Evaluation of Available Tools for Assessment of Emerging Risks of Nanomaterials

*David G. Rickerby, Iria M. Rio Echevarria and Andreas N. Skouloudis**

The environmental and health effects of nanomaterials represent significant emerging risks. However, there is at present rather limited knowledge regarding the ways in which nanomaterials might be released from products and enter the environment or how they are transported and accumulate in ecosystems. Additional data is therefore needed to estimate the possible release of nanomaterials at various stages of the life- cycle to allow identification of potential pathways into the environment. Available tools for risk assessment of nanomaterials are reviewed with the aim of identifying unknowns and uncertainties and data requirements. To carry out risk assessment it is first necessary to determine where nanomaterials are likely to present hazards that are different from those of conventional chemicals and therefore where the challenges will be greatest. Some of the limitations of current risk assessment methodologies for nanomaterials are examined.

I. Introduction

New technologies generate a complex set of emerging risks that necessitate integrated approaches to risk assessment and safety management[1, 2]. Examples include hydrogen energy, carbon capture and storage, biofuels and nanotechnologies. The inherent uncertainties connected with application of these new technologies create particular difficulties in assessing the emerging risks. In the case of nanomaterials there are at present relatively few data concerning the release of nanoparticles from products into the environment, or how they could be transported, transformed or accumulate in ecosystems[3]. For this reason, there is an urgent need to increase our knowledge on the environmental fate and impact of these novel materials. It is also necessary to evaluate the extent to which existing regulatory frameworks and associated risk assessment strategies, methodologies and tools can be applied, or will have to be modified to take into account mass production, use, and final handling and disposal of nanomaterials.

The current regulatory framework for chemicals and hazardous wastes may not be adequate to deal with emerging risks due to large scale industrial production and use of nanomaterials. While there is no explicit mention of nanomaterials they would in principle also be covered by the pertinent existing regulations. Under the REACH legislation[4] it is the duty of manufacturers to ensure that substances do not adversely affect human health and the environment. The EU Waste Directive[5], which obliges Mem-

* David G. Rickerby and Iria M. Rio Echevarria are both based at the Institute for Health and Consumer Protection; Andreas N. Skouloudis is affiliated with the Institute for Environment and Sustainability. Both Institutes are part of the European Commission's Joint Research Centre (JRC). The research leading to this paper has received funding from the European Union 7th Framework Programme (FP7/2007-2013) under grant agreement n° 247989.

1 Aleksander S. Jovanović and Daniel Baloš, "iNTeg-Risk Project: Concept and First Results", 16 *Journal of Risk Assessment* (2013), pp. 275-291.

2 Aleksander S. Jovanović and Vladimir Pilić, "Dealing with Risk-Risk Interdependencies and Trade-offs in Relation to Development and Use of New Technologies", 16 *Journal of Risk Assessment* (2013), pp. 393-406.

3 David E. Meyer, Mary A. Curran and Michael A. Gonzalez, "An Examination of Existing Data for the Industrial Manufacture and Use of Nanocomponents and Their Role in the Life Cycle Impact of Nanoproducts", 43 *Environmental Science and Technology* (2009), pp. 1256-1263.

4 Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation 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, OJ 2006 L 396/3.

5 Directive 2006/12/EC of the European Parliament and of the European Council on waste, OJ 2006 L 114/9.

ber States to adopt measures to ensure that waste treatment does not have an adverse impact on health and the environment, would apply also to the disposal of products containing nanomaterials. The previous Integrated Pollution Prevention and Control Directive[6] requirements for industrial installations to limit emissions was similarly pertinent to the production of nanomaterials. From 7 January 2014 this directive was amended by the Industrial Emissions Directive[7], which provides an integrated approach to prevention and control of emissions into air, water and soil and to waste management.

The available scientific knowledge on nanomaterials characterisation, detection, measurement, transport, toxicology, exposure, persistence and fate[8] is still insufficient to allow accurate and reliable assessment of their impact on the environment. However, the increasing amount of nanomaterials produced worldwide raises important questions about their behaviour when released into the environment and on possible hazards due to accumulation in animals, plants and the human body. Nanomaterials can be extremely resistant to degradation and may aggregate, be transported and accumulate in soils, groundwater and sediments, resulting in modification of their properties compared to isolated nanoparticles. Models developed to predict the fate, transport, and human health impacts of conventional environmental contaminants thus need to be modified to take into account the specific properties of nanoparticles that may lead to additional risks[9].

Current regulations are based on parameters that may not be appropriate for nanoparticles in solution or in suspension. Future legislation should be based on reliable scientific evidence regarding the effects of specific nanomaterials and their mobility in the environment. Although it has been found that some nanomaterials have toxic properties in laboratory tests, relatively little is known at present about their migration and uptake in organisms. Additional research is therefore needed on the interactions between nanoparticles and environmental matrices, including ecotoxicity studies. Reliable data on the physicochemical properties, toxicokinetics and degradability of nanomaterials are crucial to understanding where, in which form and in what amounts they can be expected to occur in different environmental compartments, in order to support risk assessment.

Existing methods of estimating environmental exposure may be insufficient to address the emerging risks related to nanomaterials and current risk assessment procedures consequently need to be adapted to account for their specific hazards. Risk assessment needs to consider toxicology, ecotoxicology, exposure, environmental and biological fate, transport and transformation as well as process safety management for the prevention of accidental releases. Nanomaterials may have higher toxicity than conventional chemicals with the same chemical composition and their long term behaviour in the environment might be different. These uncertainties must be properly taken into consideration when carrying out the risk assessment.

A key challenge is to understand to what extent current risk assessment methods and tools are valid or need to be refined, adapted or modified to account for the distinctive features of nanomaterials. The impacts on natural systems resulting from accidental release and leakage and from long term cumulative exposure and waste disposal need to be reliably determined; an initial step towards this goal consists of estimating the potential environmental concentrations[10]. In the present work methods and tools are identified that could be, or are already being, applied to assess and manage the emerging risks to the environment from manufactured nanomaterials and indicate gaps where risk assessment methods or data are not currently sufficient.

II. The EU Regulatory Framework

A review of relevant EU legislation concluded that the existing regulatory framework is sufficiently flex-

6 Council Directive 2008/1/EC concerning integrated pollution prevention and control, OJ 2008 L 24/8.

7 Directive 2010/75/EU of the European Parliament and of the Council on industrial emissions (integrated pollution prevention and control), OJ 2010 L 334/17.

8 Stephen J. Klaine, Pedro J.J. Alvarez, Graeme E. Batley et al., "Nanomaterials in the Environment: Behaviour, Fate, Bioavailability and Effects", 27 *Environmental Technology and Chemistry* (2008), pp. 1825-1651.

9 Christine Ogilvie Hendren, Michael Lowry, Khara D. Grieger et al., "Modelling Approaches for Characterising and Evaluating Environmental Exposure to Engineered Nanomaterials in Support of Risk-Based Decision Making", 47 *Environmental Science and Technology* (2012), pp. 1190-1205.

10 Nicole C. Mueller and Bernd Nowack, "Exposure Modelling of Engineered Nanoparticles in the Environment", 42 *Environmental Science and Technology* (2008), pp. 4447-4453.

ible to deal with the risks of nanomaterials[11]. However, it advised that present legislation might require modification as new information becomes available. Details of the applicable regulations are given in the accompanying staff working document[12]; those relating to environmental risks are summarised below.

1. Chemicals

Chemicals regulation already provides a framework for dealing with health, safety and environmental risks. REACH is intended to replace progressively the previous directives and regulations for chemicals. This approach transforms the regulatory process by shifting the responsibility from the authorities to manufacturers, importers and users, extending the scope for registration, and creating a single harmonised European system. The legislation complements existing regulations, for example those applicable to product safety. Although it contains no explicit reference to nanomaterials, it does refer to some relevant application areas.

A technical dossier, for substances produced or imported in quantities of one tonne or more per year, and a chemical safety report, for substances produced or imported in quantities of ten tonnes or more per year, must be submitted to the European Chemicals Agency. Substances already on the market in bulk form that are produced or imported in nano form without modifications are not considered to be different from the bulk material for registration purposes. It is thus possible to include the nano form in the same registration as the bulk substance. Where the properties or uses of the nano and the bulk form differ, supplementary information is required regarding properties and uses, safety assessment, hazardous properties, risk management and operational conditions. Additional testing or information may be required and test guidelines may need to be modified to address the specific hazards associated with the nano form.

Substances must be registered if they are intended to be released from products during use. Substances of very high concern are subject to notification if they are present in the product at a concentration of greater than 0.1 wt%. There exists an obligation to update and register new information with respect to changes in the quantities produced or imported, new uses or new knowledge of risks to human health or to the environment. This may necessitate changes in the safety data sheet or the chemical safety report, or changes in the classification and labelling. In the case of increased quantities produced or imported, more information may have to be submitted to fulfil the regulatory requirements.

The authorities may request the provision of additional information after evaluation. Dossiers are first examined by the European Chemicals Agency to review testing proposals to ensure that unnecessary animal tests and costs are avoided, and to verify compliance with registration requirements. Further evaluation is carried out by the Competent Authorities when there is a reason to suspect that a substance may present a risk to human health or the environment. On the basis of this evaluation additional information can be requested beyond the minimum required by the regulations.

For substances of very high concern authorisation is required for use and placing on the market. Substances subject to authorisation are those that are carcinogenic, mutagenic or toxic for reproduction, persistent, bioaccumulating and toxic, or known to have probable serious effects on humans or the environment. The conditions under which a substance may be authorised are based on the risk management measures, socio-economic benefits, the availability of alternatives and risks related to these alternatives. Authorisations are issued for a limited time and may be subject to conditions, such as monitoring arrangements. Specific provisions allow the review of authorisations, when the changes in the conditions of the original authorisation affect the risk to human health or the environment, and for updating of information.

Restrictions are imposed on the manufacturing, marketing and use of dangerous substances, preparations and products. It is obligatory to notify the European Chemicals Agency of substances subject to registration and dangerous substances. Irrespective of the quantities, suppliers of a dangerous substance or preparation must provide a safety data sheet, containing the data required by REACH. This also ap-

11 Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee on Regulatory Aspects of Nanomaterials, COM(2008)366 final.

12 Commission Staff Working Document: summary of legislation in relation to health, safety and environment aspects of nanomaterials, regulatory research needs and related measures SEC(2008) 2036.

plies in cases where a safety data sheet would not ordinarily be obligatory but the substance is subject to authorisation, to restrictions or where information is required to enable appropriate risk management measures to be implemented. Suppliers of products that contain substances subject to authorisation in concentrations above 0.1 wt% must provide sufficient information to allow safe use.

The most recent EU regulation relating to labelling, packaging and use of dangerous substances and preparations[13] is aligned with the Globally Harmonised System (GHS) of classification and labelling of chemicals adopted at UN level. It will gradually replace the existing system based on the Dangerous Substances Directive[14] and the Dangerous Preparations Directive[15] by June 2015. While the main features of classification and labelling are similar there are some differences due to hamonisation with the GHS. The new system adopts the hazard classes from the GHS which correspond closest to those of the Dangerous Substances Directive. These are divided into hazard categories which consider the severity of the effect or the route of exposure. While the scope of the classification is comparable to that used previously, the number of hazard classes is increased. The Seveso III Directive[16] also contains technical updates that take account of these changes in classification.

Nanomaterials, whether in the form of a substance, a preparation or contained within a product, clearly fall under the scope of the REACH regulations and their health and environmental effects must be assessed accordingly. All the provisions of REACH are therefore equally applicable to nanomaterials, including those that relate to the control of risks. Advice on exposure assessment and hazard and risk characterisation for nanomaterials has been provided by the REACH Implementation Project on Nanomaterials[17]. Its objectives included the development of exposure scenarios, evaluation of operational conditions and risk management or mitigation measures.

2. Pollution Prevention and Control

The Integrated Pollution Prevention and Control Directive[18] requires industrial and agricultural activities with a high pollution potential to have a permit. Issuance of this permit carries an obligation to prevent or reduce emissions, including measures relating to waste. National Competent Authorities can only issue a permit if all appropriate preventive measures are taken against pollution, no significant pollution is caused and waste is either avoided, or recovered or disposed of in a way that avoids or reduces the impact on the environment. The permit application must provide information on the nature and quantities of foreseen emissions and identify significant effects of the emissions of the environment, and the methods used to prevent or reduce emissions from the installation. Annexes V-VIII of the Industrial Emissions Directive[19] contain some mandatory emission limit values; however these do not refer specifically to nanomaterials.

The Directive promotes application of the best available techniques (BAT) and a set of reference documents facilitates consistent implementation. The permit conditions include an emission limit value (ELV) based on BAT but it is not specified what units are to be used. Usually mass concentration is employed but values could be expressed in terms of alternative units (e.g. surface area) to allow more appropriate specification for dealing with releases of nanomaterials. The implementation of this Directive as a regulatory tool for nanomaterials would require the assessment of releases only from installations that it covers, whereas releases may be expected also from installations falling outside its scope. At present the focus is on conventional pollutants, re-

13 Regulation (EC) No 1272/2008 of the European Parliament and of the Council on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006, OJ L 353/1.

14 Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances, OJ 1967 196/1.

15 Directive 1999/45/EC of the European Parliament and of the Council of 31 May 1999 concerning the approximation of the laws, regulations and administrative provisions of the Member States relating to the classification, packaging and labelling of dangerous preparations, OJ 1999 L 200/1.

16 Directive 2012/18/EU of the European Parliament and of the Council of 4 July 2012 on the control of major-accident hazards involving dangerous substances, amending and subsequently repealing Council Directive 96/82/EC, OJ 2012 L 197/1.

17 R. Alan Aitken, Arianna Bassan, Steffi Friedrichs et al., *Specific Advice on Exposure Assessment and Hazard/Risk Characterisation for Nanomaterials under REACH (RIP-oN 3) - Final Project Report* RNC/RIP-oN3/FPR/1/FINAL (Brussels: European Commission 2011).

18 Council Directive 2008/1/EC, *supra* note 6.

19 Directive 2010/75/EU, *supra* note 7.

flecting a longstanding need to control such emissions and the available technical expertise. The capability of the Competent Authorities to monitor and enforce compliance with ELVs or other permit conditions in the case of nanomaterials will therefore need to be strengthened.

3. Waste

The legislation on waste and relating to specific waste streams and waste treatment techniques already includes general requirements for the protection of health and the environment for waste management. This covers the management of waste products that may contain nanomaterials but excludes any special provisions to address the emerging risks of the nanomaterials. The Waste Directive[20] provides definitions for waste legislation and states that Member States should take the necessary measures to ensure that waste treatment does not adversely affect health and the environment. It sets out the rules relating to administration, planning, implementation and permits for installations for treating, storing, recovering or disposing of waste, and inspection procedures. It requires Member States to adopt policies to encourage the prevention, recovery and safe disposal of waste.

Directive 91/689/EEC[21] defines which wastes are hazardous and lays down provisions for waste considered as hazardous. It covers recording and identification of waste, prohibitions on mixing different categories of waste, separation of hazardous waste, permission for facilities treating hazardous waste, packaging and labelling, national waste management plans, emergency measures and reporting. The classification refers to the Council Directive[22] on the classification, packaging and labelling of dangerous substances and its subsequent amendments. Wastes containing significant quantities of nanomaterials could be considered as hazardous provided that these materials were classified as dangerous under these provisions because they may cause adverse effects on the environment or human health. The classification of waste from nanomaterials as hazardous would initiate measures to reduce the environmental and health risks. However, the present insufficient understanding of the potential hazards means that increased knowledge regarding the behaviour of nanomaterials both during and at the end of their life-cycle would be required.

III. Environmental Risk Assessment

The basic principles of environmental risk assessment are outlined in a paper by the Royal Society of Chemistry[23]. In general, risk assessment includes the following main steps: (i) problem formulation; (ii) hazard identification; (iii) release assessment; (iv) exposure assessment; (v) risk estimation. Environmental risk assessment has a wide variety of applications and there is an extensive range of legislation that utilises the principles of environmental risk assessment with regard to chemicals[24]. Practical guidance on risk assessment procedures is usually furnished for each specific type of legislation.

Risk assessment and risk management methods are increasingly applied at every policy and regulatory level and a gradual evolution has occurred from a hazard-based to a risk-based approach. In many instances achieving zero risk is not possible or unnecessary to ensure health and environmental protection and a certain level of risk in some instances may be considered acceptable in relation to the potential benefits. Environmental risk assessment is a well-established tool for policy and regulatory agencies, which have been responsible for much of the innovation in this field. It is also becoming more widely employed by industry as a result of its application as an instrument for regulatory purposes.

Environmental risk assessment is sub-divided into: (i) human health risk assessment; (ii) ecological risk assessment; (iii) industrial risk assessment. Health and ecological risk assessment are essentially similar in nature even though they relate to different policy and regulatory requirements. Industrial risk assessment tends generally not to consider ecological systems or human health separately but is applied in practical settings and hence tends to be less theoretical than other types of risk assessment. Engineering risk assessment forms a part of the overall risk assessment and integrates the environmental

20 Directive 2006/12/EC, *supra* note 5.

21 Council Directive 91/689/EEC on hazardous waste, OJ 1991 L 377/20.

22 Council Directive 67/548/EEC, *supra* note 14.

23 Environment, Health and Safety Committee, *Note on Environmental Risk Assessment* (London: Royal Society of Chemistry, 2008).

24 Robyn Fairman, Carl D. Mead and W. Peter Williams, *Environmental Risk Assessment - Approaches, Experiences and Information Sources*, Environmental Issues Report No. 4 (Copenhagen: European Environment Agency, 1999).

and health components. It focuses on risk management with the objective of protecting human health and the environment for the purpose of limiting company liability.

The US Environmental Protection Agency has issued guidelines for improving the quality and consistency of ecological risk assessments[25]. They are not mandatory regulations but rather provide advice to the regulatory community regarding ecological risk assessment. The guidelines emphasise the importance of interaction between risk assessors, risk managers, and other interested stakeholders at the problem formulation stage and in the risk characterisation and risk assessment process. These parties have complementary roles in defining the focus of the assessment, its scope and boundaries, and ensuring that the results are used in an effective manner to support environmental decision making. Risk characterisation includes estimating, interpreting, and reporting risks to bring an ecological perspective into policy by enabling clear, transparent and consistent analysis.

A crucial step in environmental risk assessment is the estimation or prediction of the potential exposure to a chemical released in the environment due to production, use and disposal. Hazard and exposure assessment are generally carried out iteratively, applying a tiered approach. The OECD has published an overview of methods that can be employed for exposure assessment[26]. Emission scenarios were developed that include a description of sources, production processes, pathways and use patterns with the aim of quantifying emissions or releases of chemicals in specific industrial or use categories.

A commonly used risk management paradigm is the one proposed by the US National Academy of Sciences[27] for dealing with the risks of chemicals to human health. This type of approach forms the basis for EU chemicals legislation and is the predominant model for health risk assessment applied by regulatory and policy organisations. Industrial risk analysis typically includes the additional step of risk evaluation, which is also incorporated in European chemicals legislation.

Details of the method applied in the EU for environmental risk assessment for the regulation of new and existing substances are described in the Technical Guidance Document[28]. Risk evaluation requires estimation of the probability that damage or adverse effects will occur. Comprehensive risk assessment of hazardous chemicals usually involves three distinct steps: (i) effects assessment; (ii) exposure assessment; (iii) risk characterisation. The effects are estimated by identification of the hazard potential based on the physicochemical properties, ecotoxicity and intended use, and calculation of the predicted no effect concentration (PNEC), from ecotoxicity data. Exposure is determined by calculation of the predicted environmental concentration (PEC) from monitoring data, realistic worst cases scenarios and predictive modelling techniques that take into consideration release, degradation, and transport and fate mechanisms. If the PEC/PNEC ratio is less than 1 the substance can be considered to present a low risk to the environment.

The European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) has proposed a tiered approach for evaluating the health and environmental risks due to chemicals, which is available as a web-based tool[29]. This is based on targeted risk assessment (TRA) using conservative assumptions and applying broad exposure/risk models to determine where additional, more detailed risk assessment may be needed. The potential of this approach has been recognised for performing the risk assessment required under the provisions of the REACH regulations. Depending on the degree of exposure and the hazard, different levels of information are required[30]. The use of a tiered approach ensures that the degree of detail in the information included in the risk evaluation is proportional to the potential risks of a chemical, taking into account both the hazards and possible exposures.

The original TRA methodology was not considered suitable for use in evaluation of environmental

25 Environmental Protection Agency, *Guidelines for Ecological Risk Assessment*, EPA/630/R-95/002F (Washington DC: U.S. Environmental Protection Agency, 1998).

26 OECD Environment Directorate, *Environmental Exposure Assessment Strategies for Existing Industrial Chemicals in OECD Member Countries*, OECD Series on Testing and Assessment No. 17 (Paris: Organisation for Economic Co-operation and Development, 1999).

27 National Academy of Sciences, *Risk Assessment in the Federal Government: Managing the Process*, (Washington DC: US National Academy of Science, National Academy Press, 1983).

28 European Chemicals Bureau, *Technical Guidance Document on Risk Assessment* (Brussels: European Commission, 2003).

29 European Centre for Ecotoxicology and Toxicology of Chemicals, *Targeted Risk Assessment*, Technical Report No. 93 (Brussels: ECETOC AISBL, 2004).

30 Tom Feijtel, Geert Boeije, Mike Comber et al., "The ECETOC Approach to Targeted Environmental Risk Assessment", 24 *Environmental Toxicology and Chemistry* (2005), pp. 251-252.

risks under the provisions of the REACH regulations. An updated version was therefore developed[31] that included an improved tool for environmental risk assessment. This incorporates certain features of REACH, such as environmental release classes and the algorithms used in the Technical Guidance Document, in order to estimate the environmental concentrations and exposure. Information on the substance properties, emission conditions and risk management measures can also be included in the risk assessment.

IV. Risk Assessment for Nanomaterials

Evaluation of the emerging risks of nanomaterials entails an understanding of their mobility, reactivity, ecotoxicity and persistence in the environment[32]. An extensive review of the current knowledge on the release of engineered nanomaterials into the environment[33] has compared the results of experimental and theoretical studies. One method for calculating the environmental concentrations is by carrying out substance flow analysis from products to air, soil and water[34]. The input parameters required to perform the calculation are: estimated production volume; allocation of the production volume to product categories; particle release from products; flow coefficients in environmental compartments. Another alternative approach has been proposed[35] that applies probabilistic material flow analysis to determine the predicted environmental concentration (PEC), eliminating the need to consider a range of possible scenarios.

A problem encountered in this type of analysis is that the expected nanoparticle concentrations in the environmental compartments are subject to wide variation, due to uncertainties in the production volume and the different life-cycles of the products. However, an upper bound can be estimated for the potential exposures based on the available data for the production volumes[36]. Emissions may be from point sources, such as factories or landfill sites, and from diffuse sources, such as wet deposition from the atmosphere, rainwater runoff, and attrition of products containing nanomaterials[37]. Long-range atmospheric transport and transport in both saturated and unsaturated subsurface regions may occur. Prediction of the exposure to manufactured nanomaterials requires knowledge of their environmental availability throughout their life-cycle[38]. This will be influenced by the matrices in which they are embedded and the surface chemistry of the nanomaterials, which influences their transport and fate[39].

The European Commission Scientific Committee on Emerging and Newly Identified Health Risks[40] concluded that current risk assessment techniques may not be suitable and might require modification to deal with the hazards associated with nanomaterials. It was recommended that the exposure evaluation should be based on the number of nanoparticles and/or their surface area instead of the hitherto used mass concentration. Existing methods may not be appropriate for determining the environmental fate of nanoparticles. Because there have been few investigations of the behaviour of nanomaterials in the environment until now, it is necessary to discover whether they disperse and react differently in environmental media in comparison to the same compounds in macroscopic form.

Assessment of the environmental consequences of engineered nanomaterials requires characterisa-

31 European Centre for Ecotoxicology and Toxicology of Chemicals, *Addendum to ECETOC Targeted Risk Assessment Report No. 93*, Technical Report No. 107 (Brussels: ECETOC AISBL, 2009).

32 Bernd Nowack and Thomas D. Bucheli, "Occurrence, Behavior and Effects of Nanoparticles in the Environment", 150 *Environmental Pollution* (2007), pp. 5-22.

33 Fadri Gottschalk and Bernd Nowack, "The Release of Engineered Nanomaterials to the Environment", 13 *Journal of Environmental Monitoring* (2011), pp. 1145-1155.

34 Mueller and Nowack 2008, *supra* note 10.

35 Fadri Gottschalk, Roland W. Scholz, and Bernd Nowack, "Probabilistic Material Flow Modelling for Assessing the Environmental Exposure to Compounds: Methodology and an Application to Engineered Nano TiO_2 Particles", 25 *Environmental Modelling and Software* (2010), pp. 320-332.

36 Christine Ogilvie Robichaud, Ali Emre Uyar, Michael R. Darby et al., "Estimates of Upper Bounds and Trends in Nano-TiO_2 Production as a Basis for Exposure Assessment", 43 *Environmental Science and Technology* (2008), pp. 4227-4233.

37 Mark R. Wiesner, Gregory V. Lowry, Pedro Alvarez, et al., "Assessing the Risks of Manufactured Nanomaterials", 40 *Environmental Science and Technology* (2006), pp. 4337-4445.

38 Mark R. Wiesner, Gregory V. Lowry, Kimberly L. Jones et al., "Decreasing Uncertainties in Assessing Environmental Exposure, Risk, and Ecological Implications of Nanomaterials", 43 *Environmental Science and Technology* (2009), pp. 6458-6462.

39 Jose R. Peralta-Videa, Lijuan Zhao, Martha L. Lopez-Moreno et al., "Nanomaterials and the Environment: A Review for the Biennium 2008-2010", 186 *Journal of Hazardous Materials* (2011), pp. 1-15.

40 Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), *Opinion on The Appropriateness of Existing Methodologies to Assess the Potential Risks Associated with Engineered and Adventitious Products of Nanotechnology* (Brussels: European Commission, 2006).

tion of both nanoparticles and their aggregates. Quantitative analytical techniques are required to determine the environmental concentrations in order to facilitate risk and exposure assessments[41]. While these analytical methods still need further development and optimisation, particularly for nanoparticles in aqueous media, some fundamental knowledge is already available from the environmental behaviour of naturally occurring nanomaterials and colloid chemistry[42]. Small particles tend to aggregate or agglomerate and may become associated with other dissolved, colloidal and particulate matter. After release into the environment, nanoparticles may undergo dissolution, speciation, agglomeration, transformation to other chemicals, and/or mineralisation to carbon dioxide and water, thereby changing their properties.

A Defra study has examined the question of whether standard ecotoxicity methods are adequate for assessing the hazards of engineered nanomaterials[43]. It concluded that there is significant uncertainty in assessments of nanoparticle exposure using conventional test methods. Data are highly dependent on use and release patterns, environmental fate, persistence and bioaccumulation; further research is therefore needed on the main classes of nanoparticles likely to be released into the environment. A three-level risk assessment strategy has been proposed[44] that includes analysis of the fate and transport of nanomaterials and potential exposure pathways based on a qualitative description of the relationships between material and process parameters, environmental behaviour and exposure scenarios.

Because of the shortcomings of conventional risk assessment methods when applied to nanomaterials a number of nano-specific risk assessment methodologies and tools have been proposed[45], details of some of which are listed in Table 1. Two of the most commonly used tools for risk assessment of nanomaterials, will now be compared: the Nano Risk Framework, which allows a complete analysis of potentially high risk nanomaterials, and the Precautionary Matrix, which is more suitable for preliminary screening. The inclusion of all life-cycle stages is considered to be a significant advantage offered by both of these risk assessment methodologies. Additional key aspects are ease of access, availability free of cost, documentation available in English and risk assessment based on scientific data. Several of the other methodologies and tools employ essentially similar approaches to those adopted by the Nano Risk Framework or the Precautionary Matrix and for this reason are not discussed in further detail here.

1. Nano Risk Framework

A comprehensive, practical framework has been developed for the evaluation and management of the emerging risks of nanomaterials by DuPont and Environmental Defense[46, 47]. It provides a systematic and rigorous methodology for identifying, managing, and reducing the environmental, health, and safety risks of engineered nanomaterials at every stage of the product life-cycle, including production, use, disposal, and ultimate fate. This framework provides guidance on the principal issues that have to be considered in applications of nanomaterials, and on the information needed to carry out risk evaluation and risk management decision making. It is sufficiently flexible to be applied even in situations where information is incomplete or uncertain, by making reasonable assumptions and adopting suitable risk management practices to compensate for knowledge gaps. In addition, it provides a method to guide data generation and update assumptions, decisions, and practices when new information becomes available.

The assessment is information driven and contains no implicit assumptions regarding the risk or

41 Martin Hassellöv, James W. Readman, James F. Ranville et al., "Nanoparticle Analysis and Characterisation Methodologies in Environmental Risk Assessment of Engineered Nanoparticles", 17 *Ecotoxicology* (2008), pp. 344-361.

42 Jamie R. Lead and Kevin J. Wilkinson, "Aquatic Colloids and Nanoparticles: Current Knowledge and Future Trends", 3 *Environmental Chemistry* (2006), pp. 159-171.

43 Mark Crane, Richard D. Handy, John Garrod et al., "Ecotoxicity Test Methods and Environmental Hazard Assessment for Engineered Nanoparticles", 17 *Ecotoxicology* (2008), pp. 421-437.

44 Niall O'Brien and Enda Cummins, "Development of a Three-Level Risk Assessment Strategy for Nanomaterials", in Igor Linkov and Jeffery Steevens (eds.), *Nanomaterials: Risks and Benefits,* (Dordrecht: Springer, 2009), pp. 161-178.

45 Danail R. Hristozov, Stefania Gottardo, Andrea Critto et al., "Risk Assessment of Engineered Nanomaterials: a Review of Available Data and Approaches from a Regulatory Perspective", 6 *Nanotoxicology* (2012), pp. 880-98.

46 Environmental Defense-DuPont Nano Partnership, *Nano Risk Framework* (Wilmington: DuPont, Washington DC: Environmental Defense, 2007).

47 Scott Walsh and Terry Medley, "A Framework for Responsible Nanotechnology", in Erik Fisher, Cynthia Selin and Jameson M. Wetmore (eds.), *Yearbook of Nanotechnology in Society*, Vol. 1 (Dordrecht: Springer, 2008), pp. 207-213.

Table 1: Summary list of available nano-specific risk assessment tools

Nanomaterials Risk Assessment Method	Developer	Website
Nano Risk Framework	DuPont - Environmental Defense (USA)	www.nanoriskframework.com
Precautionary Matrix for Synthetic Nanomaterials	Federal Offices of Public Health and Environment (Switzerland)	www.bag.admin.ch/nanotechnologie/12171/12174/index.html?lang=en
Risk Assessment of Manufactured Nanomaterials	New Energy and Industrial Technology Development Organisation (Japan)	www.aist-riss.jp/main/modules/product/nano_rad.html?ml_lang=en
NanoCommission Assessment Tool	Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (Germany)	www.bmu.de/en/service/publications/downloads/details/artikel/responsible-use-of-nanotechnologies-1/
Precautionary Strategies for Managing Nanomaterials	Advisory Council on the Environment (Germany)	http://www.umweltrat.de/EN/Reports/SpecialReports/specialreports_node.html
SafeNano	Institute of Occupational Medicine (UK)	www.safenano.org/
Cenarios	The Innovation Society (Switzerland)	http://www.innovationsgesellschaft.ch/images/publikationen/Factsheet_CENARIOS_english_arial2.pdf (link not available anymore).

safety of a particular nanomaterial. Where little or no information is available to inform decisions on the potential hazard or exposure, it employs "reasonable worst-case assumptions" or comparisons to materials or processes for which the information is more complete, together with appropriate risk management. Replacement of assumptions with real data is especially desirable for products that are close to the market. The framework is a tool for the organisation, documentation and communication of the available information, and for identifying and addressing information gaps. It is designed to be applied iteratively to take into account recent developments as new information becomes available. An output worksheet enables evaluation, management, and communication of the information and recording of risk management decisions. The risk assessment procedure consists of six distinct steps: (i) description of materials and applications; (ii) development of life-cycle profiles for properties, hazards and exposures; (iii) evaluation of risks; (iv) risk management; (v) decisions and documentation; (vi) review and update of the risk evaluation.

In developing the framework many of the basic principles used in existing risk analysis methods were included. However, current risk management strategies were enhanced by the addition of new features, such as data sets of the properties, hazards, and exposures for the specific nanomaterials under consideration, to improve risk evaluation and decision making. The incorporation of life-cycle profiles provides a greater amount of information on physical and chemical properties, ecotoxicity, and environmental fate. This additional data is needed due to the lack of experience with nanomaterials, the complexity of carrying out risk evaluation on the basis of the limited information available and the influence of properties other than chemical composition on the toxicity and behaviour of nanomaterials. The principal limitations of this methodology are that it pro-

vides qualitative rather than quantitative risk assessments and requires an extensive data set.

2. Precautionary Matrix for Synthetic Nanomaterials

The Swiss Federal Office for Public Health and the Federal Office for Environment have collaborated on the development of a precautionary matrix for nanomaterials[48] to enable assessment of the need for nano-specific precautionary measures and identify potential risks that might arise in development, production, use and disposal. This allows the risk potential to be classified to decide on appropriate action. Applications requiring more detailed investigation can thus be identified, and measures for health and the environmental protection reviewed and implemented. The precautionary matrix may be used to assess existing or new products and processes by adopting a structured approach for evaluation of potential risks. It also provides a basis for decision-making and risk management.

It is assumed that nano-specific risks exist only in cases where there is a possibility that nanoparticles or their agglomerates can be released. All stages in the life-cycle are considered, including research and development, production, use and disposal. A different analysis needs to be carried out for each process considered and additional subdivision into different employee activities or use conditions may be necessary. The results refer to a specific type of nanoparticle in a precisely defined environment. If the environment or conditions of use change, the analysis needs to be repeated to take the modifications into account. A new analysis must be performed also in the case of transformation of the original nanoparticles during use. Release during waste disposal, recycling or further processing is considered by means of a separate assessment.

The precautionary matrix utilises a relatively small number of evaluation parameters to estimate the potential effect on the basis of reactivity and stability. The probability and potential exposure of humans and release into the environment are determined using data relating to the physical surroundings of the nanoparticle, the quantity produced and the anticipated emissions during development, production and use. A modular approach is used to facilitate inclusion of emerging scientific information. The need for precaution is assessed in relation to the magnitude of the potential effect and the potential for exposure of humans or release into the environment. Allowance is also made for uncertainties due to knowledge gaps or inaccuracies in data. In cases for which the information is insufficient, the worst case scenario is assumed. Fewer data are required compared to the Nano Risk Framework but, while the results take into account the physical properties and reactivity, they are insensitive to the chemical composition. The method is potentially useful for preliminary screening, as part of a tiered risk analysis, to decide whether more comprehensive assessment is required.

V. Conclusion

Existing regulatory and environmental risk assessment methods need to be reviewed with regard to their applicability to the production, application, and disposal of nanomaterials. Current legislation covers to a large extent the risks associated with nanomaterials and it should be possible to deal with these under the present regulatory framework. However, modification may be required as new scientific information becomes available and the emerging risks are more clearly defined. Nanomaterials would, in principle, fall under the scope of the existing chemicals legislation and their health and environment effects must be assessed accordingly. All the provisions of these regulations apply equally to nanomaterials, including the assessment of risks. Development of appropriate industrial risk and safety decision frameworks will thus be necessary to ensure that potential risks of engineered nanomaterials are adequately dealt with.

Environmental risk assessment and management methods are increasingly applied in policy and regulation and there has been a gradual transition from hazard-based to risk-based approaches. Several nano-specific methodologies are available for hazard characterisation and environmental risk assessment; however more attention needs to be paid to the fate of nanomaterials released during use and disposal. There is still an incomplete understanding of the

48 Jürgen Höck, Thomas Epprecht, Heinrich Hofmann et al., *Guidelines on the Precautionary Matrix for Synthetic Nanomaterials* (Berne: Federal Office of Public Health and Federal Office for the Environment, 2010).

risks due to nanomaterials in the environment and how they are transported, transformed or accumulate in ecosystems. Improved knowledge of the behaviour of nanomaterials during production, use and at the end of life-cycle is therefore necessary. Assessment of the environmental and health risks of nanomaterials requires an understanding of their mobility, reactivity, ecotoxicity and persistence in the environment, involving precise characterisation of nanoparticles and their aggregates. However, there still remain many data gaps, in particular the lack of quantitative predictions of environmental releases.

Exposure, environmental fate, and transport are critical to the environmental impact of nanomaterials but there are at present no standard accepted methodologies for their determination. It is not evident to what extent the established models applied to conventional chemicals could be adapted to take into account the specific properties of nanomaterials, which may vary greatly from those of their bulk counterparts. A major difficulty in assessing the emerging risks for nanomaterials is the high level of uncertainty in the calculated concentrations for the environmental compartments, due to wide variability in estimates of the production volume and lack of information regarding the product life-cycles, with the consequence that the potential exposures cannot be accurately established.