Study to Assess the Impact of Possible Legislation to Increase Transparency on Nanomaterials on the Market

Building Blocks Report

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Author(s)	**RPA:** Marco Camboni Andrew Turley	**BiPRO:** Craig Hawthorne Yvonne Floredo Jan Vorderman
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Table of contents

List of Abbreviations

µg	Microgramme
Anses	*Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail*
ANSM	*Agence Nationale de Sécurité du Médicament et des Produits de Santé*
BALF	Bronchoalveolar lavage fluid
CLI	Classification And Labelling Inventory
CNF	Carbon Nanofibre
CNT	Carbon
CPI	Consumer Products Inventory
CPNP	Cosmetics Products Notification Portal
DNEL	Derived No Effect Level
EC	European Commission
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
ECHA	European Chemicals Agency
EEA	European Environment Agency
EFTA	European Free Trade Association
EU	European Union
EU-OSHA	European Occupational Safety and Health Agency
FNS	French Notification System
FP	Framework Programme
g	Gramme
HEPA	High Efficiency Particulate Air
HSE	Health and Safety Executive
IARC	International Agency for Research on Cancer
IFA	*Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung* (German Institute for Occupational Safety and Health)
Ineris	*Institut National de l'Environnement Industriel et des Risques*
INRS	*Institut national de recherche et de sécurité pour la prévention des accidents du travail et des maladies professionnelles*

InVS	*Institut de Veille Sanitaire*
LEV	Local Exausted Ventilation
LOEL	Lowest Observed Effect Level
m	Metre
MAK	Maximale Arbeitsplatz-Konzentration (Maximal Workplace Concentration)
MEDDE	*Ministère de l'Écologie, du Développement durable et de l'Énergie*
ml	Millilitre
MNM	Manufactured Nanomaterial
MWCNT	Multi Wall Carbon Nanotubes
NGO	Non-Governmental Organisation
NIOSH	National Institute for Occupational Safety and Health (United States of America)
nm	Nanometre
NM	Nanomaterial, as defined by the French authorities, unless otherwise stated
NOAEL	No Observed Adverse Effect Level
NRV	Nano Reference Value
OECD	Organisation for Economic Co-operation and Development
OEL	Occupational Exposure Level
PAH	Polyaromatic Hydrocarbon
PM	Particulate Manner
PNEC	Predicted No Effect Concentration
REACH	Registration, Evaluation, Authorisation (and Restriction) of Chemicals
REL	Recommended Effect Level
R&D	Research and Development
SCCS	Scientific Committee on Consumer Safety
SCOEL	Scientific Committee on Occupational Exposure Levels
SUVA	Swiss National Accident Insurance Fund
SWCNT	Single Wall Carbon Nanotubes
TWA	Time Weighted Average
UBA	*Umweltbundesamt* (German Federal Environment Agency)

UFP	Ultrafine particles
UV	Ultraviolette
VAT	Value Added Tax
XAN	The XAN number is the name approved by a specific country (X) for a cosmetics product
WATCH	Working Group on Action to Control Chemicals
WPMN	Working Party on Manufactured Nanomaterials

Executive Summary

This report is one of several outcomes of a study on transparency measures on nanomaterials within the EU.

It aims to present, without being comprehensive, relevant and reliable information with regard to hazards and risks of nanomaterials, their value chains and the potential of growth and innovation associated with nanotechnology. The overview on these different aspects will support the Commission in better defining and assess the potential measures to increase transparency and ensure regulatory oversight on nanomaterials. It also suggest a list of indicators aiming to facilitate the evaluation and monitoring of any transparency measure implemented.

The report contains:

- *A review of the literature regarding known hazards of nanomaterials and the ongoing research on their "hazard profile" characterisation;*
- *A review of the literature on the assessment of the occupational, consumers' and environmental exposures;*
- *Information on the value chains of the nanomaterials, on the basis of the data presented in the French public report and of the results of the survey on the administrative burden posed by the FNS on companies;*
- *A broad overview on growth and innovation, with statistics on private and public funding, number of patents by country and a description of some of the most promising nanomaterials and applications of nanomaterials in terms of market volumes and societal benefits;*
- *A list of indicators on fitness-for-purpose.*

The reason why manufactured nanomaterials are of such interest and offer such potentially significant benefits to society is that they often have very different properties to the same substances on the macro scale – they may be more reactive, have increased strength, etc. However, these same differences also mean that they may also be more readily absorbed into biological systems and that their hazards may be different from those of their larger forms. Nevertheless, as stated by Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR): "the hypothesis that smaller means more reactive, and thus more toxic, cannot be substantiated by the published data."

Extensive research campaigns are being conducted for the understanding of the possible hazards of nanomaterials; nevertheless, the statement that "not all nanomaterials are hazardous, not all nanomaterials are equally hazardous and there can be considerable variation in toxicity between nanomaterials with a similar chemical composition, because of their physicochemical characteristics" is still valid.

The EU has allocated €177m to a range of projects on the safety of nanomaterials and a wide debate on Occupational Exposure Limits for generic dust and ultrafine dusts is currently ongoing. As described by the European Environmental Agency in their 2013 report "Late lessons from early warnings", the development of nanotechnology has coincided with "…discussions of potential risks and the need for regulatory reform" unlike preceding technologies where the discussions of associated risks have generally been carried out after their widespread use. However, according to EEA (2013), there has been a lack of coordinated action from governments and regulatory bodies.

Despite nanotechnology receiving attention of regulators and the wider public throughout its development, there is concern about its use among consumers and NGOs. The concerns of both the public and policy makers have prompted the creation of the various initiatives under analysis.

With regard to the assessment of consumers' exposure to nanomaterials and the possible effects of nanomaterials on the environment, although there are still knowledge gaps, literature in this area is constantly increasing, especially on specific nanomaterials.

With regard to the characterisation of the value chains of the nanomaterials, on the basis of the research that has been carried out, they do not seem to have different characteristics from the value chains of "more traditional" chemical substances, if not that their market volumes still appear to be relatively low (with the exception of the "common" nanomaterials, such as carbon black, silicon dioxide, calcium carbonate, titanium dioxide and possibly pigments and dyes). As previously found by EC (2012), "in general it appears that most substances are produced all through the industrialised world, with producers in Europe, North America (mainly United States and Canada) and Japan or other traditionally industrialised countries in the Far East (…) and only for few of those substances there seems to be a concentration in a particular world region".

Data relating to public spending on nanomaterial R&D is available, but using it not completely straightforward for two reasons.

First, the science of nanomaterials is not frequently separated from the broader field of nanotechnology. Research on the manufacture of molecular machines from DNA, for example, would invariably be considered nanotechnology without pertaining to bulk nanomaterials.

Second, because of the highly interdisciplinary nature of the activity, not all nanotechnology R&D is labelled as such. There are some extremely high value national and international R&D programmes currently funding projects that focus exclusively on nanotechnology. The US National Nanotechnology Initiative is typical of these. But operating in the shadows is a host of individual projects that involve nanotechnology without explicitly saying so.

That said, the science of nanomaterials is a very significant part of nanotechnology. Additionally, it is probably the field of nanotechnology most likely to appear beneath a nanotechnology banner. Most other fields stand a higher – if still relatively small – likelihood of appearing beneath another banner. Pharmaceutical nanotechnology might, for example, be labelled healthcare for the purposes of public funding.

In general, EU spending on nanotechnology R&D has increased over the last 10–15 years, although successive funding programmes have organised work in different ways making direct comparisons difficult.

Under the Sixth Framework Programme (FP6), the EU spent €1.3bn on nanotechnology R&D (shared between 550 projects) in the five years from 2002 to 2006. It then spent €3.5bn in the seven years from 2007 to 2013 on the 'nanosciences, nanotechnologies, materials and new production technologies' theme of the Seventh Framework Programme (FP7).

It is now spending €3.85bn on 'nanotechnologies, advanced materials and advanced manufacturing and processing' under Horizon 2020, which will run for seven years from 2014 to 2020.

The US National Nanotechnology Initiative (NNI) has supplied about €15bn ($20bn) of public money to nanotechnology R&D since its launch in 2000. Its annual budget grew steadily through the 2000s, but then stalled in the wake of the 2007–8 global financial crisis at about €1.4bn ($1.9bn). The budget fell significantly in 2013 but has since levelled out at about €1.1bn ($1.5bn).

Chinese public spending on nanotechnology R&D is estimated at €960m ($1.3bn) in absolute terms and €1.65bn ($2.25bn) assuming purchasing power parity. With the US allocating only €1.6bn ($2.18bn) to the field in 2011, China become for the first time the biggest spender globally.

Japan has a reputation as a country that invests heavily in R&D, and in relation to nanotechnology it has more or less played to type, spending €280m ($380m) of public money on the field.

Nanotechnology is regarded as being one of the technologies from which a great deal of future growth will be generated. In this sense it has been defined by the European Commission as one of the Key Enabling Technology (KET) and represents one of the elements which will generate a great proportion of future employment growth, research and development and technological innovation. The Council highlighted in 20-21 March 2014 the crucial importance of KETs, for the enhanced industrial competitiveness (with cleantech as a cross-cutting element).

The quantification of the effects that nanotechnology has on the economy is subject to much research and speculation. According to some studies nanotechnology impacted € 182.7 billion (US$ 254 billion) worth of products in 2009 and this impact is forecasted to grow to € 1.799 trillion (US$ 2.5 trillion) by 2015. However, the economic crisis occurring since 2008 has decreased somewhat the estimations of nanotechnology market size. In this context particularly the decline in the cyclical automobile and construction industries was estimated to have the strongest negative effect on demand for nanotechnology and particularly on nanomaterials and composites .

As a result of the above described trends, the number of workers employed in the nanotechnology sector worldwide is expected to reach 2 million by 2015, of which 0.8-0.9 million would be in the United States and 0.3-0.4 million in Europe. Other estimates state that the estimated number of nanotechnology jobs is to reach 1 million in the US by 2014.

1 Introduction

1.1 Overview

The overall aim of this study is to provide support to the European Commission in the preparation of an impact assessment to identify and develop the most adequate way to increase transparency and ensure regulatory oversight for nanomaterials. The contractor is expected to:

- Gather relevant information on the experience from other nanomaterials register-like schemes;
- Provide information on health and safety, markets and research trends of nanomaterials for the better definition of the policy options to be assessed; and
- Support the impact assessment of the policy options.

The technical specifications set out a detailed framework for the study and identified five different tasks, namely:

- Task 1: Lessons learned from other schemes;
- Task 2: Background information for building blocks of policy options;
- Task 3: Organise and carry out public consultations;
- Task 4: Support for the option assessment; and
- Rask 5: Validation workshop.

This Building blocks report documents the findings of Task 2 and should complement the information provided in the Evaluation report (based on the findings of Task 1) and the findings of the public consultation (launched in early May and closed on 5 August 2014). Moreover, the validation Workshop was held in Brussels on 30 June 2014, aiming to discuss with different stakeholders the preliminary findings of the study. The main points of discussion are presented in the Workshop report. When the discussion focused on some of the aspects of this report, this has been highlighted in the appropriate Sections.

1.2 Task Objectives

Main objective of Task 2 has been the gathering of information to support the Commission in defining the optimal policy options.

The task has been divided into the following subtasks:

- Profiling risks and hazards with a view to assessing potential risks (Task 2.1);
- Characterisation of the value chain (Task 2.2);
- Overview on growth and innovation (Task 2.3);
- Setting up of a system of indicators for the monitoring of the transparency measures (Task 2.4).

1.3 Structure of the Building Blocks Report

The remainder of this report has been organised as follows:

- Section 2 provides an overview on the known hazards and risks of nanomaterials and the surrounding uncertainties;
- Section 3 describes the value chains of the nanomaterials;
- Section 4 provides an overview on growth and innovation; and
- Section 5 provides a list of indicators for the evaluation and monitoring of any potential transparency measures to be implemented.

2 Profiling Risks and Hazards with a View to Assessing Potential Risks

2.1 Introduction

The reason why manufactured nanomaterials are of such interest and offer such potentially significant benefits to society is that they often have very different properties to the same substances on the macro scale – they may be more reactive, have increased strength, etc. However, these same differences also mean that they may also be more readily absorbed into biological systems and that their hazards may be different from those of their larger forms. Nevertheless, as stated by Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR): "*the hypothesis that smaller means more reactive, and thus more toxic, cannot be substantiated by the published data*."[1] The increasingly growing body of literature on health and safety aspects of nanomaterials is focusing on those insoluble or with very low solubility: "*From a toxicological point of view, nanomaterials of poor solubility in biological fluids are of special importance, because they maintain their nanostructure after contact with the human body. Nanomaterials that are enclosed in an insoluble matrix are of minor importance, but may become relevant as soon as they are released by e.g. mechanical forces*". It should be noted that "*most of currently relevant nanomaterials occur in a solid aggregate state and have a (very) low solubility*".[2]

Although the potential effects of nanomaterials on human health can vary from those of the chemical agents in macro-forms due to their specific physicochemical characteristics, the possible mechanisms for the generation of harm remain the same: the causation can be direct, through contact, or indirect, through the production of some form of energy which can have an adverse effect on human health. In the first case, exposure might result in an "acute effect", when the harm becomes apparent rapidly or even immediately after contact, or in a "chronic effect", when the harm appears in the long term, normally due to repeated exposure over time. Moreover, the term "local effect" is used if the harm becomes apparent at the point of contact; "systemic effect" denotes harm that appears in any point of the body regardless of the place where the contact occurred, normally following a process of absorption and distribution through the body. "*The smallness of nanomaterials can lead to an increased potential to cross barriers in living organisms which increases the number of organs that can be affected*" (EU-OSHA, 2009). Nanomaterials could also cause harm by fire or explosion.

Extensive research campaigns are being conducted for the understanding of the possible hazards of nanomaterials; "*Not all nanomaterials are hazardous, not all nanomaterials are equally hazardous and there can be considerable variation in toxicity between nanomaterials with a similar chemical composition, because of their physicochemical characteristics*".[3]

Currently, three substances in nano-form (silicon dioxide, silver and titanium dioxide) are undergoing the Evaluation process under REACH. In addition, through the OECD's Sponsorship Programme for

[1] SCENIHR (2009): Risk Assessment of Products of Nanotechnologies, Opinion adopted at its 28th plenary on 19 January 2009. Available at: http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_023.pdf

[2] EU-OSHA (2009): Workplace exposure to nanoparticles, European Risk Observatory Literature Review, the European Agency for Safety and Health at Work (EU-OSHA), available from the EU-OSHA Internet site: http://osha.europa.eu/en/publications/literature_reviews/workplace_exposure_to_nanoparticles

[3] HSE (2013): Using nanomaterials at work, Including carbon nanotubes (CNTs) and other biopersistent high aspect ratio nanomaterials (HARNs), Health and Safety Executive, UK.

the Testing of Manufactured Nanomaterial, a further ten MNMs (fullerenes C60, SWCNTs, MWCNTs, iron nanoparticles, aluminium oxide, cerium oxide, zinc oxide, dendrimers, nanoclays and gold nanoparticles) are currently being evaluated and tested for approximately 59 endpoints relevant to environmental safety and human health.[4]

Methods for the assessment of health effects are usually divided in four groups:

- Epidemiology/occupational medicine;
- In vivo methods with animals;
- In vitro methods;
- Methods for the determination of physicochemical properties.

As reported by the Commission Staff Working Document accompanying the General Report on REACH "*…further adjustment of the OECD Test Guidelines is currently being discussed by the OECD Working Party on Manufactured Nanomaterials (WPMN). Eight test guidelines have been identified as requiring adaptation. A dedicated working group within WPMN is examining the applicability of alternative testing methods to nanomaterials*",[5] with a particular care on the sample preparation and dosimetry.

Moreover, the EU has allocated €177m to a range of projects (grouped in the EU Nano Safety Cluster)[6] on the safety of nanomaterials through the Seventh Framework Programme (FP7)[7]. Currently there is a wide debate on the basis for Occupational Exposure Limits for generic dust.[8] In Germany, the MAK Dust Committee has developed a proposal for limiting exposures to respirable dusts in the form of a GBS[9] particle limit, based on outputs from two analyses: the first by the Fraunhofer Institute, is based on low level exposure-effect relationships, while another approach developed by Pauluhn (2010 and 2011) is based on modelling alveolar/macrophase overload. This latter model is based on the effect being linked to particle density (with a focus on insoluble forms) and is particularly relevant because the dataset used includes several nano-size substances. The MAK Committee has suggested that the limit value for generic dust should be set at 1.3 mg/m3 for the respirable fraction. At the same time, they are also considering what might be necessary in the case of ultrafine dusts (which include nano-sized particles) and are currently considering the suitability of adoption of a value equal to either one tenth or one twentieth of the general dust value (pers. comm.).

In the UK the current limit values are set at 10 mg/m^3 for the inhalable fraction and at 4 mg/m^3 for the respirable fraction but various bodies (including the Institute of Occupational Medicine) have raised concerns regarding the extent to which these are adequate to ensure safety.[10] Also, the WATCH[11] scientific committee of the Health and Safety Executive (HSE) could not define a lower

[4] OECD (2012): Important Issues on Risk Assessment of Manufactured Nanomaterials, the Organisation for Economic Co-operation and Development (OECD), available from the OECD website: http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono%282012%298&doclanguage=en

[5] EC (2013): Commission Staff Working Document accompanying the document General Report on REACH, Report from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions, in accordance with Article 117(4) REACH and Article 46(2) CLP. Available from http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SWD:2013:0025:FIN:EN:PDF

[6] http://www.nanosafetycluster.eu/

[7] Part of the budget comes from the Sixth Framework Programme.

[8] Where with "generic dust" is intended not a specific substance dust.

[9] Granular bio-durable particles without known significant specific toxicity http://www.baua.de/en/Publications/Expert-Papers/F2083.html

[10] IOM (2011): The IOM's position on occupational exposure limits for dust, 5th of May 2011.

[11] Working Group on Action to Control Chemicals

threshold below which there would be no lung function decline when the respiratory tract was exposed in sufficient quantities to poorly soluble dust. It is opinion of this Committee that increasing exposure results in increasing adverse health effects and, although the reviewed literature only considered kaolin, carbon black and coalmine dust, the Committee felt that "*the results could probably be generalised to all other low toxicity dusts*". It was suggested that setting stricter limit values (proposed at 5mg/m^3 for inhalable dust and at 1 mg/m^3 for respirable dust) would result pro rata in a reduction in the risk of COPD in the future. However, in December 2010 the HSE Board concluded that "*only limited benefits would accrue from reducing the exposure limits for airborne dust and that it would not therefore be seeking to do this in pursuit of a long-term reduction in respiratory disease*" (IOM, 2011).

At EU level, SCOEL is reviewing TiO_2 in the nanoform but as yet no proposal has been agreed or circulated for comments (pers. comm.). Moreover, ECETOC is working on particles overload and trying to define NOAELs[12] that could be used to inform assessments to inform REACH, while the European Commission Joint Research Centre (JRC) is working on the feasibility of identifying generic occupational exposure limits for nanomaterials.

One of the main problems for the establishment of occupational exposure limits for nanomaterials is that, usually, OELs are based on a mass concentration metric "*but the most optimal dose metrics is still undefined for nanoparticles*".[13] Fibre-like substances for which the dose-response relationship is expressed as the 'number of fibres per volume' are an exception (e.g. asbestos). There is growing evidence that a mass-based approach is not the most appropriate for nanomaterials[14] and that a number-based approach or a particle's surface area based approach fit better the observed effects, though the recent work of Pauluhn (2010 and 2011)[15] has suggested that a volume-based cumulative lung exposure dose metric may be most appropriate as a basis for a generic limit. Currently, however, with regard to risk assessment of nanomaterials (or ultrafine particles) a number-based approach has considerable support. Furthermore, the detection limits for number-concentration measuring devices are generally much lower than those for devices used to measure the mass exposure.

For a few specific nanomaterials, industry and research have suggested either specific OELs/RELs or DNELs (these are summarised in Table 2-1).

DNELs were calculated in an experimental study by Aschberger *et al* (2011)[16] applying the DNEL methodology with the prescribed assessment factors to MWCNTs, fullerenes, Ag and TiO_2.

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12 No Observed Adverse Effect Level

13 Hansen and Baun (2012): European Regulation affecting nanomaterials – Review of limitations and future recommendations, Dose-Response, 10:364-383, 2012.

14 Wittmaack (2007a): In search of the most relevant parameter for quantifying lung inflammatory response to nanoparticle exposure: Particle number, surface area or what?, Environ Health Perspect 115:187-194, or Wittmaack (2007b): Dose and Response Metric in Nanotoxicology: Wittmaack responds to Oberdoerster et al and Stoeger et al, Environ Health Perspect 115(6): A290-291.

15 Pauluhn (2011): Poorly soluble particulates: Searching for a unifying denominator of nanoparticles and fine particles for DNEL estimation, Toxicology 279 (2011) 176-188, and Pauluhn (2010): Multi-walled carbon nanotubes (Baytubes®): Approach for derivation of occupational exposure limit, Regulatory Toxicology and Pharmacology 57 (2010) 78-79.

16 Aschberger *et al* (2011): Analysis of currently available data for characterising the risk of engineered nanomaterials to the environment and human health — Lessons learned from four case studies, Environment International, Volume 37, Issue 6, August 2011, Pages 1143-1156, ISSN 0160-4120, http://dx.doi.org/10.1016/j.envint.2011.02.005. (http://www.sciencedirect.com/science/article/pii/S0160412011000365)

A threshold value for Carbon Nanotubes has also been set in Switzerland in 2011 by the Swiss National Accident Insurance Fund (SUVA) at 0.01 fibres/ml (SECO, 2012).

Table 2-1: Suggested OELs and DNELs at March 2013				
Substance	**Parameter**	**OEL or REL µg/m^3**	**DNEL µg/m^3**	**Reference**
MWCNT (Baytubes)	8-hr TWA	50		Pauluhn, 2010
MWCNT (Nanocyl)	8-hr TWA	2.5		Nanocyl 2009[17]
CNT and CNF	8-hr TWA	1		NIOSH 2013[18]
MWCNT	Chronic inhalation		0.67-33.5	Aschberger *et al* 2011
Fullerenes	Chronic inhalation		270	Aschberger *et al* 2011
Ag (18-19nm)	DNEL		98	Aschberger *et al* 2011
TiO_2 (10 -100nm)	10hr/day, 40hr/week	(REL) 300		NIOSH 2011[19]

It should be noted that NIOSH "*has not assessed the extent to which exposures can be controlled during the life cycle of CNT/CNF product use, but since airborne CNT/CNF behave as classical aerosols, the control of worker exposures appears feasible with standard exposure control techniques (e.g., source enclosure, local-exhaust ventilation)*".[20] NIOSH reports that in assessing risks of workers' exposure to CNT/CNF there are still many uncertainties and more research is needed, especially on "*workplace exposures to CNT and CNF, as well as information on whether in-place exposure control measures (e.g., engineering controls) and work practices are effective in reducing worker exposures*".[21] Nevertheless, given the relative consistency of the proposed OELs for CNT/CNF across different studies, it is demonstrated that CNT/CNF need to be managed as a "*new and more active form of carbon*" (NIOSH, 2013). For instance, the permissible exposure limit for graphite or carbon black would not protect workers exposed to CNT/CNF. Moreover, "*In workplaces where CNT or CNF can't be substituted with a less hazardous or non-hazardous material then all process equipment and other equipment involved with the handling of CNT and CNF should incorporate the necessary engineering control measures to prevent worker exposure to CNT and CNF. Because of limited published workplace exposure data for CNT and CNF, it is unknown whether worker respirable mass exposures to CNT and CNF can be maintained at all workplaces below the NIOSH REL of 1 µg/m^3 EC as an 8-hour TWA. However, exposure control techniques such as source enclosure (i.e., isolating the generation source from the worker) and well-designed local exhaust ventilation (LEV) systems equipped with high efficiency particulate air (HEPA) filters have been shown to be effective for capturing airborne nanoparticles including CNT and CNF*".[22]

With regard to fullerenes, "*Pristine fullerenes have shown low toxicity and there is probably no risks expected for humans exposed to fullerenes in the workplace under good hygiene conditions. The main concern for consumers is exposure via direct dermal application of fullerenes present in cosmetics. Available studies do not indicate a short term risk from the tested fullerene types, however no extrapolation to all fullerene types and to chronic exposure can be made. In conclusion,*

[17] Nanocyl (2009): Responsible Care and Nanomaterials Case Study Nanocyl. Presentation at European Responsible Care Conference, Prague 21-23rd October 2009. http//www.cefic.be/files/downloads/04_nanocyl.pdf

[18] NIOSH (2013): NIOSH Current Intelligence Bulletin 65, Occupational Exposure to Carbon Nanotubes and Nanofibers, April 2013. Available online at: http://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf

[19] NIOSH (2011): Occupational Exposure to Titanium Dioxide, Current Intelligence Bulletin 63, April 2011. http://www.cdc.gov/niosh/docs/2011-160/pdfs/2011-160.pdf

[20] NIOSH (2013), page vi

[21] NIOSH (2013), page 71

[22] NIOSH (2013), page 58

the current dataset on fullerenes in relation to both, human exposure and hazard is limited and does not allow reaching any definite conclusions suitable for regulatory decision making".[23]

The DNEL of 0.098 mg/m^3 proposed for nanosilver by Aschberger *et al* (2011) is slightly lower than the current DNEL (systemic long-term inhalation route for workers) set on 0.1 mg/m³ for silver. However, it is opinion of SCENIHR that "*Occupational exposure to silver and silver particles –mainly via airborne material – has not been studied in full detail. A further detailed description of the occupational exposure is needed in order to perform an occupational risk assessment*".[24]

With regard to ultrafine titanium dioxide, NIOSH reports that the institute is "*not aware of any extensive commercial production of ultrafine anatase TiO_2 in the United States although it may be imported for use. Ultrafine rutile TiO_2 is being commercially produced as an additive for plastics to absorb and scatter ultraviolet light; 10%–20% of the ultrafine TiO_2 is reported to be < 100 nm in size. Engineered TiO_2 nanoparticles are also being manufactured, and like ultrafine TiO_2, they are finding commercial application as a photocatalyst for the destruction of chemical and microbial contaminants in air and water, in light-emitting diodes and solar cells, in plastics, as a UV blocker, and as a "self-cleaning" surface coating. While a paucity of data exist on worker exposure to engineered TiO_2, exposure measurements taken at a facility manufacturing engineered TiO_2 found respirable exposure concentrations as high as 0.14 mg/m^3*".[25]

To overcome the current lack of reliable hazard data for individual nanoforms with which to derive OELs and DNELs, the adoption of Nano Reference Values (NRVs) has been proposed by the Ministry of Social Affairs and Employment in the Netherlands as a pragmatic basis for establishing provisional limit values. In fact, NRVs were first proposed by the British Standards and were subsequently further refined by the German *Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung* (IFA, 2009). It must be noted, however, that the NRVs are not health-based, rather they are intended to represent a warning or concern level. If they were to be found to be exceeded, the assumption is that additional exposure control measures should then be taken to ensure a lowering of exposure within the workplace. As such, they have been proposed as a means of implementing an approach based upon the precautionary principle that overcomes the uncertainties relating to the current state-of-the-art with regard to the technology and science.

2.2 Concerns over Physical Hazards

There remains a lack of knowledge and a need for further research on the physical hazards associated with nanomaterials. By way of example, when handling nanopowders, particular attention should be paid to the catalytic effects and the risk of fire or explosion. INRS (2013[26]) note that very few nanomaterials have been specifically tested for such hazards.

Moreover, in some specific work activities, other possible hazards should be considered, for example:

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[23] Aschberger et al (2010): Review of fullerene toxicity and exposure--appraisal of a human health risk assessment, based on open literature, Regul Toxicol Pharmacol. 2010 Dec;58(3):455-73. doi: 10.1016/j.yrtph.2010.08.017. Epub 2010 Aug 26. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20800639

[24] SCENIHR (2013): Opinion on Nanosilver: safety, health and environmental effects and role in antimicrobial resistance, Scientific Committee on Emerging and Newly Identified Health Risks. Opinion approved on 10-11 June 2014. Page 37.

[25] NIOSH (2011), page 82.

[26] INRS (2013): Nanomaterials – Current situation and prospects in occupational health and safety, Paris, INRS, dated September 2013, http://www.inrs.fr/accueil/dms/inrs/PDF/cp-nanos-bilan-perspective-english/cp-nanos-bilan-perspective-english.pdf

- During the generation of a plasma via the use of high currents, hazard of electrocution might be increased;
- During work activities with possible leaks of inert protective gases there might be an asphyxiation hazard.

Due to their greater surface area, nanoparticles can be easily charged electrostatically, thus increasing the risk of ignition and the violence of an explosion. Furthermore, due to their size, they might remain airborne for longer time, thus increasing the possibility of creating potentially explosive dust clouds.

The Nanosafe2 project[27] ranked various carbon black powders, aluminium nanoparticles of different sizes and carbon nanotubes in terms of their flammability and explosivity: on a scale from 0 to 3, where 0 is "no explosion", 1 corresponds to "weak explosion", 2 to "strong explosion" and 3 to "very strong explosion", carbon black and carbon nanotubes are in the dust explosion class 1, while aluminium nanopowders, depending on the particle size, were ranked in the highest classes 2 and 3.

2.3 Concerns over Health Hazards

2.3.1 Overview

As is the case regarding the physical hazards posed by nanomaterials, there is a general lack of data on the health hazards arising from their use. However, there is generally an awareness that nanomaterials do require a thorough evaluation. As described in a recent EEA (2013) report, the development of nanotechnology has coincided with *"…discussions of potential risks and the need for regulatory reform"* unlike preceding technologies where the discussions of associated risks have generally been carried out after their widespread use.[28] However, as the EEA (2013) report highlights, there has been a lack of coordinated action from governments and regulatory bodies.

Despite nanotechnology receiving attention of regulators and the wider public throughout its development, there is concern about its use among consumers and NGOs. The concerns of both the public and policy makers have prompted the creation of various initiatives. For example, the creation of the Project on Emerging Nanotechnologies Consumer Products Inventory.[29] This inventory seeks to list consumer products that may contain nanomaterials. It is based on crowd-sourced information regarding claims about product contents and thus relies on input from third parties to ensure its accuracy. Friends of the Earth (2011) raise concerns regarding the policies surrounding nanomaterials and their health and environmental hazards associated with nanotechnology such as the use of nano-silver antibacterial products.

2.3.2 Epidemiological studies

Epidemiological studies were mainly conducted on the effects of carbon black, one of the MNMs that has been used for many decades. The International Agency for Research on Cancer (IARC) evaluates carbon black as *possibly carcinogenic to humans (Group 2B)*, as there is sufficient evidence in experimental animals but inadequate evidence in human epidemiological studies.[30] Moreover, it is not certain whether workers were exposed to carbon black at nanoscale or micro-scale. This same uncertainty also affects epidemiological studies on nano-titanium dioxide. With regard to carbon

[27] http://www.nanosafe.org/

[28] EEA (2013): Late lessons from early warnings: science, precaution, innovation, EEA Report No 1/2013, available at http://www.eea.europa.eu/publications/late-lessons-2, accessed 04 March 2014

[29] http://www.nanotechproject.org/, accessed 03 March 14.

[30] http://monographs.iarc.fr/ENG/Monographs/PDFs/93-carbonblack.pdf

black, it has to be noted that the Scientific Committee on Consumer Safety (SCCS) concluded that nano-structured form of carbon black with a particle size of 20 nm or larger can be safely use as a colorant in cosmetic products in concentration up to 10% when applied in healthy, intact skin, "*based on the current available scientific evidence which shows an overall lack of dermal absorption*."[31]

According to the Health Effects Institute[32], a growing number of epidemiological studies have been conducted over the last ten – fifteen years on the human health effects of ultrafine particles (UFP)[33]. However, the evidence of adverse effects from short-term exposure to ambient UFPs on acute mortality and morbidity from respiratory and cardiovascular diseases is suggestive rather than conclusive. Due to underlying deficiencies in exposure data, it is not possible to conclude (or exclude) that UFPs alone account substantially for the adverse effects associated with other ambient pollutants such as $PM_{2.5}$. No epidemiological studies of long-term exposures to UFPs have been conducted so far.

2.3.3 Toxicity tests

Due to the uncertain reliability of in-vitro methods to assess the health effects of nanomaterials (SCCS, 2012, p. 14) and the limited and inconclusive epidemiological evidence (HEI, 2013; IARC, 2010), in-vivo studies provide most of the data on which the current concerns have been built.

Short and medium-term duration animal studies have provided evidence of toxic effects to the lung (inflammation, cytotoxicity and tissue damage) of different types of MNMs (e.g. carbon black, titanium dioxide, carbon nanotubes, C_{60}-fullerenes and amorphous silicon dioxide) (IARC, 2010; NIOSH, 2013; NIOSH, 2011; Oberdörster, 2004). However, there is conflicting evidence on the higher potency of nanomaterials compared to micro-sized particles. Markers of inflammation in the brain were observed in rats following inhalation exposure to nano-manganese (Elder *et al*, 2006). Some preliminary studies (e.g. Poland *et al*, 2008; IOM *et al*, 2008; Pacurari *et al*, 2008) detected effects similar to those of asbestos for specific modification of carbon nanotubes. Several types of nanomaterials (e.g. biological origin materials like phospholipids, lipids, lactic acid but also various polymers, carbon, silica and metals)[34] have shown the capacity of systemic distribution in the organism; however, the toxicological implications of the availability of MNMs in further organs were not sufficiently classified for hazard end-points.

Animal studies of long-term duration raised evidence on lung toxicity following inhalation exposure to nano-carbon black and nano-titanium dioxide and lung tumours were evoked in rats (IARC, 2010; NIOSH, 2011). The intratracheal instillation of different types of MNMs (namely carbon black, aluminium oxide, aluminium silicate, titanium dioxide, and amorphous silicon dioxide) has induced tumours and a higher potency of nanomaterials compared to micro sized particles have been observed.[35] "*However, there are insufficient data to confirm the health consequences of long-term repeated exposure*" (HSE, 2013).

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[31] SCCS (2013): Opinion on Carbon Black (nano-form), Opinion adopted at its 4th plenary meeting on 12 December 2013. Available at: http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_144.pdf

[32] HEI (2013): Understanding the Health Effects of Ambient Ultrafine Particles, HEI Review Panel on Ultrafine Particles, HEI Perspective 3, Health Effects Institute, Boston, Massachusetts.

[33] The report focuses on ambient UFPs, mostly related to combustion processes. Key source of UFPs in urban areas are exhaust (result of combustion) and non-exhaust emissions (tire and break wear) from motor vehicles.

[34] See De Jong and Borm (2008); Oberdöster *et al* (2009).

[35] Pott and Roller (2005): Carcinogenicity study with nineteen granular dusts in rats. Eur J Oncol 10: 249–281.

Landsiedel *et al* (2010) describe NOAEC or LOAEC values derived from short term inhalation trials in rats. These are expressed in terms of mg/m^3 of various nanoparticles. The values reported by Landsiedel *et al* are shown in Table 2-2 for the nanomaterials that have suggested OELs (see above). It is worth noting that comparisons between the results of various studies are particularly difficult for nanomaterials in comparison to macromaterials. The studies may have been carried out using different sources of nanoparticles and thus they are likely to have a different distribution of nanoparticle sizes and shapes as these are dependent on the exact production method or source. Therefore if the study does not provide an adequate characterisation of the nanomaterial composition, it may be impossible to make comparisons their toxicological profiles.

Table 2-2: Comparison of suggested OEL/DNEL values and NOAEL and LOAEC for nanomaterials

Nanomaterial	Aerosol Concentrations tested (mg/m^3)	Suggested OEL/DNEL* (mg/m^3)	NOAEL/LOEL (mg/m^3)	Pathology	Reversibility
MWCNT	0.1, 0.5, 2.5	OEL/REL 0.05	NOAEL 0.1	Inflammation	No
Carbon Black	0.5, 2.5, 10	DNEL (for fullerenes) 0.27	NOAEL 10	No effects	-
TiO_2	2, 10, 50	OEL/REL 0.3	LOEL 2	Histocytosis	Not complete

Source: Landsiedel *et al* (2010).
Note: The sources of nanoparticles are not necessarily comparable for the studies leading to the derivation OEL/DNEL and the NOEAL/LOEL.
* OEL/DNEL reported as µg/m^3 in Table 2-1.

The US National Institute for Occupational Safety and Health (NIOSH) has determined, in light of the results of in-vivo studies, that exposure to ultrafine TiO_2 should be considered a potential occupational carcinogen, acting "*through a secondary genotoxicity mechanism that is not specific to TiO_2 but primarily related to particle size and surface area*".

Moreover, "*the higher mass-based potency of ultrafine TiO_2 compared to micro sized TiO_2 is associated with the greater surface area of ultrafine particles for a given mass*". This has led to the setting of different Recommended airborne Exposure Limits of 2.4 mg/m^3 for fine (micro sized) TiO_2 and 0.3 mg/m^3 for ultrafine (nano sized) TiO_2 (including manufactured nano-TiO_2), as time-weighted average (TWA) concentrations for up to 10 hours per day during a 40-hour work week.

Importantly, NIOSH concluded that:

the adverse effects of inhaling TiO_2 may not be material-specific but appear to be due to a generic effect of poorly soluble low-toxicity (PSLT) particles in the lungs at sufficiently high exposure. While NIOSH concludes that there is insufficient evidence to classify fine TiO_2 as a potential occupational carcinogen, NIOSH is concerned about the potential carcinogenicity of ultrafine and engineered nanoscale TiO_2 if workers are exposed at the current mass-based exposure limits for respirable or total mass fractions of TiO_2. NIOSH recommends controlling exposures as low as possible, below the RELs" (NIOSH, 2011).

A recently published report[36] by the Fraunhofer Institute for Toxicology and Experimental Medicine, on behalf of the German Federal Environment Agency (UBA), ran a large analysis on long term studies with nanomaterials in order to identify toxicity indicators and possible precursors of

[36] UBA (2014): Carcinogenicity and Mutagenicity of Nanoparticles – Assessment of Current Knowledge as Basis for Regulation, Umwelt Bundes Amt, Texte 50/2014. Available at: http://www.umweltbundesamt.de/publikationen/carcinogenicity-mutagenicity-of-nanoparticles

carcinogenicity. The authors built a relational database, populating it with more than 100 inhalation and instillation *in vivo* studies on:

- "Inert" particles or granular biopersistent dusts
  - Carbon black
  - Titanium dioxide
  - Aluminium oxide
- Silicon dioxide
- Heavy metals (elemental or oxides)
  - Silver
  - Manganese
  - Nickel
  - Iron
  - Cerium
- Carbon nanotubes
  - Single wall carbon nanotubes
  - Multi wall carbon nanotubes.

Neutrophil number, total protein and LDH content in the bronchio-alveolar lavage fluid (BALF) are frequently observed effects that can be considered as sensitive indicators of toxicity. Infiltration of inflammatory cells in the lung and increased lung weight are instead often observed effects that can be considered possible precursors of carcinogenicity. Notably, the Lowest Observed Effect Levels (LOELs) of nanomaterials are generally lower than the LOELs of the bulk or fine powder forms of the substances considered, indicating a higher potency, with differences by several orders of magnitude. Within the nanomaterials analysed, nanosilver was identified as the most toxic one.

The authors propose grouping of nanomaterials on the basis of their potential of generating inflammation and, based on inflammatory parameters, suggest a preliminary LOEL of 0.1 mg/m^3 (exposure 24 hours a day, seven days a week) to distinguish the "inert" nanomaterials from the nanomaterials with specific toxicity (which LOELs should be set at lower values). Moreover, the data analysis supports the view of nanotubes as a separate group.

2.3.4 Industrial health accidents linked to nanomaterials

A research of articles documenting and analysing any health accidents linked to nanomaterials has been carried out: two papers have been found and are presented below.

Song et al (2009): Exposure to nanoparticles is related to pleural effusion, pulmonary fibrosis and granuloma

The authors report on what appears to be a "nanomaterial-related disease". During 2007-2008, seven young previously healthy non-smoking female workers employed at a print plant were admitted, examined and treated at the hospital of the authors in Beijing. The presented symptoms were: shortness of breath, rashes and itching on the face and arms. The clinical findings showed pleural and pericardial effusions and progressive pulmonary fibrosis, leading to the death of two of the patients.

The survey of the workplace found very poor risk management measures and occupational hygiene: the seven workers were assigned to a machine used for air spray coating materials, heat and dry the coating onto polystyrene boards to be used in the printing a decorating industry; the machine was located in a 70 m^2 room without windows and with one single door that was kept closed due to the outside temperature. The ventilation unit of the machine broke five months before the occurrence

of the disease. The coating material was a mixture of polyacrylic ester. Table 2-3 presents the components of the polyacrylic ester paste handled by the workers.[37]

Table 2-3: Components of the polyacrylic ester paste handled			
Substance	**EC number**	**CAS number**	**Classification**
Butanoic acid	203-532-3	107-92-6	Harmonised classification: H314 Cause severe skin burns and eye damage
Butyl ester	204-658-1	123-86-4	Harmonised classification: H226 Flammable liquid and vapour H336 May cause drowsiness or dizziness
N-butyl ether	205-575-3	142-96-1	Harmonised classification: H226 Flammable liquid and vapour H315 Cause skin irritation H319 Causes serious eye irritation H335 May cause respiratory irritation H412 Harmful to aquatic life with long lasting effects
Acetic acid	200-580-7	64-19-7	Harmonised classification: H226 Flammable liquid and vapour H314 Cause severe skin burns and eye damage
Toluene	203-625-9	108-88-3	Harmonised classification: H225 Highly flammable liquid and vapour H304 Maybe fatal if swallowed and enters airways H315 Causes skin irritation H336 May cause drowsiness or dizziness H361d Suspected of damaging the unborn child H373 May cause damage to organs
di-tert-butyl peroxide	203-733-6	110-05-4	Harmonised classification: H225 Highly flammable liquid and vapour H242 Heating may cause a fire H341 Suspected of causing genetic defects
1-butanol	200-751-6	71-36-3	Harmonised classification: H226 Flammable liquid and vapour H302 Harmful if swallowed H315 Cause skin irritation H318 Causes serious eye damage H335 May cause respiratory irritation H336 May cause drowsiness or dizziness
Acetic acid ethenyl ester	203-545-4	108-05-4	Harmonised classification: H225 Highly flammable liquid and vapour H332 Harmful if inhaled H335 May cause respiratory irritation H351 Suspected of causing cancer
Isopropyl alcohol	200-661-7	67-63-0	Harmonised classification: H225 Highly flammable liquid and vapour H319 Causes serious eye irritation H336 May cause drowsiness or dizziness
Ethylene dioxide	204-661-8	123-91-1	Harmonised classification: H225 Highly flammable liquid and vapour H319 Causes serious eye irritation H335 May cause respiratory irritation H351 Suspected of causing cancer

[37] The components reported in the paper have been searched on the Classification and Labelling Inventory and the EC number, CAS number and classifications reported in the table. All components have harmonised classifications.

Nanoparticles of around 30 nanometres in particle size were found through electron microscopy in both the paste and the dust. Although the analysis is limited due to the absence of environmental monitoring data of the workplace and the subsequent inability in estimating the accurate concentrations of the polyacrylate nanoparticles that the workers were exposed to, around 6 kilogrammes of paste were used typically every day. It should be noted that, although the authors list the components of the paste (probably based on the consultation of the paste producer), the same authors state lately in the paper that the actual composition of the nanoparticles is still unknown. They also report that polyacrylate is often enhanced (to make it stronger and more resistant to abrasion) through the addition of surface coated nanomaterials of various substances, such as silicon, zinc oxide, titanium dioxide and silver.

The 30 nm nanoparticles were found in chest fluid, lung tissues and bronchoalveolar lavage fluid (BALF) of the patients.

The authors infer that the main route of exposure was inhalation and the secondary route of exposure was dermal. The smoke generated by the spraying, heating and drying of the boards is highly reactive and damaging and might explain, in the opinion of the authors, the deposition of the nanoparticles in the respiratory tract and in the BALF. Dermal exposure might explain the rash and itching reported by the patients.

The authors draw a parallel between the results of *in vivo* and *in vitro* studies and the results of the analysis of the consequences observed on the patients and suggest that the nanoparticles themselves might have caused the injuries. They also suggest that the components of the paste used are low in toxicity (despite the classifications reported in Table 2-3: a substance with a low toxicity requires large doses to produce mild symptoms) and unlikely to cause disease of the severity seen in these patients, concluding that the patients' illness appears to be a "nanomaterial-related disease". The same authors suggest however that, given "*the detailed description of their working, the duration of the daily exposure, the dosage of the material used every day, the space of their workplace and the serious results of long-term exposure give us some important information that the concentrations of the polyacrylate nanoparticles that the workers were exposed to may be very high*". In a subsequent study (Song *et al*, 2011), the authors identified the nanoparticles found in the lung fluids and tissues of the patients as amorphous silica nanoparticles.

The authors call for further research and for the implementation of effective protective methods.

Journeay and Goldman (2014): Occupational Handling of Nickel Nanoparticles: A Case Report

The authors report the case of a young non-smoking female formulation chemist that, in 2010, started a new task involving the handling of dry nickel nanopowder. Table 2-4 reports the harmonised hazard classifications of nickel.

Table 2-4: Harmonised classification of nickel

Nickel (EC number: 231-111-4; CAS number: 7440-02-0)	H317: May cause an allergic skin reaction H351: Suspected of causing cancer H372: Causes damage to organs H412: Harmful to aquatic life with long lasting effects

Source: ECHA Classification and Labelling Inventory

She previously worked in formulation of polymers, coatings and metallic inks without any symptom. The task involved the weighing, processing and repackaging of the nanopowder and the subsequent cleaning of the tools used. The worker wore latex gloves just during the cleaning but no respiratory

protection or any other personal protective equipment. It was the first time she was handling nickel powder. Within one week she developed throat congestion, "post nasal drop" and flushing of the face on a daily basis. She then experienced skin reaction to the metal amalgams of her earrings and belt buckle. The symptoms kept appearing even once she was moved to a different floor, due to indirect exposure to the nickel powder handled by other workers. When far from the working premises, the patient' symptoms were markedly reduced.

The powder handled was composed by highly pure (over 99.9%) nickel with particle size of 20 nm and surface area between 40-60 m^2/g.

The authors highlight the importance and effectiveness of engineering controls and personal protection in reducing occupational exposure to nanomaterials and note that, in the case reported, the risk reduction measured implemented were not adequate. Although it is not known if the patient would have developed the same reaction if exposed to bulk preparation of the nickel powder, the authors note that nanoscale nickel powder has different properties, with a higher propensity to become airborne and possibly higher immunogenicity and irritant effects, as the small total mass of the particles handled seems to suggest. This higher potency might be linked to the high surface area.

The authors conclude that it is increasingly important to appreciate the differences between bulk and nanosized materials, in order to implement adequate exposure controls.

2.3.5 Nanomaterials in consumer products

As should be apparent from the preceding text, much of the information concerning exposure to nanomaterials is related to occupational exposures. Of course, consumers may also be exposed to nanomaterials present in a range of products. There is a significant number of reports and studies on how the presence of nanomaterials could be measured, but reports on actual measurements are more difficult to find, although literature in this area is constantly increasing, especially on specific nanomaterials, such as nanosilver[38]. In the Netherlands, some work has been undertaken by RIVM[39] but, given the lack of exposure data, it is not surprising that RIVM notes*: Possible health effects of consumers of using nano-products are not known.*[40]

The difficulties lie on the fact that each step of the consumer exposure assessment poses a challenge:

- Firstly, the consumer products containing nanomaterials need to be identified;
- Secondly, various characteristics of the nanomaterials and of the product containing the nanomaterials need to be analysed;
- Thirdly, the type of exposure (direct/indirect), the duration and the frequency, the route of exposure and the number of consumers exposed need to be determined.

These three main steps are further described below.

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[38] For example: Oomen *et al* (2011), Nazarenko (2011), Quadros and Marr (2011), Benn *et al* (2010), Lorenz *et al* (2012), Geranio *et al* (2009), Von Götz *et al* (2013a), Echegoyen and Nerín (2013), Quadros *et al* (2013), Peters *et al* (2011), as quoted in SCENIHR (2014).

[39] RIVM (2011): Nanomaterial in consumer products: Detection, characterisation and interpretation, Report 320029001/2011. Available at: http://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2011/mei/Nanomaterial_in_consumer_products_Detection_characterisation_and_interpretation

[40] http://www.rivm.nl/en/Topics/C/Consumer_exposure_to_chemical_substances/Nanomaterials_in_consumer_products

Step 1: Identification of the products containing nanomaterials

Several attempts to identify consumer products containing nanomaterials have been made in the past years. Some of these resulted in the building of publicly available inventories, for example:

- The Project on Emerging Nanotechnologies (based on a partnership between the Woodrow Wilson International Centre for Scholars and the Pew Charitable Trusts);[41]

- The NANO Supermarket – It is an initiative of the non-profit organisation Next Nature Network, aiming "*to visualize, research and understand the implications of this next nature on our everyday life*." It provides information on different product categories and technologies that might shape our next future, ranking them by their likelihood and feasibility.[42]

- Nanowerk Nanotechnology Products and Applications – It is a database aiming to give "*an idea of how and where in industry nanoscale materials, devices, structures and processes are being used.*"[43]

It should be noted that among the transparency measures analysed in the Evaluation report, only the Cosmetic Product Notification Portal and the Danish system gather information on consumer products containing nanomaterials.

In order to show the challenges in identifying products on the consumer markets, the consultants describe more in detail the Consumer Products Inventory of the Project on Emerging Nanotechnologies and highlights some shortcomings identified and some problems reported. This discussion is also very important when considering the potential uses by different stakeholders of the information provided and their desired (or non-desired) effects.

The Consumer Products Inventory (http://www.nanotechproject.org/cpi/) aims to provide information to the public on how nanotechnology is entering the market; currently, the inventory provides information on over 1,600 consumer products based on nanotechnology. Registered users are encouraged to submit evidence-based data. The managers of the inventory decide on what to include following three criteria: the product can be readily purchased by the consumers; the product is identified as nano-based by the manufacturer or another source; the claim that the product is nano-based seems reasonable. Each entry provides information on:

- The manufacturer;
- Country of origin;
- Product category;
- Claims supporting the application of nanotechnology;
- The date on which the entry was last updated;
- If provided by the manufacturer, information on the nanomaterial, nanomaterial function, nanomaterial location/characterisation, potential exposure pathway, and coatings is also provided.

Products are placed in different Product Categories and Sub-categories:

- Appliances (Heating, cooling and air; large kitchen appliances; laundry and clothing care);
- Automotive (Exterior; maintenance and accessories);

[41] http://www.nanotechproject.org/cpi/
[42] http://www.nanosupermarket.org/
[43] http://www.nanowerk.com/index.php

- Goods for Children (Basics; toys and games);
- Electronics and Computers (Audio; cameras and film; computer hardware; display; mobile devices and communications; television; video);
- Food and Beverage (Cooking; food; storage; supplements);
- Health and Fitness (Clothing; cosmetics; filtration; personal care; sporting goods; sunscreen);
- Home and Garden (Cleaning; construction materials; home furnishings; luxury; paint);
- Cross-Cutting (Coatings).

A ranking system (from 1 "Extensively verified claim" to 5 "Not advertised by manufacturer") of the confidence level on the information has also been developed.

Professor Maynard, one of the co-founder of the Project on Emerging Nanotechnologies Consumer Products Inventory (CPI), has recently discussed the risks linked with the misuse of the information provided through the inventory, in a recent piece titled "No, metal oxide nanoparticles in your food won't kill you"[44] and published online on "The Conversation" website[45]. He reports on an article published on the American publication Mother Jones[46] relating on the presence of "*tiny metal oxide particles*" in food and linked dangers. He sustains that the information sources for the article[47] have been misused: the journalist refers to a Friends of the Earth report that in turn refers to the CPI that in turn refers to a paper[48] published in the journal Environmental Science & Technology in 2012. Professor Maynard clarifies that the CPI was conceived as a way to "*better understand the increasing number of consumer products that were using engineered nanomaterials*" and "*never meant to be comprehensive or authoritative*". According to professor Maynard, the 2012 study reported an analysis of 90 food products for the presence of titanium dioxide, concluding that some products contained titanium dioxide in concentrations of 0.4% by weight or below. Following its publication, the CPI was updated with some of the food products analysed in the paper. Subsequently, Friends of the Earth used the CPI to claim a sharp increase of food products contained nanomaterials on the market. The problem is that food grade titanium dioxide (in the European Union, E171) is not normally a nanomaterial (the majority of the particles has particle size of hundreds nanometres) and that, as clarified by professor Maynard, the inventory is updated on the basis of intermittent web searches and other sources of intelligence, not necessarily mirroring the real situation on the market but just providing clues on what kind of products nanomaterials can be found.

Another problem is the reliability of the information provided. As mentioned, the CPI has a ranking system in order to give less or more "trustworthiness" to the information presented, on the basis of the source and the possibility to check it online.

The consultants browsed the inventory by substance, and their attention was captivated by the entry regarding Lead. Lead is a notorious neurotoxic element that can have adverse effects even at low levels. Selecting "Lead" in the inventory, one product is presented as containing lead nanoparticles, with a confidence level category 2 (Verified claim), although the product has now been put in the archive (availability/nano claim can no longer be verified). The product[49] is presented as a sunscreen manufactured in the UK and easily available to consumers. The

[44] https://theconversation.com/no-metal-oxide-nanoparticles-in-your-food-wont-kill-you-27545

[45] "*The Conversation is a collaborative initiative between editors and academics to provide informed news analysis and commentary that's free to read and publish*", source: https://theconversation.com/uk

[46] "*Mother Jones is a non-profit news organisation that specialises in investigative, political, and social justice reporting*". Source: http://www.motherjones.com/about

[47] The article has been updated reporting the correction of the inventory. Available at: http://www.motherjones.com/tom-philpott/2014/05/nanotech-food-safety-fda-nano-material

[48] Weir *et al* (2012): Titanium Dioxide Nanoparticles in Food and Personal Care Products, Environ. Sci. Technol., 2012, 46 (4), pp 2242–2250.

[49] http://www.nanotechproject.org/cpi/products/optisoltm-sun-defence/

description of the product reports that microscale (not nano) titanium dioxide has been conditioned incorporating a small amount of manganese in order to avoid the formation of free radicals. The description actually refers only to the active component of the sunscreen, more precisely a new UV filter. In the description, there is neither mention of nanomaterials, nor of lead nanomaterials. Following the link to the source[50], a better description of the technology behind the UV absorber can be found, but again, no mention of nanomaterials. Checking the ingredients list[51] of the products using this UV absorber technology, only one substance is listed as (nano): Methylene bis-benzotriazolyl tetramethylbutylphenol. Neither titanium dioxide nor manganese oxide are labelled as nano, nor, more importantly, there is mention of lead among the ingredients. The misunderstanding seems to derive from the description of the new UV absorber technology as a "lead product" on the manufacturer website, meaning however "leading product".

Step 2: Characterisation of the nanomaterials and of the products containing nanomaterials

Once the products containing nanomaterials have been identified, information on the physicochemical parameters of the nanomaterials (chemical entity, particle size, shape, specific surface area, etc.), their concentration in the products and the status of the nanomaterials in the products (agglomerated, aggregated, free particles, bound to the other non-nano materials) must be determined.

Subsequently, information on the form of the products needs to be gathered (solid/coating, liquid, spray, dispersion).

Step 3: Exposure scenarios

Once the nanomaterials and the products containing the nanomaterials have been characterise, information on the type of exposure have to be collected: the ways the products are used will determine the type (direct or indirect) of exposure the consumers might have. An assessment of the use setting needs to be performed (outdoor/indoor) in order to determine the possible concentrations of the free/released nanoparticles or the potential release of the nanomaterials from products exposed to the weather elements.

The duration and the frequency of the exposure events need to be determined as well as the number of users exposed.

Finally, the route(s) of exposure need to be identified.

As reported in the SCENIHR opinion on nanosilver[52], Hansen *et al* (2007) proposed a grouping of nanomaterials based on the combination between location of the nanomaterials in the system/material and the uses of the nanomaterials in the products. "*Products containing free nanoparticles with direct human exposure (e.g. food supplements or sunscreen products) are considered to have a high potential exposure. Conversely, products in which nanomaterials are integrated into larger scale materials with indirect human exposure (e.g. food storage bags or computers) are considered to have a low potential exposure*"[53].

[50] http://www.isis-innovation.com/news/news/oxonica-apr05.html

[51] http://www.boots.com/en/Soltan-Once-Face-Moisturising-Suncare-Cream-SPF30-50ml_1314649/

[52] SCENIHR (2014): Opinion on nanosilver: safety, health and environmental effects and role in antimicrobial resistance, Scientific Committee on Emerging and Newly Identified Health Risks, Opinion approved at the 6th plenary of 10-11 June 2014.

[53] SCENIHR (2014), page 31.

Following this system, exposure scenarios are ranked on the basis of the likelihood and magnitude of exposure.

In a subsequent paper, Hansen *et al* (2008) proposed the grouping of consumer products containing nanomaterials in three exposure categories:

- Expected to cause exposure: direct contact, for example with nanoparticles in liquids or aerosols, is expected;
- May cause exposure: the nanomaterials are applied to the surface of the product and some wear and tear cannot be excluded;
- No expected exposure to the consumer: the nanomaterials are bound to the macromaterials in the product.

2.4 Concerns over Environmental Hazards

Since 2006, OECD has published over 40 authoritative documents[54] on the 'Safety of Manufactured Nanomaterials', providing up-to-date information on the diverse activities related to human health and environmental safety of nanomaterials. Throughout there has been a recognition that methods to measure and assess environmental pathways and resultant effects on the environment will be required. By inspection of the more recent publications, it is apparent that considerable knowledge gaps remain. By way of example, OECD (2012)[55] presents a long list of research needs to reduce the inherent uncertainties including:

Ecological Effect Research Needs: Understanding the disposition of nanomaterials (i.e. ADME) within whole organisms in all trophic levels. This information will provide an understanding as to whether standard ecotoxicological studies are an effective indicator of toxicity for nanomaterials, as well as provide insight on mode of toxicity and species sensitivities

Persistence, Bioaccumulation, Fate and Distribution: Identify mechanisms of bioaccumulation, as well as developing means for predicting bioaccumulation, as well as potential for food chain transfer. Bioaccumulation and food chain transfer are crucial in conventional chemical risk assessments, however, there is no confidence that approaches employed for chemicals are applicable to nanomaterials.

In addition, there is an emerging consensus that some nanomaterials may present a risk to the environment. By way of example, in a recent study for the Swiss authorities[56], it is reported that nano-titanium dioxide (as used in some sun-screens) and nanosilver (as an anti-microbial agent) are hazardous to the aquatic environment. SCENIHR (2014) concludes that:

.. while in the environment Ag-[silver nanoparticles] may be a particularly effective delivery system for silver to organisms in soil, water and sediment and may act as sources of ionic silver over extended periods of time. Therefore, additional effects caused by widespread and long term use of Ag-NPs cannot be ruled out.

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54 http://www.oecd.org/science/nanosafety/publicationsintheseriesonthesafetyofmanufactured nanomaterials.htm

55 OECD (2012): Important Issues on Risk Assessment of Manufactured Nanomaterials, http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono%282012%298&doclanguage=en

56 TA-SWISS (2013); Nanomaterialien: Auswirkungen auf Umwelt und Gesundheit, Zurich. Available at: https://www.ta-swiss.ch/en/projects/nanotechnologies/nano-and-environment/

Nanomaterials can be released from a variety of sources and during various phases of their life cycles including manufacturing, delivery, use, and disposal. Nanomaterials can reach the different compartments of the environment (water, soil, air and biota) finding their way into solid waste and wastewater effluents from disposed products containing nanomaterials; through direct discharge or accidental spillage from industrial sources and then transported to aquatic systems by wind or rainwater runoff. They can also be released from coatings materials and plastic composites via weathering processes, such as abrasion and sunlight-induced degradation.

Due to their characteristics, nanomaterials can remain suspended in air and water for long periods of time and thus be transported over greater distances than larger particles of the same material.[57] Moreover, carbon or metal based nanomaterials may threaten the environment due to their bioaccumulative nature within food chains.

As for consumer exposure, the attention has been focused on specific nanomaterials, such as nanosilver and carbon nanotubes. Attempts to include environmental impact as a design parameter in the synthesis process of CNTs have been conducted since 2008. MIT researchers characterised the chemical content of the CNTs and then traced the nanotubes into the air, water and soil. They observed that CNTs, even after purification, contained residues of metals (chromium, copper and lead) and measurable levels of PAHs, which might result in the release of these contaminants into the environment.[58]

Another area with a constantly growing literature is the characterisation of ultrafine particles emitted by industrial plants and municipal waste incinerator plants.[59]

Nanosilver is probably the nanomaterial that most attention has received with regard its potential effects on the environment. Several studies have been conducted to measure the silver nanoparticles concentrations in water bodies and sediments in different regions of the world[60]. Some of them, tried to characterise fate and behaviour in the different compartments, with others trying to quantify the effects on aquatic systems, aquatic organisms, bacteria, plants and soil animals and microorganisms. When released, nanosilver undergoes several transformations, the most important ones being dissolution and speciation, with the formation of silver chloride and silver sulphide. These processes directly influence the bioavailability and toxicity of silver in the environment. Another important factor that seems to determine the toxicity expressed is the eventual coating of the silver nanoparticles.

Few studies have attempt to determine bioaccumulation and authors are still debating on whether the parameter was effectively assessed, since the protocols applied do not allow for a proper assessment[61].

Much concern was raised on the possible effect of silver nanoparticles on bacterial resistance. During the last decade, many articles have been published focusing on bacterial susceptibility and bioavailability to silver and silver nanoparticles, however, "*more data are needed to better understand bacterial response to ionic silver and Ag-NPs exposure*"[62].

[57] http://www.epa.gov/athens/research/nano.html
[58] http://cee.mit.edu/system/files/October_08_On_Balance.pdf
[59] http://www.journals.elsevier.com/science-of-the-total-environment/virtual-special-issues/nanomaterials-in-the-environment/
[60] See SCENIHR (2014), page 55.
[61] SCENIHR (2014), page 63.
[62] SCENIHR (2014), page 74.

2.5 Substances Notified to the FNS and the ECHA registered substances and CLI databases

As presented in the Evaluation report, although the French Notification System does not require information on physical, health and environmental hazards, a cross-analysis with the Classification and Labelling Inventory (CLI) has been carried out.

Each one of the substances notified to the FNS as manufactured and imported at the nanoscale has been searched for in the CLI. The search has been performed by EC number when available. When an EC number was not available or the EC number was not found, the CAS number was entered in the search field. If also the search by CAS number gave no result, a significant part of the spelling of the chemical name of the substances was entered.

Table 2-5 presents the results of the analysis.

Table 2-5: Cross-analysis of the FNS with the CLI	
Substances searched in the CLI	258
Substances not found in the CLI	40
Substances found in the CLI	218
Substances with a harmonised classification	8
Substances found in the CLI but without classification	67
Substances with a classification (including substances with harmonised classification)	151
Substances with "nanomaterial" as one of the forms notified to the CLI	**23**

Table A3-4 in the Evaluation report presents the list of substances notified to the FNS that have been found in the CLI with classifications referring to the nanoform(s). Three of the substances with nanoforms notified to the CLI have a harmonised classification, namely:

- Nickel monoxide (EC number: 215-215-7, CAS number: 1313-99-1);
- Copper(I) oxide (EC number: 215-270-7, CAS number: 1317-39-1); and
- Zinc oxide (EC number: 215-22-5, CAS number: 1314-13-2).

Table 2-6 shows the number of substances with nanoforms that have been notified to the FNS presenting a defined DNEL, PNEC and/or OEL. These values have been gathered from the ECHA registered substances database: it is important to note that they are not specific to the nanoforms of the substances.

For the Occupational Exposure Levels, the values for the European Union and for three countries (France, United Kingdom and Germany) have been reported as illustrative examples.

Table 2-6: Number of substances with nanoforms notified to the FNS with DNELs, PNECs and OELs (non-specific to the nanoforms)	
DNELs (exposure route/local or systemic/ long-term or short-term (acute)/ worker or consumer)	**No.**
Inhalation local long-term worker	50
Inhalation local short-term worker	5
Inhalation systemic long-term worker	63
Inhalation systemic short-term worker	10
Inhalation local long-term consumer	14
Inhalation local short-term consumer	4
Inhalation systemic long-term consumer	45
Inhalation systemic short-term consumer	6
Dermal local long-term worker	3

Table 2-6: Number of substances with nanoforms notified to the FNS with DNELs, PNECs and OELs (non-specific to the nanoforms)	
Dermal local short-term worker	2
Dermal systemic long-term worker	54
Dermal systemic short-term worker	5
Dermal local long-term consumer	2
Dermal local short-term consumer	2
Dermal systemic long-term consumer	52
Dermal systemic short-term consumer	5
Oral local long-term worker	0
Oral local short-term worker	0
Oral systemic long-term worker	1
Oral systemic short-term worker	0
Oral local long-term consumer	1
Oral local short-term consumer	1
Oral systemic long-term consumer	71
Oral systemic short-term consumer	4
PNECs	
Freshwater	39
Freshwater sediment	37
Marine water	34
Marine water sediment	36
Sewage Treatment Plant (STP)	64
Soil	50
Intermittent release (IR)	24
Air	0
Terrestrial organisms	1
Secondary poisoning	9
OELs	
European Union	1
France	12
United Kingdom	20
Germany	9

3 Value Chain Characterisation

3.1 Introduction

This section is based on the information presented on the French public report, on data gathered via the online consultation and associated research.

3.2 The French Notification System

Some preliminary data were published in the French public report and Figure 3-1 shows the distribution of the notifiers across the supply chain.

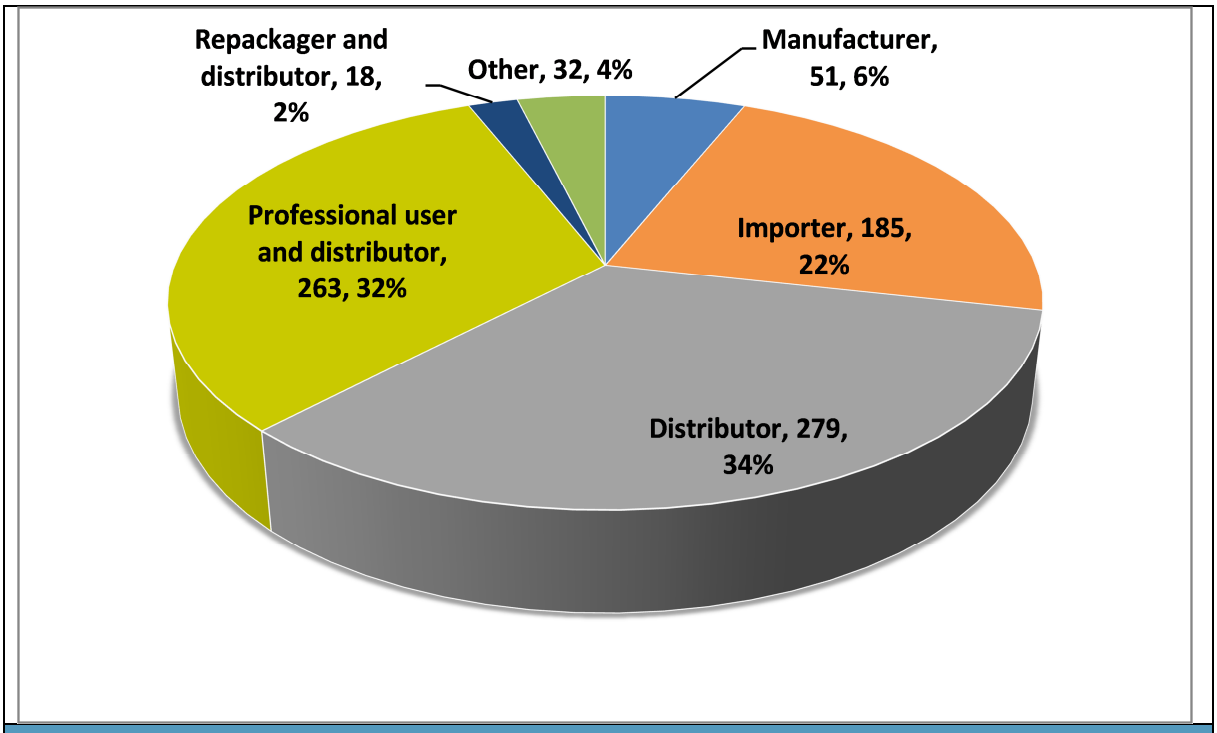

Figure 3-1: Distribution of the notifiers across the supply chain. Source: French public report (2013)

Table 3-1 presents the average number of notifications per role in the supply chain. No information has been reported on the 32 entities that indicated "other" as role in the supply chain. It must be noted that the notifiers could indicate multiple roles for each notification.

Table 3-1: Average number of notification per role in the supply chain

Role	No. of notifications	Average No. of notifications
Manufacturer	149	3
Importer	923	5
Distributor	1,121	4
Professional user and distributor	982	4
Repackager and distributor	35	2
Other	(32)	n/a

Table 3-2 provides the analysis of the number of substances per notified sectors of use (as already presented in the Evaluation report).

Table 3-2: Number of substances per notified sectors of use (SU)			
Code	**Supplementary descriptor: Sectors of end-use**	**NACE codes[63]**	**NMs**
SU1	Agriculture, forestry, fishery	A	60
SU2a	Mining, (without offshore industries)	B	3
SU2b	Offshore industries	B 6	1
SU4	Manufacture of food products	C 10,11	8
SU5	Manufacture of textiles, leather, fur	C 13-15	7
SU6a	Manufacture of wood and wood products	C 16	3
SU6b	Manufacture of pulp, paper and paper products	C 17	18
SU7	Printing and reproduction of recorded media	C 18	5
SU8	Manufacture of bulk, large scale chemicals (including petroleum products)	C 19.2+20.1	9
SU9	Manufacture of fine chemicals	C 20.2-20.6	27
SU 10	Formulation [mixing] of preparations and/or re-packaging (excluding alloys)	C 20.3-20.5	132
SU11	Manufacture of rubber products	C 22.1	24
SU12	Manufacture of plastics products, including compounding and conversion	C 22.2	70
SU13	Manufacture of other non-metallic mineral products, e.g. plasters, cement	C 23	10
SU14	Manufacture of basic metals, including alloys	C 24	2
SU15	Manufacture of fabricated metal products, except machinery and equipment	C 25	7
SU16	Manufacture of computer, electronic and optical products, electrical equipment	C 26-27	6
SU17	General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment	C 28-30,33	21
SU18	Manufacture of furniture	C 31	3
SU19	Building and construction work	F	28
SU20	Health services	Q 86	7
SU23	Electricity, steam, gas water supply and sewage treatment	C 35-37	2
SU24	Scientific research and development	C72	32
SU0	Other		147
Not reported			1
Note: It must be noted that the numbers do not add up as for each substance different sectors of use have been notified			

The nanomaterials are present across different sectors, notably 132 different substances have been notified as being used at the nanoscale in:

- C 20.3 Manufacture of paints, varnishes and similar coatings, printing ink and mastics (72 substances were also notified as being used in product category PC9a “Coatings and paints, thinners, paint removers” and 22 in PC18 “Ink and toners”);
- C 20.4 Manufacture of soap and detergents, cleaning and polishing preparations, perfumes and toilet preparations;
- C 20.5 Manufacture of other chemical products.

[63] Notifiers have to submit information on the Sectors of Use. Corresponding NACE codes have been assigned to Sectors of Use by ECHA.

Sixty substances have been notified to be used at the nanoscale in the broad sector A "Agriculture, Forestry and Fishing". From the further analysis of these substances, most of them are pigments and dyes used for agricultural colouring requirements. Other 28 substances were notified as being used at the nanoscale in the broad sector F "Construction".

Twenty-seven substances have been notified as being used at the nanoscale in:

- C20.2 Manufacture of pesticides and other agrochemical products;
- C20.6 Manufacture of man-made fibres.

Notably, 32 substances are used for research and development purposes.

Table 3-3 reports the nanomaterials manufactured and/or imported in France in 2012 above 1,000 tonnes. Although Table 10 in the French public report provides figures for nanomaterials above 100 tonnes per year, those figures might be erroneous due to partial notifications by companies or partial analysis of the notifications by the French authorities.

Table 3-3: Nanomaterials manufactured and/or imported in more than 1,000 tonnes in France in 2012

Chemical name	Tonnes
Carbon Black	≈ 275,000 tpa
Silicon dioxide / amorphous silica	≈ 155,000 tpa
Calcium carbonate	≈ 34,500 tpa
Titanium dioxide	≈ 14,300 tpa
Aluminium oxide	≈ 2,200 tpa
Copolymer of vinylidene chloride (declared name)	≈ 1,600 tpa

Source: reproduced from French public report (2013), Table 10.

Figure 3-2 provides the shares on the total tonnage of nanomaterials on the French market in 2012.

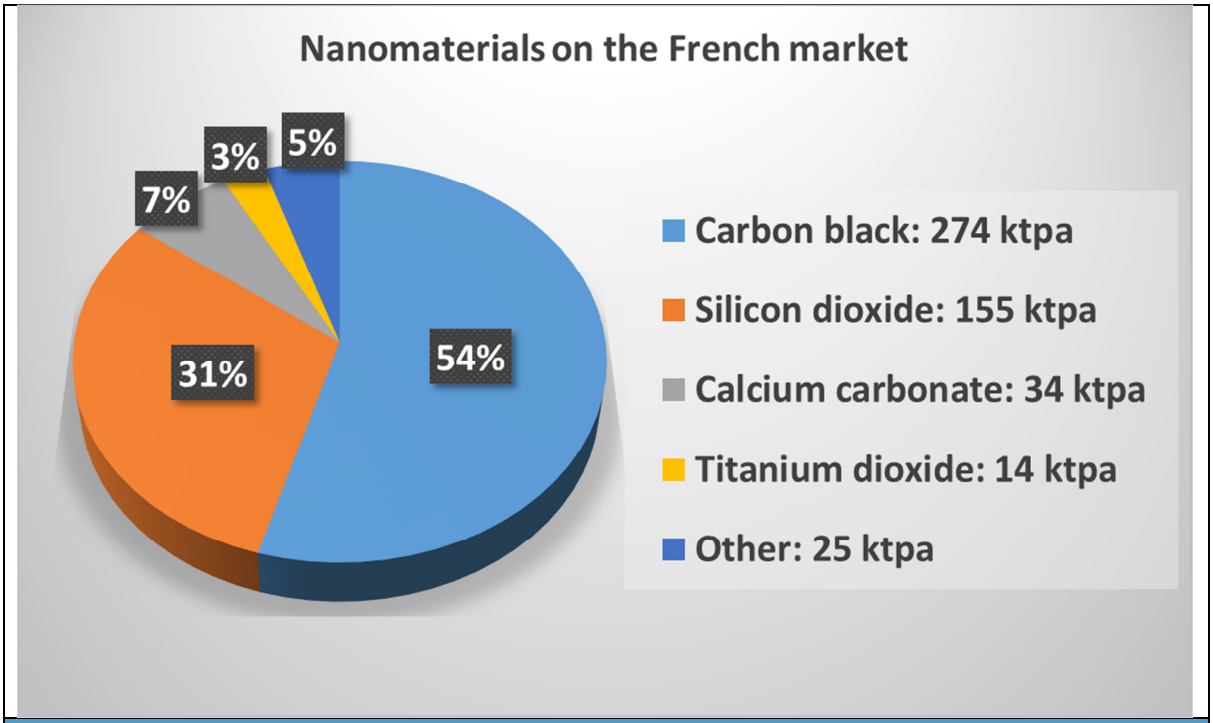

Figure 3-2: Shares on the total tonnage of nanomaterials on the French market in 2012

The market is dominated by four nanomaterials:

- Carbon black (over 50% of the market);
- Silicon dioxide (over 30%);
- Calcium carbonate; and
- Titanium dioxide.

The remaining five percent of the nanomaterials' tonnage on the French market is made up of the other 254 substances, of which over 150 have been identified[64] as pigments and dyes.

More information and a comparison of the data presented in the French public report with other sources have been presented in Section 6 of the Evaluation report.

3.3 Results of the Survey on the Administrative Burden of the Notification Systems

3.3.1 Introduction

The online survey on the administrative burden posed by the FNS and the CPNP was launched at the end of February 2014 in English and French. Its aim was to gather relevant information on the experiences of companies providing information to the French Notification System (FNS) and the Cosmetic Products Notification Portal (CPNP), in particular on the direct costs and the impacts on research and innovation. In total, 52 replies were received (status: 5 June 2014; 32 replies to the French questionnaire version, 20 replies to the English version). Moreover, the *Union des Industries Chimiques* submitted a position document highlighting some key points on behalf of its members.

The analysis of the administrative burden has been presented in Section 5 of the Evaluation report. This section proposes again some of the information relevant for the characterisation of the supply chains of the nanomaterials.

3.3.2 Country of origin

Over 60% of the answers were received from companies based in France. Seven enterprises with headquarters in Germany and four Belgian companies also participated in the survey. Other six replies have been received from companies based in Czech Republic, the Netherlands, Poland, Spain, Sweden and Switzerland.

Table 3-4: Number of respondents by country of origin

Country	Number of respondents	Share
France	35	67%
Germany	7	13%
Belgium	4	8%
Czech Republic	1	2%
Netherlands	1	2%
Poland	1	2%
Spain	1	2%
Sweden	1	2%
Switzerland	1	2%
Total	**52**	-

[64] With the help and support of Cefic, NIA and their members.

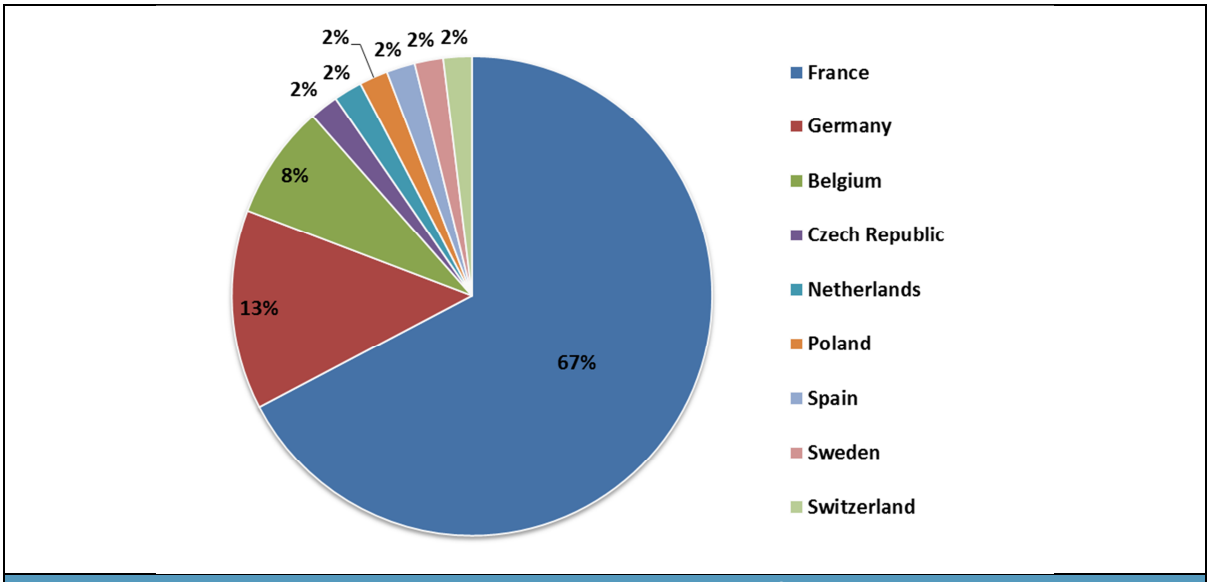

Figure 3-3: Respondents by country of origin

3.3.3 Company size

The participants to the survey were asked to provide number of employees and annual turnover in two separate questions, rather than asking for the company size, in order to facilitate the answers. The replies have been combined and the profile of the companies checked trough internet searches, in order to determine whether SMEs were actual autonomous enterprises or partner/linked enterprises (with effect on their SME status[65]). No information has been asked with regard to annual balance sheet total to avoid overcomplicating the survey. The results are provided in Table 3-5 and presented in Figure 3-4.

Table 3-5: Respondents by company size

Company size	Number of respondents	Share
Small enterprise	3	6%
Medium enterprise	9	17%
Large enterprise	40	77%
Total	52	-

Around 80% of the replies (40 respondents) have been received from large enterprises (companies with over 250 employees and annual turnover over €50 million). Seventeen percent of replies (9 respondents) classifies as medium enterprises (companies with fewer than 250 employees and turnover of less than €50 million). Only three replies (6%) came from small enterprises (companies with fewer than 50 employees and turnover of less than €10 million). No micro enterprises (companies with fewer than 10 employees and turnover of less than €2 million) participated in the survey. The size of the sample and its composition (not statistically significant) do not allow to extrapolate the results for the analysis of the companies' size across the different supply chains of the nanomaterials (the manufacturers that participated in the survey are large global players; medium sized enterprises participating in the survey declared multiple roles across the supply chains and were distributed homogenously in the different roles).

[65] For further information on the EU definition of SME, see: http://ec.europa.eu/enterprise/policies/sme/files/sme_definition/sme_user_guide_en.pdf

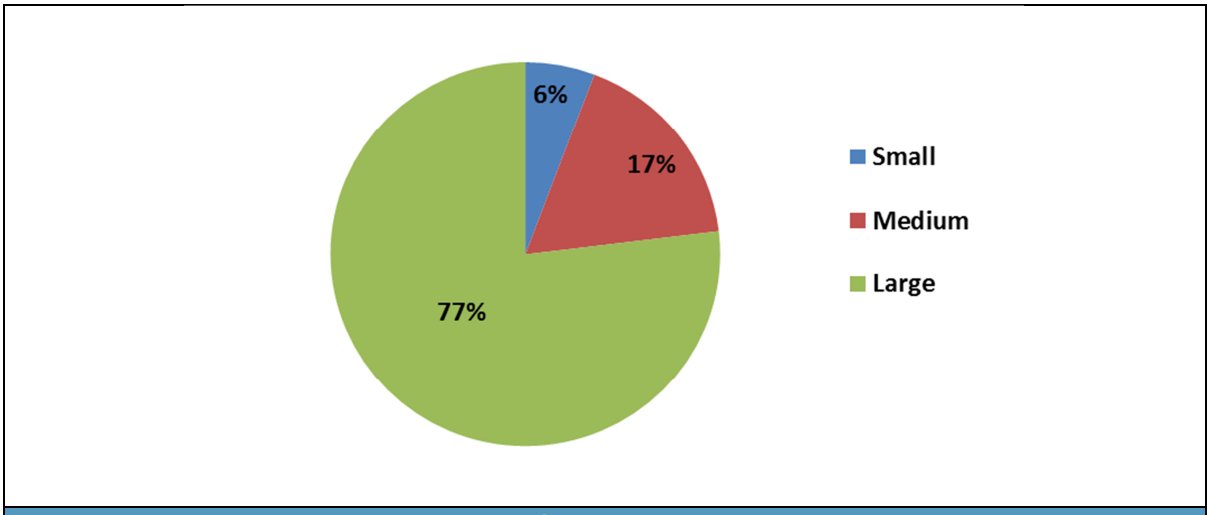

Figure 3-4: Share of respondents by company size

Companies were also asked to provide an estimate of the turnover (in terms of ranges) directly linked with the manufacturing, importing or commercialising of nanomaterials and mixtures or articles containing nanomaterials. Twenty-eight companies provided an estimate: these are presented in Table 3-6 along with overall annual turnovers.

Forty companies provided an indication for the annual turnover, with most of them (65%) declaring an annual turnover over €50 million and another 25% declaring an annual turnover between €10 and €50 million. Three companies declared an annual turnover between €2 million and €10 million and one company an annual turnover of less than €250 thousand.

Table 3-6: Annual turnover of companies and the nanotechnology related share

Range in Euro	Number of respondents (and %) per annual turnover	Number of respondents (and %) per nanotechnology-related turnover
< 250 k	1 (2.5%)	13 (46%)
250 k ≤ 2 m	0 (0%)	1 (4%)
2m ≤ 10m	3 (7.5%)	5 (18%)
10m - 50m	10 (0.25%)	4 (14%)
> 50m	26 (65%)	5 (18%)

It was indicated by nearly 50% of the companies that the nano-products related turnover lies beneath €250,000. Other 50% of the respondents that provided an estimate (14 over 28 companies) indicated a nanotechnology-related turnover higher than €2 million.

3.3.4 Primary business sector

Companies were asked to indicate their primary business sector (52 replies[66]), and if applicable their secondary business sector(s) (15 replies). Table 3-7 presents the primary business sector of the respondents. Seven companies provided only 2 digits for NACE code C20 "Manufacture of chemicals

[66] 45 respondents provided NACE codes, six respondents provided national codes equivalent to NACE codes and one company did not indicate the primary role as their business cover several NACE codes. For the latter, a NACE code has been assigned on the basis of the highest revenue among the company business sectors.

and chemical products": some of them might be active across the different groups and classes[67]. Four companies provided 3 digits for NACE code C20.4 "Manufacture of soap and detergents, cleaning and polishing preparations, perfumes and toilet preparations", C20.5 "Manufacture of other chemical products" and G46.3 "Wholesale of food, beverages and tobacco".

Table 3-7: Overview on the primary business sector of the companies	
NACE primary business sector	No.
C20.4.2 - Manufacture of perfumes and toilet preparations	8
C20 - Manufacture of chemicals and chemical products	7
C20.3.0 - Manufacture of paints, varnishes and similar coatings, printing ink and mastics	7
C20.1.2 - Manufacture of dyes and pigments	5
C20.1.3 - Manufacture of other inorganic basic chemicals	5
C20.5.9 - Manufacture of other chemical products n.e.c.	5
G46.7.5 - Wholesale of chemical products	4
C20.4 - Manufacture of soap and detergents, cleaning and polishing preparations, perfumes and toilet preparations	2
G46.4.5 - Wholesale of perfume and cosmetics	2
C10.8.9 - Manufacture of other food products n.e.c.	1
C20.1.4 - Manufacture of other organic basic chemicals	1
C20.2.0 - Manufacture of pesticides and other agrochemical products	1
C20.4.1 - Manufacture of soap and detergents, cleaning and polishing preparations	1
C20.5 - Manufacture of other chemical products	1
G46.3 - Wholesale of food, beverages and tobacco	1
M72.1.9 - Other research and experimental development on natural sciences and engineering	1
Total	52

3.3.5 Characterisation of the supply chains of the respondents

This subsection characterises the respondents in terms of the role(s) played in the supply chains of nanomaterials and provides some data on the number of completed notifications.

Role in the supply chains of nanomaterials

Thirty-two companies indicated to play multiple roles in the supply chains of nanomaterials, with just eight companies indicating to be only manufacturers, five indicating to be only importers, other five indicating to be professional users and distributors and two indicating to be only distributors. Table 3-8 presents the different roles as indicated by the respondents (multiple ticks and indication of primary role possible[68]).

Table 3-8: Overview on the supply chain position of the companies		
Supply chain position	No. of companies	of which primary role
Manufacturer	26	**25**
Distributor	26	**11**
Importer	26	**11**
Professional user (PU) & distributor	15	**12**
Repackager & distributor	4	**2**
European representative	2	**1**

[67] For the detailed structure of NACE code C20 Rev.2, see page 65 at: http://epp.eurostat.ec.europa.eu/cache/ITY_OFFPUB/KS-RA-07-015/EN/KS-RA-07-015-EN.PDF

[68] For companies, who only selected one role, the selected role was considered as their primary role. For companies indicating more than one role, but without stating one of the roles as being their primary role, all selections were equally counted as primary role.

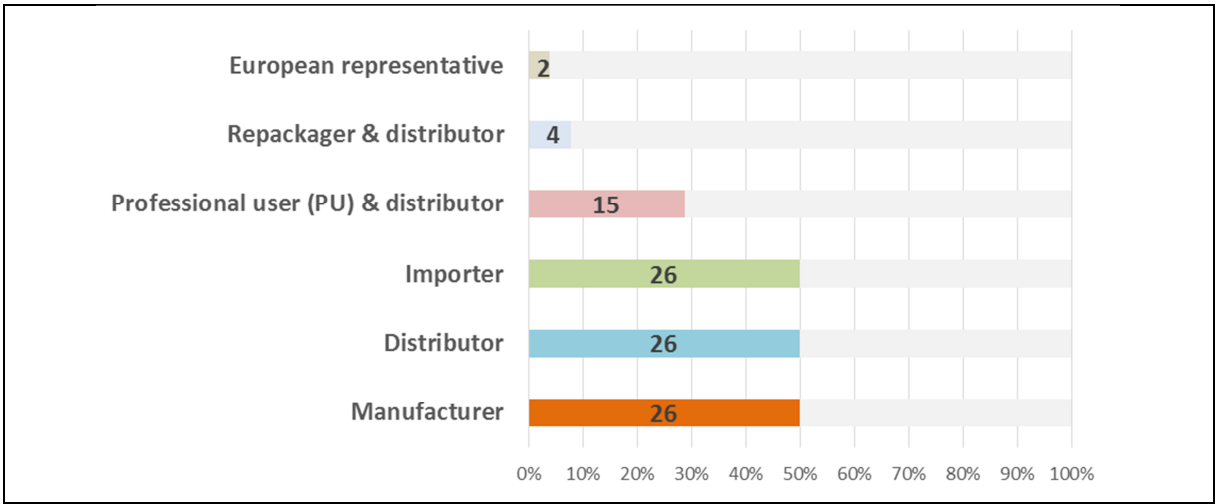

Figure 3-5: Overview of the supply chain by company role

Number of notifications

Companies were asked to provide the number of notifications completed in 2013 and completed or planned for 2014.

Overall, in 2013, 933 companies completed around 3,409 notifications: 52 companies (around 6% of the total number of notifiers) participated in the survey and indicated to have completed around 800 notifications (24% of the total number of notifications). It can be concluded that many of the big actors on the French market participated in the survey.

With regard to notifications in 2014, respondents generally provided or the same number of notifications or a higher number or the additional number of notifications: it can be concluded that 2013, being the first year of implementation of the system, has been a "learning" period for companies. This seems to be confirmed also by the fact that in 2014 the French authorities received three times the number of notifications than in 2013.

3.3.6 Information on customers and suppliers

Companies were asked to provide information with regard the number of customers and suppliers of nanomaterials. Nearly half of the respondents (49%) declared to have more than 100 customers (see Figure 3-6). Conversely, more than 80% of the companies who participated in the survey have less than 16 suppliers.

When looking at companies´ size and primary role in the supply chain, large companies tend to have a large portfolio of customers (64% declared more than 100 customers) irrespective of the position in the supply chain. The number of replies do not allow to identify any definite trend with regard to SMEs.

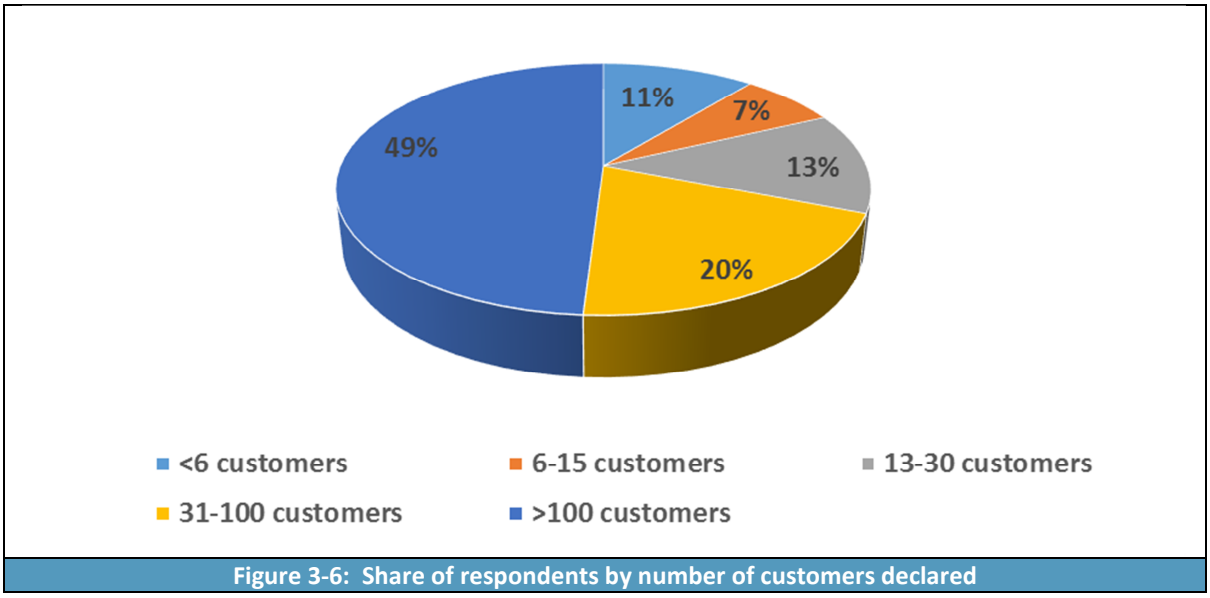

Figure 3-6: Share of respondents by number of customers declared

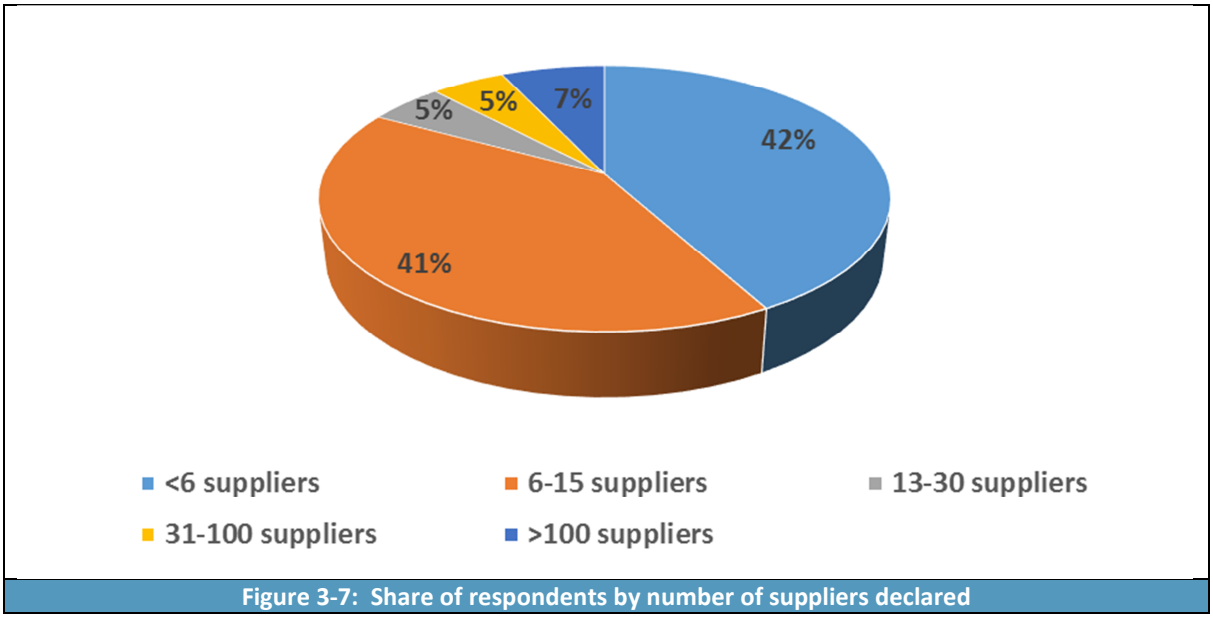

Figure 3-7: Share of respondents by number of suppliers declared

3.3.7 Overview on the distribution of nano-related products on different markets

Companies were asked to provide information with regard to the number of nano-related products (substances in nanoform as well as mixtures and articles containing nanomaterials) put on the French, European and global markets. The results are presented in Tables 3-9, 3-10 and 3-11.

Only around half of the respondents were in the position to estimate the number of nanomaterials and mixtures containing nanomaterials commercialised on the different markets: companies had difficulties with the definition of nanomaterials and thus with their identification. Moreover, in large companies, the provision of this information required the person in charge of filling out the questionnaire to contact different departments in different countries. With regard to the number of articles containing nanomaterials, the low rate of replies to this question might also indicate that the respondents were primarily manufacturers, importers and distributors of chemical products and not

of articles treated with nanomaterials. Notably, two companies declared to put on the French market more than 1,000 nanomaterials: this response is inconsistent with the response regarding the number of notifications submitted in 2013 (and 2014); rather than no compliance with the FNS, this suggests a misinterpretation of the question.

However, the majority of respondents declared a number of nanomaterials commercialised on the different markets fewer than six, consistently with the number of notifications submitted and the low turnover directly related with nanotechnology.

It should also be noted that around the same number of nano-related products are commercialised on the French, European and global markets, suggesting that, once the scaling up to industrial production has been successfully performed, nanomaterials and nano-related products have a global market.

Table 3-9: Number of nanomaterials put on the French, European and global market

	French market	EU Market	Global market
<6 NMs	17	14	11
6-10 NMs	1	1	2
11-50 NMs	2	3	3
51-100 NMs	1	0	0
101-250 NMs	2	0	0
251-500 NMs	0	1	0
501-1000 NMs	0	1	2
>1000 NMs	2	2	2
No. of respondents	25	22	20

Table 3-10: Number of mixtures containing nanomaterials put on the French, European and global market

	French market	EU Market	Global market
<6 mixtures containing NMs	12	12	10
6-10 mixtures containing NMs	2	1	0
11-50 mixtures containing NMs	8	4	4
51-100 mixtures containing NMs	4	2	1
101-250 mixtures containing NMs	2	2	2
251-500 mixtures containing NMs	1	2	2
501-1000 mixtures containing NMs	0	1	2
>1000 mixtures containing NMs	4	4	4
No. of respondents	33	28	25

Table 3-11: Number of articles containing nanomaterials put on the French, European and global market

	French market	EU Market	Global market
<6 articles containing NMs	8	6	6
6-10 articles containing NMs	0	0	0
11-50 articles containing NMs	1	2	0
51-100 articles containing NMs	0	0	0
101-250 articles containing NMs	1	1	0
251-500 articles containing NMs	0	0	0
501-1000 articles containing NMs	1	0	0
>1000 articles containing NMs	1	1	1
No. of respondents	12	10	7

3.4 Findings of the Supply Chain Characterisation

Aim of this Section was to identify information on the relevant competitive position of EU companies and production sites, as well as on margins and profits and direct and indirect employment and growth trends.

However, on the basis of the research that has been carried out, the value chains of nanomaterials do not seem to have different characteristics from the bulk forms of the chemical substances, if not that their market volumes still appear to be relatively low (with the exception of the "common" nanomaterials such as carbon black, silicon dioxide, calcium carbonate, titanium dioxide and possibly pigments and dyes). As previously found by EC (2012), "*in general it appears that most substances are produced all through the industrialised world, with producers in Europe, North America (mainly United States and Canada) and Japan or other traditionally industrialised countries in the Far East (…) and only for few of those substances there seems to be a concentration in a particular world region*"[69].

The research of relevant information is problematic due to diverging definitions (of "nanomaterial" and "nanotechnology"), to the lack of specific information (with the exception of road categories such as nanotubes or quantum dots, nanomaterials are considered as advanced forms of the same materials) and to the R&D stage of many nanomaterials, where information tend to be highly confidential.

However, the information that has been gathered through the analysis of the French public report and the results of the survey give a firm basis for the extrapolation of the market volumes per nanomaterials categories to the EU level (see the Option Assessment report).

In terms of market values, despite the predictions of double-digits growth annual rates and heavy investments in R&D by major players[70], from the results of the survey it seems that the "new" nanomaterials did not reach yet consolidated positions on the markets. This might be due to still higher prices than alternatives made of "traditional" materials and to problems in scaling up the manufacturing of nanomaterials from the lab to industrial production[71].

Due to the lack of specific statistics on nanomaterials and the "no differentiation" between nanomaterials and other chemicals, an estimate of the direct and indirect employment is very difficult. Even if all the data gathered through the FNS were published, the estimate would still require the consultation of all the notifiers in order to gather information on the number of persons directly employed to work on nanomaterials. Even so, the apportionment of the workforce to nanomaterials related tasks would be challenging, given that there is no such a neat distinction between nanomaterials and other forms of the substances on the workplace and employees are likely to work with different forms of the substances.

[69] EC (2012), Appendix 2, page 45.

[70] For example, see http://www.lucintel.com/lucintelbrief/globalnanomaterialsopportunity-final.pdf

[71] A good deal of research funding is addressed to the development and optimisation of industrial-scale production of nanomaterials, see for example: http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/h2020/topics/2482-nmp-05-2014.html

4 Overview on Growth and Innovation

4.1 Proxies for Innovation

Innovation is typically measured via imperfect proxies owing to the inherent difficulty of measuring it directly. Such proxies include:

- R&D spending;
- Number of people employed in R&D;
- Patent applications and approvals;
- Journal papers published.

While each of these relates to innovation in obvious ways, they all come with limitations.

Crucially, R&D is an input to innovation outputs rather than a measure of innovation occurring in an economy. The relationships between R&D and innovation outputs are likely to vary with time and occur with uncertain lags, and they may be non-linear.

There are similar problems with the relationships between patents and innovation outputs, but patents are at least likely to be more closely related to those outputs. Both R&D and patents measure innovation with error: a certain proportion of R&D and patents will have no impact on technological growth, productivity or GDP. For this reason, it is important that they be viewed together when drawing conclusions about innovation.

As a proxy for innovation, patents are limited in other ways. For example, a patent application may be submitted under the name of a subsidiary, rather than the parent company. Also, it is perfectly possible for the research to be conducted in one region and the corresponding patent application to be submitted in another.

In addition, a significant proportion of technological innovations in manufacturing do not result in patent applications, however this should not affect the usefulness of patent data for measuring trends as long as the average propensity to patent does not change over the period under investigation.

Proxy data are discussed here and the limitations of such data, as outlined, should be noted.

4.2 R&D Spending

4.2.1 Public

Data relating to public spending on nanomaterial R&D is available, but using it not completely straightforward for two reasons.

First, the science of nanomaterials is not frequently separated from the broader field of nanotechnology. Research on the manufacture of molecular machines from DNA, for example, would invariably be considered nanotechnology without pertaining to bulk nanomaterials.

Second, because of the highly interdisciplinary nature of the activity, not all nanotechnology R&D is labelled as such. There are some extremely high value national and international R&D programmes currently funding projects that focus exclusively on nanotechnology. The US National

Nanotechnology Initiative is typical of these. But operating in the shadows is a host of individual projects that involve nanotechnology without explicitly saying so.

That said, the science of nanomaterials is a very significant part of nanotechnology. Additionally, it is probably the field of nanotechnology most likely to appear beneath a nanotechnology banner. Most other fields stand a higher – if still relatively small – likelihood of appearing beneath another banner. Pharmaceutical nanotechnology might, for example, be labelled healthcare for the purposes of public funding.

Here then, we have reviewed nanotechnology in general where – as is frequently the case – the degree of demarcation in the relevant reference sources is insufficient to facilitate a meaningful discussion of nanomaterials in isolation.

EU

In general, EU spending on nanotechnology R&D has increased over the last 10–15 years, although successive funding programmes have organised work in different ways making direct comparisons difficult.

Under the Sixth Framework Programme (FP6), the EU spent €1.3bn on nanotechnology R&D (shared between 550 projects) in the five years from 2002 to 2006. It then spent €3.5bn in the seven years from 2007 to 2013 on the 'nanosciences, nanotechnologies, materials and new production technologies' theme of the Seventh Framework Programme (FP7).[72]

It is now spending €3.85bn on 'nanotechnologies, advanced materials and advanced manufacturing and processing' under Horizon 2020, which will run for seven years from 2014 to 2020[73].

Data from Georgalis and Aifantis show that annual spending through these programmes increased steadily from 1997 to 2009 (Georgalis & Aifantis, 2013).

EU member states

The UK research councils and other public funding organisations provide money for nanotechnology R&D. Of these, the Engineering and Physical Sciences Research Council (EPSRC) most likely provides the most. At the time of writing, live EPSRC grants with the socio-economic theme nanotechnology accounted for €217m (£176m) of funding[74]. As grants are typically provided for periods of more than one year, this figure represents funding for several years.

According to a report from industry group Materials UK and the Knowledge Transfer Networks (KTNs), the UK government provided €790m (£640m) for nanotechnology over the 12 year period from 1998 to 2010 (Materials UK, 2010). The breakdown of this spending is shown in Table 4-1.

Table 4-1: Estimated UK government support for nanotechnology based on Department for Business, Innovation & Skills data

Year	Estimated amount (millions of €/£)
2009/2010	102 / 83.2
2008/2009	96 / 77.6
2007/2008	91 / 73.5

[72] Around €177m was the budget dedicated to the research focusing on health and environmental impacts of nanomaterials.

[73] http://horizon2020projects.com/industrial-leadership/nanotechnology/

[74] http://gow.epsrc.ac.uk/NGBOListSocioThemes.aspx

Table 4-1: Estimated UK government support for nanotechnology based on Department for Business, Innovation & Skills data	
Year	**Estimated amount (millions of €/£)**
2006/2007	82 / 66.2
2005/2006	81 / 66.0
2004/2005	81 / 65.8
2003/2004	75 / 60.8
2002/2003	50 / 40.6
2001/2002	62 / 50.0
2000/2001	44 / 35.5
1999/2000	14 / 11.0
1998/1999	15 / 12.4

The German government directed €400m of public money into nanotechnology R&D in 2010 (Federal Ministry of Education and Research (BMBF), 2011), up from $500m in 2008 (Materials UK, 2010), making the German government one of the biggest spenders globally.

France ran a €2.3bn national public–private nanotechnology R&D programme, Nano2012, from 2008 to 2012 (five years)[76]. In 2009, the French government announced it would commit €457 in public money to the programme[75], which was led by STMicroelectronics, a French–Italian semiconductor company.

In 2013, the French government announced that it would be contributing to €600m to Nano2017, the follow-up to Nano12[76]. Like its predecessor, the programme is set to run for five years, will focus on nanotechnology and involve both public money, including €400m from the EU, and private money, including €1.3bn from some stakeholders.

According to reference sources, France spent €210m of public money on nanotechnology R&D in 2008 (Materials UK, 2010).

The rest of the world

The US Government has apportioned about €15bn ($20bn) of the Federal budget to the National Nanotechnology Initiative (NNI) member agencies since its launch in 2000[77]. The supplied annual budget grew steadily through the 2000s, but then stalled in the wake of the 2007–8 global financial crisis at about €1.4bn ($1.9bn), as can be seen in Table 4-2. The budget fell significantly in 2013 but has since levelled out at about €1.1bn ($1.5bn).

[75] http://www.electronics-eetimes.com/en/nano2012-r-d-program-is-officially-launched.html?cmp_id=7&news_id=218501185

[76] http://www.nanotechia.org/news/news-articles/french-prime-minister-launches-eur-35-billion-public-private-partnership-nano

[77] http://www.nano.gov/about-nni/what/funding

Table 4-2: NNI annual budget	
US fiscal year	Allocation (millions of €/$)
2015	1130 / 1540*
2014	1130 / 1540**
2013	1140 / 1550
2012	1370 / 1860
2011	1360 / 1850
2010	1400 / 1910
2009	1250 / 1700
2008	1140 / 1550
2007	1050 / 1430
2006	992 / 1350
2005	882 / 1200
2004	727 / 989
2003	559 / 760
2002	512 / 697
2001	341 / 464
*Proposed; **estimated	

The NNI budget represents only part of the public money available for nanotechnology R&D in the US. It does not included, for example, money from state initiatives. In the 2011 fiscal year, the NNI reported funding for €1.36bn ($1.85bn), but Cientifica, a market research firm, estimated total government spending at $2.18bn[78].

The Russian strategy towards funding of nanotechnology R&D coalesced in 2007 in the form of the Development Programme for Nanoindustry in the Russian Federation (Connolly, 2013). Through this program, the government planned to spend about €2.12bn (руб100bn) from 2008 to 2015. Specifically, it created a federal targeted programme (FTP) and a state corporation, Rusnano (formerly Rusnanotekh), which together would use the money to realise the aims of the development programme through investment in infrastructure and funding for R&D.

This large injection of state money had an immediate impact. Indeed, in 2009, when the money came online fully, Russia became the biggest spender globally. Only two thirds of that money went towards R&D, however. In the years leading up to the 2007 push, Russia had spent comparatively little on nanotechnology, and as a consequence a large proportion of the investment was need needed for basic development of the relevant infrastructure.

Cientifica estimated Chinese public spending on nanotechnology R&D at €960m ($1.3bn) in absolute terms and €1.65bn ($2.25bn) assuming purchasing power parity (ppp)[78]. With the US allocating only €1.6bn ($2.18bn) to the field in 2011, China become for the first time the biggest spender globally.

Japan has a reputation as a country that invests heavily in R&D, and in relation to nanotechnology it has more or less played to type, spending €280m ($380m) of public money on the field (Materials UK, 2010).

The Taiwanese government directed €88m ($120m) of public money into nanotechnology R&D in 2010 (Materials UK, 2010).

In 2007, the India government approved Nano Mission, a national nanotechnology R&D programme, with an allocation of €124m (Rs1000crore) for five years.

[78] http://www.cientifica.com/research/white-papers/global-nanotechnology-funding-2011/

4.2.2 Private

Several market research firms (Lux Research, Cientifica) have produced widely quoted reports on private spending on nanomaterial R&D but these are not readily available.

Additionally, not all companies publish their information about nanomaterials (ObservatoryNANO, 2011):

> *As it has been noted in this paper, companies do not always publicize their research in nanotechnology. In fact, depending on the industry, some companies are fearful of making it known. This factor not only may skew numbers such as the true count of nanotechnology companies, but it can also play an impact in driving (or discouraging) future nanotechnology research. If a company feels nanotechnology research will be punished rather than lauded, it will be more hesitant to pursue such developments. This is just one of many barriers a nanotechnology company may face. While barriers to commercial success have been identified, further investigation could be made to better understand the possible solutions to overcome such barriers.*

It may be possible however to construct a qualitative picture of private spending by profiling companies with nanomaterial business and large R&D budgets. The profiles of two global players are presented below as illustrative examples.

BASF

BASF spent €1.8bn on R&D in 2013, split six ways, as shown in Table 4-3.

Table 4-3: BASF 2013 R&D spending by business segment

Segment	Spending (€m)	Proportion of total (%)
Chemicals	184	10
Performance products	367	20
Functional materials and solutions	367	20
Agricultural solutions	477	26
Oil and gas	55	3
Corporate research, other	385	21

The segments can be divided into sub-segments, as shown in Table 4-4. By inspection of the sub-segments, it might be expected that nanotechnology applications are most likely to be found in 'performance products' and 'functional materials and solutions'.

Table 4-4: BASF business segments and sub-segments		
Segment	**Sub-segment**	**Description on BASF website[79]**
Chemicals	Petrochemicals	Basic products: ethylene, propylene, butadiene, benzene, alcohols, solvents, plasticizers, alkylene oxides, glycols and acrylic monomers Specialties: Special plasticizers such as Hexamoll® DINCH®, special acrylates
	Monomers	Basic products: isocyanates (MDI, TDI), ammonia, caprolactam, adipic acid, chlorine, urea, glues and impregnating resins, caustic soda, polyamides 6 and 6,6, standard alcoholates, sulfuric and nitric acid Specialties: Electronic chemicals, metal system
	Intermediates	Basic products: butanediol and derivatives, alkylamines and alkanolamines, neopentylglycol, formic and propionic acid Specialties: specialty amines such as tert-Butylamine, gas treatment chemicals, vinyl monomers, acid chlorides, chloroformates, chiral intermediates
Performance products	Dispersions and pigments	Polymer dispersions, pigments, resins, high-performance additives, formulation additives
	Care chemicals	Ingredients for skin and hair cleansing and care products, such as emollients, cosmetic active ingredients, polymers and UV filters Ingredients for detergents and cleaners in household, institution or industry, such as surfactants, chelating agents, polymers and products for optical effects Solvents for crop protection formulations and products for metal surface treatments Superabsorbents for the hygiene industry
	Nutrition and health	Additives for the food and feed industries, such as vitamins, carotenoids, sterols, enzymes, emulsifiers and omega-3 fatty acids Flavors and fragrances, such as geraniol, citronellol, L-menthol and linalool Active ingredients and excipients for the pharmaceutical industry, such as caffeine, ibuprofen and pseudoephedrine as well as binders and coatings for tablets, synthesizing pharmaceutical substances and intermediates for our customers
	Paper chemicals	Dispersions for paper coating, functional chemicals, process chemicals, kaolin minerals

[79] http://www.basf.com/group/corporate/en/about-basf

Table 4-4: BASF business segments and sub-segments		
Segment	**Sub-segment**	**Description on BASF website[79]**
Performance products (cont.)	Performance chemicals	Antioxidants, light stabilizers, pigments and flame retardants for plastic applications Fuel and refinery additives, polyisobutene, brake fluids and engine coolants, lubricant additives and basestocks, components for metalworking fluids and compounded lubricants Process chemicals for the extraction of oil, gas, metals and minerals, chemicals for enhanced oil recovery, water treatment chemicals, membrane technologies Auxiliaries for the production and treatment of leather and textiles
Functional materials and solutions	Catalysts	Automotive and process catalysts Battery materials Precious and base metal services
	Construction chemicals	Concrete admixtures, cement additives, underground construction solutions, flooring systems, sealants, solutions for the protection and repair of concrete, high-performance mortars and grouts, tile-laying systems, exterior insulation and finishing systems, expansion joints, wood protection solutions
	Coatings	Coatings solutions for automotive and industrial applications Decorative paints
	Performance materials	Polyurethane systems and specialty elastomers, engineering and high-performance plastics, biopolymers and epoxy resins, insulation and specialty foams
Agricultural solutions	Fungicides	Protecting crops from harmful fungal attacks; improving plant health
	Herbicides	Prevention of nutrient and water deprivation caused by weeds
	Insecticides	Combating insect pests in agriculture
	Functional crop care	Products beyond traditional crop protection for plant health and increased yield potential, such as biological control products, seed treatments, polymers and colorants
	Pest control	Non-agricultural applications: public health, professional pest control, landscape maintenance
Oil and gas	Exploration and production	-
	Natural gas trading	-

Geographic distribution of R&D

One of BASF's stated aims is to move more of its R&D outside Europe.[80] In 2013, it conducted '28%' of its R&D outside Europe and it is aiming for 50% by 2020.

Key areas of interest

In its annual press release on innovation, BASF highlighted its interest in several nanomaterials and fields of nanotechnology R&D:

- Insulation materials. BASF markets polyurethane foams with nano-scale (50-100nm) pores.
- Microencapsulation. Active compounds, for a range of applications, can be encapsulated in a micro-scale shell of another substance, typically a wax, a polymer or an oil-based substance, to facilitate a delayed release profile. BASF is interested in nano-scale control of the shell thickness and nano-structuring of the shell as ways to fine-tune the release of the encapsulated compound.
- Graphene for use in organic light emitting diodes (OLEDs), electronic displays, batteries and catalysts.
- Colour filters for liquid display (LCD) components. BASF has manufactured filters comprising particles of less than 40nm in diameter.
- Nanomaterial toxicology and eco-toxicology.

Mode of action

BASF has partnered with many universities to conduct nanotechnology R&D. In 2013, for example, the company established an 'advanced materials' programme with three US universities: Harvard University, Massachusetts Institute of Technology and the University of Massachusetts, Amherst[81]. The referenced source (a press release) suggests that a significant part – if not all – of the funded R&D might be considered nanotechnology R&D:

> *Topics already identified include micro- and nanostructured polymers with new properties, as well as biomimetic materials that emulate nature. For example, the scientists are working on lightweight construction materials for wind turbines and automotive construction and on new color effects for cosmetic applications.*

One part of the programme is about 'pharmaceutical nano-formulations'[82].

BASF did not disclose the amount of money it was contributing when it announced the programme, but it said that it would fund 20 post-doc positions over the five year period. The move built on a €15m ($20m) 2007 programme between BASF and Harvard that focused on biofilms and chemical formulations for drugs, food and cosmetics.

[80] http://www.basf.com/group/pressrelease/P-14-237. The source document (a press release) does not indicate the measure of R&D used for the percentage. We assume the figure is based on R&D spending.

[81] http://www.basf.com/group/corporate/en_GB/news-and-media-relations/news-releases/news-releases-usa/P-13-291.

[82] http://research.initiative.seas.harvard.edu/research.html

Solvay

Solvay is a major international chemical company with nearly 30,000 employees in over 50 countries. It also has 15 research and innovation (R&I) centres with 2,000 staff and spends nearly €250m per annum on R&I as shown in Table 4-5.

Table 4-5: Solvay 2013 R&I spending by business segment		
Segment	**Spending (€m)**	**Proportion of total (%)**
Performance Chemicals	20	8.4%
Advanced Formulations	52	21.9%
Advanced Materials	90	38.0%
Functional Polymers	22	9.3%
Corporate & Business Services	53	22.4%
Total	**237**	**100.0%**
Source: http://www.solvay.com/en/binaries/2013-annual-report-EN-164627.pdf		

Priorities for Nanotechnologies

Solvay is keen to develop nanomaterials and nanotechnology within three broad areas[83]:

- electronics and IT
- manufacturing and materials
- healthcare and life sciences.

Some examples of specific applications are presented in Table 4-6. No published information is available as to the levels of R&I expenditure in these specific areas.

Table 4-6: Solvey Development in Nanomaterials		
Material Classification	**Material**	**Specific Examples**
Nanomaterials	Fluorides – Superfine	MgF2, CaF2, BaF2, TiOF2
	Nano Barium Sulfate	Improvement to resistance to scratch, abrasion, impact etc., hardness, rigidity etc.
		Keeps transparency in resins, varnishes, and polymers – polycarbonate, acrylic, epoxy, polysulfone
	Nano-PTFE	Microemulsion (10.60 nm particle size)
		PTFE bimodal dispersion for coating
	Precipitated Calcium Carbonate	

[83] Miltner (2010): The potential of Nanotechnologies for SOLVAY, a Chemicals and Pharmaceuticals Company, presentation available from: https://eng.kuleuven.be/studenten/programma/interdepmasters/nanotechnology/HEM-SOLVAY_IMEC-Apr26-2010.pdf

Table 4-6: Solvey Development in Nanomaterials		
Material Classification	**Material**	**Specific Examples**
Nano-intermediates	NanoVin® a commercialised product	Plastisols for thick coating, soft grip for tooling
	Functional PerFluoroPolyEthers	Soft Lithography refers to a group of techniques for micro- and nano-fabrication using a soft elastomeric stamp – applications include Microlenses, Microfluids, etc.
		PFPEs functionalised with reactive end-groups (Flurolink MD700, 5112X) are ideal raw materials for manufacturing elastomers
Nano-enabled products	Fenofibrate	Used for the treatment of Dyslipidemia
Source: https://eng.kuleuven.be/studenten/programma/interdepmasters/ nanotechnology/HEM-SOLVAY_IMEC-Apr26-2010.pdf		

Other Large Companies

Research into a number of other large companies (including Evonik, Air Liquide, Linde, Yara, DSM and AkzoNobel) indicated significant expenditure on R&D (or R&I) with some companies providing information on their development of nanotechnologies. However, specific data on R&D expenditure on nanomaterials/nanotechnologies were not readily available.

SMEs

Nanomaterials and nanotechnologies are also being developed and implemented by small and medium sized enterprises (SMEs). Investigation into several likely SMEs was undertaken by reviewing information on companies claiming to manufacture nanomaterials on the Nanowerk website[84].

As for the large companies considered above, it was possible to derive some basic company information (size, products, etc.) and areas of interest in nanomaterials. However, no specific data on R&D expenditure on nanomaterials/nanotechnologies were identified. Some examples are listed in Table 4-7.

Table 4-7: Examples of SMEs involved in Nanotechnology		
Company (Country)	**Main Activity**	**Comment**
CAN GmbH (Germany)	Production of various nanoscaled materials like fluorescent, magnetic and catalytically-active nanocrystals. Also undertake consulting and contract research	These products are marketed under the brand CANdots and are dispersible in polar or unpolar media readily available for applications in research and industry.

[84] http://www.nanowerk.com/nanotechnology/nanomaterial/suppliers_plist.php?page=1&mat=&subcat1=np

Table 4-7: Examples of SMEs involved in Nanotechnology		
Company (Country)	**Main Activity**	**Comment**
IBU-tec advanced materials (Germany)	Manufacturer of nanopowders.	12.5% of their employees do research and development
MBN Nanomaterialia S.p.A. (Italy)	Producer of nanopowders such as nanostructured metal alloys, ceramics and metal-ceramics nanocomposites, polymeric alloys, fillers and nanostructured additives	Active at EU level through Nanofutures platform
Metal Nanopowders (UK)	The company is dedicated to the production of metal powders at the sub-100nm scale.	A spin-off from the University of Birmingham
Particular (Germany)	The company manufactures custom nanoparticle dispersions and also provides nanoparticle coating for metallic products, for instance for medical instruments.	
Yorkshire Bioscience (UK)	The company provides services and reagents for molecular biology research. Among its products are nanodiamonds.	
Sources: *CAN GmbH (Germany): http://www.can-hamburg.com/english/home.html* *IBU-tec advanced materials (Germany): http://www.ibu-tec.de/* *MBN Nanomaterialia S.p.A. (Italy): http://www.mbn.it/eng/* *Metal Nanopowders (UK): http://www.metalnanopowders.com/* *Particular (Germany): http://particular.eu/startseite.html* *Yorkshire Bioscience (UK): http://www.york-bio.com/*		

4.2.3 Strategic priorities

A multitude of programmes and organisations within the EU are currently spending public money on nanotechnology R&D. A comprehensive quantitative analysis of the strategic priorities of all of these is beyond the scope of this report. In order to gain a picture of this environment, a qualitative analysis of the German strategy on nanotechnology is provided below.

Germany spends the most on nanotechnology R&D, publishes the most journal articles and applies for the most patents. Furthermore, most of public money for nanotechnology R&D in Germany is delivered via the national R&D programmes.

In 2007, the German Ministry of Education and Research (BMBF) published a national strategy for nanotechnology R&D, the Nano-Initiative Action Plan 2010. This gave five key objectives:

- Opening up future markets, introducing new sectors;
- Improving general conditions;
- Behaving in a responsible manner;
- Informing the public;
- Identifying the future demands for research.

The first of these, 'opening up future markets, introducing new sectors', was broken down as follows:

- Branch level industrial dialogues[85];
- Lead innovations;
- Promoting networking;
- Supporting SMEs.

In 2011, the BMBF followed up the 2007 strategy with the Action Plan Nanotechnology 2015, which committed Germany to:

- Use nanotechnology to contribute to growth and innovation in Germany;
- Make nanotechnology safe and sustainable;
- Tap the potential of nanotechnology in education and research;
- Tap the potential of nanotechnology to meet global challenges.

The programme aims to:

- Secure the contributions of nanotechnology to the protection of environment and climate, to securing of energy supply and to the creation of a knowledge-based bioeconomy;
- Utilise the possibilities of nanotechnology for health;
- Use the possibilities of nanotechnology for sustainable agriculture and food safety;
- Achieve environmental and energy-saving mobility through nanotechnology.

Table 4-8 shows the focus of research funding around so-called global challenges.

Table 4-8: Global challenges under the German Action Plan Nanotechnology 2015

Climate and energy	Nanotechnology for higher energy efficiency	Nanomaterials for adaptive building technology	New high insulation and fireproof materials
			Thermochromic house paints
			Passive and active smart glazing
			Micro-mirror arrays
			Switchable insulation materials or phase change materials as latent heat accumulator
		Nanomaterials for decentralised energy supply	Nanomaterials for electrical and thermal energy storage
	Nanotechnologies for the adaption to climate changes	Development of filtering techniques	Water filtering
			Catalytic processes associated with water filtering
			De-salination of sea water
		Improvement of hygiene	Filters for hygiene requirements
	Protection of environment and resources	NanoNature: Nanotechnologies for the protection of the environment	Procedures for water and air cleaning, soil rehabilitation and water treatment
			Procedures for product preparation, resource recovery and environmentally friendly separation processes
			Methods for the reduction of discharges of substances into the environment
		Material efficiency, substitution of scarce raw materials and	Nanotechnologies enabling substitution of scarce raw materials
			More material-efficient recycling through joining

[85] These should help industrial sectors to understand the opportunities offered by nanotechnology to explore the ways in which nanotechnology might be used. They would focus on sectors with little previous access. to the results of nanotechnology R&D and in particular SMEs within those sectors. Dialogues should be carried out in the following areas: automotive, construction, textiles, IT, the life sciences, optics, chemistry, energy and the environment.

Table 4-8: Global challenges under the German Action Plan Nanotechnology 2015			
		recycling	technologies, such as nanobonding
			Nanocatalysts for alternative chemical reaction paths
		Carbon nanomaterial – substitution and efficiency	Impact of carbon nanotubes on human health
			Conservation of natural resources through the use of carbon nanomaterials
		Low wear and environmentally friendly friction materials	Lubricating technologies that enable better performance and lower impact on the environment
		New materials for sustainable water management	Efficient nanofiltration membranes
			Environmentally friendly reagents and catalysts
			Nanomaterials for adsorptive procedures
		Funding activity "Nano goes Production"	Environmentally friendly production of nanomaterials
		New and safe components through multiscale simulation	Simulation of nanoscale properties behaviour of materials for improved products and production processes
		Survey on potential reduction of environmental pollution	Tools for the evaluation of life-cycle benefits enabled by nanotechnologies including, efficient use of raw materials, reduced energy consumption and reduced emission of pollutants
Health–nutrition and agriculture	Health	Molecular imaging	Diagnostic tools (nanoparticle contrast agents, sensors)
			Imaging methods
			Pharmaceuticals
			Theranostics
		Tailor-made therapies and nano-medicine	Controlled release coatings and matrices
			Drug delivery systems
		Personalised implants and prostheses for long-term rehabilitation	Enhanced implants with improved tissue compatibility
		Regenerative medicine and nanostructured biomaterials	Nanotechnologies and nanomaterials for replacement tissues and organs
	Nutrition and agriculture	Nanotechnology for improved plant protection products and methods	
		Controlled carrier systems for the specific release of active agents for defined physical or chemical impacts	
		Impact assessment of nanomaterials for controlled application in agriculture (risk assessment of the chemical, physical and ecotoxicological properties of active agents and carrier agents and of their discharge into the ecosystem as well as discharge of the raw material flows	
		Nanotechnology for quicker, more cost-effective and precise diagnostic procedures in case of animal and plant diseases	
		Analysis methods for the detection and quantification of nanoscale food ingredients	
		Easy-to-clean nanocoated surfaces in food storage, transport and processing	
		Nanotechnology for functional food packaging	
		Nanotechnology for increased bioavailability of desired food ingredients	
		Nanotechnologies for energy generation from renewable sources linked to agriculture	

Table 4-8: Global challenges under the German Action Plan Nanotechnology 2015		
Mobility	Nanotechnology for cost-effective and resource-saving mobility	Filters and cleaning components for exhaust fumes
		Lightweight components
		Catalysts
		Coatings for injection systems
		Components for injection systems
	Nanotechnology for electric mobility	Electrode and conductor materials for energy storage (via batteries) and transport
		Super-capacitor components
		Nanomaterials for hydrogen fuel cells
	Nanomaterials for intelligent streets	Sensors for road-to-car communication
		Transport infrastructure materials with noise reducing properties
Communication	Quantum communication as a basis for tap-proof communication	Quantum repeaters for secure data transfer
	Organic or printable electronics	Improved displays
		OLEDs
		Nanoparticles for conducting pastes and inks
Security	Document protection and product security through product identification and marking systems for the generation of optical security features	Fluorescent nanoparticles for product identification and marking systems
		Biological materials for security inks
	Development of nanotechnological materials for the managing of potential consequences of major incidents	Improved decontamination products
		Filters
		Self-cleaning nanostructured surfaces
		Catalytically active nanoparticles for coatings
	Development of stab and bullet-proof nanoscale materials for protection systems for policemen and rescue workers	Integrated protection systems for the protection against hazardous substances, explosion impacts, fires and projectiles
		Polymer nanocomposites (shock-proof carbon nanotube fibers, shear-thicking nanofluids) for stab- and bullet-proof textiles
		Clothes with self-healing properties

4.3 Patents

4.3.1 Introduction

Patents applications and approvals might be used as a proxy for innovation. This approach has some well documented limitations (see 'Proxies for innovation'), but can be informative nonetheless provided it is neither viewed in isolation nor over interpreted.

Previous reports on the status of nanotechnology have included discussions on patents. Typically, however, the most recent data used for these is from 2010. The European Nanotechnology Landscape Report, for example, examined patent data from 2000 to 2010. Its findings can be summarised as follows:

- Germany filed many more nanotechnology patents than any other country. Indeed, the number of patents applications filed by Germany (3730) is almost equal to the number of patents filed by the other EU member states combined (3767).
- The states publishing high numbers of nanotechnology journal articles (Germany, the UK, France) are also filing high numbers of patent applications.
- The Netherlands stands out as a country that produces more patent applications than journal articles. In general, countries produce more of the latter.
- There is considerable variation between sectors in terms of patent applications. Some produce a lot others, very few.

Historically, separating the data on patents relating to nanotechnology from wider the data on patents has not been straightforward and as such the research community has made many attempts to design the best possible strategy for the identification of nanotechnology patents (Zheng *et al*, 2014). The USPTO[86] recently created over 250 cross-reference art collection subclasses in Class 977, Nanotechnology[87], intended to provide for disclosures:

- Related to research and technology development at the atomic, molecular or macromolecular levels, in the length of scale approximately 1-100 nanometre range in at least one dimension
- That provide a fundamental understanding of phenomena and materials at the nano-scale and to create and use structures, devices and systems that have novel properties and functions because of their size.

This class features in the "Calendar Year Patent Statistics General Patent Statistics Reports Available For Viewing" in the Patent Counts By Class By Year'[88]. It does not, however, appear on the list of classes with "Patenting In Technology Classes Breakouts By Geographic Origin (State and Country)"[89].

Meanwhile, patent offices worldwide have started to classify nanotechnology uniformly under the International Patent Classification (IPC) system[90]. A new symbol, B82Y, was introduced into the IPC on 1 January 2011, replacing the Y01N symbol used previously by the EPO. These tags could be used

[86] United States Patent and Trademark Office (USPTO)
[87] http://www.uspto.gov/patents/resources/classification/class_977_nanotechnology_cross-ref_art_collection.jsp
[88] http://www.uspto.gov/web/offices/ac/ido/oeip/taf/cbcby.htm
[89] http://www.uspto.gov/web/offices/ac/ido/oeip/taf/tecstc/classes_clstc_gd.htm
[90] http://www.epo.org/news-issues/issues/classification/nanotechnology.html

in conjunction with appropriate keyword-search strategies to generate data on patents relating to nanotechnology (Zheng *et al*, 2014).

The OECD produces such data across the following areas:

- Patent applications to the EPA, years to 2010;
- Patent grants at the USPTO, years to 2008;
- Triadic patent families, years to 2010;
- Patent applications filed under the Patent Co-operations Treaty (PCT), years to 2011;
- Patent grants at the EPO, years to 2008.

Statnano, part of the Iranian Nanotechnology Council Initiative, produces data on patents relating to nanotechnology, based on Orbit.com, a full-text patent search system familiar to independent information professionals (Wolff & Adams, 2010).

According to Figure 4-1, which is based on Statnano data, 21,379 patents related to nanotechnology were granted by the USPTO in 2013, representing a 60% increase compared with 2012. According to the USPTO, in 2013, the US had a share of 57% of all patents issued, which is more than the sum of all other countries. This is followed by Japan with a 15% share and the EU28 with a 14% share (as broken down in Table 4-9). The rest of the world had almost the same share of patents issued as the EU28, where the majority of the patents were issued to China, Taiwan, Switzerland and South Korea.

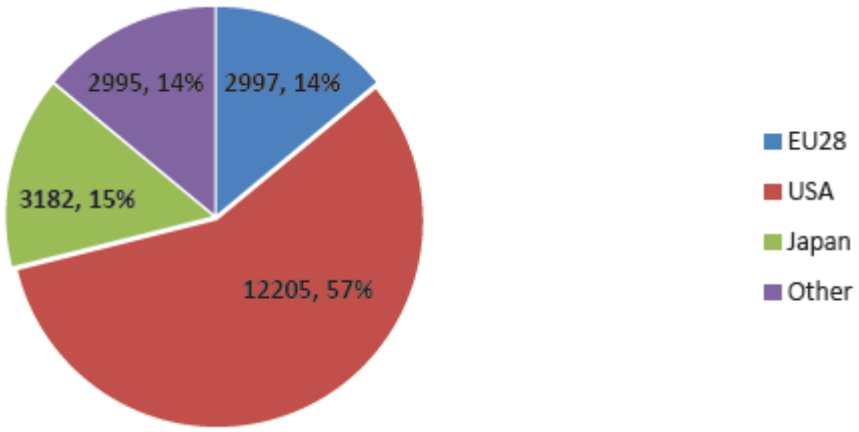

Figure 4-1: Number of patents issued by the USPTO in 2013

Source: *Nano Statistics (2014): Nanotechnology published patent applications in USPTO. Available at: http://statnano.com/report/s89 on 17 February 2014.*

Table 4-9: Number of patents issued by the USPTO in 2013 to EU28 member states

EU member state	Number of patents 2013	EU member state	Number of patents 2013
Germany	886	Portugal	7
France	561	Czech Republic	7
Netherlands	397	Estonia	5
UK	266	Hungary	5
Belgium	113	Romania	3
Italy	97	Cyprus	3
Sweden	82	Poland	2

Denmark	63	Slovenia	2
Ireland	62	Lithuania	2
Finland	61	Croatia	2
Spain	39	Bulgaria	1
Austria	37	Latvia	0
Luxembourg	21	Slovakia	0
Greece	8	Malta	0

Source: Nano Statistics (2014): Nanotechnology published patent applications in USPTO. Available at http://statnano.com/report/s89 on 17 February 2014.

As can be seen, the number of patents to some extent corresponds to the size of the country as well as the level of industrialisation.

For another perspective, we also looked at the number of patents issued by the European Patent Office (EPO). From Figure 4-2, it can be seen that in 2013, the EPO issued 41% of all patents to EU28 member entities, which is slightly lower than in 2012, when 42% of patents were issued to EU member states, even though the number of patents issued increased 4,622 (in 2013) from 4,241 (in 2012).

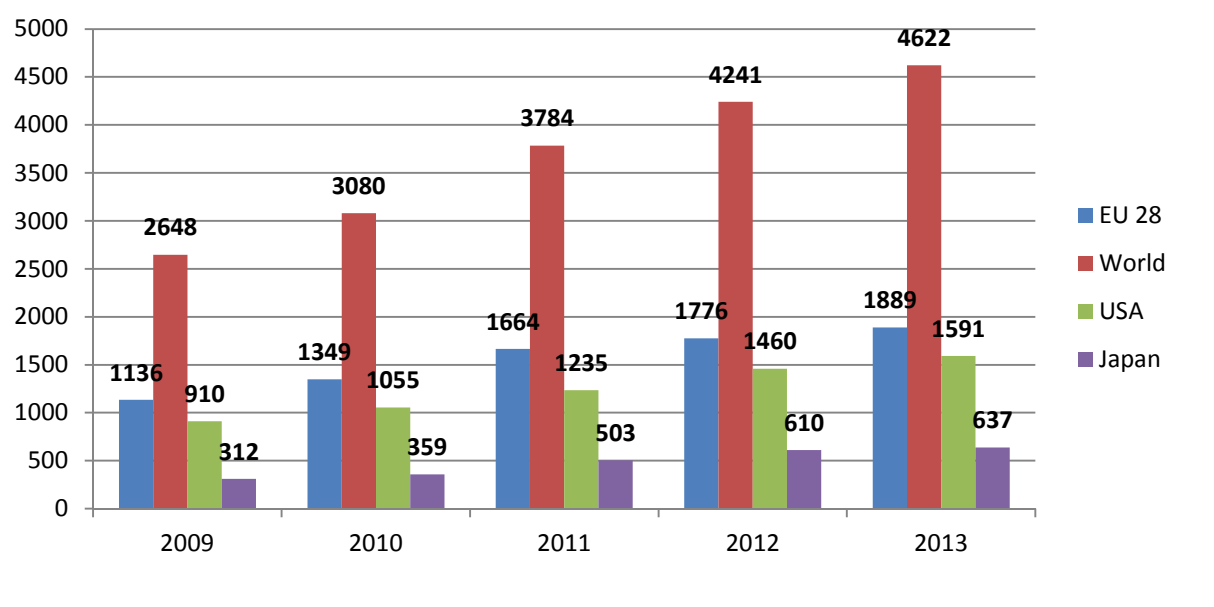

Figure 4-2: Number of patents issued by the EPO (2009-2013)

Source: *Nano Statistics (2014): Nanotechnology published patent applications in EPO. Available at: http://statnano.com/report/s95 on 17 February 2014.*

In Table 4-10, we present the number of patents issued by the EPO to individual EU28 member states for the period 2009 to 2013. Again Germany leads the pack with a share of 41% of all patents issued by EPO in 2013. This is disproportionately high with respect to other EU member states; Germany had, for example, twice as many patents issued as the second placed France. This highlights the fact that Germany seems to be the innovation leader in terms of nanotechnology patents. Following France are the Netherlands, the UK and Belgium. In others words, the most industrialised countries in the EU28 produce the most patents by this measure.

Table 4-10: Total number of patents issued by the EPO to EU28 member states (2009-2013)					
	2009	2010	2011	2012	2013
EU 28	1136	1349	1664	1776	1889
Germany	430	484	665	693	775
France	233	288	368	344	379
Netherlands	124	147	157	188	182
UK	83	110	130	136	151
Belgium	51	60	76	84	76
Italy	66	67	60	92	70
Sweden	34	37	45	58	55
Denmark	27	46	54	51	51
Austria	20	32	26	40	40
Spain	17	12	24	24	31
Finland	15	27	12	24	23
Ireland	14	16	20	15	16
Luxembourg	7	4	5	5	10
Czech republic	4	6	7	3	9
Slovenia	0	0	4	2	5
Greece	4	1	3	1	5
Poland	3	2	0	7	4
Portugal	0	2	3	2	3
Lithuania	0	1	0	0	2
Hungary	1	3	3	2	1
Latvia	0	1	1	0	1
Cyprus	1	1	0	0	0
Romania	0	0	0	0	0
Croatia	2	1	0	1	0
Estonia	0	0	1	3	0
Slovakia	0	1	0	1	0
Bulgaria	0	0	0	0	0
Malta	0	0	0	0	0
Source: Nano Statistics (2014): Nanotechnology published patent applications in EPO. Available at http://statnano.com/report/s95 on 17 February 2014.					

4.4 Scientific Literature

Based on analysis of 1998-2009 data (ObservatoryNANO, 2011), the countries publishing the most nanotechnology journal articles are Germany, the UK, France and Switzerland. Each of these countries published over 1000 such articles from 1998 to 2009. Together, they accounted for two thirds of the total. Table 4-11 shows the full data set:

Table 4-11: Nanotechnology journal articles published by country from 1998 to 2009	
Country	**Number of articles**
Switzerland	1031
Finland	494
Sweden	816
Germany	6449
Austria	590
United Kingdom	2688
Netherlands	650

Table 4-11: Nanotechnology journal articles published by country from 1998 to 2009	
Country	**Number of articles**
Denmark	191
Ireland	151
Belgium	319
Estonia	39
France	1491
Slovenia	40
Czech Republic	191
Hungary	180
Luxembourg	8
Italy	955
Cyprus	12
Greece	161
Lithuania	35
Slovakia	56
Spain	409
Bulgaria	56
Poland	280
Portugal	73
Romania	71
Latvia	7
Source: (ObservatoryNANO, 2011)	

4.5 Future Market Trends

Nanotechnology is regarded as being one of the technologies from which a great deal of future growth will be generated. In this sense it has been defined by the European Commission as a Key Enabling Technology (KET)[91] and represents one of the elements which will generate a great proportion of future employment growth, research and development and technological innovation.

Cientifica identified four countries with the combination of academic excellence, technology-hungry companies, a skilled workforce and the availability of early stage capital to ensure effective technology transfer[78]: Germany, the US, Japan and Taiwan.

The quantification of the effects that nanotechnology has on the economy is subject to much research and speculation. According to some studies nanotechnology impacted € 182.7 billion[92] (US$ 254 billion) worth of products in 2009 and this impact is forecasted to grow to € 1.799 trillion[5] (US$ 2.5 trillion) by 2015[93,94]. Older Lux Research's estimates from 2007 predict that the size of the global market size, assuming steep growth, would reach € 1.9 trillion[95] (US$ 2.6trillion) in 2014,

[91] http://ec.europa.eu/enterprise/sectors/ict/key_technologies/index_en.htm

[92] Using average ECB exchange rate for 2009 i.e. $/€ 1,39

[93] CEFIC (2010): Nanotechnology: A sustainable basis for competitiveness and growth in Europe. Dated December 2010. Available at http://ec.europa.eu/enterprise/sectors/ict/files/kets/3_nanotechnology_final_report_en.pdf on 17 February 2014.

[94] Lux Research and Forfás (2010): Ireland's Nanotechnology Commercialisation Framework 2010-2014. Dated August 2010. Available at http://www.forfas.ie/media/forfas310810-nanotech_commercialisation_framework_2010-2014.pdf on 17 February 2014.

[95] Using average ECB exchange rate for 2007 i.e. $/€ 1,37

which was 70% higher than their original estimate from 2005[96]. However, the economic crisis occurring since 2008 has decreased somewhat the estimations of nanotechnology market size. Lux Research estimated in 2009 that the global market size of nanotechnology would be € 1.799 trillion[5] (US$ 2.5 trillion) by 2015, which is 4 % less than the 2007 estimates. In this context particularly the decline in the cyclical automobile and construction industries was estimated to have the strongest negative effect on demand for nanotechnology and particularly on nanomaterials and composites[97].

As a result of the above described trends, the number of workers employed in the nanotechnology sector worldwide is expected to reach 2 million by 2015, of which 0.8-0.9 million would be in the United States and 0.3-0.4 million in Europe[98] (see Figure 4-3). Other estimates state that the estimated number of nanotechnology jobs is to reach 1 million in the US by 2014[99].

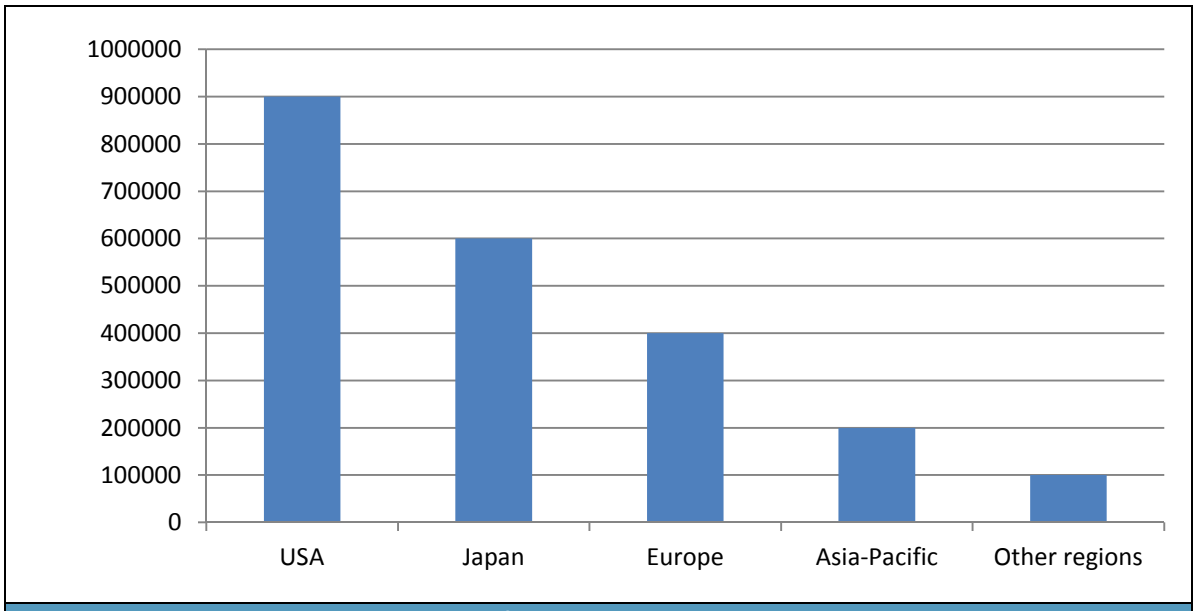

Figure 4-3: Number of Nanotechnology jobs by 2015 globally

Source: *OECD (2009): Nanotechnology: an overview based on indicators and statistics. Dated 25 June 2009. Available at http://www.oecd.org/dataoecd/59/9/43179651.pdf on 17 February 2014.*

Nanotechnology is expanding its reach to different economic categories such as consumer goods, aerospace, medicine, automobile industry etc. and is regarded as being one of the technologies of the future. It affects an ever increasing part of economic production and according to some studies nanotechnology impacted €183 billion[5] (US$ 254 billion) worth of products in 2009, which is projected to grow to around €1.8 trillion[5] (US$ 2.5 trillion) by 2015.

The global market for nanotechnology (on its own) is valued at about € 14.9 billion in 2012 and is expected to increase to more than € 18.9 billion in 2015 and € 35.2 billion in 2017. As indicated in Figure 4-2 and Table 4-1, the largest segment of nanotechnology are nanomaterials. The market for

[96] Lux Research (2007): The Nanotech Report 2006: Investment Overview and Market Research for Nanotechnology. New York: Lux Research Inc.

[97] Lux Research (2010): The Recession's impact on Nanotechnology. Boston: Lux Research Inc.

[98] Christos Tokamanis, KET Open Day on Nanotechnologies, 27 Oct. 2010

[99] OECD (2012): The Economic Contributions of Nanotechnology to Green and Sustainable Growth. Dated 12 March 2012. Available at http://www.oecd.org/sti/nano/49932107.pdf on 17 February 2014.

nanomaterials stood at about € 6.6 billion in 2009 and is expected to increase to more than € 14.3 billion in 2015 and € 26.8 billion in 2017.

Research for the National Science Foundation (NSF) in the United States looked at a range of scenarios for the potential world market for nanotechnology in 2015 with estimates ranging from conservative € 376 billion to the more "optimistic case" of 1.5 trillion. As indicated in Figure 4-4 the majority of nanotechnology will be applied in materials (nanomaterials) and electronics, where they will represent an estimated 31 % and 28 % respectively. Other segments where nanomaterials will be applied to use are also the pharmaceutical industry (17%), chemical manufacturing (9 %) and Aerospace (9%).

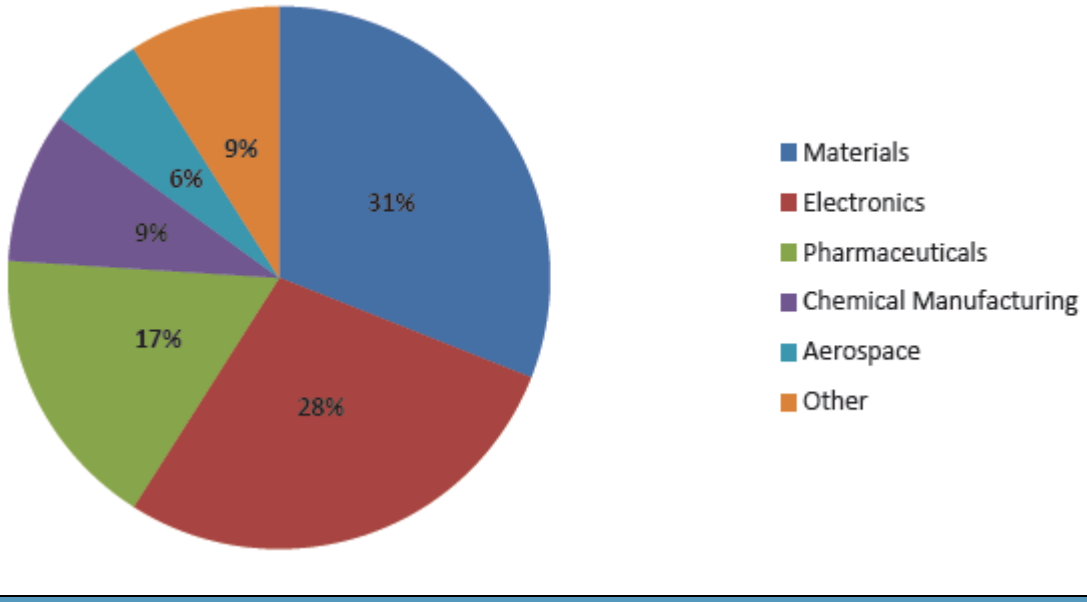

Figure 4-4: Distribution of Nanotechnology related products by industry by 2015

***Source: C.** Tokamanis, KET Open Day on Nanotechnologies, 27 Oct. 2010*

4.6 Emerging Nanomaterials, their Properties and Applications

4.6.1 Introduction

The volume and diversity of nanomaterials, nano-scale phenomena and applications under investigation is very large indeed. They include, for example:

- Quantum dots for use as bio-imaging agents;
- Ferrofluids;
- Anti-counterfeiting products;
- Printed electronics;
- Nano-enabled sensors for security applications;
- Self-cleaning, super-hydrophilic thin films;
- Anti-bacterial silver nanoparticles;
- Gold nanoparticles;
- Carbon nanotubes;
- Mesoporous silica nanoparticles drug delivery;
- Hierarchical nanoparticle assemblies;
- Metamaterials;

- Anti-biofouling paints for boats;
- Surfaces that reduce build-up of snow on antennas and windows;
- Self-cleaning windshields for automobiles;
- Microfluidic components;
- Lab-on-a chip devices.

The identification of the emerging nanomaterials, applications and technologies which could become widely used is very difficult, but it is surely related with the ease to move from the laboratory scale to the industrial production scale.

5 Indicators on Fitness-for-Purpose

5.1 Introduction

This Section presents some indicators that could be used in order to facilitate the monitoring of the implementation and impact of transparency measures and support future review if implemented.

An indicator can be defined as a quantitative or qualitative factor or variable against which we can measure changes associated with particular policies. They allow us to perceive difference, improvements or developments relating to a desired change, and over a specific time period when set against a baseline. As such, they must be practical and realistic, in this case relying on existing data sets to feed into the assessment. Key components of indicators include the following:

- What is going to be measured;
- Unit of measurement to describe the change;
- Status at the baseline year;
- Size, magnitude or dimension of the intended change;
- Quality or standard of the change to be achieved;
- Target populations;
- Timeframe.

This may include indicators of three possible types:

- Output indicators, which assess progress against specific operational activities, i.e. the establishment of procedures for enforcement;
- Outcome indicators, which assess progress against specified outcomes, i.e. are enforcement procedures resulting in compliance; and
- Impact indicators, which provide a broad picture of whether the desired change is actually occurring on the ground, i.e. are the objectives of the transparency measures being achieved.

Indicators should be SMART, i.e. Specific, Measurable, Achievable, Relevant and Timed. In ensuring that indicators are SMART, we will apply the set of questions presented in Table 5-1 below to each indicator.

In order to develop the indicators on fitness-for-purpose of transparency measures, some studies proposing indicators for the evaluation and monitoring of chemicals legislation have been reviewed and presented below.

Table 5-1: Questions for ensuring indicators are SMART	
Specific:	Is it clear exactly what is being measured? Has the appropriate level of disaggregation been specified? Where is the change happening? At what level (National, EU, global)
Measurable:	Are changes objectively verifiable? What unit of measurement will be used? Is it qualitative or quantitative? Is it a reliable and clear measure of results? Is it sensitive to changes in policies and programmes?
Achievable:	Are data sources known? Are data actually publically available at reasonable cost and effort? How reliable, complete and coherent (i.e. same units) is the data?
Relevant:	Will the indicator effectively demonstrate whether the desired change has taken place? Is it relevant to the intended outputs and outcome? Is the association of the indicator and measured change with the policy sphere credible?
Timed:	Is data available for this indicator for today? Is data available for the baseline year?

5.2 Studies Proposing Indicators for the Evaluation and Monitoring of Chemicals Legislation

5.2.1 Eurostat *et al* (2012): The REACH Baseline Study

Eurostat undertook the initial development of a multi-stranded approach that was intended to facilitate the collection of relevant data to inform subsequent modelling on the impacts arising from REACH. This started with the commissioning of a study to develop a 'snap shot' of data for the year 2007 with the intention that this would provide the baseline against which future comparisons could be made (Eurostat, 2008 and 2009).

While seeking to establish a wider set of metrics than just the impact of chemicals on human health and the environment, the Eurostat baseline system was never intended as a comprehensive tool to address **all** potential issues that arise from the REACH implementation. Rather, it sought to establish a number of metrics which could be grouped into three different types (or 'pillars' as described in Eurostat, 2009) of indicator (see Table 5-2). These represent:

- **Administrative indicators:** used to monitor the REACH process. These refer to the registration, evaluation, authorisation and restriction steps defined by REACH and include, for example, the numbers of substances registered and the number of chemical safety reports documented by ECHA;
- **Risk and quality indicators:** intended to link to two of the main aims of REACH, the reduction in nominal risks of chemicals for humans and the environment and the improvement in the quality of publicly available data. These indicators are assessed on the basis of a defined sub-set of 237 substances; and
- **Supplementary indicators:** these relate to those REACH objectives not covered by the other two indicator types, including increase in the quality of safety data sheets and the use of alternative test methods.

Table 5-2: Objectives of REACH as Interpreted by the Eurostat Baseline Study			
Central elements & objectives of REACH	**Baseline Study Indicator System**		
	Administrative indicators	**R&Q indicator system**	**Supplemental indicators**
Registration of chemicals	X		
Evaluation of chemicals	X		
Authorisation and restriction of chemicals	X		
Establishment of a central agency	(indirect)		
Protection of human health and the environment		X	X
Improvement of knowledge on properties and safe uses of chemicals		X	X
Assessment of existing and new chemicals in a single, coherent system			X
Increased transparency and consumer awareness			X
Promotion of alternative methods for assessment of hazards of chemicals			X
Maintenance and enhancement of the competitiveness of the EU chemical industry	Not within the scope of the Baseline Study		
Prevention of fragmentation in the internal market	Not within the scope of the Baseline Study		
Conformity with EU's international obligations under WTO	Not within the scope of the Baseline Study		
Source: Eurostat (2009)			

5.2.2 RPA *et al* (2012): Human and Environmental Benefits of REACH

The aim of the REACH Benefits Study was to provide an understanding of the benefits to human health and the environment stemming from the implementation of REACH to date. It included the development of a framework for assessing the human health and environmental benefits of REACH.

The proposed framework draws on a review of the methodologies that have been used in the past (or that could otherwise be used) to provide qualitative or quantitative information on the benefits of REACH, including the economic value of human health (mainly workers and the general public) and environmental benefits. A key conclusion from this work was that, at the time of writing, it was not possible to quantify benefits, and the assessment has to rely on the use of a series of qualitative information together with a limited set of quantitative indicators; the latter are the types of

indicators being reported on by the REACH Baseline Study[100]. In the longer term, the scope for a more quantitative assessment should increase.

The framework for assessing the benefits of REACH starts with the identification of:

- The **drivers of benefits** within REACH, where these are the set of legal provisions which are expected to trigger direct or indirect human health and/or environmental benefits. The drivers considered within the study were registration, requirements for information through the supply chain, authorisation and restrictions;
- The **pathways** through which the drivers deliver these benefits, in other words they describe the cause and effect links between the drivers and benefits;
- **Indicators** of benefits, which can act as a direct measure or a proxy of the effects stemming from any cause-effect link; and
- **Enhancers**, which are those provisions that help to realise the benefits through support, control and enforcement and thus assist or ensure compliance with the main obligations. The study considered the provision of guidance, evaluation, inspection and enforcement activities.

The key indicators of benefits used for the **registration** driver were:

- Number of newly classified substances and number of substances which have changed classification as a result of new information (new data on substance properties lead to new classifications or changes in existing substance classifications, higher data quality and (re-assessment of risks);
- Changes in DNELs, PNECs, etc. (the degree to which information on previously unknown uses became known to registrants; linked to this is the number of uses subsequently 'advised against' as they are not/no longer considered 'safe');
- Changes in recommended Risk Management Measures (the extent to which REACH may have triggered the implementation of more stringent operating conditions or RMMs);
- the number of substances withdrawn from the market due to hazardous properties (where the use of alternatives does not lead to an increase in exposure to other hazardous substances);
- Linked to the above is information on the number of new, non-hazardous (or potentially low hazard) substances added to the market and the degree to which this varies from the numbers and hazard profile of such substances being newly notified before REACH; and
- the number of newly identified PBTs or vPvBs.

Potential indicators of benefits were also identified to act as proxies for the impacts that the **communication** of safety data may have in terms of realising health and environmental benefits. These include:

- The extent to which ES set out more stringent use conditions (operational conditions and/or RMM) to be implemented by Downstream Users in their processes;
- Queries and information provision to suppliers from Downstream Users;
- The number of Downstream User chemical safety assessments (although it may be too early for there to be many of these); and
- Queries from consumers about the content of substances of very high concern in articles.

The indicators related to **authorisations** identified were:

[100] Oko-Institut, FoBiG, DHI and INERIS (2011): REACH Baseline Study: 5 Years Update, Progress Report IV, Eurostat study Reference No 2010/S 167-255573, Freiburg, December 2010.

- Number of substances identified as meeting the criteria as a SVHC;
- Number of chemicals included in the candidate list (Art.58), and as a % of those meeting criteria as a SVHC;
- Number of substances (and % of all SVHCs) subject to authorisation (inclusion in Annex XIV);
- Percentage of substances with SVHC properties listed in Annex IV of CLP and in Annex XIV compared to the total expected number of SVHCs;
- Percentage of Annex XIV substances for which safe alternatives are introduced over specified time frames (e.g. first 10 years of REACH);
- Number of applications for the continued use of substances and the associated percentage of the total volume pre-candidate listing;
- Number of decisions taken regarding Article 60 using the adequate control route or the socio-economic route.

With regard to **restrictions**, they were:

- Number of restriction proposals introduced for substances, mixtures or articles;
- Number of new restrictions adopted on uses of substances and mixtures, and on articles;
- Average (and minimum/maximum) time taken to reach regulatory decision on a restriction proposal.

The study identified four main enhancers within REACH: Evaluation; Inspection and enforcement; Synergies with other legislation; and Guidance and other support, including the dissemination of information to external stakeholders.

With regard to dossier **evaluation** the indicators listed below were considered:

- Number of dossiers opened;
- Draft decisions sent to registrant;
- Final decisions;
- Quality observation letters sent;
- Compliance check concluded without further action.
- With regard **to inspection and enforcement** the indicators considered were:
- Number of inspection performed by member states and different categories of actors;
- Number of measures due to non-compliance.

5.2.3 RPA *et al* (2012b): Technical Assistance to prepare the Commission Report on the operation of REACH

The Technical Assistance study to prepare the Commission report on the operation of REACH was undertaken to support the Commission in meeting its reporting obligations under Article 117(4). The analysis undertaken was therefore based primarily upon the Article 117(1) reports provided to the Commission by Member States (MS) and the Article 117(2 & 3) reports provided to the Commission by the European Chemicals Agency (ECHA). Further information was provided by the Commission studies running in parallel to this study.

Several indicators were applied for the assessment of the different aspects of the operation of REACH. For the analysis of the organisation of the European Chemical Agency, number and contract types of the Agency's workforce working on the different tasks have been used, as well as performance indicators as number of dossiers analysed, reply rate to queries from the industry etc.

A questionnaire developed by the Commission was submitted to the Competent Authorities in each Member States to collect their point of view on the operation of REACH[101].

The output indicators that were used to measure enforcement activities in each Member State were:

- Number of inspections that addressed registration and number of non-compliances found;
- Number of inspections that addressed information in the supply chain and number of non-compliances found;
- Number of inspections that addressed downstream use and number of non-compliances found;
- Number of inspections that addressed authorisation and number of non-compliances found;
- Number of inspections that addressed restriction and number of non-compliances found;
- Number of inspections that addressed other REACH duties and number of non-compliances found;
- Number of investigations prompted by complaints and concerns raised;
- Number of investigations prompted by incidents or dangerous occurrences;
- Number of investigations prompted by monitoring;
- Number of investigations prompted by results of inspection/follow up activities;
- Number of inspections and investigations resulting in no areas of non-compliance;
- Number of inspections and investigations resulting in verbal or written advice;
- Number of inspections and investigations resulting in formal enforcement short of legal proceedings;
- Number of inspections and investigations resulting in initiation of legal proceedings;
- Number of convictions following legal proceedings.

The questionnaire tried also to classify these data in terms of the type (manufacturer, importer, distributor, downstream user) and size (small, medium, large enterprise) of the duty holders that were subject to enforcement.

RPA analysed the answers to inform the Commission Report on the operation of REACH and found that the lack of a clear definition of the actors gave space to different interpretations by respondent. Some Member States were also unable to provide the data at such detailed level. A major problem was the estimate of the number of duty holders by type, where often a duty holder can be at the same time manufacturer and importer of basic chemicals, formulator of mixtures and distributor of chemical products.

5.3 Possible Indicators for the Evaluation and Monitoring of Transparency Measures

5.3.1 Introduction

The transparency measures implemented and proposed across different countries and sectors and analysed in the Evaluation report vary in scope (e.g. nanomaterials and mixtures containing nanomaterials for professional users, nanomaterials in mixtures and articles for the consumers

[101] The answers are now being made available by Client Earth on this website: http://www.clientearth.org/health-environment/health-environment-publications/progress-reports-reach-1184

market), duty-holders, object of notifications and information requirements, ultimately reflecting slightly different objectives.

When using the list of indicators suggested below for comparing the transparency measures, these differences should be taken into account.

5.3.2 Indicators

Three different types of indicators are suggested:

- Output indicators, which assess progress against specific operational activities: i.e. the establishment of procedures for enforcement;
  - Number of notifications per year;
  - Number of notifiers per year/number of companies identified as manufacturing/importing/distributing/using nanomaterials;
  - Number of different nanomaterials notified;
  - Number of (consumer) mixtures containing nanomaterials notified;
  - Number of (consumer) articles containing nanomaterials notified.
- Outcome indicators, which assess progress against specified outcomes, i.e. are enforcement procedures resulting in compliance:
  - Number of substances newly identified as nanomaterials;
  - Level of awareness among consumers on nanotechnology;
  - Level of awareness among consumers on societal benefits of nanotechnology;
  - Level of awareness among consumers on health and safety risks of nanotechnology;
  - Compliance check concluded without further action;
  - Number of inspection performed on different actors across the supply chain;
  - Number of measures/fines due to non-compliance;
  - Number of inspections addressing substance characterisation and number of non-compliances found;
  - Number of inspections addressing tonnages and uses and number of non-compliances found;
  - Number of inspections addressing information on the identity of customers and number of non-compliances found;
  - Number of investigations prompted by complaints and concerns raised;
  - Number of investigations prompted by incidents or dangerous occurrences;
  - Number of investigations prompted by monitoring;
  - Number of investigations prompted by results of inspection/follow up activities;
  - Number of inspections and investigations resulting in formal enforcement.
- Impact indicators, which provide a broad picture of whether the desired change is actually occurring on the ground, i.e. are the objectives of the transparency measures being achieved:
  - Number of registration dossiers submitted with information specific to nanomaterials, following the notification/implementation of the transparency measure;
  - Number of chemical safety assessments with information specific to nanomaterials, with exposure scenarios setting out more stringent use conditions (operational conditions and/or RMM) to be implemented by Downstream Users in their processes;

- Number of notifications to the Classification and Labelling Inventory specific to nanomaterials, following the notification/implementation of the transparency measure;
- Changes in recommended Risk Management Measures (the extent to which transparency measures may have triggered the implementation of more stringent operating conditions or RMMs, following the identification of nanomaterials in the workplace);
- Changes in DNELs, PNECs, etc. (the degree to which information on previously unknown uses became known to notifiers; linked to this is the number of uses subsequently 'advised against' as they are not/no longer considered 'safe');
- Number of changes in classification and labelling of nanoforms of substances previously classified and labelled differently;
- Number of nanomaterials included in the Community Rolling Action Plan list of substances, following their notification/implementation of the transparency measures;
- Queries and information provision to suppliers from Downstream Users;
- Queries from consumers about the content of nanomaterials in articles;
- Number of nanomaterials withdrawn from the market;
- Number of consumer products claiming nano-properties;
- Number of consumer products claiming to be "nano-free";
- Cost of the notification process/administrative burden posed by the transparency measure on companies;
- Cost entailed by the public authorities in the implementation of the transparency measure.

It should be noted that some of the indicators listed above, especially among the impact indicators, aim to measure indirect effects that can be achieved only through the synergy with other pieces of chemicals legislation, such as the REACH and CLP Regulation or the health and safety legislation. Moreover, depending on the declared objectives of the transparency measures, the indicators could be moved between the three categories suggested.

In order to screen the list of indicators, a simple scoring and weighting system has been developed to allow the comparison of the different indicators in a consistent and transparent manner. Four criteria have been chosen, namely:

- Specificity: how closely does the indicator match the objective?
- Quality of information: is the data robust based upon its source and the extent of quality control that is apparent within data sets?
- Cost: how easy will it be to collect the data and what extent of additional analysis will be required?
- Confounding Factors[102]: how extensive and significant are the confounding factors, and to what extent can these be adjusted for?

For each of these factors, scores will be assigned according to a series of definitions (summarised in Table 5-3). The scoring of the indicators and the comparison of the transparency measures on the basis of the indicators selected will be carried out in the option assessment report. For each indicator, the reasoning behind the assignment of the score will be recorded and weights will be assigned according to the importance of each criterion. This will allow to provide an overall score for each indicator.

[102] Confounding factors relate to objectives where there is crossover with other changes that may also have caused or contributed to that effect, such as other legislation which may have come into force or common practices may have changed thus contributing towards the effect.

Table 5-3: Scoring Criteria for Indicators			
Specificity: How closely does the indicator match to the objective at EU level?	**Quality of information: Is the data source robust?**	**Cost: How easy will it be to collect the data and what extent of additional analysis is required?**	**Confounding Factors: How significant are the confounding factors and how easily can these be addressed?**
1.**Questionable**: tenuous fit with the objective and will inform on a non-EU level only	1. **Unreliable**: no apparent quality control in place	1. **Very high**: requires collection of new data through extensive monitoring/analysis (possibly with development of new methodologies) or extensive surveys specifically to gather data	1.**Very high confounding**: many confounding factors that it will be difficult to address
2. **Limited**: limited fit with sub-objective and may inform only on a non-EU level	2.**Borderline**: collecting organisation has some quality control measures in place, but no cross-checking is possible	2. **High**: requires collection of new data through additional monitoring/analysis (using existing methodologies) or surveys in co-operation with other organisations	2. **Some confounding**: some confounding factors with limited potential for correction
3.**Moderate**: reasonable fit with objective but may inform only on a non-EU level	3. **Reasonable**: some independent cross-checking of information is possible	3. **Medium**: requires collection of new data (monitoring or surveys) but this can be undertaken at little or no cost to Defra, or may involve addition of some questions to existing questionnaire survey	3. **Moderate**: some confounding factors but with some potential for correction
4.**Good fit**: reasonable fit with objective and relates to EU relevant data	4. **High**: information collected by authoritative source but quality control unspecified	4. **Moderate**: data already collected, but significant additional analysis required	4. **Quite specific:** some confounding factors but they can be largely corrected
5. **Specific**: excellent fit for the objective and relates to EU specific data	5. **Robust**: information collection by authoritative source and is subject to recognised quality control	5. **Very low**: already collected on on-going basis in a usable format from a reliable source with no data protection issues. May need some reformatting or limited additional analysis	5. **No confounding:** no confounding factors

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Risk & Policy Analysts Limited
Farthing Green House, 1 Beccles Road
Loddon, Norfolk, NR14 6LT, United Kingdom

Tel: +44 1508 528465
Fax: +44 1508 520758
E-mail: post@rpaltd.co.uk
Website: www.rpaltd.co.uk