Research roadmap for nanosafety
Part III: Closer to the market (CTTM)

Closer to the market Roadmap (CTTM)

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LIST OF ABBREVIATIONS

BSI – British Standards Institute

CENF – Cellulose Nanofibers

CNF – Carbon Nanofibers

CNTs – Carbon Nanotubes

CSA – Coordination Support Action (an EU funding instrument)

CTTM - Closer-to-the-Market-Roadmap

ECHA – European Chemicals Agency

EMA – European Medicines Agency

EPA – Environment Protection Agency

ETUC – European Trade Union Confederation

FP6 – Framework Programme 6 of the European Commission (2002-2006)

FP7 – Framework Programme 7 of the European Commission (2007-2013)

H2020 – Horizon2020 – the EU funding mechanism (2014-2020)

HCA - Health Care Assistant Program

IARC – International Agency for Research on Cancer

IFA/DGUV - Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung

KPIs - Key Performance Indicators

LEV - Local Exhaust Ventilation

MNMs – manufactured nanomaterials

NEP – Nano-enabled product

NGOs – Non-governmental Organisations

NIOSH – National Institute for Occupational Safety & Health

NMs - nanomaterials

NRVs – Nano Reference Values

NSC – NanoSafety Cluster

MWCNTs – Multi-walled Carbon Nanotubes

NEDO - New Energy and Industrial Technology Development Organization

OECD – Organisation for Economic Cooperation and Development

OELs - Occupational Exposure Limits

OSH - Occupational Safety and Health

OHSMS - Occupational Health and Safety Management Systems

PPE – Personal Protection Equipment

QSAR – Quantitative structure activity relationship

REACH – Registration, Evaluation and Authorisation of Chemicals

RIVM - National Institute for Public Health and the Environment

RMM - risk management measures

RPE - respiratory protective equipment

SCOEL - Scientific Committee on Occupational Exposure Limits

SbD - Safer by Design approach

SCCS – Scientific Committee on Consumer Safety

SDS - safety data sheets

SME – small or medium enterprise

SPE - skin protective equipment

TDI - Tolerable daily intake

TRL´s - Technology Readiness Levels

VHTS - Virtual High Throughput Screening

GLOSSARY OF KEY TERMS USED IN THE REPORT

Nanomaterial – definition: "*material with any external dimension in the nanoscale or having internal structure or surface structure in the nanoscale*"; in this document, the term nanomaterial is restricted to manufactured (i.e.; nanomaterial intentionally produced to have selected properties or composition) and/or engineered nanomaterials.
Source: ISO/TS 80004-1:2015;

Nano-enabled [product] – definition: "*exhibiting function or performance only possible with nanotechnology*"
Source: ISO/TS 80004-1:2015

[Market] implementation – "*the act of putting a plan* [nanotechnologic developments; nano-enabled products; etc.] *into action* [on the market; to customers, consumers, end-users, etc.] *or of starting to use something*"
Source: http://dictionary.cambridge.org/dictionary/english/implementation

Safe by Design approach – "*Safe by design is a concept and movement that encourages construction or product designers to "design out" health and safety risks during design development. The concept supports the view that along with quality, programme and cost; safety is determined during the design stage.*"
Source: https://en.wikipedia.org/wiki/Safety_by_design

For several definitions of terms used in the CTTM, please see the ISO Vocabulary "ISO/TS 80004-1:2015":
http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=68058&commid=381983

One can also use the ISO Online Browsing Platform which gives access to all ISO definitions. https://www.iso.org/obp/ui/

Executive Summary

Nano-products and nano-enabled applications need a clear and easy-to-follow human and environmental safety framework for the development along the innovation chain from initial idea to market and beyond that facilitates navigation through the complex regulatory and approval processes under which different product categories fall. The missing framework results in a lack of (i) solid data regarding roadblocks to market penetration of nano-enabled products as well as the absence of (ii) transparency in terms of which products (e.g. containing nanomaterials (NMs); nano-enabled products) are on the market (e.g. registries) and voluntary schemes and labelling requirements for cosmetics and food, which processes are used for manufacturing nano-enabled products, and (iii) meager inclusiveness in the dialogue (between all stakeholders) most likely exist as a result of the missing framework. The Closer-to-the-Market-Roadmap (abbrev. CTTM) aims at speeding up the progress towards market implementation of nanotechnologies by outlining the steps needed to develop such a framework. In its current form it is addressed towards policy makers, but the ultimate framework will be designed for use by SME and enterprise organisations.

The CTTM identifies the key challenges to be tackled immediately and outlines a step-by-step approach to establishing a framework to deliver of nano-enabled products to the market: (i) building an inclusive collaboration network, (ii) bringing together the scientific and entrepreneurial experts, (iii) strengthening dialogue of all stakeholders (inclusiveness!) and exchange to raise synergies and safe resources, (iv) implementing of a novel risk assessment framework supported by the regulatory initiatives and implemented by contract research organisations, and (v) building service provider platforms which function as consulting agencies assisting companies to bring their products towards market implementation.

Along these actions, the respective skillset development, educational training and formation of job profiles and recognition certificates shall be established. The accompanying tasks will be to continue the dialogue (e.g. risk communication, safety awareness, dissemination dialogue, needs assessment, debate on key topics, consultation on proposed activities/solutions, etc.) with different stakeholder groups (such as e.g. public authorities, broad public, opinion leaders, NGO´s, etc.) with the objective to increase the level of information via visualization and communication, in order to address all the current gaps listed within the CTTM. This will enable a transparent and open communication process.

Along with facilitating the market implementation of nano-products and nano-enabled applications, the consumers and end users of these products shall be provided with a clear and validated declaration regarding the use and function of NMs in products. Such information will show, in a balanced and standardized way the risks and benefits of the nano-enabled vs. the previously established products and of course addressing the unique new products and applications enabled by nanotechnology. This will increase understanding (and potentially support building trust) among stakeholders about safety issues, reduce the uncertainties for SMEs and enterprises about how to address the nano-enabled products (and NMs) properly, and minimise the impact of risk and safety assessment processes on hampering the innovation potential.

Following the recommendations of the EU REACH system (Article 13) and regarding ethical aspects, the risk assessment procedures should be performed with possible

reduction of living animals' use. Whenever possible, alternative methods such as *in vitro* and *in silico* (computational) testing should be applied for replacing experiments with higher animals. Moreover, the use of computational modelling for supporting Safer-by-Design (SbD) and High Throughput Screening (HTS) might be an interesting option for the innovative industry, since it enables to extend the number of considered solutions without increasing costs.

The actions proposed in the CTTM will reduce the uncertainties for all stakeholders, increase the safety of nano-enabled products while reducing their time to market, and increase the market confidence in this technology and the acceptance of the safe nano-enabled products by businesses and consumers.

Recommendations

Market implementation shall be envisaged based on solid operational knowledge (high level of scientific expertise and robust accumulated datasets) about nanotechnologies' impact on human health and the environment. It is recommended to build this knowledge via the establishment of an ongoing dialogue between science (e.g. nanosafety research), industry (e.g. innovators), and public bodies (e.g. regulatory authorities, panels and committees, policy makers, politicians, NGOs, etc.).

An inclusive European approach, accompanied by strong global interaction and taking into account the high level know-how of organizations and authorities globally shall facilitate realisation of, and reduce barriers to achieving, the positive economic impact promised by nanotechnologies. This shall be reached by bundling activities in all European countries to maximise synergies and progress, establishing an ongoing global interaction and including publicly (National, European, and global) and privately funded initiatives into a cohesive, transparent and active hub of support for SMEs and enterprise regarding safe and benign nanoproducts.

Based on current knowledge and in anticipation of future regulations, easy-to-apply safety thresholds together with benchmarking of skills and jobs shall be implemented and applied to provide the public and the industry with a clear "risk and safety framework" against which to assess the safety of nano-enabled products versus the benefits of their utilisation in specific applications along their whole product life cycle. Where applicable, alternative solutions should be provided and discussed in order to improve the risk-benefit profile and enhance consumer and regulatory confidence.

Building on the strategies for Europe 2020 and for an Innovation Union, the focus of a European nanosafety expertise hub must be inclusive and representative of economic sectors/companies as well as research organizations and academia as well as authorities, bundled or coordinated via member states networks. Harmonized tools and methods (best tools) for industry to address nanosafety issues shall be created and tested in most representative European sectors, and passed to contract research organisations for routine implementation as per safety testing of chemicals, pharmaceuticals, pesticides etc. More attention should be put on the development and application of computational tools. However, the methods should be easily applicable and the rigorous validation criteria and evaluation procedures for the modelling must be established for ensuring the evidence of high quality of the predicted results.

For the national networks, it is expected that they bring together the national stakeholders, including industrial partners, and constitute a representative group of the member states' community, communicating bottom-up and top-down the state-of-the-art (scientifically relevant and real-life-applicable) findings/improvements in the CTTM-related work, and contributing actively to the continuous shaping of the European nanosafety framework and regulatory frameworks in each application area.

All the educational, risk-management and other tools and guides listed in CTTM could be utilised as a blue-print for use by different sectors, and a central nanosafety centre could work with each of the sectoral industry associations to tailor them appropriately, combining the sector-specific expertise of the industry association and the nanosafety expertise of the European centre.

The CTTM-European network shall define (and continuously observe and adapt) an overall concept and a suitable approach to address the needs and objectives of this roadmap, building a hub of best-practice that facilitates rapid deployment across all member states, with a focus on increasing uptake of nano-technologies in the new member and accession states. This should be established initially by core funding from member states and the EU, via the establishment of an EU-wide knowledge hub. To ensure that accumulated knowledge and experience is not lost post the funding cycle, and to support ongoing developments including in other emergent technological areas, strong two-way linkages with established industry organisations is required, including potentially leveraging funding from these for nano-specific activities in the longer run.

For development of a nanotechnology market it can be said that in terms of addressing safety aspects, the nano-related industry is ahead of the curve, and one of the goals of CTTM is that the activities in the nano-field shall be supported by dedicated funding of nanosafety research (interdisciplinarity of research) to support responsible research and innovation in the nanotechnology field.

1. INTRODUCTION:

1.1. NanoSafety Cluster - First layer - Basic scientific knowledge

The rapid initial translation and introduction of nanotechnology-based products into the market has brought the question of its long-term safety and the resulting risk management measures. This, and the current lack of practice to transfer nanotechnology risks to the insurance sector, has led to a slowing down of translation / commercialisation activities, uncertainty regarding legal liabilities and insurance aspects, slowed venture capital investment, and a significant change in attitude by companies producing nano-enabled products with regard to their claims and publicity regarding nanotechnologies. To address these concerns, considerable effort has been undertaken by FP6 and FP7 projects to answer basic scientific and technical questions and will continue under H2020. Updates from these projects are provided in the annual NanoSafety cluster compendium[1], and research needs to 2025 have been outlined in the research roadmap launched by the NanoSafety cluster[2].

1.2. NanoSafety Cluster - Second layer - Research to support regulation

A second layer of activity consists of supporting the regulatory aspects including validation of methods and supporting translation of scientific development into regulatory practice. Examples of regulatory support activities include provision of the technology, skills and conventions necessary for science based implementation of existing rules and consistent development of new ones. This effort takes two main directions.

1.2.1. Enabling regulation of existing NMs by competent authorities based on robust data, sound scientific understanding, and new tools/assays demonstrated to be suitable for use with NMs which can be used to improve regulatory decision-making.

1.2.2. To reduce the potential for health risks along the product life cycle by developing and stimulating safe-by-design and benign-by-design concepts.

In the short term these objectives are covered by three projects.

- NANoREG, which is a 50M€ project funded by the FP7, the EU-member states and industry. It is running since March 2013.
- The follow-up project (i.e. 'NanoReg II'), which will address the safe-by-design aspects – has started in September 2015.
- The Coordination and Support Action (CSA) entitled 'PROSAFE - Promoting the Implementation of Safe(r)-by-Design started in February 2015 and will run for two years.

Furthermore, technical projects are providing these three with scientific data, e.g. NanoMile and NanoSolutions (hazard, both 2013-2017), NanoFASE (fate, Sept. 2015-

[1] Ref. to NanoSafetyCluster-Compendium – download: http://www.nanosafetycluster.eu/home/european-nanosafety-cluster-compendium.html

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

2019), GuideNano (risks, 2013-2017), SUN (risks; safe use; 2013-2017), etc. – further projects and details can be found on the NanoSafety cluster homepage[3].

In the long term regulatory research activities will be addressed as defined in the Roadmap regulatory research (corresp. author: Vicky Stone).[4]

1.3. NanoSafety Cluster - Third layer - Nanotechnology Market

Beside research and regulations, a third layer, which has received less attention in FP7, but is a central feature of H2020, is the market layer, which focusses on research to support commercialisation of nano-innovations and nano-enabled products along the whole value chain. The market layer is the subject of this roadmap.

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

[4] Link to the regulatory roadmap shall be provided (not available at the moment Feb. 16th, 2016)

2. NANOSAFETY CLUSTER - THIRD LAYER - NANOTECHNOLOGY MARKET

2.1. Setting the framework

It is usual that once a technology enters the market the safety management can only be done thereafter. As this is true for all kinds of new technologies, to enable the safety of a technology is in itself a market i.e. professional services supply and demand and provision of contract research services to generate the data needed for regulatory approvals.

Companies bring products to the market that are safe for the intended use. Over time, there will be assessed new uses, a.o. because we learn more about the safety in different circumstances. Hence, the level of safety achieved from application of any new technology will usually increase over time. Safety and risk are usually also put in the context of the benefits the new technology can offer for a society (risk-benefit analysis). The decision to be made in each case is "how much of today's resources ought to be invested for the benefits of tomorrow?" in terms of both Health and Environment.

Each new technology application is based on regulation developed either in generic terms or in sector/application specific terms. Implementation of the regulation should be possible in non-ambiguous conditions.

Development of any new regulation (i.e. new rules/practices) will be based on solid scientific knowledge and will have to be enforceable.

Comprehensive and unambiguous information on the risk of each new technology should be made available and communicated to the end-user. However, for each new product/application combination it may be different. Three main groups should receive information on potential risks within the lifecycle of a NM or nano-enabled product:

- **Workers** handling (or transporting) NMs and/or nano-enabled products
- **Professional users** of nano-enabled products; and,
- **Consumers** buying and using products containing NMs as part of a formulation or nano-enabled products.

In addition, information on the risks from nanotechnologies is important to underwriters so that they can develop robust practices to transfer these risks from the nanotechnology industry to the insurance sector and thus facilitate R&D investment into new nanotechnology products.

2.2. Scope

The scope of this CTTM is to identify best practice and unfulfilled gaps in terms of where and how the scientific / research community, via H2020 and member state funding initiatives, can support the commercialization of this new technology. Such support could take the form of provision of the technology, skills, processes, trained personnel, and tools necessary for implementation of science-based nanosafety best practices in the industrial & commercial activities in order to facilitate sustainable and responsible creation of marketable products and goods, which will be successful on the market and bought/used by society. This effort takes three main directions, irrespective of the regulatory regime applicable to the specific product / application: Setting minimum requirements for nanosafety-related jobs, skills and/or tools. This is provided in the form

of a roadmap which is a plan that matches short-term and long-term goals with specific solutions to help meet those goals (see chapter 2.5 and 2.6). It is a plan that applies to a new product or process, or – in this case – to an emerging technology, nanotechnology. CTTM has three major uses: it helps reach a consensus about a set of needs and the technologies required to satisfy those needs; it provides a mechanism to help forecast technology developments; and it provides a framework to help plan and coordinate technology developments.

2.2.1. Building capacity for formalisation of jobs

- Risk monitoring

Risk monitoring means monitoring of exposure in view of compliance with a benchmark level. Ideally, this benchmark level is health-based. However, only for a few NMs do such health-based levels exist currently. For instance NIOSH has proposed Recommended Exposure Limits for TiO_2 and CNTs; the SCOEL committee recommends occupational exposure limits to the EC[5], however currently NMs are not on their agenda. In Japan the NEDO-project has also proposed 'limit values' for CNTs. The situation is further complicated by the fact that for specific types of CNTs, e.g. Baytubes[6] (Pauluhn, 2010) or the Nanocyl MWCNTs (Ma-Hock et al., 2009) slightly different 'Occupational Exposure Limits (OELs) were proposed as a result of their different properties leading to different degrees of health risk. Still, for most NMs such benchmark levels are currently lacking. Therefore non-specific benchmark levels have been proposed. BSI (UK) launched an initiative for 'generic' NM benchmark levels (BSI 2009) relevant for granular biopersistent NM without specific toxicity, whereas IFA/DGUV (Germany) adapted these values to comply with a generic threshold value of 0.1 mg/m^3 for hazardous substances[7]. This was then further adapted in the Netherlands, where the concept of Nano Reference Values (NRVs) was accepted. So in practice such a benchmark level is used as a surrogate to evaluate exposure levels with respect to risk. However, this is possible only for granular (i.e. non fibrous) NMs without specific toxicity. Currently, registration of 'nano workers' or job titles with high probability of exposure to NMs is in an early stage in some EU countries, e.g. France and the Netherlands. Epidemiological studies are in pilot phase and therefore cannot contribute to an adequate risk monitoring at this stage. However, these studies should focus on early markers of effect rather than on clinical health outcomes. Clearly, such studies should be conducted using harmonised protocols to enable future data pooling in order to enhance the power of such studies.

- Risk Assessment, risk characterization

Risk is a function from hazard and exposure. The **risk assessment** (RA) is an established procedure, recognised by several regulatory agencies and international organizations such as ECHA, EPA, OECD and the WHO, which estimates the likelihood of adverse health and/or environmental effects due to exposure to chemical substances. The RA framework is composed of hazard and exposure assessment, risk characterization and uncertainty analysis. Specifically, the hazard assessment involves hazard identification and dose-response analysis. The **hazard assessment** is carried out by evaluating relevant

[5] http://ec.europa.eu/social/main.jsp?catId=148&langId=en&intPageId=684
[6] No longer on the market
[7] http://www.dguv.de/ifa/Fachinfos/Nanopartikel-am-Arbeitsplatz/Beurteilung-von-Schutzma%C3%9Fnahmen/index-2.jsp

physicochemical and toxicological information from *in vitro* and *in vivo* tests to assess the intrinsic hazard of a substance. The dose-response analysis characterizes the relationship between the dose of the substance and the incidence of adverse health effects in the exposed population in order to establish a "safe" or "tolerable" dose (i.e. TDI). This generally involves the estimation of a Point of Departure (PoD) (e.g. Benchmark Dose or a No-observable Adverse Effect Level) based on data obtained from animal studies, and the extrapolation of this PoD for animals to a TDI for humans by means of uncertainty factors. The exposure assessment is typically based on exposure measurements in occupational, consumer and/or environmental settings and/or the estimation of exposure levels by means of models. This is always performed for one or more exposure scenarios (ES), which describe(s) the operational conditions in which the substance (on its own or in mixture or an article) is handled or used. In the **risk characterization** step, the estimated exposure levels are compared to the TDI or a Reference Exposure Limit (REL). If the estimated exposure exceeds the human effect threshold, or the REL, a conclusion can be made that the risk for the target population is not acceptable.

Unfortunately, the data for a proper science based RA of nanomaterials are limited (e.g. biokinetic data are missing). This is why the development of methods and tools to generate such nano-specific data has become a dynamic area of research, which resulted in an array of test protocols for sample preparation, physicochemical characterization, and *in vitro* and *in vivo* toxicology, which have been developed in many FP6, FP7 and H2020 projects, including but not limited to MARINA, SUN, GuideNano, NanoMile, NanoDefine, NanoSolutions, NANoREG. In addition, risk categorization and control banding tools have been proposed, including a hazard identification tool (Hristozov et al., 2014b), an occupational exposure prioritization tool (Hristozov et al., 2014a), the TEARR risk ranking tool (Grieger et al., 2015), the Swiss Precautionary Matrix (Höck et al., 2010), NanoRiskCat (Hansen et al., 2013), the Control Banding Tool (Paik et al., 2008), the ANSES system (Ostiguy et al., 2010), Stoffenmanager Nano (Duuren-Stuurman et al., 2011), and NanoSafer (Jensen et al., 2013). Moreover, Decision Support Systems for risk assessment and management of nanomaterials are currently being developed in the SUN and GuideNano projects.

- Risk reduction by prevention, Risk minimization

Risk reduction by prevention and hence reducing uncertainty[8] has been indicated already in the context of REACH implementation. Risk minimization is usually an outcome of a scientific based risk assessment. Based on scientific data risks for certain types of NMs are calculated. This results in an understanding of "safe" or "tolerable" doses (i.e. the tolerable daily intake or TDI). Based on this, acceptable amounts of NMs in certain products can be derived. However, currently data for a proper science based risk assessment are limited (e.g. biokinetic data are missing).

Risk and waste management practices currently applied to NOAA [e.g. Engineering Controls (fume hoods, local exhaust ventilation, enclosed glove boxes), administrative controls (HEPA-filtered vacuum cleaner or wet wiping methods), Personal Protective Equipment (respirators)] do not significantly depart from conventional safety practices

[8] See Schaafsma et al (2008): «REACH, non-testing approaches and the urgent need for a change in mind set », J.of Regulatory Toxicology and Pharmacology, DOI 10.1016/j.yrtph.2008.11.003.

for handling chemicals. These procedures are based upon the properties of the bulk form or the solvent carrier and not on nano-specific characteristics.

Only recently, Safe by Design (SbD) has become a national initiative in the US. This approach aims to retain the functionality of materials and products, while reducing their health and environmental risks. The development and implementation of SbD risk control strategies is a major challenge to overcome in order to ensure the sustainability of nanotechnologies. However, it is presently constrained by: (i) the knowledge gaps, still existing on nano EHS issues and (ii) the control of costs.

Various research projects (e.g. Scaffold[9], NanoMICEX[10], Sanowork[11], SUN[12], Guidenano[13]) have attempted to overcome these challenges and provided good examples to demonstrate the SbD proof of concept, however, SbD has not yet been fully integrated into material, product and process development, despite having already achieved a high level of NM manufacturing development, as presented by RIVM recently within the NANoREG project.

In the context of SbD, it would be highly beneficial to develop and apply in near future Virtual High Throughput Screening (VHTS) strategies based on computational modelling and simulations. In this way, it should be possible to considerate much larger libraries of nanoparticles containing much larger variation in the nanoparticles' structure without significantly increasing the amount of experimental work. Along with this idea, the experimental data obtained for only few nanoparticles being representative for a group, can be utilized for developing models and then making predictions for the remaining members of the group. At the final stage, only few virtually selected "best" nanostructures should be tested experimentally to confirm their properties. At this moment, the usefulness of such tools as (Quantitative) Structure-Activity Relationships ([Q]SAR) modelling and/or read-across for hazard (toxicity) assessment has been demonstrated by the six EU "modelling projects" (NanoPUZZLES[14], MODERN, PreNanoTox, ModENPTox, MembraneNanoPart, and eNanoMapper) funded under FP7 and working jointly within NanoSafety Cluster as well as by COST MODENA action.

Risk awareness is an important factor that determines the attitude of workers and their safety behaviour as well. Education and training have been demonstrated to be fundamental tools to improve worker's safety behaviour. Practical tools have been developed to support risk awareness e.g. NanoSmile[15], however, integration of such tools with training programs is needed.

NanoEIS[16] CSA surveyed the skills needs of industrial and societal employers with regards to nanotechnologies. Furthermore, in this project it compared the needs to the current provision of nanotechnology education, and determined significant gaps at university in terms of health and safety and environmental safety provision, with employers requiring these skills now and in 5 years time.

[9] http://scaffold.eu-vri.eu/
[10] http://www.nanomicex.eu
[11] http://www.sanowork.eu
[12] http://www.sun-fp7.eu
[13] http://www.guidenano.eu
[14] http://www.nanopuzzles.eu
[15] http://www.nanosmile.org/index.php?lang=en
[16] http://www.nanoeis.eu/

- Risk mitigation

Once all potential risks are identified, assessed and thoroughly evaluated, risk reduction strategies should be considered in a systematic approach. Essentially, there are two ways of mitigating or reducing the risk: *hazard control* through modification of NM properties while maintaining their original features and functionality and *exposure control* reducing the release of NM from industrial processes or consumer products or limiting the exposure of workers and consumers to NM by means of administrative measures and behavioral guidelines. It has been recommended that these risk management measures are applied according to an established hierarchy of control (Figure 1). Although it is widely agreed that traditional methods used to control exposure to particles can be implemented to NMs, there is a need to confirm their effectiveness against NMs[20].

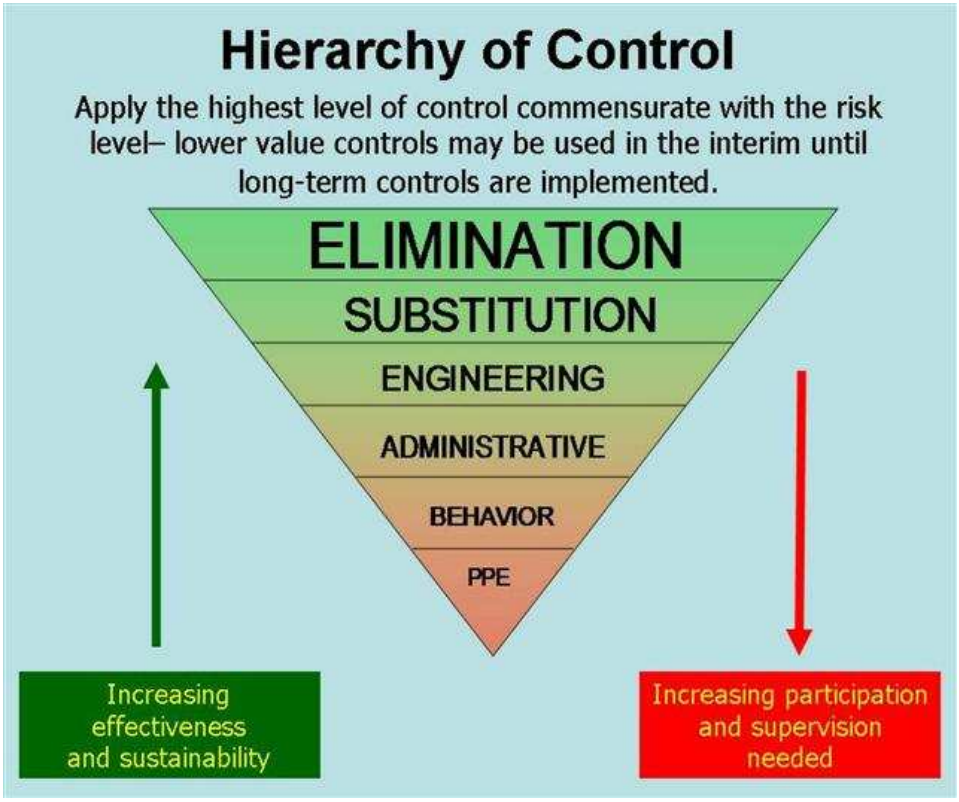

Figure 1: Hierarchy of risk controls applicable to NMs.

If the application of elimination and substitution techniques does not effectively mitigate risks below acceptable levels, engineering control measures should prevent releases or emission of NMs into the (workplace) air and measures that affect the transport of the NMs through the air to the worker or systems that prevent or reduce explosion/fire of very reactive NMs. If the engineering control measures does not effectively mitigate the risks, administrative control should cope with this by defining work practices in documented form. This is explicitly demanded under the 'process control' requirements of the ISO 9000 standard, which state that work shall be performed under controlled conditions, including use of process documentation, where lack of such documentation could reasonably be expected to adversely affect risk management. Such administrative measures are typically combined with occupational guidelines to prevent workers' behaviours that could increase their exposure to the chemicals and the associated risks. Unfortunately, there are still no administrative and behavioural control measures specifically tailored to NM, but the H2020 project caLIBRAte (H2020; webpage not yet

available) will perform research in this context. Personal protective equipment is considered the last resort with respect to risk mitigation. The empirical evidence of the effectiveness of control measures for conventional substances has been documented in an on-line library (Ecel[17]), however, there is currently little information on the specific effectiveness of the controls for NMs and it has not been inserted into a library so far. Risk banding tools, e.g. Stoffenmanager Nano (NL) and Nanosafer (DK) have libraries with information on exposure control measures, which would be the first step to extract 'best practices' for handling and other processes. Similar information can be retrieved from on-line libraries, e.g. Good nano Guide[18].

The selection of adequate risk management measures (RMM), including Local Exhaust Ventilation (LEV) systems, filtration, respiratory protective equipment (RPE), skin protective equipment (SPE), safety goggles and protective clothing, as well as fire/explosion or runaway chemical reaction protection systems, plays a crucial role in the safe handling and use of NMs. In most cases, a combination of partly elimination, substitution, engineering controls, administrative controls, process safety protective systems and personal protective equipment (PPE) are chosen to effectively control the risks. Most of these exposure control methods are applicable to NMs, but their performance to control ENM exposure should be further evaluated under different exposure scenarios. This has been addressed in a growing number of European and international efforts, including FP7 projects such as MARINA, SUN, SANOWORK, Scaffold, Nanomicex and NanoSafePack, and GUIDEnano.

To support sustainable jobs in nanotechnology, ensuring nanosafety is critical. To support this goal, the available but currently scattered information on risk prevention and control should be collated into easy accessible libraries. SUN started collecting the available knowledge into a Techonological Alternatives and Risk Management Measures (TARMM) inventory located in Ecel[19], which includes information on efficiency and costs, but future projects should take up this initiative in a continuous commitment. Moreover, national and virtual (collaborating) transnational nanosafety centres, which function as nodes for nanosafety-researchers, should collate information on 'best practices' and, depending on national regulations, act as focal points for risk monitoring activities, which may include (exposure) registration and future efforts towards epidemiological studies.

- Risk Communication

Nanotechnologies are an evolving area of technological advancement and as with many chemicals, the hazard and risk information pertaining to these new forms of materials is often complex, conflicting and incomplete, yet there is still a need to adequately convey such information to stakeholders (industry, regulators, NGOs, the public); ECHA is working on that, and so does the NANoREG-project[20]. Risk communication involves providing information on levels of health and environmental risks, their significance and their management (e.g. NanoDialog - Germany[21]).

[17] http://www.ecellibrary.com/Account/SignIn?ReturnUrl=%2fHome%2fOverview
[18] https://nanohub.org/groups/gng
[19] http://www.ecellibrary.com/Account/SignIn?ReturnUrl=%2fHome%2fOverview
[20] http://www.nanoreg.eu
[21] http://www.nano-sicherheit.de/Expertendialoge

- Risk transfer

One considerable obstacle that hinders investment in nanotechnologies and their successful commercialisation is the lack of practice to transfer their risks to the insurance sector. This issue stems from the ambiguity surrounding the safety of nanotechnologies, which prevents the underwriting community from understanding the risks and adopting legal-organisational-commercial risk transfer mechanisms such as captives, self-insurance, and risk sharing). The lack of the practice to disperse risk through access to insurance markets affects especially the SMEs, because due to their size and access to capital, they are vulnerable to changes in risk perception. Despite the clear interest of the insurance industry to engage with the science and regulatory communities in developing underwriting protocols for nanotechnology risks, it currently lacks the tools to do so. The development of such decision making tools and robust risk transfer practices is essential and should take into account the existing regulatory, legal and actuarial practices. This is one of the aims of the H2020 project caLIBRAte.

2.2.2. Building capacity for formalisation of skills

- Standardisation

Standardisation is one of the key elements in research and development to provide reproducible results. ISO defines a standard document as "document that provides requirements, specifications, guidelines or characteristics that can be used consistently to ensure that materials, products, processes and services are fit for their purpose". This standardisation process leads to an improved and consensus development of new technologies to be used safely for economy and social purpose[22]. One of the biggest problems in standardisation of NM test methods (characterisation and toxicity) is missing standardisation guidelines and protocols to be followed by all means as well as missing reference materials, however, this is work underway under the frame of OECD-sponsorship program and in ISO/TC 229 as well as by JRC towards a repository. In addition, OECD is responsible for harmonization of toxicity test methods. A pre-requisite is method validation, typically achieved by blinded study design to test a larger set of chemicals with known outcome. Beforehand typically the method is defined by round robin exercises. So far only a limited amount of round robins have been performed for nano-testing methods and no specific method validation has started.

Furthermore, due to the different properties of engineered NMs they can interfere with available test systems for hazard assessment, which were established for their bulk form or they may have different matrix interactions in analytics, which hampers quantification. The same problem is visible for computational toxicity predictions, where the models are developed and – what is more important – are validated according to different, non-standardised protocols. At this point it is also necessary to start with standardisation of characterisation methods before focusing on standardizing toxicity screening methodologies for NMs to evaluate properties, morphologies, chemical stability and biokinetics. Furthermore a characterisation in relevant media to exploit changes in behaviour when getting in contact with different media (e.g. agglomeration, aggregation, bundling, etc.) has to be performed. Despite the fact that all scientist agree that the characterization inside the test medium is important, no generally accepted guidelines exist. After the characterisation of NMs they might be grouped (not yet in place)

[22] ISO. (2013). International Organization for Standardization. Retrieved July 31, 2013, from www.iso.org

according to their behaviour shown and application used (human and environmental exposure). Following a proposed case-by-case approach exposure can be estimated and scenarios deducted to focus in the next step on adaption and/or establishment of existing/new toxicity methods[23]. In line with this, the standardisation skills may include knowledge about materials, products, processes and technologies, models, experience in preparing guidelines and SOP's, and shall be included in education actions.

- Education

The need for education has featured prominently in European policy texts such as the European Commission's Strategy for Nanotechnology of 2004[24] and its Nanosciences and Nanotechnologies Action Plan of 2005,[25] which aims to *'Promote networking and disseminate 'best practice' for education and training in N&N.'* Along with similar policy mandates for education on European member states and in other parts of the globe, this has resulted in a wide range of nanotechnology education activities over the last decade[26]. Also, NanoEIS[27] identified that educating for the general public is best achieved by including nano topics in primary and secondary education as that way it filters into homes as families discuss what children learned at school. Combined with a plethora of activities on national and regional levels, the question for nanotechnology education is not what education materials to develop, but how to make best use of the available material. There is already a Teacher's net[28], which has a mandate to develop teaching materials, and will translate them (free of charge) to any EU language upon request from just 3 teachers! This is not sufficiently widely known, nor utilised, so again, compilation and communication of existing resources is key. To gain value added for society, these skills may be build up in schools by involvement of N&N already in secondary school, as well as in basic lectures of relevant scientific studies. Ideally, all chemistry and materials science programmes in the EU should have at least one module covering safety and environmental assessment aspects, such that those developing materials have at least a basic understanding of the consequences of their developments. This was also called for with respect to Green Chemistry, as a means of embedding the concept into common experience.[29]

Ongoing research projects continuously push the edge of knowledge in the nanosafety research field, and it is important to disseminate this evolving frontier to educate young scholars and professionals across the public and private sectors. Training courses and workshops are being organised in most NSC projects, trying to provide an understanding of their scientific outputs and the achievements. Although not all NSC projects have specific work packages dedicated to education, most of them have budgets to perform training to ensure a high level of skills and consistency within the consortiums and to transfer the new knowledge for education of both young and experienced professionals from academia, industry, regulatory agencies etc.

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[23] Geys, J., Nemery, B., & Hoet, P. H. M. (2010). Assay conditions can influence the outcome of cytotoxicity tests of nanomaterials: better assay characterization is needed to compare studies. Toxicology in Vitro : An International Journal Published in Association with BIBRA, 24(2), 620–9. doi:10.1016/j.tiv.2009.10.007

[24] European Commission (2004). Towards a European Strategy for Nanotechnology. COM(2004) 338 http://ec.europa.eu/nanotechnology/pdf/nano_com_en.pdf

[25] European Commission (2005). Nanosciences and nanotechnologies: An action plan for Europe 2005-2009. COM (2005) 243 http://ec.europa.eu/research/industrial_technologies/pdf/nano_action_plan_en.pdf

[26] http://nanoeis.eu/ ; http://nanofutures.eu/community/group/skills-and-education

[27] http://www.nanoeis.eu/

[28] http://teachers.net/

[29] Green Engineering Principle, American Chemical Society.

Although many nanosafety training schools and workshops are taking place in projects each year, until now there has been no coordination of these events on the NSC level. Therefore, the SUN project developed and coordinates a NSC WG on Training. This WG aims to support nanosafety education through aligning the training agendas of the NSC projects to achieve the following objectives: i) Perform trainings where partners collaborate across the boundaries of projects and disciplines; ii) Ensure a high level of skills and consistency within the projects; iii) Transfer the knowledge generated in the projects to external stakeholders; iv) Enhance training offerings through collaboration and sharing of experience.

- Professional training and certification

Like for any other compounds, companies handling NMs must ensure a safe workplace and must be able to confirm that this objective is achieved. This is particularly difficult in the current context of

- knowledge gaps on hazards from and exposure to NMs, and on the efficiency of personal prevention and precaution measures and equipment towards NMs[30].
- frequent lack of detailed information about the product composition and their possible nano-specific health and safety issues and frequent loss of the information available from the raw material manufacturer while stepping down the value chain[31] [32].

Research projects have produced valuable information for Occupational Safety and Health (OSH) practices regarding NMs. There is the need for organizing and bringing this information to the industry in the form of science-based training and certification on nanosafety at the workplace, especially to SMEs or to OSH service providers (and also to many small research teams not familiar with industry's OSH procedures.

This work has already been started, for example:

- The French research and service institutes INERIS and CEA have developed a training and certification course for nanosafety at work[33]. More than 200 trainees from industry have received the training and, after successfully completing the exam, a certificate. The offer includes an on-site certification of the workplace. Developments are still welcome, such as on Personal Protection Equipment.
- The FP7 project Scaffold[34], developed and implemented training modules for the construction sector, along with a risk management model. However, one of the main results of the project, the Toolkit, works in a specific mode of operation only, specifically designed for training reasons. This mode allows access to an extensive library of knowledge (processes, hazards, toxicology, devices and methods of measuring exposure, exposure databases, best practices, protective measures, etc.) and a set of tools for managing nano-risks in construction (risk assessment, KPIs, OHSMS diagnosis, implementation, and audit, etc).
- FP7 project NanoValid[35] has produced a set of documents called "Nano to Go!": Nano to Go![36] is a practically oriented guidance on safe handling of nanomaterials

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

[31] FIEC *et al.*, 2009: "Nanotechnology in the European Construction Industry -State of the art 2009 - Executive Summary",

[32] EU-OSHA, 2012: "European Risk Observatory – Literature Review", https://osha.europa.eu/en/tools-and-publications/publications/literature_reviews/workplace_exposure_to_nanoparticles

[33] NANO-CERT, one day for workers, 3 days for OSH managers, in French and in English http://www.ineris.com/ineris_formation/detail/1344

[34] http://scaffold.eu-vri.eu/

[35] http://www.nanovalid.eu/

(NMs) and other innovative materials at the workplace. It was developed within the NanoValid project by the German Federal Institute for Occupational health (BAuA).
- Some European trade unions or similar bodies (notably ETUC member organisations, such as national occupational health institutes) have already produced corresponding information destined for workers.[37][38]

There is the need to consolidate and develop these first initiatives so as to make available to industry and other stakeholders concerned a European-wide, up-to-date, science-based, complete training and certification system for nanosafety in the workplace. However, education is not only needed with respect to occupational safety.

- The German Federal Institute for Risk Assessment (BfR) has developed in cooperation with the European Infrastructure project QualityNano[39] a training event specifically dedicated for risk assessors with a focus on consumer safety, which took into account specific issues for material characterization and toxicity testing. It addition current regulation (e.g. REACh, cosmetics, novel food and biocides regulation) was explained and discussed.
- EMA has developed training events specifically dedicated to understand risk assessment for nano drugs.

An overview of different types of trainings, especially for scientists and laboratories, can be found on the QualityNano webpage[40], although this is not being updated any longer. The NanoSafety Cluster website has a calendar of upcoming events, including training provided by FP7 and H2020 projects, and the new Training sub-group is developing an updated and projected to the next several years roadmap of the training planned in FP7 and H2020 projects to allow oversight, consolidation of offers and gap analysis.

2.2.3. Building reliable tools for nanosafety at work

- Risk management model

As for OSH training and certification, there is a need for the development, testing, validation and dissemination of holistic, consistent and cost effective RMM to manage occupational exposure to NMs in the different industrial sectors. These RMMs should be based on state-of-the-art safety management systems (OHSAS 18001 + ISO 31000) and should organize the different tools and data available for OSH consultants and managers, including:

- Tools for analysis of occupational risks along the life cycle of NMs and nano-enabled products
- Valid or newly proposed globally harmonized Occupational Exposure Limits (OELs), as well as reactivity parameters (e.g. explosion & flammability limits)
- Exposure measurement protocols
- Control banding tools
- Risk management diagnosis, implementation and audit
- Etc,..

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[36] http://www.nanovalid.eu/nanoToGo/nanoToGo-flyer.pdf

[37] Guidance on the protection of the health and safety of workers from the potential risks related to nanomaterials at work - Guidance for employers and health and safety practitioners (2014); http://ec.europa.eu/social/BlobServlet?docId=13087&langId=en

[38] https://www.etuc.org/press/workers%E2%80%99-protection-lost-nano-space-etuc-reaction-european-commission-second-regulatory-review#.VsM4Ho-cFu0

[39] http://www.qualitynano.eu/

[40] http://www.qualitynano.eu/the-qnano-knowledge-hub.html

The first sectorial-specific initiatives, such as Scaffold for the construction sector and NanoMicex for paints and pigments should be consolidated and developed at a European-wide, multi-sectorial scale.

Project Scaffold produced a “Library of Solutions for Risk Management” including a specific handbook, four quick guides (risk prevention, risk assessment, risk protection and risk management) and a Toolkit (software), based on OHSAS 18001 + ISO 31000, to facilitate the diagnosis, implementation and audit of nano-risk management in large companies and SMEs, in construction. Recently, the CEN/TC 352 "Nanotechnologies" committee decided to accept a New Work Item (NWI) proposal relating to CEN/TS "Manufactured nanomaterials (MNMs) in the construction industry: Guidelines for occupational risk management”[41], lead by partners of the Scaffold project.

- Safety Data Sheets

The main routes of hazard and risk communication are pictograms, signal words (e.g. “danger”, “warning”), hazard and risk phrases and the provision of information via safety data sheets (SDS). The transmission of the nanosafety information through the Safety Data Sheets is generally very incomplete, and information provided is often for the bulk form. The result is a frequent lack of detailed information about the product composition and their possible nano-specific health and safety issues, and frequent loss of the information available from the raw material manufacturer while stepping down the user chain (FIEC *et al*., 2009; EU-OSHA, 2012).

Transcription processes to support the translation of scientific knowledge into the SDS have to be established and implemented, and should be done at the EU-level. The development of high quality SDS is therefore a fundamental element underpinning the safe and responsible development of NMs and nano-enabled products. Some efforts in this direction have already been made, such as the Swiss effort, and could be built upon. Indeed, guidelines are now available in Switzerland which may help in the preparation of SDS for NMs and nano-containing products and better support the appropriate communication of risk information throughout the supply chain[42],[43]. However, some discussion of whether these and acceptance by all member states and globally harmonised version of these would be required (potential topic for globally harmonised system).

- Occupational Exposure Limits (OELs) and Toxicological Reference Values (TRVs)

Occupational Exposure Limits (OELs, for assessing occupational exposure) and Toxicological Reference Values (TRVs, for assessing exposure of the population) exist for very few NMs (like SiO_2, TiO_2). For chemically reactive nanoparticles, safety parameters (such as explosivity and flammability parameters) should also be provided. There is a strong need to translate the scientific data on hazards and especially toxicology into such values. Based on the available data on the toxicological properties of the NMs selected by project Scaffold, recommendations for occupational exposure limit values

[41] See ISO/TS 12901-2:2014: http://www.iso.org/iso/catalogue_detail.htm?csnumber=53375

[42] SECO. (2012). Safety data sheet (SDS): Guidelines for synthetic nanomaterials. Available at: http://www.bag.admin.ch/nanotechnologie/12171/12176/index.html?lang=en [accessed 16th October 2014]

[43] SECO. (2012). Two examples for the guidelines: Safety data sheet (SDS) for synthetic nanomaterials. Available at: http://www.bag.admin.ch/nanotechnologie/12171/12176/index.html?lang=en [accessed 16th October 2014]

have been proposed for TiO_2, SiO_2, Carbon Nanofibers (CNF), Cellulose Nanofibers (CENF) and Nanoclays.[44] Of course, the setting of limits, the routes of communicating with the organizations doing that, and the way how it is done have to be made transparent and need to be science based.

2.3. Organisation/Inventory

The challenge of managing safety is given to a certain extend to the regional, national and/or international nanosafety platforms in European countries. However, this is still done uncoordinated on European level, which shall be changed by recent activities (e.g. CSA NMBP-27-2016-project, etc.). A wide variety of national and (EU) regional platforms and centers can be observed which are dedicated to either research or dissemination of nanosafety. Broadly three categories can be distinguished: NanoSafety Research Centers, NanoSafety Expert Platforms, and NanoSafety Collaborations;

2.3.1. **NanoSafety Research Centers**. Virtual stand-alone academic or collaborative entities between research institutes/ universities with focus on nanosafety research with national (e.g. governmental) funding.

- Examples are the Finnish NanoSafety Research Centre[45], the Danish Nano Safety Centre[46], Namur NanoSafety Centre[47], NanoSafety-Austria/EURO-NanoTox, etc.

2.3.2. **NanoSafety Expert Platforms**: Collaboration on the level of (academic) experts, mainly focused on dissemination of nanosafety. Within the field of occupational safety and health, these platforms share knowledge, seek collaboration and provide scientific interpretation.

- KIR nano (Risks of Nanotechnology Knowledge and Information Centre)[48]

  KIR nano was initiated by the Dutch government and is currently jointly sponsored by three Ministries. The target groups of KIR nano are staff at the ministries and other government organisations and EHS professionals. On a national level, KIR nano participates for instance in the interdepartmental working group on risks, in which various ministries are represented.

- BioNanoNet Forschungsgesellschaft mbH[49]

  BioNanoNet is an Austrian Network that combines a wide range of expertise in numerous medical and pharmaceutical disciplines, with a strong focus on nanomedicine and nanotoxicology. BioNanoNet serves as the Austrian NanoSafety hub. The BioNanoNet GmbH has the clear aim of supporting innovative interdisciplinary research by forming cooperative networks and synergistic collaborations in order to initiate and coordinate national and international research projects. In addition to providing BioNanoNet's nanosafety

[44] http://www.scaffold.eu-vri.eu/
[45] http://www.ttl.fi/en/Pages/default.aspx
[46] http://nanosafety.dk/
[47] https://www.narilis.be/research/research-centers-groups-1/namur-nanosafety-center
[48] http://www.rivm.nl/Onderwerpen/N/Nanotechnologie/Kennis_en_informatiepunt_risico_s_KIR_Nanotechnologie
[49] http://www.bionanonet.at/health-nanosafety

expertise, the renowned BioNanoNet members include top-level scientists that work on several TRL's to advance the safe implementation of nanotechnology.

❖ SAFENANO[50]

SAFENANO is dedicated to providing the highest quality expertise to help nanotechnology emerge and develop on a safe and sustainable basis, maximising its commercial potential, through a continuous development and improvement of our knowledge, equipment and practice.

Vision: To be the leading multidisciplinary independent authority on nanosafety and partner of choice for industry and regulators, ensuring the safe and sustainable development of nanotechnology.

Values: We develop and maintain valued relationships with our clients and stakeholders across the nanotechnology community. We uphold our independence and integrity. We set high standards of excellence both personally and professionally.

2.3.3. **NanoSafety <u>Collaborations</u>:** Collaboration between academic experts/ institutes and industry

❖ EHS - Advance[51]

EHS-Advance is a Competence Centre distributed, promoted by the nanoBasque Agency, funded by the regional Basque Government (Spain) and currently under implementation phase by the technological centers GAIKER-IK4[52], TEKNIKER-IK4[53] and the corporation TECNALIA[54], within the framework of a Strategic Research project funded by the Basque Government. The initiative sets out to provide industry and other interested parties with service and support in the areas relating to the Environment, Health and Safety (EHS) whenever nanotechnologies are incorporated into its products and processes. The center seeks synergistic effects by merging capabilities of assessment, analysis and testing, and highlighting the existence of specific infrastructures in the Basque Country, with a strong relationship with organizations with the same interests at the European level thereby creating a *One stop shop for nano EHS issues*. The current offer includes: 1) Studies, analyses & tests (OECD, ASTM, ISO, CEN … in the areas of toxicology in vitro & in vivo, ecotoxicology), 2) Risk assessment & control, in processes (industrial safety & OHS), 3) Training, dissemination & awareness, 4) Development & implementation of methods and standards.

❖ Nanocentre[55]

Nanocentre is initiated by TNO in cooperation with RIVM and Syntens (Innovationplatform for SMEs) to support SMEs with safely innovation using NMs by providing **tailored** dissemination of knowledge <u>on nanosafety and</u>

[50] http://www.safenano.org/
[51] http://www.ehsadvance.com/en/
[52] http://www.gaiker.es/ing/index.aspx
[53] http://www.tekniker.es/en/
[54] http://www.tecnalia.es/en/
[55] www.nanocentre.nl

innovation by nanotechnology or NMs. This information is provided by the website, where information can be retrieved, and where an interactive Q/A function, and a module for new questions can be accessed. In addition to the website, SMEs/ contact persons who signed up for the newsletter, are regularly invited for workshops with various topics related to safe use of NMs. Some of the workshops provide aspects of training/ instruction.

Nanocentre partners use their own resources, however, both TNO and RIVM are indirectly supported by Government (i.e. the Ministries of Socials Affairs and Employment and Infrastructure and the Environment).

- NanoHouse[56]

The aim is to develop added value by initiating the application of nanotechnology within businesses. To realize this ambition, NanoHouse is the knowledge broker and project leader for businesses who are interested in applying nanotechnology. NanoHouse is interested in receiving worldwide information concerning: NMs functionalities, intermediate applications, and (international) research programs. The information will be freely distributed towards potential interested businesses to develop innovation projects and business clusters.

NanoHouse is located in the South of the Netherlands and is working in parts of Belgium, the Netherlands and Germany. The reasoning is that many large and medium-sized companies and research institutes are located in this region and cooperation will be beneficial. NanoHouse consists of an advisory board, board and project office.

- INERIS[57] and CEA[58], French institutes linking research and industry

The French research and service institutes INERIS and CEA have developed an offer of services for the industry, from physico-chemical characterization and (eco)toxicology study to nanosafety at the workplace and integrated risk assessment, in the form of studies, training, and certification.

- CRANN institute at Trinity College Dublin[59]

CRANN (the **C**entre for **R**esearch on **A**daptive **N**anostructures and **N**anodevices) is one of the largest research institutes in Trinity College Dublin and Ireland's leading nanoscience institute.

CRANN brings together over 300 researchers including 37 leading Investigators based across multiple disciplines including Trinity's Schools of Physics, Chemistry, Medicine, Engineering and Pharmacology. The centre delivers internationally leading materials research that is industrially and clinically informed with outputs including new discoveries and devices in ICT, medical device and industrial technology sectors. The centre has a strong emphasis on linking industry to research programmes and the aim of the centre is to develop safe products that directly impact everyone's quality of life such as the development of the next generation societal wellbeing.

[56] http://www.nanohouse.nl/nl/english
[57] http://www.ineris.com/theme_presta/1754
[58] http://www.minatec.org/recherche/rd-interventions-sur-terrain
[59] http://crann.tcd.ie

CRANN institute is supporting industry-academia research for industrial transfer (from low to mid-high TRL) with strong infrastructural and technical strengths in the areas of microscopy, computation and environmental health and safety assessment. On the latter, the group has built strong infrastructure and characterization know-how, which is enabled by strong collaboration at international level.

❖ FENAC at the University of Birmingham[60]

FENAC (Facility for Environmental Nanoscience Analysis and Characterisation) is a UK Natural Environment Research Council funded facility offering (funded) access to a suite of state of the art NMs synthesis, characterisation and impact assessment capabilities at expertise at the University of Birmingham. Access is provided on a the basis of peer-reviewed proposals for pilot projects or full investigations on all aspects of NMs interactions in living systems (with a focus on environmental aspects at present, although the remit is currently being expanded). A suite of additional services for SMEs, regulators and other stakeholders (e.g. water companies, city councils etc.) is currently being developed for launch in late 2016. A strong focus on characterisation of NMs in complex environmental and product matrices is a feature of FENAC's expertise, with facilities for characterisation of interactions with biotic and abiotic matrix components.

2.4. International cooperation

Global cooperation is needed to along all nanosafety work. Some examples of international cooperation which are already dealing with nano-related topics are listed below.

❖ Communities of Research[61]

➔ A platform for scientists and other interested stakeholders from academia, government, industry, and NGOs in the US, EU, and beyond to develop a shared repertoire of protocols and methods to overcome research gaps and barriers and to enhance their professional relationships in the area of NMs safety assessment.

❖ Latin America[62]

➔ NMP-DeLA is a support action funded by the EU under FP7 for two years from 1st September 2013. It aims to facilitate the deployment of advanced and enabling technologies in areas of major social challenge in Latin America. The NMP-DeLA project brings together partners and experts from across Latin America and Europe to develop a series of activities between the two regions, to strengthen the local research and training potential, as means to achieve the goal of deployment of new, advanced and enabling technologies in areas of major social challenge in Latin America: water, energy and health.

[60] http://www.birmingham.ac.uk/facilities/fenac/index.aspx
[61] http://us-eu.org
[62] http://NMP-DeLa.eu

❖ Australian Initiatives (NICNAS; ARC Centre of Excellence in Convergent Bio-Nano Science & Technology)

➔ The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) is a statutory scheme administered by the Australian Government Department of Health. NICNAS aids in the protection of the Australian people and the environment by identifying out the risks to occupational health and safety, to public health and to the environment that could be associated with the importation, manufacture or use of industrial chemicals, and by maintaining a national standard for cosmetic products.

➔ The ARC Centre of Excellence in Convergent Bio-Nano Science and Technology is a national innovator in bio-nano sciences and an incubator of the expertise and technological excellence required to develop next generation bio-responsive NMs.

- Needs Assessment

The development (and consolidation) of a suite of NanoSafety Services into a European one stop shop will reduce the uncertainties, increase the confidence in this technology, and will lead to acceptance of nano-enabled products.

The needs of the various concerned stakeholders have to be further elaborated within future activities (e.g. consultation rounds, polls, interviews, etc.); comments of initial analysis are outlined below:

➔ Industry and market view

Nanotechnology is making advances faster than the safety management related to it. Development of new methods, strategies and tools for risk management based on solid scientific knowledge may take a longer time than their market presence. European industry is already manufacturing NMs and nano-enabled products and workers might be exposed to nanomaterials. Consequently, efforts should be made to provide the industry with intermediate management solutions, based on the state of the art, to make decisions with minimal uncertainties. This would mean the need to translate and encapsulate the results of current research into a battery of practical methods, strategies and tools for the management of nano-risks, directly usable by industry and companies that provide services to industry.

In addition, there is a need to establish adequate strategies to manage and communicate risks of NMs and nano-enabled products further down the supply chain, to both professional and consumer users of the product(s), where appropriate. There are already a couple of interesting sources of information like the “Nanorama Laboratory”, an online, interactive tool to help laboratory personnel understand how to safely handle nanomaterials [63]. Collecting, evaluating and presenting of up-to-date scientific facts in an easy comprehensible way is the main focus of the project DaNa 2.0.[64] A scientific expert team prepared the latest research findings from the field of human and environmental nanotoxicology and present these together with material

[63] http://nano.dguv.de/nanorama/bgrci/en/

[64] http://www.nanopartikel.info/en/projects/current-projects/dana-2-0

properties and possible applications for interested laymen, stakeholders and other scientists. These data and together with further facts on nanotechnology are publicly available on the internet platform "Nanoobjects".[65]

Industry is not only responsible for ensuring the quality and safety of the product it produces, but also has a corporate responsibility to communicate information regarding risks downstream workers / consumers may be exposed to.

Communicating with consumers about well understood risks can help to provide assurance that such risks are being actively managed, improving the acceptance of nanotechnology by end-users. Work with consumer agencies (e.g. Which? in the UK) could be facilitated to allow direct comparison of products with/without NMs (e.g. sunscreen) such that the real benefits to consumers are demonstrated clearly and in an unbiased manner. Such activities could be built into the stakeholder engagement activities of an EU NanoSafety Centre.

➔ Science view

From the scientific perspective there has been an accelerated evolution and in depth knowledge generated around nanosafety across the many research projects and flagship initiatives, which have been funded towards the creation of good reliable data, safety-by-design approaches, decision-making processes, safety value chain and methodologies for assessing safety from *in vitro* and *in silico* models to worker protection and environmental safety. Development of experimental and computational methodologies, characterization and standardisation are at the basis of the scientific data to be provided for the assessment of MNMs.

The next critical phase is the consolidation of this knowledge, in order to re-assess which of the previous knowledge-gaps have now been filled, where established and validated protocols exist and should be utilised as standard, and where research effort should now focus (e.g. on testing of appropriately aged NMs, on longer term exposures / chronic studies, on more realistic *in vitro* models that are predictive of *in vivo* effects, etc.). EU FP7 project NanoMILE (www.nanomile.eu) is taking an initiative in this direction to develop consensus reports on several key aspects of nanosafety during 2016, including methods for NMs characterisation in complex matrices (with NanoValid and MARINA), high throughput and omics methods (with NanoSolutions) and on environmental assessment (with GuideNano and NanoFASE), based on NANoREG-project's output. These consensus papers will facilitate contract research organisations and regulatory authorities to converge on agreed test methods for regulatory dossiers, and facilitate contract research organisations to take over the assays and SOPs and deliver them as services for enterprise and SMEs.

➔ Further views

In addition to the above highlighted views, it would be of utmost importance to consider the governmental view in several states in Europe, which will enable regional differences in perception, engagement, and structuring to be taken into account. Key to a common approach in Europe will be the integration of national stakeholders points of view with the tasks and needs on European level from EC, and the translation of guides for SMEs and others into all EU languages. Hence, a coordinated structure which enables taking into account lessons learned from the

[65] http://www.nanopartikel.info/en/glossary/193-nanoobject

past, combining this with new aspects recommended in this roadmap, the inclusiveness throughout all European countries as well as with global players will ensure to gain acceptance in all communities.

- Timeline for further needs assessment

Mid 2016 – implementation of existing strategies and consolidation of resources

Mid 2016 – start preparation of Research- and CSA-topics for the future calls, addressing the identified bottlenecks.

2017 – next call for proposals addressing “CTTM”-roadmap- actions

2018 – start development of CTTM-call topics looking at the needs from 2020-2030

2.5. Current bottle-necks (hindering large scale access to the market of MNMs)

2.5.1. Occupational safety: sustainable marketing requires that employees and employers are confident in the safety of the processes implemented for their protection:

Please note: the Bottle-necks are NOT ordered by any means; if needed, they could be prioritised in a next step.

Bottle-neck	Solutions	Layer(s) concerned
Lack of awareness of employees and employers	• Operational OSH solutions • Communication / training • Application of a diligent and precautionary approach to labelling • Proper SDSes	1. Scientific knowledge **3. CTTM**
Uncertainty in efficiency of prevention/protection measures	• Improve knowledge • Develop adequate portable (personal) measuring equipment, including SOPs • Develop safer processes anyway (e.g. less release during production, fire/explosion, massive release protection systems) • Standardized protocols to support the evaluation of the effectiveness of common RMMs	1. Scientific knowledge **3. CTTM**
Uncertainties in risk assessment and in regulation	• Improve and stabilize the regulation • communicate uncertainties	2. Regulatory research **3. CTTM**
Lack of validated reference control banding tools	• Operational OSH solutions • Standardisation	1. Scientific knowledge **3. CTTM**
Lack of validated methods (toxicological and analytical) for nanosafety assessment	• Equipment • Harmonization • Round robins • validation studies • General guidelines how to standardise nano-specific protocols	1. Scientific knowledge **3. CTTM**
Lack of Occupational Exposure Limits (OELs) and safety parameters for reactive NMs (explosion/fire, runaway reactions)	• Transcription from scientific knowledge and OSH expertise to Occupational Exposure Limits and reaction safety Limits; link with SCOEL. • Harmonization, validation, Standardisation of protocols to	1. Scientific knowledge 2. Regulatory research **3. CTTM**

	measure the levels of exposure in the workplace. • Personal measuring equipment	
Lack of transmission of nanosafety information through the Safety Data sheets	• Transcription processes from scientific knowledge to the SDS • Development of high quality SDS reflecting as best as possible current knowledge in the field	2. Regulatory research **3. CTTM**
Lack of nanosafety management systems Lack of integration of nanosafety issues into industry process management systems.	• (sector specific) nanosafety management systems, proportional to the respective situation • Standardisation, training and certification • Translate and encapsulate the results of research in a battery of practical methods, strategies and tools for the management of nano-risks • Harmonized standards	1. Scientific knowledge **3. CTTM**
Lack of support for the implementation of the previous items	• Helpdesk, Q&A platforms • Translation into EU languages • Collaboration with sector-specific industry associations and trade unions	**3. CTTM**
Lack of trust towards employers in the field of Nano-OSH	• Open two-way communication with open results • OHS Training for nano-workers in addition to companies working with nano (including online) to inform workers of their rights and responsibilities. • Voluntary Nano-exposure registries whereby workers handling NMs can volunteer for periodic health checks as a means to initiate long-term exposure monitoring and epidemiological studies. [66]	1. Scientific knowledge **3. CTTM**
Lack of regulation specifying requirements to ensure the safety and health of workers exposed to nano-risks (*the game board*)	• New or improved regulation • Harmonized standards	2. Regulatory research **3. CTTM**

[66] Michaela Kendall, Iseult Lynch, (2016), Long Term Monitoring for Nanomedicine Implants and Drugs, Nature Nanotechnology.

2.5.2. Public safety: sustainable marketing requires that consumers are confident in the safety of the products they purchase:

Bottle-neck	Solutions	Layer(s) concerned
Improve the trust towards regulation (REACH: adapted to nanos?)	• Follow and communicate safety and labelling rules. These laws and their related regulations are intended to protect consumers from health hazards and deceptive practices and to help consumers make informed decisions regarding product purchase. • Integrate latest knowledge into regulation (e.g. if/if not labelling, clear definitions and tools to measure, etc.) • Open two-way communication with open sharing of results • Promotion of REACH implementation as a key action in nanosafety projects	2. Regulatory research **3. CTTM**
Lack of Toxicological Reference Values (TRVs)	• Transcription from scientific knowledge and risk assessment expertise to Toxicological Reference Values	1. Scientific knowledge **3. CTTM**
Improve trust towards employers in the field of Nano-OSH	• Open two-way communication	**3. CTTM**
Lack of Risk characterization awareness	• Open two-way communication sharing of outcomes even where unfavourable towards use of nanotechnologies • Cooperation with consumer organisations (e.g. Which?) to assess nano/non-nano products and communicate the results openly. If benefits are for the company (e.g. improved process) or the environment (for example) rather than consumer, need to be open about this and allow consumer freedom of choice; e.g. using LCA-approach.	**3. CTTM**
Lack of Risk characterization awareness	• Open two-way communication with open sharing of results • Option for consumers also to participate in voluntary exposure and health monitoring	**3. CTTM**

	programmes? This could also be linked to food, cosmetics and nanomedicines, and could operate as an important assessment of impacts of cumulative exposures to different NMs from different products, which is an area we genuinely know very little about at present.	

2.6. Actions proposed/CTTM-future topics

For the identified bottle-necks proposals for actions to be taken are shown in this chapter. The identifier shows the abbreviation for this roadmap CTTM, a numbering and suggests a timeline to implement the action (st = short term 2018-2020; lt = long term 2020 and beyond).

CTTM 01 st Occupational Safety	**Objective** **Employees and employers are confident in the safety of the processes implemented for their protection**	
Current challenges	**Activities**	**Timeline**
Lack of awareness of employees and employers	• **Networking** ▪ Interaction and adequate communication between existing platforms (e.g; NanoSafety cluster) and industry/SMEs/trade unions to raise awareness ▪ Development of an European nano-network ▪ Networks should be open for all stakeholders • **Reporting** ▪ Reporting of studies, guidelines etc can provide sufficient and useful information, after performing a mandatory quality check • **Communication** ▪ Successful communication and outreach, in order to ensure safety and consolidate the trust and the confidence required ▪ Interaction and adequate, unbiased, targeted and reliable communication/networking in order to promote the application of up-to-date safety culture • **Standardization** ▪ Establish a “universal” definition of key terms (i.e. nanomaterials) including means to measure • **Assistance to new-comers** ▪ Scientific inclusiveness and information sharing within the nano-network approach • **Assistance to regulators** ▪ Training of persons which are involved in regulation or risk assessment (e.g.; ECHA initiatives such as their science meetings, and recent activities around e.g. omics) **Professional training and certification** ▪ Development of first initiatives so as to make available to industry and other stakeholders concerned a global, up-to-date, science-based, complete training and certification system for nanosafety. This should be for employers / OSH managers, but also for employees handling NMs in order that they have full understanding of potential risks and their rights and responsibilities.	Short term
Uncertainty in efficiency of prevention/protection	• **Networking** ▪ Networking of existing platforms, including the NanoSafety cluster, at European level	Short term

measures	and cooperation with third countries to improve knowledge • **Benchmarking** ▪ Assess and increase safety in regulatory terms, and the capacity to develop and implement safety-by-design processes and products with the aim of keeping safety level above pre-defined values • **Data Collection** ▪ Data generation based on harmonized and standardized protocols should precede 'raw' data collection to ensure that scientifically solid data are collated (e.g.; eNanoMapper project, Exposure Scenario library and the Exposure Efficacy Control Library, NANoREG database) • **Reporting** ▪ Reporting of studies, guidelines etc can provide sufficient and useful information • **Communication** ▪ Successful communication and outreach, in order to ensure safety and consolidate the trust and the confidence required • **Standardization** ▪ Development of harmonized, validated methods, which ideally are generally (i.e. internationally) accepted (preferable OECD, ISO, CEN)	
Uncertainties in risk assessment and in regulation	• **Networking** ▪ Networking of existing platforms, including the NanoSafety cluster, at European level and cooperation with third countries to improve knowledge • **Communication** ▪ Interaction and adequate, unbiased, targeted and reliable communication/networking in order to eliminate uncertainties in risk assessment and in regulation • **Assistance to new-comers** ▪ Development of guidelines and best practices guide for the safe handling and use of NMs in different sectors; as well as new tools to support the implementation of relevant pieces of regulation, including REACH regulation • **Feedback for agreeing next research priorities** ▪ Involvement of highly renowned actors in the research and industrial field and the interaction with several stakeholders (e.g. European as well as global active bodies in standardization, regulation, etc.) to determine and agree future research priorities • **Professional training and certification** ▪ Training of persons which are involved in regulation or risk assessment (e.g.; ECHA	Short term

	initiatives such as their science meetings, and recent activities around omics and HCA)	
Lack of trust towards employers in the field of Nano-OSH	• **Communication** ▪ Successful communication and outreach, in order to ensure safety and consolidate the trust and the confidence required • **Assistance to new-comers** ▪ OHS Training for nano-workers in addition to nano-active companies to inform workers of their rights and responsibilities • **Professional training and certification** ▪ Training of workers would also help to reduce mis-trust of their employers ▪ Establish epidemiological studies and monitoring (e.g.; voluntary EU-wide monitoring of exposure and health over the long term)	Short term

CTTM 02 st - lt **Occupational Safety**	**Objective** **Validated, standardized safety tools are available.**

Current challenges	**Activities**	**Timeline**
Lack of validated reference control banding tools	• **Standardization** ▪ Harmonized, standardized and validated control banding tools based on state-of-the-art safety management should be available for OSH consultants and managers	Long term
Lack of validated methods (toxicological and analytical) for nanosafety assessment	• **Standardization** ▪ General guidelines how to standardise nano-specific protocols ▪ Development of harmonized, validated methods, which ideally are generally (i.e. internationally) accepted ▪ Standardization workshop with competent experts ▪ Harmonization of protocols and inter-lab training ▪ Round Robins, involving external labs e.g. standard metrology labs	short term
Lack of Occupational Exposure Limits (OELs) and safety parameters for reactive NMs (explosion/fire, runaway reactions)	• **Standardization** ▪ Implementation of valid globally harmonized Occupational Exposure Limits (OELs), as well as reactivity parameters (explosion & flammability limits) e.g.; via transcription from scientific knowledge and OSH expertise to Occupational Exposure Limits and reaction safety Limits	Short term

Lack of transmission of nanosafety information through the Safety Data sheets	• **Reporting/Standardization** ▪ Development of "nano SDS" i.e.; SDS which includes hazard and risk phrases, detailed information about the product composition and their possible nano-specific health and safety issues	Long term
Lack of nanosafety management systems **Lack of integration of nanosafety issues into industry process management systems**	• **Reporting/Networking** ▪ Development, testing, validation and dissemination of holistic, consistent and cost effective RMM • **Certification of methods** ▪ Transferability of RMM methods need to be demonstrated in a second stage, typically be performing round robin exercises	Short term
Lack of support for the implementation of the previous items	• **Networking** ▪ Interaction and adequate communication between existing platforms (e.g; NanoSafety cluster) and industry/SMEs to raise awareness • **Communication** ▪ Successful communication and outreach, in order to ensure safety and consolidate the trust and the confidence required ▪ Interaction and adequate, unbiased, targeted and reliable communication/networking in order to promote the application of up-to-date safety culture	Long term
Lack of regulation specifying requirements to ensure the safety and health of workers exposed to nano-risks (the game board)	• **Networking** ▪ Networking of existing platforms, including the NanoSafety cluster, at European level and cooperation with third countries to improve knowledge • **Communication** ▪ Interaction and adequate, unbiased, targeted and reliable communication/networking in order to eliminate uncertainties in risk assessment and in regulation ▪ provide an overview on which guidance documents already exist and link them such that market actors • **Assistance to new-comers** ▪ Development of guidelines and best practices guide for the safe handling and use of NMs in different sectors; as well as new tools to support the implementation of relevant pieces of regulation, including REACH regulation • **Feedback for agreeing next research priorities** ▪ Involvement of highly renowned actors in the research and industrial field and the interaction with several stakeholders (e.g. European as well as global active bodies in standardization, regulation, etc.) to determine and agree future research priorities	Long term

	• **Professional training and certification** ▪ Training of persons which are involved in regulation or risk assessment (e.g.; ECHA initiatives such as their science meetings, and recent activities around omics and HCA)	

CTTM 03 st-lt **Public Safety**	**Objective** **Consumers are confident in the safety of the products they purchase**		
Current challenges	**Activities**	**Impact**	**Timeline**
Improve the trust towards regulation (REACH: adapted to nano?)	• **Integration of latest knowledge into regulation** • **Promotion of REACH implementation as a key action** ▪ Supply a translation which suits the consumers' needs • **Communication** ▪ Open two-way communication with open sharing of results ▪ Science-based cooperation between stakeholders ▪ Unbiased, targeted and reliable communication • **Networking** at global level	**Assistance to regulators, special training for persons involved in regulation**	Long term
Lack of Toxicological Reference Values (TRVs)	• **Transcription from scientific knowledge and RA expertise to Toxicological Reference Values (TRVs)**	**Realization of science-based human risk assessment for risk-based management**	Short term
Improve trust towards employers in the field of Nano-OSH	• **Communication** ▪ Open two-way communication with open sharing of results	**Professional training and certifications**	Short term
Lack of Risk characterization awareness	• **Communication** ▪ Open two-way communication with open sharing of results • **Cooperation with consumer organisations to assess nano/non-nano products and communicate the results openly** • **Option for consumers also to participate in voluntary exposure and health monitoring programmes**	**Reliably informed unbiased consumers,** **Freedom of choice for consumers**	Long term

2.7. Expected outcome

2.7.1. Guidance to market actors (industry, public authorities)

Currently guidance documents are established from various regulatory panels and other stakeholders. For instance the EU Scientific Committee on Consumer Safety (SCCS) has published a document (SCCS/1524/13)[67], which addresses the relevance, adequacy and quality of data in safety dossiers of NM in cosmetics. The European Chemicals Agency (ECHA) has published outcomes from expert meetings on best practices on physicochemical and substance identity information for NMs[68], on best practices for REACH registrants on assessing human health and environmental hazards for NM[69] as well as guidance on human health and environmental exposure assessment and risk characterization of NM[70]. EFSA published a guidance document for risk assessment of NM in food and feed[71]. Also at the OECD level various guidance documents are developed such as the guidance document on sample preparation and dosimetry[72]. Finally SCENHIR has published a guidance document for risk assessment of nanomaterials[73].

However, regulation is differently organized in various sectors, i.e. different regulations applies in e.g. cosmetics, food, biocides, and chemicals. Therefore, as a first tier it may be highly useful to provide an overview on which guidance documents already exist and link them such that market actors, in particular SME, can have easy access. In the second tier, it may furthermore be highly useful to have a closer look into these guidance documents. Several of them are rather unspecific. Some of them also include a compilation of research needs, rather than giving specific guidance. Therefore in a second tier, the information currently contained in already existing guidance documents could be extracted and summarized as a set of specific actions SMEs should undertake.

67 Scientific Committee on Consumer Safety (SCCS), (2014), Memorandum on Relevance, Adequacy and Quality of Data in Safety Dossiers on Nanomaterials; http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_142.pdf

68 European Chemical Agency (ECHA), (2013), Best practices on physicochemical and substance identity information for nanomaterials; http://echa.europa.eu/documents/10162/5399565/best_practices_physiochem_subst_id_nano_en.pdf

69 European Chemical Agency (ECHA), (2013), Assessing human health and environmental hazards of nanomaterials - Best practice for REACH Registrants; http://echa.europa.eu/documents/10162/5399565/best_practices_human_health_environment_nano_en.pdf

70 European Chemical Agency (ECHA), (2013), Guidance on human health and environmental exposure assessment and risk characterization of NM - Best practice for REACH registrants; http://echa.europa.eu/documents/10162/5399565/best_practices_human_health_environment_nano_3rd_en.pdf

71 European Food Safety Authority (EFSA), (2011), EFSA published a guidance document for risk assessment of NM in food and feed, EFSA Journal 9(5):2140 [36 pp.]; DOI: 10.2903/j.efsa.2011.2140

72 OECD, (2012), Guidance on Sample Preparation and Dosimetry for the Safety Testing of Manufactured Nanomaterials - Series on the Safety of Manufactured Nanomaterials No. 36; http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2012)40&doclanguage=en

73 Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR), (2009), Risk Assessment of Products of Nanotechnologies; http://ec.europa.eu/health/ph_risk/committees/04_scenihr/docs/scenihr_o_023.pdf

Finally, in a third tier, more specific guidance documents e.g. for each sector could be established, again in close collaboration with sector-specific industry associations, which specifically do address also technical issues and give methodological details (e.g. how to measure a certain group of NM in a given matrix). The third tier may require additional method establishment or validation and thus is dependent on close interactions to other points already mentioned in this document. Aligning such activities via a specific research infrastructure dedicated to support and enable NMs regulation could facilitate such activities via the Joint Research Activities.

2.7.2. Best practice

To be elaborated within future projects, but directed via the ongoing gap analysis identified in the CTTM roadmap and resulting activities.

Specific examples that could be addressed in the medium term include support for SMEs in determining the “sameness” of their NMs/nano-enabled products to already approved substances / articles. This could be via a service provision, funded for example, via an EU infrastructure project.

2.7.3. Standards, technical approvals

To be elaborated within future projects but directed via the ongoing gap analysis identified in the CTTM roadmap and facilitated via the specific activities identified above where the CTTM implementation via a CSA or research infrastructure around standardisation, such as supporting projects in writing their standardisation section (including the steps required, their timing and costings), as well as consolidation with ongoing activities and support in identifying the experts needed.

2.7.4. Environmental protection

To be elaborated within future projects but directed via the ongoing gap analysis identified in the CTTM roadmap and aligned with the industry employer needs identified in the FP7 NanoEIS educational needs analysis which highlighted a lack of training / expertise in end of life cycle, environmental assessment and waste management tools.

2.7.5. Operational certification systems

To be elaborated within future projects but directed via the ongoing gap analysis identified in the CTTM roadmap, aligned with developments in the regulatory landscape (and the regulatory roadmap) and building on existing offerings such as that from INERIS/CEA.

2.7.6 Epidemiological studies

A key opportunity identified in this CTTM roadmap is the potential for utilising the above-mentioned training and certification systems as a means to identify cohorts or workers potentially exposed to NMs and recruit such individuals/organisations for long-term exposure and health monitoring. This could be funded at the individual member-stage level (via an ERA) or more effectively via a research infrastructure project (with a longer-term follow-up funding solution found beyond that) to facilitate longitudinal data collection. This needs to be done anyway, and linking it to the CTTM roadmap and activities seems like an optimal way to ensure buy-in and cooperation of all relevant stakeholders in the nano arena.

2.8. Impact

Following the recommendations of the CTTM, the European Nano-EHS-ecosystem will enable the long-term success of nanotechnologies on the market. Gaining trust via working transparently and cooperating with global players, will ensure acceptance of the CTTM-actions across all sectors involved. However, the cooperation has to clearly focus on market-support oriented stakeholders and definitely not on “creating a risk-market” activities. On route to the development of the CTTM-roadmap it became clear, that this exercise only gains the expected impact, if the so-called key-players are integrated into this work fully.

According to the identified key challenges, already the first action of building an inclusive collaboration network which has to include and be supported by a huge number of international states will ensure high impact because it is not a “pre-selected closed group” but an open inclusive team or nanosafety community. In addition to this, the bringing together of the scientific experts of each country further boosts the impact of this activity and will indeed be beneficial for all involved countries and their market players. The proposed actions in chapter 2.6 will create value-added via strengthening the dialogue and interaction to raise synergies and provide safety-assessment resources and best practices from across Europe for researchers, regulators and industry. This will also reduce the timespan from idea to the market especially by accompanying activities to support the development of products and applications via sharing of existing knowledge, route to market experience, and indeed learning from past failures.

Very high potential can be expected also during the implementation of the safety assessment framework (supported by the regulatory initiatives), which may start via building service provider platforms (e.g. one in each country strongly connected with the central node) which deal as consulting agencies on their products, and facilitating and advising on its way towards market implementation. Via these actions, the market share of safety-assured nano-enabled products and applications will tremendously increase which shows the high value of the implementation of the CTTM recommendations.

General impact of the research priorities

- The improvement of efficacy of toxicology studies of nanomaterials and certification of methods
- To provide industrial stakeholders and the general public with appropriate knowledge on the risks of nanoparticles and NMs for human health and the environment.

- The establishment of an ongoing dialogue between all stakeholders to additionally overcome the existing lack of knowledge transfer in the economic and societal point of view.
- The value chain from Idea to Market (and beyond) very much depends on research management (lower TRLs), Pilot technology and Industrial scale-up management (middle TRLs) and innovation and commercialisation management (higher TRLs). The implementation of CTTM-topics will enable that earlier building of "Business Plan(s)" of any product supports the better and the faster movement towards the market. Hence, the earlier we integrate in the "Business Plan" the nanosafety dimension, the faster and better the safety requirements can be taken into account at each TRL level and permit industry to "internalise" in their plans the safety issues, the bankability of safety can be increased and become part of the "market asset" of the product.

2.9. Timeline and next steps

First step is underway by a coordination and support action bringing together nanosafety management platforms and institutes of the member states, in which they have invested to build, staff and operate. Furthermore, joint calls will be implemented to pool national funding from member states and third countries (e.g. USA) to finance Nano-EHS-Research and market-oriented accompanying measures which are of common interest for the platforms the timeline is to get the action operational end 2016. The aim is to use this CSA to develop further actions.

The platforms provide services and support for stakeholders (e.g. industry, governments, researchers etc.) to create in a sustainable way marketable, societal approved products and goods.

The CTTM will be part of the NanoSafety Cluster strategic research and innovation agenda which shall be launched end of 2016.

Legal notice:

Andreas Falk, Christa Schimpel, Andrea Haase, Benoît Hazebrouck, Carlos Fito López, Adriele Prina-Mello, Kai Savolainen, Adriënne Sips, Jesús M. Lopez de Ipiña, Iseult Lynch, Costas Charitidis, Visser Germ: “Closer to the market”-Roadmap (CTTM), 2016.