European Commission, Joint Research Centre –
Institute for Health and Consumer Protection – Ispra/Italy

Examination and assessment of consequences for industry, consumers, human health and the environment of possible options for changing the REACH requirements for nanomaterials

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BiPRO

Beratungsgesellschaft für integrierte Problemlösungen

In cooperation with

Öko-Institut e.V.
Institut für angewandte Ökologie
Institute for Applied Ecology

Disclaimer:

This report presents the results of the NANO SUPPORT project (TASK II) and does not represent the official view of any Commission service or of the European Chemicals Agency.

Content

Executive Summary

The objective of the project “Scientific technical support on assessment of nanomaterials in REACH registration dossiers and adequacy of available information ("NANO SUPPORT")” is to evaluate how the risk and safety of nanomaterials have been assessed in selected REACH registration dossiers, and based on this, to develop a set of possible **options** for modifications to the current REACH provisions to better address nanomaterials. The results of the first tasks have already been published, in March 2012.

The aim of the current work that forms the basis of this report has been to conduct an examination and assessment of the **consequences** for industry, consumers, human health and the environment if these options for modifications of REACH are implemented.

Important elements of the applied methodology for this assessment include:

- Development of a **baseline scenario** and investigation of the relevance of discussed options in close collaboration with a Project Steering Group.
- Identification of **suitable case studies** and assessment of economic, health, environmental and societal impacts of all options for these case studies. For this purpose the project team gathered data from expert interviews, stakeholder responses, its own investigations and from literature. The methodology followed the EU Guidelines for Impact Assessments of 2009. A time frame of 10 years from the year 2012 to 2022 was considered and adopted.
- **Extrapolation** of the case studies results in an estimation of the impacts of different options to the total 'market for nanomaterials'. This takes into account the future market structure and the different information requirements for the respective tonnage bands of the registered nanomaterials.

In the course of this project it became apparent that only 9 of the 21 originally proposed modification options would be subject to the assessment. The other 12 options need to be regarded as already implicitly part of current REACH requirements, or are addressed by following the advice provided by experts of the European Chemicals Agency (ECHA), however, not representing an official ECHA position.

The total **costs** for implementing the 9 options amount to between **€11 million and €73 million** as a cumulative effort for all concerned companies for a time period until 2022. The split of total costs on single options shows big differences between options with high or medium efforts, and hence high or medium costs, and options with no or very little additional costs (see Table ES-1).

Table ES-1 Total costs for industry, allocated option-wise, after implementation of 9 options of option scenario

Option	Description of the option	Additional costs (€1,000)
6	Include information on dustiness	210 - 640
11	Require acute toxicity data for the most relevant route of exposure	1,280 – 9,400
12	Change "particles" to "nanoparticles" for repeated dose toxicity studies (inhalation)	0
13	Require non-bacterial in-vitro gene mutation study	2,000 – 9,600

Option	Description of the option	Additional costs (€1,000)
16	Consider water solubility in relation to test waiving	5,090 – 29,540
17	Specify that long term testing should not be waived based on lack of short term toxicity	1,800 – 15,270
18	Specify that algae testing should not be waived based on insolubility	0
19	Require that testing on soil and sediment organisms is prioritised	770 – 7,660
21	Require considerations of most appropriate/relevant metric with preferable presentation in several metrics	200 – 800
	Resulting additional costs for industry:	**11,400 – 73,000**

The assessed costs take into consideration an extensive grouping and read-across approach, as specified in the provisions of the REACH Regulation. Without this approach the final costs would multiply drastically up to **€100 million** and **€600 million.**

Registration of nanomaterials after 2018 will also entail costs. However, these costs are not quantifiable since no exact predictions on the affected number of nanomaterials can be made. It can reasonably be argued that registrants would profit from experiences gained in the meantime by registration of nanomaterials which would facilitate the efficient registration of nanomaterials. Furthermore, it is expected that by this time updated/new testing methods are available specifically addressing the characteristics of nanomaterials.

The **quantification** of total benefits of the 9 options in monetary terms is hampered by considerable uncertainties. Related to health benefits, an average of **€165 million** (with a range between **€83 million** and **€248 million**) for cumulative savings for a period until 2042 could be calculated. It needs to be mentioned that, due to latency effects, most of the health benefits are expected to occur with significant delays after implementation of the options. Hence, investigating a period until 2022, health benefits are expected to be significantly lower. It needs to be further mentioned that health benefits do not automatically occur as a consequence of the options but will be achieved only if appropriate risk reduction measures are taken, which in turn could lead to additional costs. Following this, a direct comparison between monetary costs for registration and benefits is not feasible. Increased information on nanomaterials as a consequence of several options will lead to increase of health benefits. It is estimated that the increase of health benefits per substance in average will amount to about 20% of the health benefits per substance to be obtained as the total potential of REACH. This share is based on a judgment of a plausibility range between 10% and 30%, estimated during a set of expert interviews.

Besides the quantifiable benefits, additional added value is expected through implementation of the proposed options. This concerns in particular the reduction in uncertainty regarding potentially adverse effects on the environment and the increased ability to react promptly and appropriately in cases where risks are suspected or identified. Furthermore, increased knowledge is likely to stimulate innovation processes within companies searching for new and better solutions. Nanomaterials identified as being hazardous to human health and/or the environment can be subject to substitution activities within the concerned companies. It will consequently help to improve the image of companies in the public view

and provide options for concerned companies to communicate that non-hazardous nanomaterials are used in the manufacturing process. The conclusion is that these non-quantifiable effects should not be neglected.

The impact assessment shows that additional costs for companies result in a reduced uncertainty about potentially adverse effects, which might – in combination with appropriate risk reduction measures – contribute considerably to health, environmental and societal benefits.

1 Background and objectives

Nanotechnologies are enabling technologies, and may lead to considerable benefits for consumers, workers, patients, and the environment, as well as perhaps generating growth and jobs[1]. On the other hand, nanotechnologies and nanomaterials may pose new risks to humans and the environment, and currently the knowledge on (eco)toxicity and exposure of nanomaterials is still insufficient to decide on that. From a regulatory perspective, it is therefore crucial to ensure that society can benefit from novel applications of nanotechnology, while at the same time providing for a high level of protection of health, safety and the environment.

In June 2007 the new EC Regulation 1907/2006 on the **R**egistration, **E**valuation, **A**uthorisation and **R**estriction of **Ch**emicals (REACH) entered into force. Its main objective is to ensure a high level of protection of human health and the environment, by increasing knowledge about hazardous properties of chemicals. REACH is based on the precautionary principle, and manufacturers, importers and downstream users have to ensure that they manufacture, place on the market or use such substances that do not adversely affect human health or the environment. REACH in principle applies to chemical substances in all their forms, whatever size, shape or physical state, and thus, its previsions also apply to substances in nanoforms.[2] Until now there have been no specific provisions related to nanomaterials in REACH.

On 3 October 2012 the European Commission has published the Second Regulatory Review on Nanomaterials[3] which assessed the implementation of EU legislation for nanomaterials and as a response to issues raised by the European Parliament or the Council. In that it has also consulted the opinion of SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks) of 19 January 2009 and concluded "that as there is not yet a generally applicable paradigm for nanomaterial hazard identification, a case by case approach for the risk assessment of nanomaterials is recommended. The Commission remains convinced that the REACH Regulation is the best possible framework for the risk management of nanomaterials when they occur as substances or mixtures, but within this framework more specific requirements for nanomaterials have proven necessary."

Parallel to this, the Commission Services have initiated numerous activities to address and evaluate the applicability of requirements under REACH to nanomaterials. For instance, three REACH Implementation Projects on Nanomaterials (RIP-oN) were initiated to evaluate the applicability of the existing REACH guidance to nanomaterials and how the guidance could be updated to better reflect nanomaterials[4]. This resulted in the amendment of REACH guidance to specifically address nanomaterials in May 2012. A generally agreed recommendation of a definition of nanomaterials was first published only in 2011.[5]

1 http://ec.europa.eu/enterprise/sectors/ict/files/kets/hlg_report_final_en.pdf

2 More information on how REACH applies to nanomaterials can be found in the Commission Staff Working Document on Regulatory Aspects of Nanomaterials:
SEC 2008. Commission Staff Working Document. Accompanying document to the Communication from the Commission to the European Parliament, the Council and the European Economic and Social Committee. Regulatory Aspects of Nanomaterials. Summary of legislation in relation to health, safety and environment aspects of nanomaterials, regulatory research needs and related measures {COM(2008) 366 final}

3 EU Commission: Communication Second Regulatory Review on Nanomaterials:
(http://ec.europa.eu/nanotechnology/pdf/second_regulatory_review_on_nanomaterials_-_com%282012%29_572.pdf)

4 http://ec.europa.eu/environment/chemicals/nanotech/index.htm#ripon

5 On 18 October 2011 the Commission adopted the Recommendation on the definition of a nanomaterial: Nanomaterial refers to materials containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1nm-100nm. (Commission Recommendation 2011/696/EU, OJ L 275, 20.10.2011)

Despite that there is still considerable uncertainty with regard to substance identification of nanomaterials in the context of REACH.

As part of the activities DG ENVIRONMENT has asked in an Administrative Agreement (AA; signed December 2010) the Institute for Health and Consumer Protection (IHCP) of the Joint Research Centre (JRC) to perform and coordinate the NANO SUPPORT project[6]: "Scientific technical support on assessment of nanomaterials in REACH registration dossiers and adequacy of available information", with the aim to provide a scientific and technical assessment of certain key aspects of the implementation of REACH with regard to registration and risk assessment of nanomaterials. Within this AA the European Chemicals Agency (ECHA) and the Joint Research Centre (JRC) have established an agreement (signed March 2011) to work in close cooperation on the specific tasks.

The NANO SUPPORT project was divided into 2 tasks:

> **Task I** (Task I step 1-5 and Task II step 1) of the project involved the analysis of information provided in a selected number of REACH registration dossiers addressing nanomaterials (either as a substance or as a form of a substance) and an assessment of how the nanomaterials have been risk/safety assessed. Based on this analysis and assessment, the project terms of reference (TOR) stated that options for modification to the current REACH provisions for nanomaterials would be developed. These options would address registration information requirements and requirements for conducting Chemical Safety Assessment of nanomaterials, i.e. mainly options for modification of the REACH annexes. However, if justified the options would also cover the enacting terms of the REACH legal text.
>
> **Task II** (Task II step 2) of the project was to assess the consequences for industry, consumers, human health and the environment (i.e. an impact assessment) should the proposed options for adapting REACH be implemented.

The assessment and analysis performed on 25 selected REACH registration dossiers undertaken in Task I of the project essentially involved a documentation of key deficiencies in the information included in these dossiers. The specific information needed to rectify these deficiencies was drafted as so-called "Options for adapting REACH" in the Task I report; note that these "Options" are mostly the deficiencies reformulated as recommendations for improving dossier quality. As it was explicit in the project Terms of Reference (TOR) that the assessment would not involve a compliance check in the context of dossier Evaluation under REACH, the deficiencies and associated recommendations were not bench-marked against current REACH requirements. It is important to highlight that they are termed as "Options for adapting REACH" due to the TOR of the project and need in effect to be considered solely in the context of the NANO SUPPORT project. Furthermore the work performed under Task I was carried out mostly prior to the release of the Commission recommendation of a nano-definition and the ECHA guidance specific for nanomaterials. In other words, the conclusions of Task I reflect recommendations based on generic quality observations and lack of nano-specific information as the assessments could not be carried out as true compliance checks. Therefore one needs to be careful in extrapolating these "options" outside the context and history of the current project.

[6] "NANO SUPPORT Project – Scientific technical support on assessment of nanomaterials in REACH registration dossier and adequacy of available information". The final report of the finalised steps (Task I and Task II step 1) is available at: http://ec.europa.eu/environment/chemicals/nanotech/pdf/jrc_report.pdf

The project-based context of the proposed “Options” has led to a key challenge in task II of the project as the implementation of these “Options” into REACH required the definition of a baseline; i.e. which of the proposed “Options” could be considered to be part of current REACH requirements for nanomaterials and as such should not be subjected to an impact assessment. For that ECHA experts were consulted, which helped in decision, which options would be subject to the assessment.

The aim of this project as described in this report, as the last step of the NANO SUPPORT project, is to conduct an examination and assessment of the consequences for industry, consumers and human health if the proposed modification options were to be implemented. These consequences have been addressed in a quantitative manner as far as possible. Consequences to the environment could not be addressed in quantitative terms due to a lack of knowledge of exposure-response functions.

2 Methodological Approach

This chapter describes how consequences were assessed for the set of different options identified and given in the previous steps of the NANO SUPPORT project. Direct as well as indirect benefits and costs were considered wherever appropriate. While direct effects are thought to occur directly after implementation of the options, many indirect effects only begin to appear in the long run (e.g. effects on human health or environment in cases of long latencies or effects on innovation etc.).

It has to be emphasised that the impact assessment was hampered by limited information. The market for nanomaterials is in a quick development phase, and information, especially on the relevant features of nanomaterials, is still limited. The expected impacts of the option scenario itself comprise a reduction of these knowledge and gaps, e.g. on exposure assessment and as a follow-up on the adequate scope of risk management measures.

Consequently, the quantification of indirect effects is very difficult and impacts of implementing single options on health and environment, as well as effects on innovation or on small and medium-sized enterprises are therefore described in a qualitative way. However, in order to provide at least an illustration of the potential magnitude of health benefits[7], we have adapted "top-down" estimates of the health benefits of REACH to estimate the health benefits that may be expected as a result of implementing the options for specific nanomaterial provisions. As a reference point for the calculations, impact assessments conducted prior to the implementation of REACH were used.

In order to examine direct effects on industry that would result from the implementation of specific nanomaterial provisions, three representative nanomaterials (nano titanium dioxide (TiO_2), nano zinc oxide (ZnO), nano diamond) selected in a joint effort by the contractor and the Project Steering Group were thoroughly analysed. The results of these case studies were extrapolated to approximate the effects on the entire market for nanomaterials.

Cornerstones of the overall approach

Cornerstones of the methodology, each addressed in one of the following chapters, are:

- Examination of the market for nanomaterials in the EU-27, providing an overview on both number and company size of manufacturers/importers (Chapter 3)

  This has mainly been done by review of literature and studies (including those provided by the authorities of the Steering Group), supplemented by selected expert interviews.

- Identification of suitable case studies for the subsequent impact assessment (Chapter 4)

  A set of suitable case studies were selected, taking into account different criteria such as:

  - Data availability
  - Expected tonnage bands
  - Expected number of registrants

[7] Due to the unavailability of meaningful data, environmental effects have solely been described in a qualitative manner.

- Estimated/expected hazardous properties (in relation to the group of nanomaterials under examination)

- Baseline Scenario Development for Case Studies (Chapter 5)

  The development of the Baseline Scenario followed the EU Guidelines for Impact Assessments of 2009, as far as these Guidelines are readily applicable for emerging and rapidly developing technologies such as the market for nanomaterials. Therefore, the applicability of all guideline requirements was checked for justification in details and supplemented by the advice and interpretation of the European Chemicals Agency (ECHA) which conditions of future development should be assumed and already covered by the baseline assumptions. A time horizon of 10 years is set to include registration dates of all phase-in substances (latest registration deadline for substances supplied at t ≥1 t/y: June 2018), at the same time allowing reliable predictions to be made (2012 to 2022).

- Development of the "Option Scenario" (Chapter 6)

  The option scenario is defined as covering those options not already covered by the baseline, i.e. going beyond current REACH requirements and requiring additional legal elements (as evaluated by experts of the European Chemicals Agency (ECHA), however not representing an official ECHA position).

- Impact Assessment for Case Studies (Chapter 7) – Quantitative Analysis of Economic, Social, Health and Environmental Impacts

  The two decisive economic impacts identified are the additional impacts to industry due to obligations with regard to new or updated registration dossiers and possible impacts on authorities. Both can be expressed in monetary units (€), however only the first is considered in the options scenario. Impacts on authorities can not be attributed to additional options but rather to the baseline (see Annex 4 for an estimation).

  Health impacts due to the option scenarios are described primarily in qualitative terms. In addition, monetary estimates are calculated in a top-down approach, based on benefit transfer from an existing extended impact analysis of the Commission on benefits of the application of the REACH Regulation and further similar studies.

- Extrapolation of the case studies' results to approximate the effects on the entire market for nanomaterials (Chapter 8)

  This takes into account the future market structure and the different REACH requirements in the respective tonnage bands.

Detailed information on the analysis is included in separate annexes:

- **Annex 1 ("Option profiles")** is intended to provide an overview on the proposed modification options. It is indicated whether the respective options are attributed to the baseline and to the option scenario.

- **Annex 2 ("Case studies of option scenario")** provides detailed information on the financial burden imposed on industry as a result of the implementation of the proposed modification

options. The results are based on the analysis of three case studies (nano titanium dioxide, nano zinc oxide and nano diamond).

- **Annex 3 ("Impacts on Health and the Environment")** outlines the impacts on human health and the environment as a consequence of the implementation of the proposed options. This analysis comprises a detailed qualitative description of impacts for the three case study nanomaterials (nano titanium dioxide, nano zinc oxide and nano diamond) and generic description for the other seven representative nanomaterials.

- **Annex 4 ("Baseline Scenario and Cost of Compliance")** describes in what way the current situation would evolve without adaptation of the REACH regulation, focusing on the three case study nanomaterials (nano titanium dioxide, nano zinc oxide and nano diamond). As some of the options can be regarded as already implicitly part of current REACH requirements, Annex 4 provides figures that are considered as costs of compliance which should be regarded as part of the baseline. This Annex also gives an overview on the impacts on authorities, which are as well considered part of the baseline.

- **Annex 5 ("Questionnaires")** comprises the results of a survey among members of both, the Zinc REACH Consortium and the Titanium Dioxide Industry Consortium (TDIC) that aimed to offer the most accurate picture possible with regard to current registration practice. This Annex is considered to contain business-sensitive information and will therefore not be made publicly available.

An overview of the combination and follow-up of all steps is given in Figure 2-1.

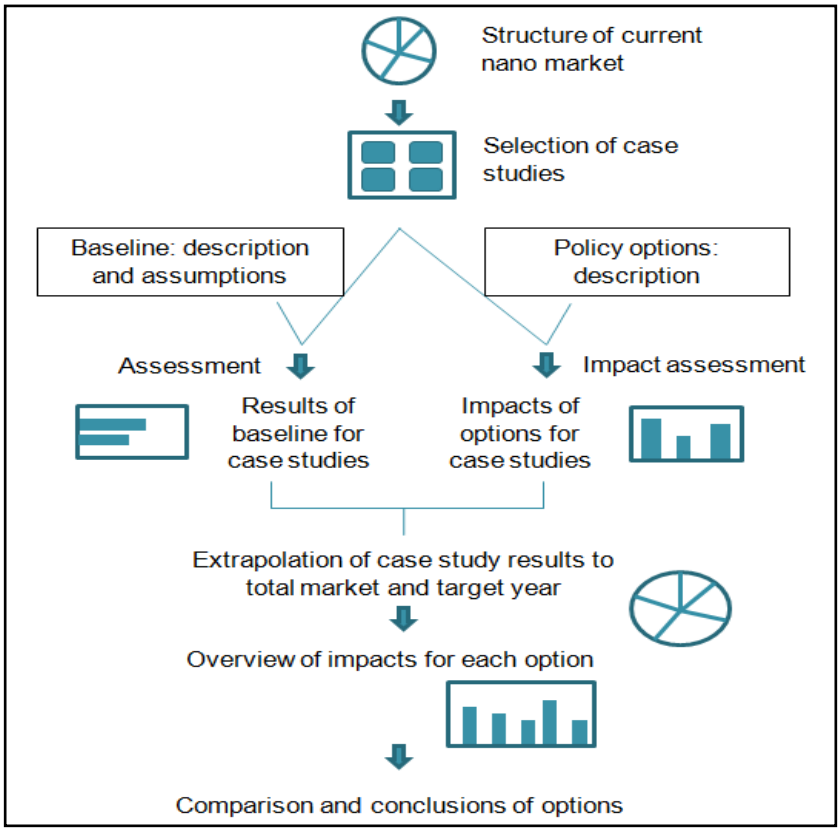

Figure 2-1 Overview of methodology and approach

3 Overview of Nanomaterials

Nanomaterials have found widespread application in material science, industry, research, medicine, and consumer products. Their unique physico-chemical properties in comparison to the corresponding bulk materials are imparted to products and industrial processes of various kinds. Along with physical characteristics such as an altered melting point, altered surface charge, exceptional mechanical stability and altered surface properties due to curvature-imposed restrictions, chemical properties may also be different. Most remarkably the comparatively increased exposure of individual atoms in objects in the nanometer range, as opposed to larger objects/particles, leads to a drastic increase in specific surface area and, proportionally, chemical reactivity.

The responsive surfaces of nanoparticles are often modified to maintain these unique properties (protect against agglomeration) or to introduce desirable characteristics such as changes in hydrophilicity or biotic targeting. Many applications do not require the existence of free nanoparticles of a given substance but fuse them in material complexes with other substances, thus altering desirable material properties such as chemical resilience, mechanical stability, magnetic or electrical properties, etc. Nanomaterials of many different forms and substances are used not only in high-tech applications such as information technology, energy generation and conservation, or space flight technology but also in everyday items such as food and food packaging, cosmetics, plastics and rubbers, clothes and many more to which humans can be directly exposed.

The high reactivity and/or the strong catalytic properties that are initially desirable also make nanomaterials prone to pick up unintentional modifications along their lifecycle in a given application (for more detailed discussion see Annex 3). This may also influence their fate in the human body or in the environment and their (eco)toxicity. The risk of nanomaterials to humans and the environment depends on their hazardous properties, their uses, and the exposure to them, which can be different from their bulk counterpart. Their assessment may also require new information requirements to better characterise and assess their risks.

In order to provide an overview of possible economic, social, human health, and environmental impacts, ten nanomaterials have been selected to serve as examples for the similarities and differences that can be found between individual substances when their particle sizes are reduced to the nanometer range.

The ten materials thus reflect a mixture of considerations such as production volumes, relative toxicities within the group of selected nanomaterials (a list obviously by no means comprehensive) either regarding human health or the environment, applications (including considerations on foreseeable consumer and workforce exposure) and potential for future growth.

The project team has selected from this list three materials to be studied as in depth case studies within this report. The same considerations as for the selection of the initial ten nanomaterials were re-applied. It was deemed of particular importance to also include a nanomaterial considered to provide immense promises for the application to current societal problems and to have very low toxicity. For this reason nano diamond was selected. In this context it should be pointed out that BiPRO is acting as Secretary of the diamond consortium.

4 Case Studies

The identification of suitable case studies for the subsequent impact assessment addressed in this chapter is based on a set of selection criteria, such as data availability, expected tonnage bands, expected number of registrants, and estimated/expected relative hazardous properties.

Prior to the preparation of this report several studies focussing on comparable issues were screened for relevant figures – from these, two[8,9] specific studies have been taken into account for the assessment of costs and benefits.

Key data identified (based on literature research):

- Between 500 and 2,000 nanomaterials are expected to be placed on the EU market. Most (around 80%) of the manufacturers and/or importers of nanomaterials are micro companies or SMEs[8].
- the estimated total number of European nanomaterials manufacturers is expected to be between 200 and 300[9]

Although these data are a rough estimate and indicate only a broad range, they can nevertheless be used for establishing best case and worst case scenarios. Generally, no distinction is made between manufacturers and importers and they are treated equally. In the "Study on REACH contribution to the development of emerging technologies" it was indicated that 20 % of all companies participating in a survey were importing nanomaterials from outside the European Economic Area (EEA). There is no precise data on the number of "Only Representatives". Referring to ECHA´s publicly available registration statistics, 27,684 joint submissions have been submitted up to 31 October 2012. Only 14 % of the submitted joint submissions could be allocated to registrants whose company size is small or medium. The remaining 86 % of joint submissions can be allocated to large companies. The share of small and medium enterprises (SMEs), however, might be in tendency larger for the smaller tonnage bands of the two forthcoming registration dates.

In order to cover a diversified range of various parameters, the project team has decided on the following substance (classes) to establish a solid data basis. This data basis serves in a subsequent step as the starting point for the aforementioned upscaling procedure. All nanomaterials have in common that they are already in use (some for a few decades, such as carbon black), and are used in substantial volumes (such as nano carbon black, synthetic amorphous silica) or have potential to be produced in substantial volumes (such as carbon nanotubes (CNTs)).

The list of nanomaterials reads as follows:

8 Risk & Policy Analysts Limited. (2012). Impact Assessment of the REACH Implementation Project on Substance ID for Nanomaterials. Norfolk.

9 Kauhanen, L., Rissanen, J., & Crawley, T. (2011). Study on REACH contribution to the development of emerging technologies.

Case studies:

- **Nano TiO_2**
- **Nano ZnO**
- **Nano diamond**

Additional nanomaterials:

- Synthetic Amorphous Silica (SAS)
- Carbon black
- Carbon Nano Tubes (CNTs)
- Fullerene
- Nano silver
- Nano copper
- Quantum dots (e.g. Cadmium sulphide)

As initially indicated, the selected nanomaterials cover a broad range of various parameters. For instance nano SiO_2, nano TiO_2 and carbon black are nanomaterials which are produced on a larger scale (> 1,000 t/y per manufacturer) – on the other hand there are indications that nano diamond would be manufactured in a volume which would merely exhibit the threshold of 1 t/y per manufacturer. The second criterion for choosing the listed nanomaterials is the broad range of hazardous effects which the nanomaterials might induce with regard to (eco)toxicity. For instance, TiO_2 is suspected to be carcinogenic (IARC 2b). However, it should be pointed out that the underlying effects may have been caused by a severe lung overload in the test settings which may put into perspective the testing results. On the other hand nano diamond is currently expected to pose no hazardous effects (information by manufacturers; in this context it should be pointed out that BiPRO acts as Secretary of the diamond consortium), however, scientific evidence for such expectations is not yet complete. Due to their tubular shape, there are concerns that certain types of carbon nanotubes (CNTs; long, rigid) may induce similar hazardous effects as asbestos fibres[10] and nano ZnO might be classified as very toxic to aquatic organisms based on the classification of the bulk form of ZnO (see Annex 3). Finally, the selected nanomaterials are used in a broad range of applications – consequently, a broad range of identified uses in the lead dossiers would be covered. For further elucidation on the individual materials and the reasons for roughly grouping them as we have done here please refer to Annex 3 (Impacts on health and the environment in detail).

Based on the aforementioned overview, the project team has categorised the selected list of nanomaterials upon the following criteria (see Table 4-1):

- Tonnage band for registration
- Number of expected registrants
- Hazardous properties

[10] van Noorden, R. (2008). Carbon nanotubes behave like asbestos. Royal Society of Chemistry. Retrieved October 5, 2012, from http://www.rsc.org/chemistryworld/News/2008/May/20050802.asp

Table 4-1 Selected list of nanomaterials and criteria for categorisation

Nanomaterial	Tonnage band for registration (t/y)				Number of expected registrants			Relative hazardous properties
	1-10	10 -100	100 -1,000	> 1,000	1-10	11-30	> 30	
Synthetic Amorphous Silica				●		●		
Nano TiO_2				●			●	
Nano ZnO			●			●		
Carbon black				●			●	
Carbon Nano Tubes (CNTs)			●			●		
Fullerene	●				●			
Nano diamond	●				●			
Nano silver		●				●		
Nano copper	●				●			
Quantum dots (e.g. CdS)	●				●			

Relative hazards: ■ low; ■ medium; ■ high

Please note that the categorisation in Table 4-1 is just a preliminary and rough indication and reflects the project team's point of view. This table should be considered as an orientation in order to emphasise the fact that the project team has selected nanomaterials with an eye towards a broad range to the drawn up categories. The categorisation was mainly based on literature and data that are publicly available. The "hazard" properties cover both the toxicological and the ecotoxicological hazards and grade the nanomaterial relative to each other in rough terms. Grading the relative hazard was preferred over grading the risk because the uses of nanomaterials are extremely diverse. One consequence of this is the highly variable exposure of humans and the ecosystem to nanomaterials which directly affects their risk assessment.

5 Options for adapting REACH

The NANO SUPPORT Project report on the first tasks from March 2012[11] describes 21 options in total. The options are described in detail in section 3.2, 4.2 and 5.2 and summarised in chapter 6 of the same report. These options are presented in Table 5-1 and refer to five categories, namely

- Substance identification and physico-chemical properties
- General aspects of human health, environmental fate, environmental hazards
- Specific aspects of human health hazards
- Specific aspects of environmental fate & hazard
- Exposure assessment and risk characterisation.

The original categorisation from the part I NANO SUPPORT report into fundamental and additional options has not been considered as relevant for the current assessment and was therefore not further applied. Instead within this report the 21 options have been classified according to the criterion distinguishing between the **baseline scenario** versus **option scenario**. Some of the options have been regarded as already implicitly part of current REACH requirements (see Table 5-1) and have been classified as baseline scenario. Options not already part of current REACH requirements have been classified as option scenario. This conclusion results from communications within the NANO SUPPORT steering group and a final agreement between the project team and ECHA experts. In this context it should explicitly be pointed out that the outlined and proposed attribution of the options is not an official position of ECHA. Implementation of the baseline options would simply make the requirements more transparent and are therefore considered to help businesses to register in full compliance with the current rules. This could be achieved e.g. by better explanation in the guidance or better communication. Consequently, costs that result from the implementation of such options are to be regarded rather as compliance costs that need to be considered part of the baseline. Most of these baseline options do not only concern nanomaterials but all complex substance types. The categorisation in (nano)particle-specific and non-nano specific has been identified during the examination of the options.

Different combinations of these characteristics within the categorization of these options can be found in Table 5-1.

The baseline and the option scenarios will be explained in the following chapters.

Suboptions/cases:

In both the baseline and the option scenario, two suboptions/cases for nano-specific properties (such as size or surface treatment) are analysed: Size or surface modification interpreted either as a characteriser or as an identifier according to REACH. Defining “size or surface treatment of a substance“ as a characteriser or an identifier can lead to the following scenarios:

- registration of bulkforms and nanoforms as different substances in one dossier or

[11] Frans M. Christensen et al.: NANO SUPPORT Project; Scientific technical support on assessment of nanomaterials in REACH registration dossiers and adequacy of available information *AAN°07.0307/2010/581080/AA/D3* Report on analysis and assessment (Task I, step 3&4&5) and options for adapting REACH (Task II, step 1); European Commission; 2012

- registration of different nanoforms as distinct substances in separate dossiers.

The latter has the consequence that nanoforms may be treated in separate SIEFs, and separate registration dossiers would be necessary.

In addition, in the option scenario a distinction is made between cases in which an exposure assessment and a risk characterisation are required – i.e. when a tested nanoform is placed on the EU market in an annual tonnage volume of more than 10 t/y and if the substance is classified as hazardous - and in cases where it is not required.

Annex 1 provides an overview on brief characterisations of the 21 options described in the **JRC NANO SUPPORT project report**. These "option profiles" are used as an instrument

- to clarify the content of the different options;
- to analyse whether the options are already addressed by newer guidances;
- to identify information needs related to the options

In addition, the profiles were used by the project team to collect first indications on costs, benefits and risks related to the options. In this way they have supported the preparation of the impact assessment carried out in detail in Chapter 7.

In the following, the three case study nanomaterials selected in chapter 4 are briefly presented. Relevant information to describe the case studies was taken from the ECHA's website for registered substances or other publicly available sources. ECHA did not provide any other information to the project team. These case studies are presented in more detail in relation to the baseline and option scenario in Annex 4 and 2 respectively.

For the case studies the following current and future market developments are considered:

- Current and expected future applications of nanomaterials, indicating expected registration tonnage bands for single substances;
- Information on companies manufacturing and/or importing substances with nanoforms;
- Trends in registration updates and new registrations
- Existence of 'learning curves' and that knowledge on nanosafety is rapidly developing
- Expected changes in other relevant legislation/regulation that could affect the uses and thus the amount of nanomaterials produced in or imported into the EU.
- Actions and legislation already decided or proposed, and impacts of these actions

Case study nano TiO_2:

In 2010 a lead registrant dossier for titanium dioxide was submitted to ECHA. The dossier covers a tonnage band of more than 1,000 tonnes per year and was elaborated under the auspices of the Titanium Dioxide REACH Consortium (TDIC).

During the development of the lead dossier several forms of TiO_2 were assessed and included in this dossier: the bulk form of TiO_2, nano TiO_2 or surface treated (e.g. silanised) nano TiO_2.

The TDIC received a questionnaire (see Annex 5 for the completed questionnaire) in which, amongst others, the consideration of nano TiO_2 in the current lead dossier, nanospecific uses or the aspect of surface treated/surface functionalised nano TiO_2 have been subject to an inquiry.

Relying on the indications made by the TDIC, neither an update nor an elaboration of a separate lead dossier for nano TiO_2 and/or surface treated/surface functionalised nano TiO_2 are envisaged. In fact, TDIC considers that TiO_2 and its accompanying various (nano)forms are sufficiently characterised by standard tests. Surface treated nano TiO_2 was also addressed in the questionnaire. There is currently no general consensus or recommendation at hand on how to register surface treated nanomaterials under REACH. This aspect is explained in detail in the RIP-oN1 report (p.28) but no consensus opinion has been reached so far. The consortium indicated that surface treated (nano) TiO_2 has been registered in a way that the surface treating substance would be registered separately. With this strategy the consortium/lead registrant has followed the current practice for registering mixtures.

Case study nano ZnO:

In 2010 a lead registrant dossier for zinc oxide was submitted to ECHA. The dossier covers a tonnage band of more than 1,000 tonnes per year and was elaborated under the auspices of the Zinc REACH Consortium.

Tests for several forms of ZnO (bulk form, nano form, surface treated forms (triethoxycaprylylsilane-coated ZnO and dimethoxy-diphenylsilane/triethoxy-caprylylsilane crosspolymer-coated ZnO)) were undertaken in the course of the elaboration of the dossier, and the correlating testing results are publicly available via ECHA´s website for registered substances. The Zinc REACH Consortium received a questionnaire (see Annex 5 for the completed questionnaire) in which, amongst others, the consideration of nano ZnO in the current lead dossier, nanospecific uses or the aspect of surface treated/surface-functionalised nano ZnO have been subject to an inquiry. With regard to the completed questionnaire, an update of the current lead dossier is planned in which especially the aspect of surface treated nano ZnO will be considered in more detail.

Case study nano diamond:

In 2011, a consortium called the “FEPA REACH consortium for diamond” has submitted to ECHA a lead registrant dossier for crystalline synthetic diamond in the tonnage band 100-1,000 tonnes per year. The substance specification defined by the consortium excludes materials in the nano scale, which means that nano diamond is not covered by this registration.

According to information from SIEF questionnaires, at the moment there is only a very small number of approximately 5 companies of which each produces/imports nano diamond in a tonnage band barely exceeding the threshold of 1 tonne per year (t/y).

Considering particle size as a characteriser or as an identifier would have various implications on the registration approach: in the case of considering size as a characteriser nano diamond may be defined as another form of bulk diamond (one substance). Considering particle size as an identifier would result in identifying nano diamond as a distinct substance leading to a separate registration.

The question whether size is a characteriser or an identifier has great influence on the information requirements for registration of nano diamond. Due to the low tonnage and thus limited information requirements (Annex VII only), elaboration of a separate lead dossier for nano diamond would be much cheaper than updating the existing lead dossier for bulk diamond (information requirements according to Annexes VII-IX). However, the lead dossier includes all information requirements related to the maximum tonnage band within the joint submission. The extent of the information requirements is triggered by the aggregated volume of a legal entity, but is not triggered by aggregated volumes of a joint submission.

Only one company producing/importing diamond in the nano range is a member of the existing diamond consortium. All other members do not produce nano diamond. It is unlikely that the members of the REACH consortium for diamond would consider updating their lead dossier to cover nano diamond. At this stage of the report the project team has no further information on probable future update activities for the lead dossier, nor can the project team assume which registration strategy the single manufacturer of nano diamond would approach. Furthermore, it can be expected that the highest tonnage band of diamond in total (aggregated volumes of manufactured and imported volumes of diamond and nano diamond in Europe) is in the range of 100-1,000 t/y and a registration dossier covering all forms of diamond has to satisfy information requirements of REACH Annexes VII - IX.

Nano diamond, as well as synthetic micron diamond, is surface treated to achieve the properties required for special applications. However, so far these surface treated nano diamond products are produced by individual companies in volumes/tonnages below 1 t/y. Therefore, it is expected that only one (untreated) form of nano diamond will be subject to registration until 2018. Since BiPRO is acting as Secretary for the diamond consortium, no questionnaires were prepared and communicated.

Table 5-1 Overview of originally identified 21 options, covered in the Baseline Scenario versus the Option Scenario

		Substance identification and physico-chemical properties		
1	**3.1**	Explicitly require registrants to describe the scope of the registration dossier	Baseline scenario	In principle not nano-specific and equally applicable to any complex substance that exists in multiple forms
2	**3.2**	Explicitly require registrants to provide more detailed characterization of nanomaterials/nanoforms	Baseline scenario	
3	**3.3**	Require that nanoforms are explicitly addressed in the endpoint sections	Baseline scenario	
4	**3.4**	Require detailed description of the test material/sample and sample preparation	Baseline scenario	
5	**3.5**	Require scientific justifications for grouping/read-across/QSAR and other non-testing approaches for different forms	Baseline scenario	
6	**3.6**	Include information on dustiness	Option scenario	(Nano)particle-specific
		General options for human health hazards, environmental fate, environmental hazards		
7	**4.1**	Require that nanoforms are explicitly addressed in endpoint sections	Baseline scenario	Not nano-specific, applicable to any complex substance that exists in multiple forms or compositions
8	**4.2**	Require detailed description of the test material/sample and sample preparation	Baseline scenario	
9	**4.3**	Require scientific justifications for grouping/read-across/QSAR and other non-testing approaches for different forms	Baseline scenario	Not nano-specific, applicable to any complex substance that exists in multiple forms or compositions
10	**4.4**	Decide on the most appropriate metrics	Baseline scenario	

		Human health hazards		
11	4.5	Require acute toxicity data for the most relevant route of exposure	Option scenario	(Nano)particle -specific
12	4.6	Change particles to '(nano)particles' for repeated dose toxicity studies (inhalation)	Option scenario	
13	4.7	Require non-bacterial in vitro gene mutation study	Option scenario	
		Environmental fate & hazards		
14	4.8	Require that bioaccumulation is addressed specifically for the nanoform	Baseline scenario	Nano-specific, considered to be addressed by Guidance updates based on the RIP-oN2 and 3 reports
15	4.9	Specify that adsorption/desorption behaviour of nanomaterials should not be assessed based on K_d values derived from K_{OC} and K_{OW}	Baseline scenario	
16	4.10	Consider water solubility in relation to test waiving	Option scenario	(Nano)particle -specific
17	4.11	Specify that long term testing should not be waived based on lack of short term toxicity	Option scenario	
18	4.12	Specify that algae testing should not be waived based on insolubility	Option scenario	
19	4.13	Require that testing on soil and sediment organisms is prioritised	Option scenario	(Nano)particle -specific
		Exposure assessment and risk characterisation		
20	5.1	Require identification of uses and exposure assessment of the nanoform	Baseline scenario	Not nano-specific, applicable to any complex substance that exists in multiple forms or compositions
21	5.2	Require considerations of most appropriate/relevant metrics	Option scenario	Not nano-specific, generic

Baseline Scenario (No policy change)

The baseline scenario describes how the current situation would evolve without adaptation of the REACH regulation. It forms the basis for the subsequent analysis and evaluation of impacts that are likely to occur as a result of the implementation options developed as part of the NANO SUPPORT project. The Baseline Scenario followed the EU Guidelines for Impact Assessments of 2009. A time horizon of 10 years has been set to include registration dates of all phase-in substances (latest registration deadline for substances supplied at a tonnage ≥ 1 t/y: June 2018), and at the same time allowing reliable predictions to be made (2012 to 2022).

The baseline scenario used in this report comprises 12 out of the original 21 options identified, i.e. the option numbers:

- 1, 2, 3, 4, 5, 7, 8, 9, 10, 14, 15 and 20.

For an overview of all options please refer to Table 5-1.

The options which are concerned with the precise description of the scope of the dossier at hand and the physico-chemical properties of the material in question, allows accurate definition of whether or not a material can be considered a nanomaterial/-form. Most of these options (but not all) correspond to the fundamental options as defined by part I NANO SUPPORT report.
One of the key challenges that registrants of nanomaterials are facing refers to discussions about substance identification of nanomaterials. Although ECHA has recently published specific guidance on nanomaterials, there are still considerable uncertainties as to whether or not size and surface treatment are to be considered as characteriser or identifier of nanomaterials[12]. These uncertainties have been taken into account in the course of the impact assessment and therefore cost estimates have been developed for both scenarios.

[12] This issue is still a matter of controversial debates and has been addressed in the course of RIP-oN 1 on Substance Identification of Nanomaterials.

6 Description of the option scenario

The “option scenario” is considered to comprise all relevant options for changing the REACH requirements for nanomaterials which are not considered as comprised by current REACH requirements. They represent new technical requirements and have to be addressed by additional legal elements. For these options the consequences for industry, consumers, human health and the environment are assessed within this report. The contents of all options covering baseline and option scenario, are described in detail in Annex 1: Option Profiles.

The option scenario comprises the following option numbers:

- 6, 11, 12, 13, 16, 17, 18, 19 and 21.

For an overview of all options please refer to Table 5-1.

The options of the option scenario are end-point related, which means that they are concerned with the human health hazards, environmental fate and environmental hazards. While specific guidance still needs to be provided in some cases (the appropriateness of available tests to nanomaterials is still under discussion), these options outline necessities for accurate experimental research to allow for a reasonable hazard assessment. Furthermore, these options address the application of read-across and QSAR approaches in an attempt to define when such alternative methods can be reasonably applied in the case of nanomaterials.

7 Impact Assessment for case studies (baseline scenario and option scenario)

This chapter presents the impacts on industry, on human health and the environment for the additional options scenario assessed for the three case studies of nano TiO_2, nano ZnO and nano diamond. The assessment is made for the target year 2022. The geographical scope is the European Economic Area (EEA), i.e. the EU-27 countries plus Norway, Liechtenstein and Iceland, corresponding to the application area of the REACH Regulation.

Results from the impacts of the individual 21 options identified in the JRC NANO SUPPORT project report, each applied to the three case studies of the substances nano titanium dioxide, nano zinc oxide and nano diamond, are described in detail in Annexes 2 and 4.

In 2007, the European Chemical Industry Council (CEFIC) commissioned the Berlin based Social Science Research Centre (Wissenschaftszentrum Berlin für Sozialforschung – WZB) to carry out a major study to investigate the prices for laboratory testing services and testing capacity across Europe[13]. The study and the output of this so-called Fleischer list have become a benchmark for the costs charged by SIEFs. The WZB found large disparities in costs across European laboratories, particularly between small and big operators, even when carrying out identical tests. These costs have been used as a basis, however, due to uncertainties with regard to the longer term trends in these costs it is still difficult to assess the accuracy of early predictions of costs of registration and testing required by REACH.

The initial predictions from around five to seven years ago on total registration and testing costs in REACH ranged from less than **€ 1 billion** to over **€ 15 billion**. At the time that was equivalent to 0.25% to more than 3% of the European chemical industry's total annual revenue, although far less in terms of total revenue over the 11 years of REACH's entire registration process[14]. The project team has prepared several lead dossiers in the last few years including lead registration dossiers for the 2010 and 2013 deadlines. Against this background the project team has a good overview on current laboratory costs, considered in the calculation of the expected costs in the following options. It is difficult to estimate whether efforts for testing nanomaterials will be higher compared to studies performed on bulk materials, as the official OECD guidelines have not yet been adopted accordingly and laboratories do not yet offer routine analysis of nanomaterials (see detailed explanation on this topic in preamble of Annex 2). Although it can be expected that some animal studies might be more expensive for nanomaterials due to more difficult atmosphere monitoring, in most cases prices are expected to be in the same range for nanomaterials and bulk materials. Therefore prices, irrespective of the physical state of the testing material, from different European laboratories and prices, indicated in the abovementioned Fleischer-list, have been used for indication of a range of cost calculations.

[13] Fleischer, M. (2007). Testing cost and testing capacity according to REACH requirements–results of a survey of independent and corporate GlP laboratories in the EU and Switzerland. J. Business Chem, 4(3).

[14] http://www.soci.org/Chemistry-and-Industry/CnI-Data/2011/2/REACHing-for-a-price-tag

7.1 Impacts on industry

Impacts on industry for the baseline and options scenario (for overview please refer to Table 5-1) have been assessed for the three case studies. Within the registration process the lead registrants of the three selected case nanomaterials have applied different registration strategies: in case of TiO_2 and ZnO, the existing lead dossiers do already cover nanomaterials. In contrast, the existing lead dossier for synthetic diamond does not cover nano diamond due to a lack of interest in registration by SIEF members. In summary, it can be concluded that implementation of requirements of the baseline scenario would nevertheless lead to costs for registrants in order to attain a REACH-compliant level of their dossier(s). For instance, performing of bioaccumulation tests (according to information requirements of Annex IX) or taking the most relevant metric into account for testings would lead to considerable costs (if e.g. the appropriate overall tonnage volume of more than 100 t/y is exceeded for the case of performing tests on bioaccumulation). This is independent from whether an existing lead dossier already covering nanomaterials had to be updated or whether an individual registration dossier for nanomaterial had to be submitted.

Additional options which result in extended information requirements, such as additional data on dustiness or additional information on aquatic toxicity due to exclusion of solubility-based waiving would result in additional costs (options scenario) either due to more information needs or due to alternative methods to satisfy data requirements such as waiving being no longer applicable. The impact of options in this case is dependent on the strategy chosen by registrants and on the decision whether nanomaterials are considered individual substances under REACH. For materials like nano ZnO or nano TiO_2, which are produced in high amounts: > 1,000 t/y, there is little difference between updating a common lead dossier and elaboration of individual dossiers.

Most nanomaterials, however, are produced in much lower volumes than bulk materials. The elaboration of a separate lead dossier is less costly than updating a dossier covering all forms of a substance. This is the reason for assessing both scenarios (identifier/characteriser). Nevertheless, in cases where an existing lead dossier does not yet cover nanomaterials and particle size is considered to be a characteriser (which is assumed to be the preferred legal interpretation), such as for nano diamond, the costs resulting from implementation of the options are expected to be in the same order of magnitude as for updating a dossier already covering nanomaterials to be compliant with the requirements implemented by the proposed options. Normally, the lead registrant submits all the required physico-chemical, eco-toxicological and toxicological information on behalf of all members of a joint registration. The extent of the information requirements correlates to the maximum tonnage band of the joint submission and is triggered by volumes of a legal entity, but is not triggered by aggregated volumes of a joint submission.

The uncertainties associated with the case studies are discussed in the sensitivity analysis provided in Chapter 8 on extrapolation to the market for nanomaterials.

Table 7-1 shows the estimated costs for industry for the three case studies of nano TiO_2, nano ZnO and nano diamond. Please refer to Annex 2 of this report for details on these calculations.

Table 7-1 Costs for option scenario on industry for TiO_2, ZnO and nano diamond

Options of the option scenario and resulting additional costs (€)							
No.	**No. JRC**	**Nano TiO_2***		**Nano ZnO****		**Nano diamond*****	
		Size as characteriser	**Size as identifier**	**Size as characteriser**	**Size as identifier**	**Size as characteriser**	**Size as identifier**
6	**3.6**	2,700	2,700	4,300	4,300	2,100	2,100
11	**4.5**	12,800 – 23,500	12,800 – 23,500	25,600 – 47,000	25,600 – 47,000	12,800 – 23,500	12,800 – 23,500
12	**4.6**	0	0	0	0	0	0
13	**4.7**	0	0	60,000 – 72,000	60,000 – 72,000	20,000 – 24,000	20,000 – 24,000
16	**4.10**	103,900 – 154,095	8,600 – 154,095	121,400 – 178,126	17,200 – 178,126	60,700 – 89,063	8,600 – 12,741
17	**4.11**	48,000 – 101,830	48,000 – 101,830	48,000 – 101,830	48,000 – 101,830	24,000 – 50,915	0
18	**4.12**	0	0	0	0	0	0
19	**4.13**	27,250 – 56,815	6,850 – 56,815	20,550 – 57,789	20,550 – 57,789	0	0
21	**5.2**	4,000	4,000	6,000	6,000	2,000	2,000
∑:		**198,650 – 342,940**	**82,950 – 342,940**	**285,850 – 467,045**	**181,650 – 467,045**	**121,600 – 191,078**	**45,500 – 64,341**
Average per nanoform		**99,325 – 171,470**	**41,475 – 171,470**	**95,283 – 155,682**	**60,550 – 155,682**	**121,600 – 191,078**	**45,500 – 64,341**

*: Two forms are assumed to be subjected to an update process or elaboration of a new registration dossier: nano TiO_2 and surface-coated nano TiO_2. Resulting costs might increase with further nanoforms of TiO_2.

**: Three forms are assumed to be subjected to an update process or elaboration of a new registration dossier: nano ZnO and two surface-coated nanoforms of ZnO. Resulting costs might increase with further nanoforms of ZnO.

***: Only one form is assumed to be subjected to an update process or elaboration of a new registration dossier: nano diamond. Resulting costs might increase with further nanoforms of diamond.

The elaborated three case studies clearly demonstrate the range of costs which the registrants would have to cope with after possible implementations of the requirements of the additional nine options in the REACH Regulation. Furthermore the assessed costs give a good indication of the possible cost range per applied option and per tested nanoform. Based on the elaborated Table 7-2, the following overview of the proposed cost range per option can be given, which also serves as a basis for the subsequent extrapolation of costs for industry:

Table 7-2 Overview on resulting additional costs per tested nanomaterial for the four affected tonnage bands

Proposed cost for option scenario, allocated to REACH Annexes (in €)				
Option	**Annex VII**	**Annex VIII**	**Annex IX**	**Annex X**
6	2,100	2,100	2,100	2,100
11	12,800 – 23,500	12,800 – 23,500	12,800 – 23,500	12,800 – 23,500
12	0	0	0	0
13	20,000 – 24,000	20,000 – 24,000	20,000 – 24,000	20,000 – 24,000
16	8,600 – 12,741	24,700 – 32,063	60,700 – 89,063	60,700 – 89,063
17	0	0	24,000 – 50,915	24,000 – 50,915
18	0	0	0	0
19	0	0	6,850 – 19,263	17,050 – 38,039
21	2,000	2,000	2,000	2.000
Final costs:	**45,500 – 64,341**	**61,600 – 83,663**	**128,450 – 210,841**	**136,650 – 229,617**

Please note that the assessed options have different impacts on costs, depending on the tonnage band. For instance, options which would affect information requirements for Annex VII under REACH only, would also have to be fulfilled for the higher Annexes (VIII, IX and X). In contrary, options which would affect information requirements for Annexes IX and X, would have no impacts on Annex VII and VIII.

In this context it should be noted that some information on the nanomaterials' (eco)toxicity is already available from publicly funded research (data/test methodologies) or from tests which are obligatory in other chemicals-related directives/regulations (e.g. Biocides or Cosmetics Regulation). The implementation of the identified additional options might potentially either lead to multiple (unnecessary) performing of the same tests or to double-counting of the resulting costs from the same test. At this stage of the report no quantitative description of the proportion of concerned nanomaterials, for which information may already be available, can be provided.

7.2 Impacts on human health and the environment

Impacts on human health and the environmental are presented below. Because of the interconnected nature of the options, baseline and option scenarios are discussed together. They are provided for the three case studies. For detailed analysis of the nanomaterial properties separated by human health and environmental impacts please refer to the Annex 3.

- **TiO_2 nanoparticles**

TiO_2 nano particles are registered within a dossier for TiO_2 (covering all forms) that encompass more than 1,000 t/y in production volume.

TiO_2 nanoparticles can be characterised as being:

a) insoluble (no ion related effects)

b) The bulk material is not recognised as hazardous

Baseline scenario:

When applying the baseline scenario to TiO_2 nanoparticles the following information is lacking or inconclusive from the current registration dossier:

- Chronic health and environmental effects
- Bioaccumulation
- Environmental dispersion
- Effects on the food chain due to severe effects on single cellular algae

Option scenario:

All options are included (both, those belonging to the baseline and those belonging to the option scenario), which leads to thorough physico-chemical characterisation, toxicological evaluation for human health and environmental impacts, and the opportunity to generate a more complete risk assessment.

Additional data available through the option scenario vs. the baseline scenario for TiO_2 nanoparticles:

If the option scenario is implemented then option 6 will provide information on the dustiness of nanomaterials. Options 16 and 18 will provide valuable information on the dispersion of TiO_2 nanoparticles in water and their impact on algae. Both could be circumvented without the implementation of the option scenario because TiO_2 nanoparticles are not water soluble and thus the tests could be waived. Similarly the waiving of long term toxicity tests due to lack of short term toxicity (option 17), which is possible in the baseline scenario, is no longer possible and thus allows for a more complete picture of nanoparticle effects. Option 22 forces the consideration of appropriate metrics and thus has the potential to facilitate non-testing methods in the future by providing more comparable data sets.

Options 11, 12, 13 and 19 do not yield additional data as the existing requirements for the highest tonnage bands already cover these demands.

- **Zinc oxide nanoparticles**

ZnO nanoparticles were registered together with the bulk material in a dossier of over 1,000 t/y. As the bulk form is classified as toxic to aquatic organisms, the same classification is expected to be valid for the nanoform. The comparison with TiO_2 nanoparticles is interesting here because neither the bulk form nor the nano form of TiO_2 are water soluble in contrast to both forms of ZnO. Without the implementation of the option scenario some data are not collected because TiO_2 nanoparticles are not water soluble (see above). As ZnO nanoparticles are water soluble tests cannot be waived due to insolubility and thus the implementation of the option scenario has less impact on the available data of ZnO nanoparticles in contrast to TiO_2 nanoparticles (see below).

Baseline scenario:

The application of only the baseline scenario to the case study of ZnO nanoparticles leads to very few blank spots within the accumulated data. Bioaccumulation in organisms are insufficiently characterised and have the most direct effects on human health and the environment.

Due to the characteristics known from the bulk material and the production quantities, most endpoint related studies would have to be done in any case. The necessary data for a meaningful exposure assessment are nearly complete without the data on bioaccumulation. Similarly the hazard related information lacks only a few data sets. However, the available information is not sufficient to perform a satisfying risk assessment.

Option scenario:

All options are included (those belonging to the baseline and those belonging to the option scenario), which leads to thorough physico-chemical characterisation, toxicological evaluation for human health and environmental impacts, and the opportunity to generate a more complete risk assessment.

Specifically for ZnO nanoparticles the potential for bioaccumulation and important additional information for the adsorption/desorption behaviour of ZnO nanoparticles is fully analysed. Please refer to Annex 3 for a detailed description of the option impacts.

Additional data available through the option scenario vs. the baseline scenario for ZnO nanoparticles:

Because ZnO nanoparticles are water soluble and ZnO is already toxic in bulk form and in the short term, the application of the option scenario delivers significantly less new information in comparison to the baseline scenario. As mentioned above this is a noteworthy distinction to TiO_2 nanoparticles. New information is added for options 6 and 21 when the option scenario is implemented. The information added is on dustiness, and the choice of relevant metrics. The consequences of having this information are elucidated above for TiO_2 and in Annex 3.

The other seven options have no impact as these tests cannot be waived due to lack of water solubility and the tonnage band (as for TiO_2) is large enough to call for some of the data requested in the other options in any case.

- **Nano diamond**

Nano diamonds are not yet produced on a large scale. The current registration dossier for synthetic diamond lists a tonnage band of 100 – 1,000 t produced per year.

Within the three selected case studies nano diamond is a nanomaterial which is assumed to exhibit the lowest (eco)toxicological profile. For nanomaterials of low toxicity the lack of information due to non-implementation of the option scenario would have little impact on human health and the environment. This is however not known *ex ante* for every new nanomaterial or nanomaterial modification. The lack of data due to a low production or import volume and due to lack of water solubility is explained below.

For nanomaterials produced in such low production volumes there will either be no registration required or the information required will be limited to those of Annex VII.

Baseline Scenario:

Due to the starting parameters (low production volume, no dissolution in water, no hazard rating) the results for nano diamond show the largest knowledge gaps of all three case studies. This has no significant consequences in this particular case as nano diamond is considered to be of lower toxicity in comparison to other nanomaterials. The main cause for the information gaps is the dependence on the yearly production volume, which triggers the extent of the substance characterisation for the registration process under REACH.

The option scenario:

Implementation of the option scenario would yield additional data for every of the nine options. In the case of nano diamond the expected impact of the information gained for risk assessment is not very high. This is because many of the requirements made by the options have been taken care of by researchers working on nano diamond, and current information indicates low toxicity of nano diamond.

Additional information that would be of interest concerns dustiness (option 6) and the choice of appropriate metrics (option 21) to facilitate downstream comparisons with other nanomaterials and thus read-across and other non-testing methods. To this end the codification of the other endpoints in the official dossier would also provide a good example for a comparatively low toxicity nanomaterial.

Additional data available through the option scenario vs. the baseline scenario for TiO_2 NPs:

As discussed above nano diamond is an example for a nanomaterial that significantly profits from the implementation of the options. Every one of the nine options would yield additional data. For a new nanomaterial, information from options 6, 11, 12, 13, 16, 17, 18, and 19 could be crucial for risk assessment. The fulfilment of option 21 in particular, and to some degree of the other options as well, yields important information for future read-across and other non-testing approaches and thus holds the promise of reducing the cost of registration of new nanomaterials in the future.

7.3 Overall Impacts of the case studies

The three case studies highlight several information deficits in the unmodified REACH text.

- The information acquired for risk assessment is not entirely dependent on the toxicological profile of the nanomaterial in question.
  Looking at the first two case studies – nano TiO_2 and nano ZnO – it becomes apparent that although the requirements for the two nanomaterials for characterisation according to REACH are the same (due to both being grouped in the same, high tonnage band), the information yield is different. This is due to the fact that the unmodified REACH text allows for the waiving of tests due to lack of water solubility and for the waiving of long term toxicity tests – depending on the experimental design – due to lack of short term toxicity. Both aspects influence the data situation in the case of nano TiO_2 disregarding the fact that important toxicological data can be obscured. Nano ZnO is less influenced because of the solubility and the obvious short term, toxicological effects.
  Nanomaterials could have long term effects without displaying obvious short term toxicity. Their water solubility is sometimes not as important as their dispersibility in water especially when considering surface modifications that favour dispersion and persistence.
  Both factors (water solubility; long-term testing in spite of lack of short term toxicity) are taken into account when the option scenario is implemented along with important other data sets such as: *in vitro* mutation studies, dustiness, and the choice of appropriate metrics.
- Comparing the first two case studies with the third it becomes apparent that significantly less information is available for nano diamond. Similarly to the above, the water solubility and the lack of short term toxicity contribute to some of the information deficits. Additionally however the very low tonnage band of nano diamond results in the lack of information for many of the toxicological aspects in the dossier for this nanomaterial. It is stressed here explicitly that the grouping of information needs in REACH according to tonnage band is not subject to any of the options discussed in this or the previous texts of this project. Nonetheless it is also important to note that the issue of creating nanospecific information requirements at nanospecific tonnage levels is debated intensively in member states of the European Union.
  Nanomaterials can be toxic in low concentrations especially when considering that the individual nanoparticles can be surface coated with a variety of unintentional modifications (see Annex 3). As many nanomaterials are used in highly specialized applications it is imaginable that their production volumes will remain low.

Applying the option scenario will significantly ameliorate the data situation within dossiers containing nanomaterials. Concomitantly the more comprehensive and hopefully more standardized data (option 21) will allow for the efficient application of non-testing methods to lower the cost of introducing new nanomaterials into dossiers for REACH.

8 Impact assessment for the baseline scenario and the option scenario applied to the total market for nanomaterials

This chapter presents the overall impacts of the options on the market for nanomaterials for industry, on human health and the environment. In addition wider opportunity costs and benefits as well as effects on small and medium sized companies are assessed. The impact assessment focuses primarily on the option scenario but considers as well the baseline scenario.

8.1 Extrapolation of impacts on industry

Expected additional costs for industry, resulting from a possible implementation of the proposed options in the REACH Regulation are extrapolated from the three selected case studies in Chapter 7 to the total European market. Each of these case studies can be considered to be representative for a relevant share of the total nanomaterial market in the EU, and therefore for a certain number of expected REACH registrations of nanomaterials. Between 500 and 2,000 nanomaterials are expected to be placed on the EU market based on an estimation in the Impact Assessment of the REACH Implementation Project on Substance ID for Nanomaterials prepared by Risk & Policy Analysts Limited (RPA) on behalf of the European Chemical Industry Council (CEFIC) in March 2012. These figures have been used for the subsequent assessment of costs, assuming that they refer to 500 and 2,000 different nanomaterials and/or different nanoforms which are affected by registration obligations (annual production volume per manufacturer or importer > 1 ton) under REACH.

REACH information requirements and therefore also impacts of the proposed options depend on the tonnage band a nanomaterial has to be registered for. Therefore, as a first step we elaborate a scenario which provides information on the number of expected registration dossiers in each of the four REACH tonnage bands.

Nanomaterials cover a wide range of different materials. Based on the market volume, the main categories include carbon based nanomaterials (e.g. carbon black, carbon nanotubes), inorganic non-metallic nanomaterials (e.g. synthetic amorphous silica, aluminium oxide, titanium dioxide), metal nanoparticles (e.g. nano silver) and organic, macromolecular or polymeric particulate materials (e.g. dendrimers). Nanomaterials often exist in a variety of forms and modifications (e.g. surface coated materials) with individual properties or uses.

The decision whether particle size and/or surface treatment has to be considered as an identifier or a characteriser within the scope of REACH has an impact on costs for industry resulting from REACH obligations for nanomaterials after implementation of the proposed options. The available ECHA guidance[15] states that the registration dossier should include the information of the substance in both the bulk form and the nanoform when the registrant manufactures or imports the substances in both forms (p. 26/27 of the document) but does not specify whether size or surface modification triggers a different identity and consequently a separate registration. Therefore, the registration strategy is quite complicated for surface treated nanomaterials. Controversial discussions arise, as to whether these nanoforms should be treated under REACH as mixtures or not. If so, the substance itself and the coating material would be affected by registration obligations. For the purpose of this study, as a worst case scenario the project team assumed that every single form of a nanomaterial (e.g. surface treated

[15] ECHA Guidance on Registration – Version 2.0 from May 2012 (Reference: ECHA-12-G-07-EN)

material) has to be considered as an individual substance, resulting in registration obligations (registration dossiers). This approach might be valid as long as no further clarification is provided.

If the bulk and the nano forms of a substance are registered within one dossier, the overall tonnage band of all forms have to be taken into account, irrespective of the tonnage band of the nano form (e.g. bulk form > 1,000 t/y and nanoform 1-10 t/y). The information requirements for the higher tonnage band of the bulk material would consequently also have to be applied to the nanoform, requiring the registrant to provide extensive and expensive information on the nanoform in cases where a read-across from the bulk form to the nano form or between two forms is not considered as justified.

The figures shown in Table 8-1 give a distinct overview on worldwide production volumes of ten common nanomaterials – the presented figures are based on a survey among worldwide companies and have been summarised in a recent report[16].

Table 8-1 Overview on the industrial production of ten engineered nanomaterials worldwide and in Europe Source: Piccinno et al. (2012)

Engineered nanomaterial (ENM)	Worldwide (t/year) Median and 25/75 percentile	Europe (t/year) Median and 25/75 percentile
TiO_2	3,000 (550 – 5,500)	550 (55 – 3,000)
ZnO	550 (55 – 550)	55 (5.5 – 28,000)
SiO_2	5,500 (55 – 55,000)	5,500 (55 – 55,000)
FeO_x	55 (5.5 – 5,500)	550 (30 – 5,500)
AlO_x	55 (55 – 5,500)	550 (0.55 – 500)
CeO_x	55 (5.5 – 550)	55 (0.55 – 2,800)
CNT	300 (55 – 550)	550 (180 – 550)
Fullerenes	0.6 (0.6 – 5.5)	0.6 (0.6 – 5.5)
Ag	55 (5.5 – 550)	5.5 (0.6 – 55)
Quantum dots (QDs)	0.6 (0.6 – 5.5)	0.6 (0.6 – 5.5)

Table 8-1 gives a brief overview of several nanomaterials placed on the European market in higher tonnage bands – unfortunately the overview makes no distinction between untreated and surface treated nanomaterials.

According to Malkiewicz et al. (2011)[17] only some rare nanomaterials such as praseodymium oxide, erbium oxide and gallium antimonide or strontium titanium oxide were found to be pre-registered when searching the ECHA databases. Five entries for substances described specifically as nanomaterials (nano in the name) were found for the registration deadline 2018, thus implying production volumes below 100 tonnes: nano silver, carbon nanobutes and phthalocyanine-fullerene compound. Further attempts to gather and analyse information on the existence of nanomaterials on the market and their production volumes including a search of different inventories of nanotechnology-based consumer products currently on the market and various and peer reviewed articles did not provide more relevant data. These

16 F. Piccinno et al.: Industrial production quantities and uses of ten engineered nanomaterials in Europe and the world"; J Nanopart Res (2012) 14:1109

17 Katarzyna Malkiewicz, Michala Pettitt, Kenneth A. Dawson, Arho Toikka, Sven Ove Hansson, Janne Hukkinen, Iseult Lynch, Jamie Lead (2011) Nanomaterials in REACH – Project Report. Available at http://www.steptoe.com/assets/htmldocuments/SKEPP%202011%20Nanomaterials_in_REACH_report_15082011.pdf

findings of only few (pre-)registered nanomaterials are in accordance with the results of the JRC NANO SUPPORT project report where it was concluded that nanomaterials were not adequately addressed in registration dossiers from 2010 and the scope of these dossiers has in many cases not been adequately described to conclude whether nanomaterials were covered or not.

Nanomaterials can be functionalised with a variety of surface treating materials which introduce completely new and desirable properties. Nanomaterials which are functionalised with similar surface treating substances (e.g. silanes, amines) can be allocated into formgroups. For instance, silanes which have the same functional group (e.g. alkyl chains) and which only differ in the alkyl chain length, are applied as surface treating substances for nano TiO_2, and can be allocated into one formgroup. The functionalised nanomaterials can be subdivided into several formgroups (classes).

This approach derives from the application of the group concept and read-across approach, as defined in Chapter 1.5 of Annex XI of the REACH Regulation. According to this chapter, substances may be considered as a group, or 'category' of substances if physico-chemical, toxicological and ecotoxicological properties of substances are likely to be similar or follow a regular pattern as a result of structural similarity. Application of the group concept requires that physico-chemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s) within the group by interpolation to other substances in the group (read-across approach). This reduces the need to test every substance for every endpoint.

It should however be pointed out that the introduced grouping approach for the assessed nanomaterials should be applied with caution. Due to the fact that properties of the surface treated nanomaterial dominate the effect and the properties and stability of the surface treating material are dependent on the surrounding conditions or its quality (coating defects), every grouping and read-across approach should be considered carefully and should be based on experts' opinions. As it has already been stated by SCENIHR[3], a case by case approach is recommended in order to assess risks appropriately. This recommendation has also been considered in the assessment of registration costs by also indicating those cost ranges which would be incurred without applying the grouping and read-across approach, i.e. resulting costs after testing every single nanomaterial.

Based on the information provided by experts of the Steering group, it can furthermore be proposed that a broader range of nanoforms is placed on the market for higher manufactured tonnage bands of nanomaterials. Conversely it can be argued that for nanomaterials which are used only in niche applications and are therefore manufactured only in much lower quantities (1-10 t/y) the available range of formgroups is also limited and manageable. Due to reasons of simplification, the project team assumes for the current assessment that

- a large part of each surface-coated nanomaterial is manufactured in the lowest tonnage band (1-10 t/y) and
- for each nanosubstance, 10 different nanoforms/classes are available. For instance, one nanoform would be the untreated nanoform of a substance whereas the remaining nine formgroups could be subdivided into functional groups with which the nanomaterial has been derivatised (e.g. silanes, amines, etc.). The aspect of forming a group plays a key role when applying a read-across approach among the nanomaterials within the same formgroup since testing costs can be reduced significantly.

The first presumption might be substantiated by the fact that due to the current worldwide economic crisis investments in nanotechnologies may be lacking which in turn might have negative implications on enhancement of innovation or competitiveness of the nanotechnology sector.

Figure 8-1 outlines the methodology and the simplified groupings among the postulated nanoforms which were the basis for further assessment:

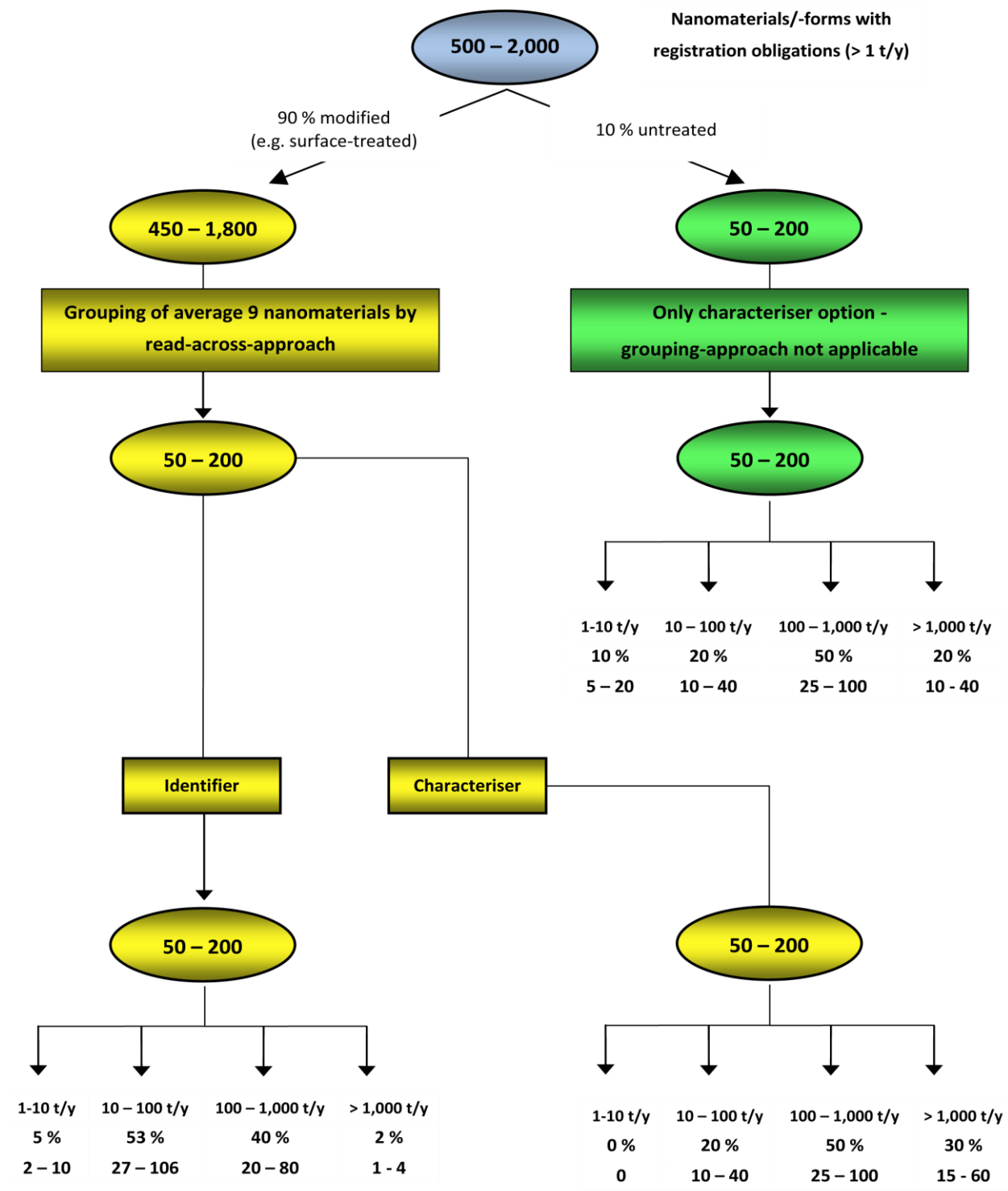

Figure 8-1 Proposed overview on nanomaterials that are assumed to be affected by registration obligations and proposed grouping approach among 500 – 2,000 nanomaterials.

Costs, correlating to option scenario:

From the 500 to 2,000 nanomaterials placed on the EU market as estimated by Risk & Policy Analysts Limited (RPA)[8] it is not known whether all of them might be affected by registration obligations under REACH or not. In order to introduce a starting point for the further proceeding of cost assessments, the project team assumes that all of the indicated 500 to 2,000 nanomaterials are manufactured in volumes of at least more than 1 t/y and that consequently all of the nanomaterials would be affected by registration obligations under REACH. The postulated range should be interpreted with caution, especially when this range is set in relation to the number of already registered substances by the first deadline in 2010 (approximately 4,500 substances; HPV chemicals and CMR substances). The final number of registered nanomaterials might finally be lower after having implemented clear registration advice especially for surface treated nanomaterials. This and other aspects, which influence the number of affected nanomaterials and the resulting costs, are discussed in the uncertainty analysis.

According to the grouping approach, as introduced above in Figure 8-1, a further simplification is introduced that approximately 10 % of the affected nanomaterials may represent non-surface-treated nanomaterials. The Guidance on Registration requires information on bulkform and nanoform of a substance to be included in one dossier – consequently, submitted dossiers would have to be updated by taking into account information on the nanoform. Based on this simplification, data for 50 to 200 nanoforms would have to be submitted together with information on the corresponding bulk form, if existing. The costs for different types of registration covering bulk and untreated or surface treated nanoforms in one or in separate dossiers are presented below.

Additional costs for registering bulk form and untreated nanoform in one dossier

Taking into account that information requirements for nanomaterials are calculated on the basis of the added tonnage bands of the nanoform and the corresponding bulk form, and considering the aforementioned overview on the already manufactured nanomaterials EU-wide, the project team assumes a distribution of lead dossiers as indicated in Table 8-2:

Table 8-2 Estimated additional costs for 50 – 200 untreated nanomaterials (valid for lead dossiers that include bulk and nanoform)

50 – 200 nanomaterials/-forms				
Tonnage band	1 – 10 t/y	10 – 100 t/y	100 – 1,000 t/y	> 1,000 t/y
Percentage distribution	10 %	20 %	50 %	20 %
Resulting lead dossiers	5 – 20	10 – 40	25 – 100	10 – 40
Testing costs per nanoform (€)	**45,500 – 64,341**	**61,600 – 83,663**	**128,450 – 210,841**	**136,650 – 229,617**
Final costs (€)	**227,500 – 1,286,820**	**616,000 – 3,346,520**	**3,211,250 – 21,084,100**	**1,366,500 – 9,184,680**
Overall final costs (€)	**5.5 – 35 million**			

Given that 10 % of the initially postulated 500 – 2,000 nanomaterials are untreated nanoforms the updating process would lead to additional costs of between **€5.5 million** and **€35 million** (accumulated final costs, according to the last row of Table 8-2.) if the majority of the updated lead dossiers (50 %) are assumed to be in the tonnage band 100 – 1,000 t/y. Testing of each nanomaterial would entail costs of **€50 million and €315 million.** The lead dossier includes all the required physico-chemical, eco-toxicological and toxicological information which is submitted on behalf of all members of a joint registration. It should in this context be pointed out that the extent of the information requirements correlates to the maximum tonnage band of the joint submission and is triggered by volumes of a legal entity, but is not triggered by aggregated volumes of a joint submission.

Paragraph 3 of Article 11 and Paragraph 2 of Article 19 (dealing with joint submission of data for isolated intermediates) provides the co-registrant with the possibility to opt-out from the joint submission under certain provisions. Disproportionate costs, disclosure of submitted confidential information or disagreement with information selected by the lead registrant are the three cases which justify submitting information separately, which should normally be submitted jointly. The extent of opt-outs cannot be assessed quantitatively since the exact number of co-registrants who would chose the opt-out-approach is not predictable.

Additional costs for registering bulk form and surface treated nanoform in one dossier

The remaining 450 – 1,800 nanomaterials, which the project team all considers as surface treated, can be registered in two different ways: either as part of an updated lead dossier which also includes information on the bulk form of the substance or in a separate lead dossier. As already assumed before, the remaining 450 – 1,800 nanomaterials can be subdivided in 9 formgroups/classes in dependence of the surface treating substance. Within each formgroup, read-across approaches could be applied if the surface treating substances exhibit similar physico-chemical and/or (eco)toxicological properties. It would therefore be absolutely sufficient and cost-efficient to perform tests with the most reactive nanoform within a formgroup/class and to use these testing results as a basis for information requirements for the remaining members of the formgroup/class. If information on the bulk form of a substance and information on all surface treated nanomaterials of the same substance have to be included in one dossier then all the manufactured tonnages would be added up and the resulting tonnage band would define the information requirements according to the correlating Annexes in REACH. It is the project team's assumption that within this process, no lead dossier for a tonnage band between 1-10 t/y would be elaborated and submitted – a more detailed overview of assumed distribution of affected lead dossiers is given in Table 8-3. As has already been pointed out, the lead dossier includes all information requirements related to the maximum tonnage band within the joint submission. The extent of the information requirements is triggered by the aggregated volume of a legal entity, but is not triggered by aggregated volumes of a joint submission.

Table 8-3 Estimated costs for elaborated formgroups within tonnage bands (valid for dossiers that include information on bulk form and surface treated nanoforms of a substance)

50 – 200 formgroups/classes (correlating to 450 – 1,800 nanoforms, subdivided in 9 formgroups/classes)				
Tonnage band	1 – 10 t/y	10 – 100 t/y	100 – 1,000 t/y	> 1,000 t/y
Percentage distribution	0%	20%	50%	30%
Resulting formgroups	0	10 – 40	25 – 100	15 – 60
Testing costs per nanoform/formgroup (€)	**45,500 – 64,341**	**61,600 – 83,663**	**128,450 – 210,841**	**136,650 – 229,617**
Final costs (€)	**0**	**616,000 – 3,346,520**	**3,211,250 – 21,084,100**	**2,049,750 – 13,777,020**
Overall final costs (€)	**6 – 38 million**			

The calculated number of formgroups would be included as part of submitted information in the lead dossier including information on the bulk form of the substance. Table 8-3 lists the resulting calculated costs for each tonnage class. The final Table A2-1 in Annex 2 lists resulting costs per nanoform which in this case can also be applied to each formgroup.

Additional costs between **€6 million** and **€38 million** (accumulated final costs, according to the last row of Table 8-3) are expected for 450 – 1,800 surface treated nanoforms for each of the 9 different formgroups. If each member of a formgroup had to be tested separately and assessed according to the information requirements of Annex IX and X the resulting testing costs would be nine times higher (between **€47 million** and **€300 million** for the tonnage bands > 100 t/y; between **€54 million** and **€340 million** for Annex VII – X). These tonnage bands are based on the assumption that the majority of lead dossiers (> 50%) include information on all forms of a substance (bulk form and surface treated nanoforms) and cover the tonnage band between 100 – 1,000 t/y. Costs can be significantly reduced by using the gathered testing results of e.g. the most reactive nanoform for read-across approaches. This approach can, however, only be performed if the testing of only one representative within one formgroup is considered as sufficient in order to fulfil the information requirements of the remaining members of the same formgroup, and if the surface treated nanoforms cannot be registered as mixtures.

Additional costs for registering surface treated nanoforms separately

If the surface treated nanoforms are registered in separate lead dossiers then read-across approaches can also be applied in order to fulfil the information requirements, leading to lower testing costs. In contrast to the aforementioned cases the project team assumes that the major part of submitted lead dossiers for nanomaterials will shift to the lower tonnage bands (10 – 100 t/y; see Table 8-4), since only the manufactured tonnages of the nanomaterial are taken into account for the resulting information requirements.

Table 8-4 Estimated costs for elaborated formgroups within tonnage bands (valid for dossiers that only include information on surface treated nanomaterials).

50 – 200 formgroups/classes (correlating to 450 – 1.800 nanoforms, subdivided in 9 formgroups/classes)				
Tonnage band	1 – 10 t/y	10 – 100 t/y	100 – 1,000 t/y	> 1,000 t/y
Percentage distribution	5%	53%	40%	2%
Resulting formgroups	2 – 10	26 – 106	20 – 80	1 – 4
Testing costs per nanoform/formgroup (€)	**45,500 – 64,341**	**61,600 – 83,663**	**128,450 – 210,841**	**136,650 – 229,617**
Final costs (€)	**91,000 – 643,410**	**1,601,600 – 8,868,278**	**2,569,000 – 16,867,280**	**136,650 – 918,468**
Overall final costs (€)	**4 – 27 million**			

As can be seen from Table 8-4, for the highest tonnage band only 1-4 lead dossiers are expected including information on a broad range of nanomaterials (9 functional classes). One of the four lead dossiers might be the already submitted dossiers for TiO_2 if a separate lead dossier for nano TiO_2 is elaborated in the future.

Performing the testing regime as proposed in the option scenario would provide its cost structure, as indicated in the last two rows of Table 8-4 (based on calculated costs for the suboption "size as identifier", as assessed exemplary for the three tonnage bands in Annex 2):

Registering surface treated nanoforms separately and applying read-across would lead to final testing costs of between **€4 million** and **€27 million** (accumulated final costs, according to the last row of Table 8-4) assuming that the major part of the lead dossiers is submitted in the tonnage band between 10 – 100 t/y. Without the outlined grouping/read-across the resulting testing costs would rise up to **€80 million** only for this tonnage band. The project team would once again like to point out the fact that the indicated ranges of nanomaterials which might be affected by registration obligations are assumptions, since a detailed overview on the EU market for nanomaterials is not provided. Given the current financial crisis in Europe and worldwide, which also might have negative implications for investments in nanotechnologies in Europe, it can also be assumed that the share of surface coated nanomaterials in the lowest tonnage band might be significantly higher than initially postulated. However, this aspect can only be mentioned in a qualitative manner and has furthermore been addressed in the uncertainty analysis.

Comparison of these figures (**€4 million** and **€27 million**) with the ones assessed for the case that surface treated nanomaterials would be registered within the same dossier as the bulk form (**€6 million** and **€38 million**), demonstrates quite clearly that this registration strategy would lead to cost reductions of approximately 27 %. Higher-tier studies (according to the information requirements of Annex IX and X) imply higher testing costs, however they also lead to a gain in additional information on e.g. (eco)toxicological behaviour. Separate registration of surface treated nanomaterials could lead to an information gap with regard to the aforementioned (eco)toxicological behaviour, since information requirements of the lead dossier are only triggered by the volume of the surface treated nanomaterial.

At this stage it should once again be explicitly pointed out that at the moment there are no clear

indications of how surface treated nanomaterials should be addressed under REACH (mixtures or phase-in or non-phase-in) resulting in completely different registration obligations.

Total costs for industry after implementation of option scenario

In order to assess the total costs for industry after implementation of the 9 options, as outlined in the option scenario, resulting costs are cumulated among concerned companies for a time period until 2022. According to the project team's postulated distribution of nanomaterials (see Table 8-1), 50 – 200 nanomaterials are supposed to be untreated. The remaining 450 – 1,800 surface treated nanomaterials can be allocated into 9 formgroups. Afterwards, two scenarios are possible: submission of a lead dossier which includes information on the bulk form of a substance and information and surface treated nanomaterials, or submission of a separate lead dossier which includes information on surface treated nanomaterials only.

The total costs for the industry, allocated option-wise, can be outlined as follows:

Table 8-5 Total costs for industry, allocated option-wise, after implementation of 9 options of option scenario

Option	Description of the option	Additional costs (1,000 €)
6	Include information on dustiness	210 - 640
11	Require acute toxicity data for the most relevant route of exposure	1,280 – 9,400
12	Change "particles" to "nanoparticles" for repeated dose toxicity studies (inhalation)	0
13	Require non-bacterial in vitro gene mutation study	2,000 – 9,600
16	Consider water solubility in relation to test waiving	5,090 – 29,540
17	Specify that long term testing should not be waived based on lack of short term toxicity	1,800 – 15,270
18	Specify that algae testing should not be waived based on insolubility	0
19	Require that testing on soil and sediment organisms is prioritised	770 – 7,660
21	Require considerations of most appropriate/relevant metric with preferable presentation in several metrics	200 – 800
	Resulting additional costs for industry:	**11,400 – 73,000**

Splitting of total costs (**€11 million** – **€73 million**) on single options reveal a broad range of costs with which the industry might be faced.

The calculated cost range is based on the assumption that extensive grouping and read-across approaches will be applied. However this approach would be applied with care and would additionally be based on experts' opinions. If it is considered that the outlined grouping approach is not applicable, the

resulting testing costs may increase due to a higher number of nanomaterials which would have to be assessed.

As already outlined in the introduction, the assessed costs cover a period until the year 2022. Similar costs per lead dossier would arise if after 2018 lead registration dossiers would have to be elaborated which include information on nanomaterials. However, it should be noted that these costs are not quantifiable since no exact predictions on the affected number of nanomaterials can be made. It can reasonably be argued that registrants would profit from experiences gained in the meantime by registration of nanomaterials. Furthermore, it is expected that by this time updated/new testing methods are available which specifically address the characterisation of nanomaterials.

Costs, correlated to baseline scenario:

In the course of this project, the project team has also assessed compliance costs for options which are regarded to be already covered by the baseline. Referring to the aforementioned scenario that 10 % of the 500 – 2,000 nanomaterials can be regarded as untreated nanomaterials, the resulting compliance costs can be outlined in Table 8-6 (the corresponding costs per nanoform can be seen in Table A4-1 in Annex 4):

Table 8-6 Estimated compliance costs for untreated nanomaterials (valid for dossiers that include information on bulk form and untreated nanoforms of a substance)

Compliance costs for 50 – 200 nanomaterials/-forms				
Tonnage band	1 – 10 t/y	10 – 100 t/y	100 – 1,000 t/y	> 1,000 t/y
Resulting lead dossiers	5 – 20	10 – 40	25 – 100	10 – 40
Testing costs per nanoform (€)	**39,050 – 54,830**	**48,633 – 77,997**	**110,633 – 257,497**	**110,633 – 257,997**
Final costs (€)	**195,250 – 1,096,600**	**486,330 – 3,119,880**	**2,765,825 – 25,749,700**	**1,106,330 – 10,319,880**
Overall final costs (€)	**4,5 – 40 million**			

As advised in the Guidance on Registration[18], a registrant placing different forms (e.g. bulk form and nanoform) of a substance on the market has to include information on these forms in the registration dossier. Taking this advice into practice would lead to final compliance costs of between **€4,5 million** and **€40 million**. Since the tonnages of the different forms (bulk and nanoform) have to be taken into account, the project team assumes that the major part of the affected lead dossiers might be shifted to higher tonnage bands.

Compliance costs for the remaining 450 – 1,800 nanoforms would lead to costs of between **€33 million** and **€270 million** if nanomaterials (see Table 8-7) are registered in a separate dossier and if the testing regime is applied to every single nanomaterial. In contrast to the option scenario, not all of the data in the baseline scenario can be used for a grouping/read-across approach as outlined in detail in the

[18] ECHA Guidance on Registration – Version 2.0 from May 2012 (Reference: ECHA-12-G-07-EN)

examples above. After an examination of the information requirements of the different options, the project team concludes that only required tests in options 4, 8, 10, 14, 15 (3.4, 4.2, 4.4, 4.8 and 4.9) can be used as a basis for a read-across or grouping approach. According to the introduced grouping-approach (see Figure 8.1), affected nanomaterials can be allocated in 9 formgroups. Within these formgroups it is postulated to apply the provisions of the option scenario on one representative nanomaterial (e.g. the most reactive form) and to apply extensive read-across approach on the remaining members of the same formgroup. After applying a grouping approach (into formgroups/ classes) the resulting compliance costs would be reduced significantly to between **€17 million** and **€120 million**.

Table 8-7 Estimated compliance costs for elaborated formgroups/classes (valid for separate dossiers that only include information on surface treated nanomaterials)

Compliance costs for 450 – 1,800 surface treated nanoforms				
Tonnage band	1 – 10 t/y	10 – 100 t/y	100 – 1,000 t/y	> 1,000 t/y
Percentage distribution	5%	53%	40%	2%
Resulting nanoforms	22 – 90	238 – 954	180 – 720	9 – 36
Testing costs per nanoform (€)	**39,050 – 54,830**	**48,633 – 77,997**	**110,633 – 257,497**	**110,633 – 257,997**
Final costs (€)	**702,900 – 4,934,700**	**11,817,819 – 74,409,138**	**19,913,940 – 185,397,840**	**995,697 – 9,287,892**
Final costs after grouping:	**450,900 – 3,434,700**	**8,361,819 – 57,449,138**	**7,433,940 – 57,717,840**	**371,697 – 2,887,892**
Overall final costs (€)	**€33 million – €270 million / €17 million – €120 million (grouping/read-across)**			

Comparison of costs with expected revenues from the market for nanomaterials

In order to emphasise the financial impact on the industry for the period until 2022, the calculated costs are being set in correlation to the expected revenues for the European market for nanomaterials by the same target time of ten years.

There are several reports or studies available in which the worldwide turnover for nanomaterials has been forecasted for the forthcoming years. For instance, BCC Research published a report in September 2012 ("Nanotechnology: A Realistic Market Assessment"), in which worldwide sales of nanomaterials are expected to be in the range between $15.9 billion in 2012 and $37.3 billion in 2017.[19]

Figures of a similar dimension have also been mentioned in a recently published European Commission's MEMO ("Nanomaterials: Commission proposes case by case approach to assessment").[20] According to this MEMO "the total annual quantity of nanomaterials on the global market is around 11 million tonnes, with a market value of roughly €20 billion".

Unfortunately neither of the quoted reports includes figures which are allocated to the European market for nanomaterials. In order to fill this information gap, the project team referred to CEFIC´s facts and

[19] http://www.bccresearch.com/report/nanotechnology-market-applications-products-nan031e.html

[20] "Nanomaterials: Commission proposes case by case approach to assessment"; Reference: MEMO/12/732 (http://europa.eu/rapid/press-release_MEMO-12-732_en.htm)

figures for the "European chemical industry in worldwide perspective"[21], which are published annually. According to the recent publication, the European Union accounts for 19.6% of total chemicals sales worldwide. Since no other information on the European Union's share of the worldwide market for nanomaterials is available, the project team assumes that the share is proportional to the aforementioned share (19.6%) of total chemicals sales worldwide.

Taking this premise into account, the project team assumes that the European Union would place nanomaterials on the worldwide market worth **€4 billion** (19.6% of €20 billion). For the forthcoming 10 years, the European Union's market for nanomaterials would contribute by placing nanomaterials on the worldwide market worth **€40 billion** (linear progress within this time period). According to the already quoted report by Risk & Policy Analysts Limited (2012)[22], between 500 and 2,000 nanomaterials are estimated to be placed on the European market. This estimation has been provided by an industry steering group that has been consulted by RPA in the course of the project elaboration. Since the aforementioned range has been used as a basis for the impact assessment, these 500 to 2,000 nanomaterials will contribute to the postulated revenues worth **€40 billion** by 2022.

Uncertainty analysis:

The expected costs for industry from implementation of the proposed options as presented above are associated with a relatively high degree of uncertainty. The following discussion addresses these uncertainties which are mainly based on data gaps and different interpretation of the REACH Regulation.

- **Size as characteriser/identifier**

  As already discussed in previous chapters and in many other reports and publications, the question of whether to consider particle size as an identifier or characteriser within the scope of REACH has an impact on the REACH obligations for nanomaterials after implementation of the proposed options, and therefore also on the costs for industry. The recently updated Guidance on Registration has addressed the registration of the bulk and nanoform of a substance within the same registration dossier. While this approach can be considered as quite reasonable for untreated nanoforms of a substance, the advised registration strategy for surface treated nanoforms still remains unclear. These aspects have been considered separately by assessing costs for industry in both sub-cases (updating/elaborating of lead dossiers which include information on the bulk form and the (surface treated) nanoform and elaboration of lead dossiers which include only information on nanoforms). Both aspects have drastic impacts on the overall tonnages, the information requirements and consequently on the final testing costs.

- **Surface treated substances**

  According to FAQ No. 6.3.8 in the Frequently Asked Question (FAQ) section of the ECHA webpage[23], the following applies to surface treated substances: „The surface treatment of a substance is a 'two

[21] "The European chemical industry in worldwide perspective - Facts and Figures 2012" (http://www.cefic.org/Documents/FactsAndFigures/2012/Chemicals-Industry-Profile/Facts-and-Figures-2012-Chapter-Chemicals-Industry-Profile.pdf)

[22] Risk & Policy Analysts Limited. (2012). Impact Assessment of the REACH Implementation Project on Substance ID for Nanomaterials. Norfolk.

[23] Frequently Asked Questions about REACH – Version 5.2 – 27 November 2012: http://echa.europa.eu/web/guest/support/faqs/frequently-asked-questions/frequently-asked-questions-about-reach

dimensional' modification of macroscopic particles (chemical reaction between the functional groups only on the surface of a macroscopic particle with a substance). For a macroscopic particle this kind of modification means a reaction of only a minor part (surface) with the surface treating substance, i.e. most of the macroscopic particle is unmodified ...".

This issue has also been addressed in the RIP-oN 1 report: according to the arguments laid out therein, surface treatment of nanomaterials has a disproportionally higher impact on nanomaterial properties due to the higher specific surface area than that of bulk materials. It is ECHA´s point of view that the aforementioned FAQ on surface treatment is not a priori applicable to nanomaterials. The FAQ was developed without reference to nanomaterials and cannot be considered to be agreed for nanomaterials. However, this issue is still subject to intense discussions between ECHA and e.g. CEFIC. Referring to statements of ECHA experts in Appendix 2 of the RIP-oN 1 report, it can be inferred that surface treated nanomaterials cannot be registered by separate registration of the nanomaterial and the surface treating substance.

There has not been any conclusion yet on whether the advised registration strategy for surface treated substances, as outlined in FAQ 6.3.8, is also applicable on surface treated nanomaterials. In the absence of a clear guidance, the project team has considered separate registrations for surface treated nanomaterials and calculated the consequences of the proposed options. Based on this assumption a number of nanoforms (450 – 1,800) with registration obligations up to 2018 seems to be realistic. If the outlined procedure, published by ECHA in the FAQ section, is applied to nanomaterials in future, a significantly lower number of nanomaterials with registration obligation are expected, as surface treated nanomaterials will be covered by separate registration of the basis substance and the surface treating substance. If surface treated nanomaterials are regarded as mixtures leading to separate registration of surface treated nanomaterials, the costs for industry to implement the proposed options to adapt the REACH regulation to nanomaterials are much lower than estimated in this report, as they will be registered at lower tonnage level or some may not even reach the threshold for registration.

- **Definition of nanomaterial**

The recommendation for a definition of nanomaterial proposed by the European Commission[5] has not yet been implemented in the REACH Regulation. Therefore, it is still unclear which materials are considered to be nanomaterials within the scope of REACH. The study is based on the assumption that the published recommendation of a definition will be accepted and integrated into the REACH system. If this is not the case, the assumed number of nanomaterials with registration obligations (500 – 2,000) may be much lower than expected, and calculated costs for implementation of the options may be overestimated in this report.

- **Limited information on the European market for nanomaterials**

Currently, there is no detailed information about the European market for nanomaterials publicly available. In future, a European register for nanomaterials – as currently under discussion – could provide more detailed information on nanomaterials used in different products on the market. So far, neither publicly available databases on products containing nanomaterials, nor the ECHA databases provide suitable information. These findings are in accordance with the results of the JRC NANO SUPPORT Project Report, in which it was concluded that nanomaterials were not adequately addressed in registration dossiers from 2010 and the scope of these dossiers has in many cases not

been adequately described to conclude whether nanomaterials are covered or not. Hence, precise and valid information on volumes and shares of nanomaterials on the European market, which could be used for extrapolation, were only partially available for the most common nanomaterials. Nevertheless, some information on the global market for nanomaterials and the global chemical market share of European companies is already available and the project team has used this information to estimate the number of nanomaterials with registration obligations in the different REACH tonnage bands. Estimations of the market size need to be taken with a certain degree of caution, although the general patterns of the estimates (i.e. order of magnitude of tonnage and market value, and relative size of market between the various materials) seem to be reliable based on the available information.

- **Registration strategies**

Registration strategies of different consortia may vary considerably, depending on the substance type, and therefore the strategy for fulfilling data requirements according to REACH for similar substances can differ significantly (e.g. intensive or no read-across); this has a major impact on the costs caused by single options. The project team has assumed that read-across among representatives of the same formgroup might be applied as a standard procedure in order to fulfil the information requirements and thereby reducing testing costs. The registration dossiers selected as case studies are considered to be representative, and registrants followed a common and reliable strategy to fulfil data requirements. It is therefore assumed that the case studies allow a reliable extrapolation to the European market for nanomaterials, although it is possible that if different registration strategies become state of the art in future, the calculated costs related to implementation may differ significantly. This could be the case if scientific evidence proves that nanomaterials do not usually represent a higher risk than bulk materials, as their (eco)toxicological behaviour is comparable. In this case registrants will make intensive use of read-across between different forms of substances, having an impact on the costs arising from implementation of the proposed options. The read-across approach and the prior application of grouping derive from the requirements that are defined in Chapter 1.5 of Annex XI of the REACH Regulation. However, the introduced grouping and read-across approach for the assessed nanomaterials should be applied carefully and should be based on experts' opinions. As it has also been stated in the European Commission´s MEMO, a case by case approach is recommended in order to assess the risks of nanomaterials appropriately.[4] This statement may also be applicable to the read-across approach.

- **Costs for laboratory studies**

Costs for laboratory studies with nanomaterials are not yet known, since routine analytical methods have not yet been implemented. The case studies are based on the assumption that (eco)toxicological studies with nanomaterials will not be more expensive than laboratory studies with bulk materials. There is currently no uniform pricing policy, as has been revealed by an inquiry among a few laboratories (for more details please refer to Annex 2 - case studies).

Costs for additional observations, like extended pathology/histology and analysis of BAL fluid (Bronchoalveolar fluid) for inhalation studies, proposed in some of the options, are not known, and only rough estimations could be used as a basis for the calculation. Although there is some uncertainty regarding costs for studies with nanomaterials, the estimations made seem to be realistic, and compared to other uncertainties of this assessment these effects are considered to be

of less influence.

In order to assess resulting testing costs quite accurately, the project team decided on using both a lower limit and a higher limit for the assessed ranges of costs. The lower limit is based on current laboratory´s prices, as received by various laboratories with which the project team has cooperated in the course of elaborating several lead dossiers. The higher limit refers to prices which are based on a paper by Fleischer et al.[24]. These prices however are costs for tests, which are not specifically for nanomaterials. Several of the assessed tests in the Fleischer paper lack the automated routine testing methods for nanomaterials and are therefore addressed in the OECD´s WPMN (Working Party on Manufactured Nanomaterials)[25]. In the recommendation, several aspects of appropriate assessment of nanomaterials (incl. characterisations as manufactured, as dosed and as taken up, and also in three metrics and all this for various nanoforms) are covered.

8.2 Impacts on Human Health and the Environment

Based on the REACH Extended Impact Assessment (EIA)[26], impacts on human health and environment are assessed by considering other relevant studies as well. A quantitative impact assessment is only possible for human health effects but not for effects on the environment. Environmental impacts are thus only considered in a qualitative manner.

Prior to the implementation of REACH in 2007, numerous studies were published that aimed to analyse the potential impacts of the new chemical legislation. According to the Extended Impact Assessment carried out by the European Commission, costs imposed by REACH would amount to between **€2.8 billion** and **€5.2 billion** during the implementation period (2007-2018)[27]. Assuming that 30,000 substances fall under REACH, these estimations correspond to average costs of between **€93 million** and **€173 million** per substance.

However, it also became evident that at the same time the quantitative consideration of indirect effects proved extremely difficult as they were expected to occur only in the long run. These indirect effects comprise, amongst others, benefits to society, for example by improving the health of the general population, as well as benefits for the environment. Impacts of nanomaterials on human health are still subject of controversial discussions. Whereas some studies concluded that there is only a limited amount of scientific evidence to suggest that nanomaterials present risks for human health[28], others express their concern with regard to the differing behaviour of nanoscale materials in comparison with their bulk counterparts, which may also lead to different toxicological properties[29].

[24] "Testing Costs and Testing Capacity According to the REACH Requirements – Results of a Survey of Independent and Corporate GLP Laboratories in the EU and Switzerland"; M. Fleischer; Journal of Business Chemistry; 2007; Vol. 4, pp. 96

[25] "IMPORTANT ISSUES ON RISK ASSESSMENT OF MANUFACTURED NANOMATERIALS" (http://search.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono%282012%298&doclanguage=en)

[26] European Commission, 2003. Regulation of The European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) on Persistent Organic Pollutants. Extended Impact Assessment.

[27] European Commission, 2003. Regulation of The European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) on Persistent Organic Pollutants. Extended Impact Assessment.

[28] Impact of Engineered Nanomaterials on Health: Considerations for Benefit-Risk Assessment, Joint EASAC-JRC Report, http://ihcp.jrc.ec.europa.eu/our_activities/nanotechnology/nanoreport-10-11/JRC-EASAC-report.pdf, p. 8.

[29] Maynard, A. D. (2011). Regulators: Don't define nanomaterials. Nature, 475, 31.

Most of these ambiguities seem to result from the unavailability of meaningful data. For instance, many chemicals – not only nanomaterials – have been associated with the development of various chronic diseases (e.g. cancer, asthma, respiratory diseases). However, without sound epidemiological knowledge, establishing a causal, stochastic link is often very difficult and even then cocktail effects and non-linear dose-response functions may perturb the outcome of these studies. Moreover, diseases are often the result of many factors acting together (e.g. genetics, lifestyle, pollution, chemicals), and responses may vary between individuals. Taking these factors into consideration, it becomes evident that a comprehensive quantitative consideration of impacts on human health and the environment is extremely difficult. In fact, some of this information might only become available as a result of the implementation of the proposed modification options[30].

We are well aware that a scientifically sound analysis of impacts cannot be provided in the context of this study. Nevertheless, it is considered of importance to provide at least some illustrative figures that indicate the magnitude of potential benefits that may be achieved as a result of implementing the modification options to better address nanomaterials under REACH.

This rough estimation of benefits represents a top-down approach of benefits. A bottom-up approach, which would estimate and evaluate benefits by incremental mortality and morbidity effects due to a change in exposure, has been examined and cancelled as it was not feasible for this assessment. Data resulting from observation of adverse effects of nanomaterials are not yet or sparsely available and therefore the intended assessment of benefits in this way was not feasible.

The most important missing data and therefore missing links of the causal chain are the following:

- Data on number of workers who are (or will be) involved in the production of the single nanomaterials in Europe.
- Data on the amount of single nanomaterials with which consumers come into contact during the life cycle of the nanomaterial.
- Knowledge of quantitative empirical dose-response functions linking exposure to nanomaterials with single human health endpoints (such as in the way they are already established for several air pollutants and heavy metals). Closing this information gap will be the very object of the option scenario, in particular the options 11, 12 and 13 addressing human health impacts).

As a reference point for our calculations, we have analysed various impact assessments that were conducted prior to the implementation of REACH. Several of these studies suggested that REACH would benefit the general community and the environment. Although many publications confined their analysis to a qualitative description of these impacts, some indicated that the health benefits may amount to as much as **€50 billion** over a 30 year time period[31]. This estimation demonstrates the potential of REACH and should not be interpreted as a best estimate of benefits. Given that at least 30,000 substances fall under REACH, these estimations correspond to an average net present value (NPV) of health benefits of approximately **€1.65 million** per substance. These estimations required assumptions as to what extent

[30] Consequently, drawing a link between certain diseases and the exposure to nanomaterials does not appear scientifically valid. This is why a "bottom-up approach" in the context of determining health benefits was not developed further.

[31] European Commission, 2003. Regulation of The European Parliament and of the Council concerning the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), establishing a European Chemicals Agency and amending Directive 1999/45/EC and Regulation (EC) on Persistent Organic Pollutants. Extended Impact Assessment.

chemicals may be the causative agent for diseases[32] and what proportion of this amount could be reduced as a result of the implementation of REACH[33]. For example, the European Commission's analysis of the impacts of REACH[34] assumed that "*positive effects on public human health would start to occur 10 years after REACH starts to be implemented*".

As indicated in the introductory chapter, REACH applies to chemical substances in all their forms, whatever size, shape or physical state, and thus, it also includes substances that occur in their nanoform. At the same time, however, an analysis of REACH registration dossiers revealed that it is currently not possible to determine if and which nanomaterials are covered by a specific registration[35]. Consequently, we have developed a "best estimate" scenario, accompanied by an uncertainty range regarded as realistic, to estimate the potential health effects resulting from the implementation of the proposed modification options to better address nanomaterials under REACH.

The best estimate is based on the assumption that some nanomaterials have already been registered together with their corresponding bulk substances and that at least some toxicological aspects specific for nanomaterials have already been considered. Taking into account what information is relevant for nanomaterials and what information is currently still missing from existing dossiers, additional nanoparticle-specific information will be collected as specified in the nine options constituting the option scenario.

Table 8-8 gives an overview of potential information which could be generated after the nine options constituting the option scenario have been applied. The information is focused on health effects and refers to expected savings from avoided health risks, especially cancer risks.

[32] An estimate of 1% has been used. This is a conservative estimate based on figures that were published in a World Bank study (K. Lvovsky et al., "Health and Environment Strategy Papers", No1, 2001, World Bank Working Paper 24096, 2001, World Bank).

[33] It has been assumed that REACH will reduce chemical-related diseases by 10 %. In fact, this estimation is also used by RPA (RPA, 2003. Assessment of the Impacts of the New Chemicals Policy on Occupational Health).

[34] European Commission, 2003. REACH extended impact assessment.

[35] European Commission, 2012. "NANO SUPPORT Project. Scientific technical support on assessment of nanomaterials in REACH registration dossiers and adequacy of available information".

Table 8-8 Additional information generated by implementing the option scenario and potential health endpoints concerned

Option	Additional information generated for	Potential health endpoints
6	Increased knowledge on dustiness	Inhalation toxicity (prevention of lung cancer)
11	Increased knowledge on inhalative exposure	
12		
13	Increased knowledge on mutagenic effects	Genetic toxicity (cancer; reproductive effects)
16	Increased knowledge on toxicological potential in environment	No direct health effects assignable
17	Increased knowledge on toxicological potential in environment after prolonged exposure	
18	Increased knowledge on toxicological potential in environment	
19		
21	Increased knowledge on nano-specific adverse effects	Inhalation toxicity (cancer); mutagenicity

This additional information, to be gained in particular by options 6, 11, 12, 13 and 21, will lead to an increase in health benefits. It is estimated that the increase in health benefits per substance on average will amount to about 20% of the health benefits per substance to be obtained as the total potential of REACH. This share is based on the judgment of a plausibility range between 10% and 30%, estimated during a set of expert interviews. It is not regarded as realistic to assume a higher share of additional information, e.g. a "worst case scenario" with 100% additional information: We know that at least in some cases nanomaterials have already been registered, either with their bulk counterparts (e.g. nano TiO_2, nano ZnO, synthetic amorphous silica) or separately (carbon black) and some information specifically for the nanoform has already been provided.

Assuming that new toxicological knowledge could be created for at least 500 nanomaterials[36], the total benefits would be in the order of magnitude of **€165 million** (€1.65 million per substance * 20% * 500 substances). Benefits will accrue to around **€0.33 million** per registered nanomaterial over the next 30 years, totalling up to **€165 million** for 500 nanomaterials with registration obligations. If the share of additional information leads to 10% or 30% additional health benefits, this range will be between **€83 million** and **€248 million**.

More than 99% of the calculated health benefits of REACH refer to avoided cancer deaths[37]. Focusing on cancer as the main endpoint for health damage may underestimate the costs from other diseases, including neurodegenerative diseases as a result of accumulation of nanoparticles in lysosomes[38].

[36] This assumption is based on the estimate of industry experts that between 500 and 2,000 nanomaterials are placed on the EU market (Risk & Policy Analysts Limited. (2012). Impact Assessment of the REACH Implementation Project on Substance ID for Nanomaterials.). Given that some of these materials may display similar toxicological properties, we have used the lower number to avoid double counting.

[37] RPA, 2003. Assessment of the Impacts of the New Chemicals Policy on Occupational Health.

[38] Recent research activities on such diseases have in particular been performed by Kenneth A. Dawson at the Centre for BioNano Interactions at University College Dublin, e.g. within the current EU 7th Framework Programme project NeuroNano (2009-2012). http://www.neuronano.eu/. Final reports and results are not yet publicly available

Considering other health effects may lead to higher health care costs, loss of jobs and income. However, reliable exposure-response functions are not yet known for this type of diseases.

Hence, taking into account the rather short temporal boundaries set at the beginning of this project (2012-2022), the potential benefits on human health resulting from the implementation of the proposed modification options would most likely not be measurable within this timeframe. However, as indicated above, this approach would significantly underestimate the benefits that occur in the long run.

The degree of magnitude of this extended impact assessment (EIA) estimation is backed by other studies with a similar focus[39] and a more detailed and traceable documentation of assumptions. Estimates of the economic costs associated with diseases under each of the end-points comprise costs of medical treatment, loss of productivity, and individual willingness to pay to reduce risks to one's own human life ("human costs"), the latter being based on values of life years lost or disability-adjusted life years. Some of these identified costs need adjustment, to the knowledge and economic situation of today (e.g. some of these studies are from 2003). However, since they progress in different directions, they thus tend to outweigh each other.

When comparing costs and benefits, it has to be emphasised that the profiles of costs and benefits over time are significantly different, as the qualitative profile characteristics show. They are demonstrated in Figure 8-2. Costs have been estimated for a time frame of 2012 to 2022. The major contributions of costs are interrelated with the remaining two REACH registration deadlines in 2013 and 2018; therefore, two cost peaks are expected around these years. In the years after 2022, further follow-up costs will be minor or even negligible. This means, extrapolating costs further from 2022 up to 2042 should not add many additional costs.

The picture is completely different regarding benefits. The majority of health benefits will occur between 2022 and 2042, due to the latency of health risks and the consecutive extension of life years lost. Restricting the estimation of health benefits to the time frame from 2012 to 2022 will cover only a minor share of health benefits. Moreover, this share and level of health benefits realised by the year 2022 is extremely difficult to estimate and would require rough assumptions on the stochastic distribution of latency and progression of cancer or other chronic diseases. Therefore, due to the different time profiles, a restriction of health benefits up to the time frame of 2022 would not be adequate and appropriate to the problem.

[39] See in particular Pearce, David and Koundouri, Phoebe: The Social Cost of Chemicals. The Cost and Benefits of Future Chemicals Policy in the European Union. A WWF Chemicals and Health Campaign Report. May 2003.

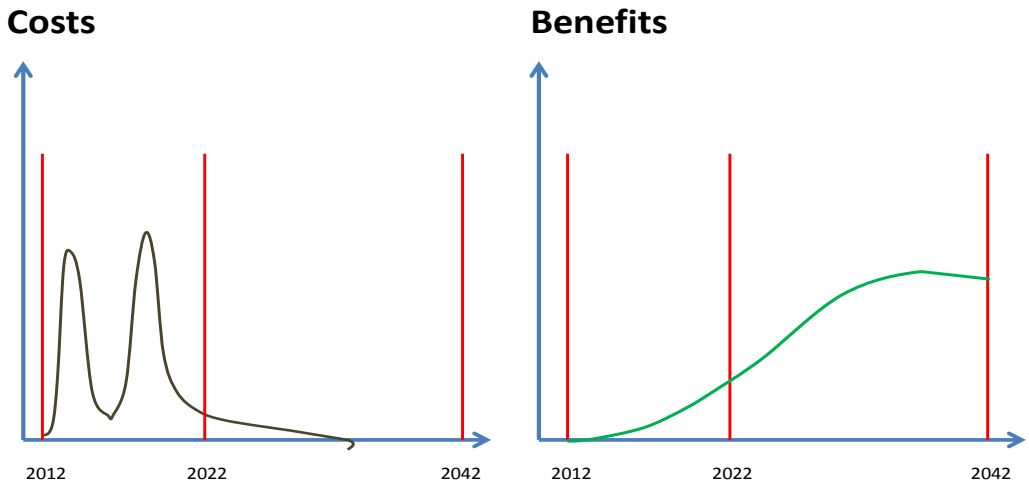

Figure 8-2 Outline of time profile for expected costs and benefits of the option scenario within the time frame of 2012 to 2042

As stated previously, the impacts on the environment are harder to grasp. This is mainly due to the lack of meaningful reference systems, i.e. ecosystems that are small enough to be useful while not being too simplistic to transfer the results to more commonplace, larger ecosystems. Possible impacts range from: probably insignificant dissolution or immediate agglomeration and precipitation, to worrisome persistence in ecosystems and organisms with genetic and morphologic consequences as well as the potential unbalancing of interspecies ratios. Some of the effects for specific nanomaterials and specific ecological environments are described in Annex 3. Next to impacts on population numbers and species diversity, other effects also well-known from chemicals can be for example bioaccumulation or toxicological effects other than death of individual organisms and populations.

There are no reliable studies on what the cost of the reduction of species diversity in a given habitat is (not to mention estimates on other less drastic effects – see above). If an animal or plant species is reduced in abundance (thus shifting the interspecies balance on that nutritional tier) or eliminated in a given habitat the repercussions are manifold and felt over time in the entire network of interdependencies above and below the complexity level of the species in question. The impacts for individual species of animal or plant life can be devastating even when indirect. Predicting where the effects of species reduction or the shift of interspecies balance will be felt within our ecosystem apart from the immediate spatial and temporal surroundings is a multivariate process that we have an awareness of, but quantification is not (yet) possible.

What can be securely predicted is that the introduction of increasing amounts of many different nanomaterials will have species-specific toxicological impacts that are dependent on the life cycle of the nanomaterial in question as well as the end-of-life circumstances it goes through.

8.3 Wider opportunity costs and benefits

In addition to the quantitative assessment, some additional implications of the developed options can be assessed in a qualitative way. These impacts include benefits from additional information (or reduced uncertainty) to be provided, which would remain unknown if the options were not implemented. Some of these effects have also been addressed by surveys in some recent studies, which are analysed in the following.

Safeguarding and improving the corporate image of companies

Companies in the nanotechnology sector are faced with public and media concern about potential problematic impacts of nanomaterials. As long as there is a high degree of uncertainty about nanomaterials in general and about specific nanomaterials and nanoforms in particular, the concern in the public opinion may remain unaddressed.

If the information as specified in the option scenario is required to be delivered in dossiers by nanomaterial producers, it can also be shared with the customers and the public (because industry has to prove that they place on the market only those substances that pose no risk). Consequently, increased testing may be used by companies to improve their corporate image. Implementation of the additional options may therefore provide some public reassurance and also demonstrate that both authorities and industry are adopting a responsible approach. In addition, for strategic planning of their product range in such an innovative technology, the company also gains early decision-making support and validation that, if the nanoproduct has passed the additional tests and requirements, it can further be utilised and optimised in the production processes. If the nanoproduct fails the tests and requirements, companies will become aware of at an early stage and can revise and adapt their product strategies to produce safer materials. In this way, further investments into materials which would have to be replaced later on could be avoided. This has an effect on innovation, described in more detail in the following.

Positive effects on public acceptance

More, differentiated information leads to increased security and reassurance to immediate customers and to the public directly or indirectly in contact with the relevant types of nanoforms. This contributes to a better informed and more differentiated opinion, attitude and level of awareness of customers and consumer protection organisations, showing that not all nanomaterials per se are dangerous or problematic. Products with nanomaterials having been tested and proved to be non-problematic will gain a higher and sustainable degree of public acceptance. This also increases the trust in industry and authorities.

Potential impacts on innovation

Inclusion of substances in the Candidate List of Substances of Very High Concern for Authorisation, in Annex XIV or XVII place companies under a certain amount of pressure to innovate and to search for and develop substitutes. This may sometimes also be induced by customers, i.e. downstream users.[40] It is expected that some companies have already anticipated potential future restrictions or authorisations and developed alternatives in order to gain a pioneer role in the case of future restrictions or

[40] This was an evident interim finding gained from a current study "Socio-Economic Analysis (SEA) in authorisation and restriction under REACH: Assessment of abatement costs of chemicals ex ante and ex post", performed by the contractor team for the German Federal Environmental Agency (Umweltbundesamt).

authorisations. Thus, an additional innovation impulse already starts before certain information becomes public.

This impact can be transferred to the information gathered by the enforcement of the additional endpoint-specific options, addressing human health hazards and environmental fate and hazards. As soon as companies have performed the additional tests required, they gain additional information on particular hazards and risks of these nanoforms and also on coherences between nanomaterial characteristics and risks. This may also induce further innovation, e.g. on alternatives with less hazards and risks.

The impact of the REACH Regulation in total on the innovativeness of the chemical industry of the EU has been subject in particular to an interim evaluation study performed by the Centre for Strategy & Evaluation Services, where the final report has become available in 2012.[41] The main findings show a complex, differentiated and ambiguous picture, but some of the findings seem to be applicable in particular to the nanomaterials market.

When addressing the question of whether a regulation impacts innovation, two different views can be identified: One view is that regulation simply increases costs and erodes competitiveness and existing innovation[42]; several answers of decision makers in companies showed that "data generation as such does not necessarily lead to conception of new ideas and innovative activity"[43]. Fulfilling the requirements of the REACH Regulation requires scarce company resources otherwise needed for other purposes, e.g. goal-oriented research and development activities.

The alternative view is that well-designed regulation can increase knowledge, help identify new opportunities and increase innovation and competitiveness. Some positive examples for such a development already exist, e.g. the successful cooperation of actors within chemical cluster regions[44]. REACH has also already led to significant organisational innovation (the implementation of a new organisational method in a firm's business practices, workplace organisation or external relations), but the full extent of organisational innovation is expected to follow after the transition period and some period of stabilisation. This also affects the external relations of the company, in particular the relationship with suppliers and customers along the supply chain, and with the public sector and external service providers.[45]

To summarise, it should be highlighted that regulations involving (increased) information requirements about substances have both decelerating and stimulating effects on innovation.

Potential impacts on downstream users

When receiving purchased products from their suppliers, downstream users are asked to implement risk management measures which are outlined in the safety data sheet. Especially for hazardous substances, downstream users have to ensure that conditions listed in the exposure scenario(s) of the safety data

41 Centre for Strategy & Evaluation Services (CSES 2012): Interim Evaluation: Impact of the REACH Regulation on the innovativeness of the EU chemical industry. Final Report and Annexes, 14 June 2012. Available at: http://ec.europa.eu/enterprise/sectors/chemicals/documents/reach/review2012/innovation_en.htm. See especially Case Study 7 – The impact of REACH on highly innovative SMEs.

42 CSES (2012), Annex, p. 56.

43 CSES (2012), p. 3.

44 This is described in detail in Case Study 2 – The effect of REACH on innovative clusters in the chemical sector. In: CSES (2012), Annex, pp. 53-56, and the website http://www.axelera.org/.

45 See Case Study 5 – REACH and marketing and organizational innovation change. In: CSES (2012), Annex, pp. 66-70.

sheet, are adequately implemented in order to guarantee safe handling and use of this substance(s). It can reasonably be assumed that in the initial phase of being supplied with a hazardous nanomaterial, bureaucratic, organisational and financial efforts might be required to implement and guarantee safe handling and use of a hazardous (nano)material. Such efforts would be required for e.g. teaching personnel appropriate handling and use of the concerned substance or for construction work (installation of ventilation equipment). It should however be noted that these requirements in general apply to hazardous substances and/or particulate materials with high dustiness and do not specifically apply to nanomaterials.

Potential impact on consumers

The aspect of impacts on consumers is not only specific to nanomaterials but may also be applied to every starting material of which the acquisition costs are passed along the supply chain. The extent of passed-down costs is determined by the principle of supply and demand.

Registration costs, which incur in the course of the elaboration of the lead dossier, can in some cases be passed down along the supply chain from the registrant to the downstream user and finally to the consumer. Given that a registered substance (nanomaterial) has caused substantial costs in the course of fulfilling information requirements under REACH, the resulting costs for the Letter of Access for this registered substance may be comparatively high if, at the same time, the number of affected registrants is quite manageable. Analogous to this, the resulting price for a Letter of Access might be comparatively moderate if the registration costs are shared among many registrants.

It can neither be predicted exactly nor be quantified whether and to what extent the high costs for the registration or the acquisition of Letters of Access are passed along the supply chain to the consumer: This is triggered by various key factors, such as the registered substance, the resulting registration costs or the number of registrants.

8.4 Effects on small- and medium-sized companies (SMEs)

The evaluation study on innovation by CSES (outlined in the previous chapter) also had a particular focus on highly innovative small and medium-sized companies (SMEs) within the chemical industry (though not in particular nanomaterial producers) and concluded that "SMEs in general probably bear a disproportionate portion of costs in the registration procedure. In addition, some of the factors that make SMEs successful as an organisational form … are negated by the processes required to comply with the REACH Regulation"[46].

The sample group from these SMEs estimated the effect of REACH on innovation at the individual company up to the present, as compared to the pre-REACH situation, as strongly negative. This negative-tendency view is also shown in the total survey group of all companies, but is less pronounced.

[46] CSES (2012), Annex, p. 81.

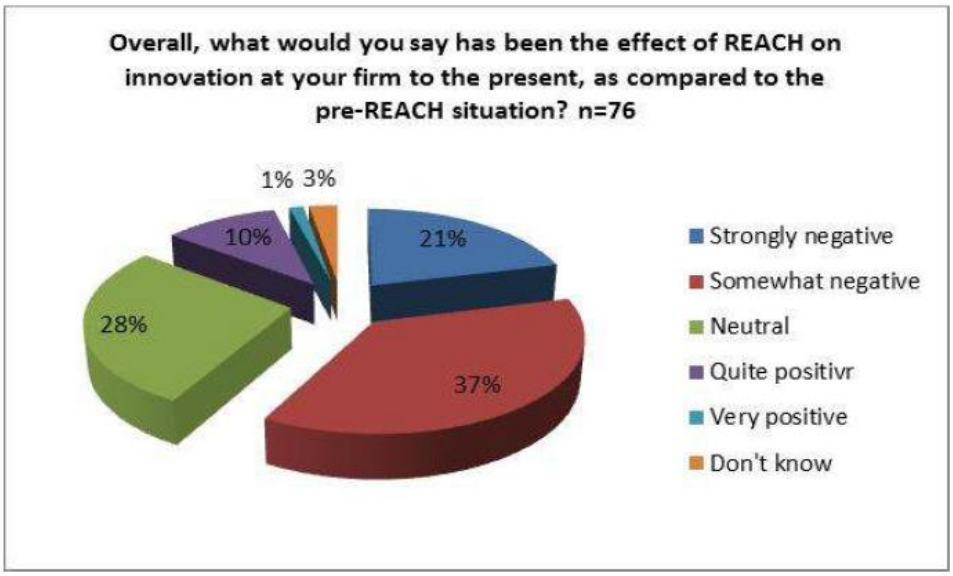

Figure 8-3 Question on the estimated effect of REACH on innovation (survey results)
Source: CSES (2012), Annex, p. 77.

Discouraging effects comprise especially administrative costs and bureaucracy, as well as the exacerbation of an uncertain business environment. The question "Do you see the position changing in the future" was also answered in a rather pessimistic way (38% "yes, more negative"; 32% "no change"; 3% "yes, more positive"; 27% "don't know").

On the other hand, SMEs and micro companies showed a higher response than the overall survey that they benefit from increased openness, in particular from the Safety Data Sheets, for the stimulation of new ideas and the conception of products.

In addition to and in support of the findings of the CSES study, which was related to the chemical industry in general, a recent nanotechnology survey by GAIA Innovative Solutions for Sustainability[47] examined in particular the market for nanomaterials. GAIA distributed a questionnaire to companies primarily developing or manufacturing nanomaterials.

The GAIA study confirmed the findings of CSES that the impacts of REACH and also of the Regulation for Classification, Labelling and Packaging (CLP) have a negative effect on the company's investment level in research and development. This was in particular indicated by those companies that had already prepared REACH registrations or had started the registration process: 44% indicated that the impact of REACH and CLP has been negative or very negative on the company's R&D investment level (44% "neutral", 6% "positive", 6% "not applicable"). The negative/very negative impacts included "increased amounts of paperwork and (perceived) unnecessary tests and certifications and other investments required by REACH".[48] Beyond that, many companies asked for better testing methods.

The companies addressed by the GAIA survey have been differentiated according to two sets of attribute specifications:

[47] Kauhanen, L./Rissanen, J./Crawley, T. (GAIA 2011): Study on REACH contribution to the development of emerging technologies. Draft on Task 1 – Situation in Nanotechnology companies in Europe. 29/11/2011. Available at: http://www.gaia.fi/files/680/Study_on_REACH_contribution_to_emerging_technologies_Situation_in_Nanotech_companies_in_Europe_DRAFT.pdf

[48] See GAIA (2011), pp. 35-37; quotation on p. 36.

Company size:
- Micro companies (1-10 employees)
- SME companies (11-250 employees)
- Large companies (over 250 employees)

Value chain position:
- Research and Development (as only position in the value chain)
- Manufacturer and/or importer
- Other companies (including users, formulators and distributors)

The overview on a distribution of responses within the combination of these groups and their involvement within REACH registrations is shown in Figure 8-4, showing that, especially within the most relevant sector of nanomaterial manufacturers and importers (section in red), micro companies and SMEs are typical for this sector and due to their tonnage bands are to a high degree affected by REACH.

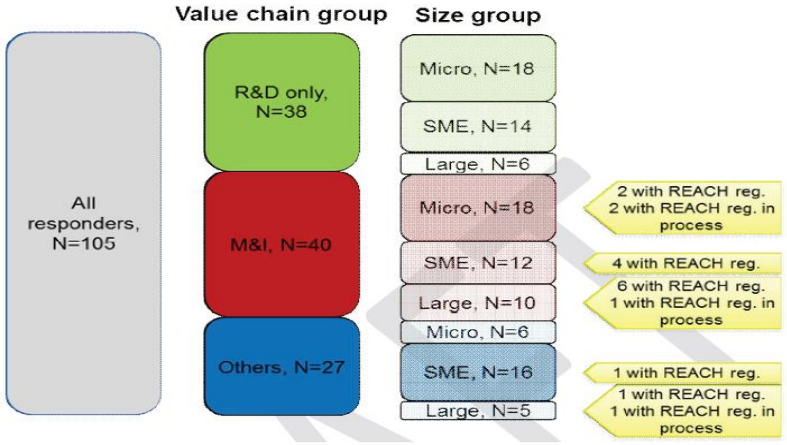

Figure 8-4 Number of responders in the different subgroup combination and REACH involvement
Source: GAIA (2011), p. 11.

Figure 8-5 shows in which fields of activity within the value chain micro companies and SMEs are active, compared to larger companies. Nearly all companies are (among others) involved in research and development of their own. All in all, there are no strictly monotonic relationships between the three company size clusters and the percentage involved in a certain field of activity within the market for nanomaterials.

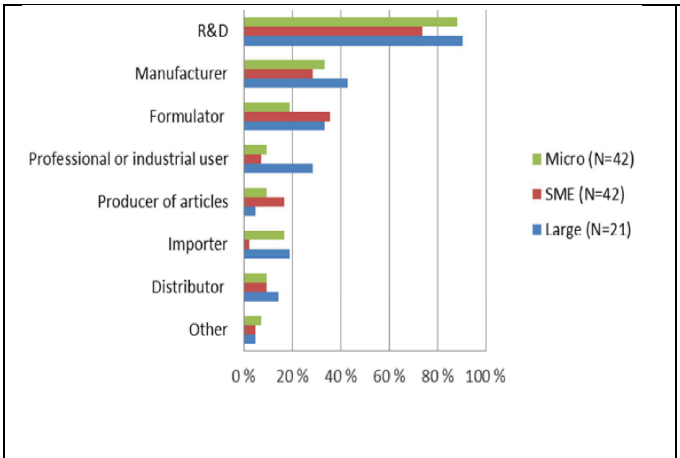

Figure 8-5 Activities in the value chain of nanomaterials by company size
Source: GAIA (2011), p. 13.

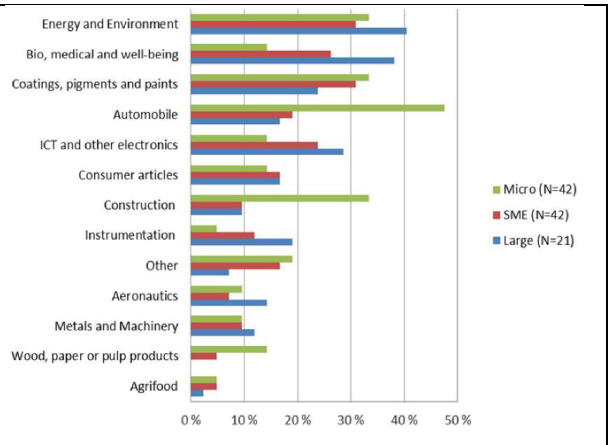

Figure 8-6 Most important customer sectors (in % of annual turnover)
Source: GAIA (2011), p. 17.

One half of the micro companies do not yet offer commercial products, but part of this group is expected to enter into commercial production by 2022.

Figure 8-6 shows the important customer sectors for micro companies, SMEs and large companies. While both SMEs and micro companies show a high involvement in the sectors of energy and environment as well as coatings, pigments and paints, micro companies participate much less in the automobile and construction sectors.

Further analysis of these survey data reveals that, although the size of the companies is positively correlated with the volume classes (tonnage bands) in which they manufacture or import nanomaterials, SMEs and even micro companies already participate to a substantial extent in the market with volumes relevant within REACH and will do this even more in an innovative and growing market. This is shown by cross tabulation of all cases within the survey in which nanomaterials are manufactured or imported (Table 8-9). Even micro companies act up to a tonnage band of 10-100 tons per year and SMEs up to a tonnage band larger than 100 tonnes per year. This indicates that, compared to the present situation, more SMEs and micro companies will have to carry out REACH registrations by 2013.

Table 8-9 Share of cases (company reporting on volume class in which nanomaterial is manufactured or imported*)
Source: GAIA (2011), p. 19 (transposed)

Tonnage band	Micro companies (N=45)	SME companies (N=22)	Large companies (N=29)	Total (N=96)
< 10 kg/year	25%	8%	5%	**39%**
10 – 100 kg/year	8%	4%	2%	**15%**
100 – 1000 kg/year	10%	2%	2%	**15%**
1 – 10 tons/year	1%	4%	1%	**6%**
10 – 100 tons/year	2%	3%	2%	**7%**
> 100 tons/year	0%	1%	18%	**19%**
Total	**47%**	**23%**	**30%**	**100%**

*) Micro companies and SMEs were asked to report on a maximum of 3 nanomaterials they produce in highest volumes, large companies to report on a maximum of 5 nanomaterials they produce in highest quantities. Nanomaterial substances reported have not been specified, so the same substance may appear for several companies as cases.

From those respondent companies that produced more than one tone of a nanomaterial, some did not produce the same substance as a conventional material at all, others also produced the corresponding bulk material in quantities larger than one tonne.

As a result from the analysis of the market structure for nanomaterials and the outcomes of the GAIA survey and the CSES study it can be concluded that costs of the option scenario on industry will to a high degree be borne by micro companies and SMES with less than 250 employees. Anticipating these additional costs and endeavours has led to pessimistic views and expectations, especially in small-sized companies producing and importing nanomaterials.

9 Conclusions

1) The project steering group concluded that 12 of the 21 originally suggested options are considered already implemented with existing legislation and guidance provided by ECHA and therefore are part of the baseline scenario. The other 9 options were considered relevant for an adaptation of the REACH regulation and therefore build the basis for the presented impact assessment.

2) The total costs for implementing the 9 options amount to a range between **€11 million** and **€73 million** as a cumulative effort for all concerned companies for a time period until 2022. These costs result from extensive application of grouping and read-across approaches under the preferences of the REACH Regulation. Without this approach the costs would multiply up to **€100 million** and **€600 million**.

3) Splitting of total costs on single options show big differences between options with high efforts (options 16, 17), options with medium efforts (11, 13, 19) and options with no or very little additional costs (6, 12, 18, 21). The dimensions of additional costs can be compared to expected revenues of concerned companies in that period of about **€40 billion**. The revenues are assumed and extrapolated on the basis of the current global turnover for nanomaterials (worth **€20 billion** per year) and the current share of European chemicals market to the global chemicals market.

4) The quantifications of the total benefits of the 9 options for human health amount to a range between **€83 million** and **€248 million** (with a best estimate of **€165 million**) of cumulative savings for a period until 2042. Most of the health benefits are, however, expected to take place with significant delays after implementation of the options. This is because implementation will not automatically occur as a consequence of the options but will only be achieved if appropriate risk reduction measures are implemented, which in turn can lead to additional costs.

5) The quantification of both, the costs and the benefits are afflicted with high uncertainties, which prevent a direct comparison between monetary costs and benefits These uncertainties include aspects, such as

    - regarding particle size as characteriser or identifier: Implementation of this parameter would lead to different registration obligations (updating of current dossier with information on nanomaterials or elaboration of lead dossier which only includes information on nanomaterials). This might especially have implications on the registration of surface treated nanomaterials.
    - surface treated nanomaterials: there is currently no clear advice available how surface treated nanomaterials should be registered, i.e. separate registrations of surface treating substances and core nanomaterials or registration of surface treated nanomaterials.
    - limited information on the European market for nanomaterials
    - costs for laboratory studies, especially for nanomaterials, since routine analytical methods have not yet been implemented.

6) Beside uncertainties, it should be considered that the time frames for calculating the costs and the expected consequences of health benefits are different.

7) Besides the quantifiable benefits, further important added values of the options are expected. These concern in particular the reduction of uncertainty regarding potentially adverse effects on human health and the environment and the ability to react to increased or new risks. Furthermore, increased knowledge can stimulate innovation processes at companies searching for new and better solutions. In addition, it can help to increase the transparency on the use and possible risks of nanomaterials. However there is also the risk that innovation could also be negatively affected if (financial) hurdles due to increased information requirements become too high. These non-quantifiable effects cannot be quantified, but should not be neglected.

8) The overall conclusion of this impact assessment shows that additional costs for companies lead to a reduced uncertainty about potentially adverse effects of nanomaterials to human health and the environment. These may lead to considerable benefits, especially if combined with appropriate risk reduction measures.

List of Abbreviations

AA	Administrative Arrangement
BAL fluid	Broncho-alveolar lavage fluid
CEFIC	European Chemical Industry Council
CLP	Classification, Labelling and Packaging
CNTs	Carbon nanotubes
CSES	Centre for Strategy & Evaluation Services
DG	Directorate-General
ECHA	European Chemicals Agency
EEA	European Economic Area
EIA	Extended Impact Assessment
ENM	Engineered nanomaterials
FAQ	Frequently Asked Questions
IHCP	Institute for Health and Consumer Protection
JRC	Joint Research Centre
OECD	Organisation for Economic Co-operation and Development
QSAR	Quantitative Structure-Activity Relationship
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RIP-oN	REACH Implementation Projects on Nanomaterials
SCENIHR	Scientific Committee on Emerging and Newly Identified Health Risks
SIEF	Substance Information Exchange Forum
SMEs	Small and Medium-sized Enterprises
TOR	Terms of Reference
t/y	tonnes per year
WPMN	Working Party on Manufactured Nanomaterials
WZB	Wissenschaftszentrum Berlin für Sozialforschung (Social Science Research Centre in Berlin)

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