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Developments in Delegations on the Safety of Manufactured Nanomaterials - Tour de Table

Series on the Safety of Manufactured Nanomaterials
No. 87

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Series on the Safety of Manufactured Nanomaterials

No. 87

DEVELOPMENTS IN DELEGATIONS ON THE SAFETY OF MANUFACTURED NANOMATERIALS - TOUR DE TABLE

IOMC
INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS
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Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris, 2018

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No. 36, *Guidance on Sample Preparation and Dosimetry for the Safety Testing of Manufactured Nanomaterials (2012)*

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Nos. 44-54, These items are the dossiers derived from the Testing Programme on Manufactured Nanomaterials which are located at:

http://www.oecd.org/chemicalsafety/nanosafety/testing-programme-manufactured-nanomaterials.htm

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No.60, *Current developments in delegations on the safety of manufactured nanomaterials - tour de table (2015)*

No.61, *Developments in delegations on the safety of manufactured nanomaterials - tour de table (2015)*

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No.66, *Categorisation of manufactured nanomaterials (2016)*

No.67, *Developments in delegations on the safety of manufactured nanomaterials - tour de table (2016)*

No.68, *Multiwalled carbon nanotubes (MWCNT): summary of the dossier (2016)*

No.69, *Fullerenes (C60): summary of the dossier (2016)*

No.70, *Single walled carbon nanotubes (SWCNTs): summary of the dossier (2016)*

No.71, *Silicon dioxide: summary of the dossier (2016)*

No.72, *Toxicokinetics of manufactured nanomaterials: report from the OECD expert meeting (2016)*

No.73, *Titanium dioxide: summary of the dossier (2016)*

No.74, *Exposure Assessment of Nano-Silver (AgNP): Case Study (2016)*

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No.77, *Gold Nanoparticle Occupational Exposure Assessment in a Pilot Scale Facility: Nanomaterials Exposure Case Study (2016)*

No.78, *Developments on the Safety of Manufactured Nanomaterials: Tour de Table from OECD Delegations (Nov.2015 - Oct. 2016)*

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No. 82, *Strategies, Techniques and Sampling Protocols for Determining the Concentrations of Manufactured Nanomaterials in Air at the Workplace (2017)*

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No. 84, *Consumer and environmental exposure to manufactured nanomaterials - Information used to characterize exposures: Analysis of a Survey (2017)*

No. 85, *Evaluation of in Vitro Methods for Human Hazard Assessment Applied in the OECD Testing Programme for the Safety of Manufactured Nanomaterials (2018)*

No. 86, *Assessment of Biodurability of Nanomaterials and their Surface Ligands (2018)*

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The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 35 industrialised countries in North and South America, Europe and the Asia and Pacific region, as well as the European Commission, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several countries with special status at the OECD, and from interested international organisations, attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

The Environment, Health and Safety Division publishes free-of-charge documents in 11 different series: **Testing and Assessment; Good Laboratory Practice and Compliance Monitoring; Pesticides; Biocides; Risk Management; Harmonisation of Regulatory Oversight in Biotechnology; Safety of Novel Foods and Feeds; Chemical Accidents; Pollutant Release and Transfer Registers; Emission Scenario Documents; and Safety of Manufactured Nanomaterials**. More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (www.oecd.org/chemicalsafety/).

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organisations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

OECD Environment Directorate,
Environment, Health and Safety Division
2 rue André-Pascal
75775 Paris Cedex 16
France

Fax: (33-1) 44 30 61 80

E-mail: ehscont@oecd.org

FOREWORD

The OECD Working Party on Manufactured Nanomaterials (WPMN) is a subsidiary body of the OECD Chemicals Committee. This programme concentrates on human health and environmental safety implications of manufactured nanomaterials (limited mainly to the chemicals sector), and aims to ensure that the approach to hazard, exposure and risk assessment is of a high, science-based, and internationally harmonised standard. It promotes international co-operation on the human health and environmental safety of manufactured nanomaterials, and involves the safety testing and risk assessment of manufactured nanomaterials.

This document compiles information, provided by delegations, on the occasion of the 18th WPMN meeting (February 2018), on current developments on the safety of manufactured nanomaterials. It aims to summarise relevant information on activities related to manufactured nanomaterials, as well as other activities on nanotechnologies at the international level.

This document is published under the responsibility of the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, pesticides and Biotechnology of the OECD.

Table of contents

1. Recent and Planned National Activities in Chemicals Regulatory Area on Health and Environmental Safety Aspects of Manufactured Nanomaterials

1.1. Australia

1.1.1. National developments on human health and environmental safety

Risk assessment decisions, including the type of: (a) nanomaterials assessed; (b) testing recommended; and (c) outcomes of the assessment

NICNAS finalised a risk assessment on a colloidal silica nanomaterial to use in industrial coatings, construction material and industrial cleaning products. Occupational health and safety recommendations were made for workers handling the nanomaterial as introduced into Australia. The assessment report was published on the NICNAS website (www.nicnas.gov.au).

To date, NICNAS has assessed four nanoscale materials.

Risk management approaches

Consistent with the OECD Council recommendation, all Australian government chemical regulators continue to utilise existing frameworks for regulating nanomaterials, with necessary adaptations.

The National Industrial Chemicals Notification and Assessment Scheme's (NICNAS) current approach to regulating industrial nanomaterials uses the existing regulatory framework applicable to conventional industrial chemicals, with some minor administrative adjustments. Significant reforms to the overall scheme are currently underway. The reforms to the regulation of industrial chemicals aim to ensure that assessment effort is proportionate to the risks posed by such chemicals, while maintaining Australia's current robust health and safety standards (further details at https://www.nicnas.gov.au/reforms). In developing the implementation detail, consideration is being given to the future regulatory approach for nano-forms of industrial chemicals.

1.1.2. Activities been initiated to implement the OECD Council Recommendation[1] (e.g. regulatory changes, guidance, voluntary, etc.)

Reforms to the overall regulatory scheme for industrial chemicals are currently underway (refer above). The implementation of these reforms will be consistent with the OECD Council recommendation.

[1] Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials

1.1.3. Developments related to good practice documents

The Australian Government Department of the Environment and Energy lead a project on problem formulation for nanopesticides in collaboration with the Australian Pesticides and Veterinary Medicines Authority, the Commonwealth Scientific and Industrial Research Organisation, and scientists from academia and the agrochemical industry.

The outcomes of this project including the conceptual framework have been published in a peer-reviewed scientific paper: Walker *et al*. (2017). Ecological Risk Assessment of Nano-enabled Pesticides: A Perspective on Problem Formulation. *J. Agric. Food Chem*. http://pubs.acs.org/doi/abs/10.1021/acs.jafc.7b02373

1.2. Austria

1.2.1. Highlight of developments

- With the caveat of some uncertainties in guaranteeing the allocation of necessary resources Austria is supervising the will work on test Guideline development regarding Aquatic (Environmental) Transformation of Nanomaterials. The work is under the auspieces of the Austrian Federal Ministry of Sustainability and Tourism (www.bmnt.gv.at); the administrative lead will be made by Environment Agency Austria with the scientific input of the University of Vienna (Frank von der Kammer). A proposal for this project has been sent to WPMN.
- As a measure of implementation of the Austrian Nanotechnology Action plan the national NANO Environment Health and Safety programme (http://www.ffg.at/nano-ehs) has been established which has been prolonged. A recent call was launched in December 2017 and deals particularly with the role of nanomaterials and „advanced materials“ in the circlular economy. This EHS programme is owned by the Federal Ministry of Sustainability and Tourism and the Federal Ministry for Transport, Innovation and Technology and is handled by the FFG - Austrian Research Promotion Agency.
- On behalf of the Ministry of Health and Women’s Affairs a survey was done to “Surface-modified nanoparticles – use in cosmetics and in the food industry, health aspects, regulatory issues”. Often results of studies contradict whether surface modifications may decrease the toxicity of a nanomaterial or even increase. Although nanoparticles can be composed of two or more materials, current rules concerning labeling requirements and safety assessments of nanomaterials in the EU do not refer to substances which are used for surface modification of nanoparticles. The survey resulted in a Nano Trust dossier (see http://epub.oeaw.ac.at/ita/nanotrust-dossiers).
- In 2018 the OECD TG318 on Nanoparticle Dispersion Stability has been adopted by the WNT and is available. The TG has been developed by the University of Vienna (Department of Environmental Geosciences, contact Frank von der Kammer) in collaboration with the German Environmental Protection Agency from where also funding was provided.

1.2.2. National developments on human health and environmental safety

Information on public/ stakeholder consultations

As a measure of implementation of the Austrian Nanotechnology Action plan the Austrian **Nanoinformation Commission** was founded by the federal Ministry of Health

to provide expertise regarding nanotechnology for consumers and decision makers. This commission comprises representatives from several ministries, agencies, NGOs, research institutions, industry and other experts. This work also includes the update of the **website on nanotechnology for the public** including chances and risks of nanomaterials: http://www.nanoinformation.at

The **Austrian Nanotechnology Action Plan** (adopted on 2nd March 2010 by the Austrian government, an English and German version can be downloaded on http://www.lebensministerium.at/umwelt/chemikalien/nanotechnologie/nano-aktionsplan.html), includes about 50 measures which will be implemented by Austrian stakeholders on national, EU and international level. The action plan was lead-managed by the Austrian Federal Ministry of Sustainability and Tourism (BMNT, www.bmnt.gv.at) (contact: renate.paumann@bmnt.gv.at) and elaborated based on a broad stakeholder involvement (see also chapter 7). The implementation report on the Austrian Nanotechnology Action plan including an English translation has been finalised after a public consultation see http://nanoinformation.at/oesterreichischer-aktionsplan/umsetzungsbericht-2012.html

1.2.3. Developments related to good practice documents

The central labour inspectorate (part of the Federal Ministry of Labour, Social Affairs and Consumer Protection) mandated a project investigating Austrian nano-workplaces to get a preliminary overview on different **uses and risk management applied**. Based on this report guidance **in German language to ensure safe and healthy workplaces regarding nanomaterials** was developed and updated end of 2013: "Leitfaden für das Risikomanagement beim Umgang mit Nanomaterialien am Arbeitsplatz". An accompanying folder summarises the results. The guidance is targeting small and medium enterprises and shall support the central labour inspectorate in advising enterprises dealing with nanomaterials. (http://www.arbeitsinspektion.gv.at/AI/Arbeitsstoffe/nano/default.htm.)

In the **committee 052 „Occupational health, ergonomics, safety techniques"** the **working group 052.73** with the title "Nanotechnologies and Nanomaterials" was established: The aim is the compilation, collection and distribution of international standardisation documents (CEN and ISO; lead-managed by Austrian Standards Institute).

1.2.4. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

The project Development of a Decision Support Tool for the Investigation of the Environmental Behaviour of Nanomaterials on the Basis of their Dispersion Stability and Solubility as a Function of Environmental Conditions was funded by the German Environmental Protection Agency and aimed at developing the scientific basis and experimental methods to determine the dispersability and dispersion stability in the context of the OECD WPNM testing framework. This project is led by the Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer). It has now lead to one of the first new nanospecific test guidelines of the OECD and has passed the 2nd commenting round recently.

1.2.5. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

The transnational Nano EHS ERANET-SIINN project NanoFarm is a collaborative project between the University of Vienna (Department of Environmental Geosciences, contact Frank von der Kammer), the Carnegie Mellon University (US), the University of Kentucky (US) and the University of Aveiro (PT). It aims to understand the benefits and impacts of inorganic nanopesticides as CuO. The project covers characterisation in environmental media, transformation and transport, plant uptake and trophic transfer as well as ecotoxicological effects.

The European Union and the United States organize on-going meetings and contacts on an expert level. This US-EU dialogue (www.us-eu.org), bridging NanoEHS research, has three goals: 1) Engage in an active discussion about environmental, health, and safety questions for nano-enabled products; 2) Encourage joint programs of work that would leverage resources; and 3) Support the communities of research. The Communities of Research (CoR) focus on specific question and activities within Nano EHS. **Albert Duschl** from the **University of Salzburg** was appointed as the European co-chair for the CoR Human Toxicity http://us-eu.org/communities-of-research/search-communities-of-research/predictive-modeling-for-human-health/

In 2018 the OECD TG318 on Nanoparticle Dispersion Stability has been adopted by the WNT and is available. The TG has been developed by the **Universitiy of Vienna** (Department of Environmental Geosciences, contact **Frank von der Kammer**) in collaboration with the German Environmental Protection Agency from where also funding was provided.

The H2020 project GRACIOuS: Grouping, Read-Across, CharacterIsation and classificatiOn framework for regUlatory risk assessment of manufactured nanomaterials and Safer design of nano-enabled products started in January 2018. The **University of Vienna** (Department of Environmental Geosciences, contact **Frank von der Kammer**) participates in this project and acts as co-leader of WP 3 Intrinsic Properties of Nanomaterials. The project aims to develop grouping and read-across strategies and tools for nanomaterials. http://cordis.europa.eu/project/rcn/212339_de.html

The **H2020 project ACENano** started in January 2017 and develops analytical tools for nanoparticle testing and risk assessment. The **University of Vienna** (Department of Environmental Geosciences, contact **Frank von der Kammer**) is scientific co-coordinator of the project and leads WP1, technical innovation. Specifically in WP1 the outcomes of the NanoEHS project DetectNano will be further developed into an instrumentation to identify ENPs based on their elemental fingerprints in collaboration with the producer and the ETH Zurich. BioNanoNet (Andreas Falk; as 3rd party of NANOfutures) collaborates in WP5 (guidelines, standardisation) and WP6 (dissemination, workshops).

In the H2020 project **PANDORA**, **Albert Duschl (University of Salzburg)** is partner and work package leader. The project is an ITN in which doctoral students work on effects of nanomaterials on the innate immune response. Since innate immunity is evolutionary old, it is highly conserved in the animal kingdom. This allows a direct comparison of human and environmental species (e.g. mussels, wood lice and earthworms). The project thus provides strong links between human nanotoxicology and environmental nanotoxicology, using the options available to both of these fields. http://www.pandora-h2020.eu/

In the FWF funded Elise Richter project Nanopesticides Dr. Melanie Kah from the University of Vienna (Department of Environmental Geosciences, contact Melanie Kah) investigates the advantages and problems arising from the use of organic, nano-enhanced pesticides (nanopesticides). Focus is on improvements in pesticide application and differences in transport, degradation and efficiency caused by the nano-specific formulations.

In the FWF funded project CNT-NOM Prof. Thilo Hofmann and Dr. Melanie Kah (Department of Environmental Geosciences, contact Thilo Hofmann, Melanie Kah) investigate the processes of natural organic matter adsorption to carbon nanotubes.

The University of Natural Resources and Life Sciences, Vienna (contact: Eva-Kathrin Sinner) leads a FWF funded project (2015–2018) called **Electroporation as method for inserting functional membrane proteins in mammalian cells**. This project aims at *in vitro* platforms based upon nanotechnology in order to provide reproducible nanoparticle assemblies and binding assays in the context of drug screening and discovery. Using cell-free synthesis and electroporation, organic nanoparticles are used to form phospholipid-based/polymeric vesicles, where functional membrane proteins are integrated. Such nanovesicles are suitable carrier systems that can be further used as models for biological membranes (e.g.to study nanomaterial-cell interactions) and, moreover, deliver functional (membrane) proteins into living cells.

The **EC4SafeNano** project, started in October 2016. It will network existing nanosafety platforms and other stakeholders around the definition and preparation of the European hub of services and support for stakeholders, EC4SafeNano. It will also develop active and effective dissemination and communication activities. **Albert Duschl (University of Salzburg)** is a partner in this project, which is intended to continue as a central European hub beyond the lifetime of the funded project.

The H2020 project **NanoFase** will develop a comprehensive modelling framework for nanomaterials in the environment, including release, transformation in waste streams, behaviour in fresh waters, estuarine and marine waters, soil and sediments. Uptake routes are addressed as well. The project is coordinated by the UK NERC. The Department for Environmental Geosciences, University of Vienna (contact: Frank von der Kammer) is involved in several work packages. The central work package on surface water and sediments is lead by University of Vienna.

The FP7 project **NanoDefine** has finished in the end of 2017 providing standardized and validated methods to characterize materials and products to be nano or not or to contain or not contain nanomaterials. The Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer) is involved in several work packages. The central work package on confirmatory methods is lead by UNIVIE.

The project **NanoTrust,** funded by the Austrian Federal Ministry for Transport, Innovation and Technology (BMVIT), the Federal Ministry of Health and Women´s Affairs, the Austrian Federal Ministry of Sustainability and Tourism and the Federal Ministry of Labour, Social Affairs and Consumer Protection is a research project to continually survey, analyse and summarise the state of knowledge regarding potential health and environmental risks of nanotechnology. Dossiers (also in English language) on specific nano-related topics are released: http://epub.oeaw.ac.at/ita/nanotrust-dossiers.

The **Research Platform Nano-Norms-Nature** (contact: Prof. Angela Kallhoff, Claudia Schwarz-Plaschg, Department of Philosophy, University of Vienna) investigates the prospects of nanotechnology in terms of environmental enhancement and the containment

and prevention of negative side-effects. The platform explores interdisciplinary approaches towards environmental nano-safety issues. Recent publication: Special Section on "Safer by Design in the Nano-Field" (2017) in NanoEthics 11/3, 277-311. Previous events: workshop on "Making Nano 'Safer by Design'" 18 May 2016; conference "Good Nano – Bad Nano: Who Decides?" 1-2 December 2016; workshop on "Standardization in the Nano-Field: For the Common Good?" 19 May 2017.

The **European Center for Nanotoxicology** (EURO-NanoTOX) is a topic-oriented platform which is co-ordinated by the BioNanoNet Forschungsgesellschaft mbH. EURO-NanoTOX develops nanosafety strategies and serves as an international node for nanotoxicology. The 5th revised edition of the ENT-expertise-catalogue will be published in September 2017. See: http://www.euro-nanotox.eu/ (contact: Andreas Falk)

In the H2020 pilot-projects **Inspired** (http://www.nano-inspired.eu/), **R2R-Biofluidics** (http://www.r2r-biofluidics.eu/), **Hi-Response** (http://hiresponseh2020.eu/index.html) and **Smart-4-Fabry** (http://smart4fabry.eu/), Austrian partner BioNanoNet is responsible for the nano-related safety-tasks. BioNanoNet is developing an integrated safety strategy together with international project partners, to reduce the potential risk upon worker's exposure to MNMs during production and manipulation processes, and to ensure the responsible implementation of nanomaterials (NMs) along the entire value chain of industrial innovation processes (contact: Andreas Falk).

BioNanoNet is partner in the H2020 MSCA-RISE project **NANOGENTOOLS** (start: January 2016; http://www3.ubu.es/nanogentools/), which aims at developing new methodologies for the identification and control of hazards associated with nanomaterials, ensuring consumer and society safety. It pursues the main objective of generating a common solid knowledge basis arising from the fruitful cross-sectorial synergy between forefront research centers in nanosafety and industry (contact: Andreas Falk).

The EU funded H2020 Research and Innovation action **BIORIMA** (start: November 2017). The acronym BIORIMA stands for Biomaterial Risk Management. The project aims to develop an integrated risk management framework for nano-biomaterials used in advanced therapeutic medicinal products and medical devices. The BIORIMA risk management framework is a structure upon which the validated tools and methods for materials, exposure, hazard and risk identification/assessment and management are allocated plus a rationale for selecting and using them to manage and reduce the risk for specific nano-biomaterials used in medical applications. BioNanoNet (contact: Andreas Falk) and Joanneum Research Department HEALTH are part of the BIORIMA consortium and will contribute their expertise to achieve the project goals.

In the H2020 project **NanoCommons** (start: January 2018) **BioNanoNet** is involved in several work packages (contact: Andreas Falk). **Albert Duschl (University of Salzburg)** is a partner and work package leader in this project. The project brings together academia, industry and regulators to facilitate pooling and harmonising of methods and data for modelling, safe-by-design product development and regulatory approval purposes, thereby driving best practice and ensuring maximum access to data and tools. NanoCommons proposes to create an openly accessible e-infrastructure of scientific and cutting edge and managerial excellence provided by a combination of research intensive academic groups and SMEs serving the current and future (unmet) needs of the key research communities and pivotal industrial users and regulators. As such NanoCommons will bring pan-European added value and innovation opportunities, by answering the increasing demands concerning the prediction of safety of existing and new nanoscale materials for health and environmental sustainability. Transnational Access will focus on

standardisation of data generation workflows across the disparate communities and establishment of a common access procedure for transnational and/or virtual access to the data, and modelling and risk prediction/management tools developed and integrated.

The project **SafeNanoKap** started in March 2017, which is funded in the framework of Austrian Nano EHS programme (duration until February 2018). The University of Natural Resources and Life Sciences, Vienna (contact: Marion Huber-Humer), in cooperation with the Austrian Academy of Sciences and the Polymerwerkstatt GmbH (http://polymerwerkstatt.com), aim at assessing the applicability of the so-called Safe-by-Design (SbD) concept using the business case on the development of food packaging that contain nanoscale additives. Polymer composites with engineered nanomaterials have a huge market potential but potential adverse environmental risks need to be minimized along the entire value chain of such advanced products (from design to waste disposal). For this, the strengths and weaknesses of the SbD concept shall be identified and summarised using the example of nanomaterial-containing coffee capsules.

DaNa 2.0 is a project financed by the German Federal Ministry of Education and Research (BMBF), which provides and extends a knowledge base on nanomaterials for the general public. The data base contains over 800 articles in German, English and French. All entries are based on carefully quality-checked scientific literature. DaNa 2.0 has become a prime information source for general nanotechnology and nanosafety topics, found under www.nanoobjects.info and www.nanopartikel.info. The project has just been extended to 2019. **Albert Duschl** from the **University of Salzburg** is one of the experts who contribute within this project to the knowledge base.

The so-called **IWWG Task Group on Engineered Nanomaterials in Waste** (IWWG: International Waste Working Group) was launched in 2014, where the University of Natural Resources and Life Sciences, Vienna, (BOKU) is one of the TG leaders (contact: Marion Huber-Humer or Florian Part). Its goal is to discuss and organize workshops and meetings about the fate of engineered nanomaterials in waste streams. End-of-life management strategies for ENM-containing products are urgently needed as many material flow models predicted that ENMs are likely to end up in waste streams (see also: https://www.tuhh.de/iue/iwwg/task-groups/engineered-nanomaterials-in-waste.html).

The University of Natural Resources and Life Sciences, Vienna (BOKU) (contact: Florian Part) became an official member – as Austrian representative – for the **European Committee for Standardization** and the technical body "**CEN-TC 352 – Nanotechnologies**". Within this committee, research approaches are identified in order to find and assess suitable procedures for handling and characterising nanomaterials – as a prerequisite for standardization.

1.2.6. Information on research or strategies on life cycle aspects of nanomaterials, as well as positive and negative impacts on environment and health of nano-enabled applications

The recently established research platform **Nano-Norms-Nature** at the University of Vienna (one section at the Department of Environmental Geosciences, contact Antonia Praetorius and Thilo Hofmann) looks into scientific, environmental, regulatory and societal implications of nanotechnology.

During the second call the transnational Nano EHS ERA NET SIINN project **FENOMENO - Fate and effect of wastewater-borne manufactured nanomaterials in aquatic ecosystems** was approved: http://www.fenomeno-nano.de/. The Research

Institute for Limnology Mondsee of the University of Innsbruck (contact: Josef Wanzenböck) is responsible for the work package 4: Environmental partitioning of manufactured nanomaterials contamination in lakes. The goal is to compare bioconcentration studies performed in the lab with the real environmental situation in Lake Mondsee along the food chain from algae to zooplankton and fish. National funding is provided by the FFG - Austrian Research Promotion Agency.

The FP7 project **SUN - Sustainable Nanotechnologies has been finished in 2017** The Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer) is involved in the development of techniques to detect and analyse nanoparticles released from products and investigation on the life cycle induced modifications of nanoparticles and how these changes affect their environmental behaviour.

1.3. Belgium

1.3.1. National developments on human health and environmental safety

The Royal Decree concerning the placing on the BE market of substances produced in nanoparticular state was published on 24th September 2014. This decree involves the registration of substances produced in nanoparticular state as well as mixtures that contain one or more of these substances.

The first annual report for 2016 has been published in April 2018. The full report is available in Dutch and French, and the summary is available in Dutch, French, German and English. A very short summary of the results is given in the next paragraph:

For the calendar year 2016, 475 registrations were submitted by 98 registrants. These registrations involve about 150 different chemical substances (based on CAS-number). In total, 75 000 tons of substances, produced in nanoparticular state, were introduced on the Belgian market, either by import or by production. The substances imported and/or produced in a quantity above 1 000 ton are amorphous silica, calcium carbonate, calcium carbonate treated with stearic acid, carbon black, diiron trioxide, iron hydroxide oxide yellow and silicon dioxide. These numbers result only from the registrations submitted for nanomaterials, placed on the market as substances.

More information about the registry can be found on the website www.nanoregistration.be.

1.3.2. Activities been initiated to implement the OECD Council Recommendation (e.g. regulatory changes, guidance, voluntary, etc.)

In the framework of the national regulation on nanoparticles, the FPS Economy, Service of Metrology – National Standards started in July 2015 a pilot study on the comparability of nanoparticles size measurement at the national level. As the new regulation requires the registration of nanoparticles dimensions measured by a traceable method, with uncertainty budget associated, this comparison is also the opportunity for researchers and companies to improve comparability of their measurements through understanding of uncertainty contributions in specific measurement methods. The goal is to achieve comparability with different measurement techniques based on different physical principles. The study involves for the moment 3 different microscopy techniques (SEM, TEM, AFM) and 2 centrifugal separation (DCS) but is opened to further collaborations.

1.3.3. Developments related to good practice documents

The BE Service for Metrology, part of the Federal Public Service Economy, has been accredited according to ISO 17025 for the dimensional measurement of spheric, non-compressible nanoparticles smaller than 200 nm and with a measurement uncertainty of 3 nm.

1.3.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Nanomaterials in products: inventarisation, characterization and exposure assessment through the air:

Nanomaterials are increasingly being used in the development of new consumer products worldwide. Yet, the possible risk of exposure through using these products is still largely unknown. Insight in this matter is important to (in)form policy makers about health risks of nanomaterials. For these reasons the Flemish service environment & health started a study entitled "Nanomaterials in consumer products: inventarisation, characterization and exposure assessment through the air". The goal of the study is the assessment of the possible exposure to nanomaterials in products. In a first step 8 products with a nanoclaim that are available on the market and are regularly used by consumers, will be tested on the presence of nanoparticles. For products containing nanomaterials, the exposure during use of the product will be determined by simulating representative exposure conditions. Based on these results a work plan for toxicological screening of the selected products will be made. The study also aims at formulating specific policy advises concerning potential exposure through the use of consumer products containing nanomaterials and more general conclusions on risks of nanomaterials. Based on these case-studies, tools for future exposure assessment of consumer products will be developed.

NANO Global Risk Assessment (NANOGRA)

The NANO Global Risk Assessment (NANOGRA) project aims at globally assessing the risks of exposure to NMs (MWCNT, Carbon black, TiO2 and Al) by addressing explosion, ecotoxicological and toxicological risks. Explosion and fire characteristics assays will focus on the generation of reliable and comparable experimental data. In addition, they will give us some indications to which extend the laws found for powders at the micro scale remain valid at the nanoscale. For ecotoxicological risk assessment, the environmental compartment studied will be sediment, as it is known to be a sink for NPs reaching the aquatic medium. Standardized bioassays on Chironomus riparius and Heterocypris incongruens will be adapted to nanoscale substances. Realistic concentrations in the environment are also intended to be studied in a second phase. Control banding approach will be applied to the scenarii of Nanogra's research activities. The choice of NMs has followed several criteria: relevant use in the Walloon region, relevancy for explosion and/or ecotoxicological assessment with sediments, and availability of data in order to validate our tests development. In 2016, a new laboratory has been set up with a 20L-sphere to conduct explosion and ecotoxicological risk assessment.

Towards a toxicologically-relevant definition of nanomaterials (To2DeNano)

Nanotechnology enters more and more the consumer market. This unavoidably results in increasing human exposure to manufactured nanomaterials (MNM) and/or manufactured

nanoparticles (MNP). Environmental (external) measurements are currently the only tools available to evaluate exposure to MNMs; only experimental methods exist to assess internal exposure to MNMs. Moreover, monitoring MNM exposure is problematic because of the lack of defined standardized metrics and protocols . This project aims to support a definition of MNM based on the most toxicologically relevant exposure metrics, and will provide some guidelines for further risk and toxicity analysis. It is impossible within the 2 year timeframe allocated to this programme to consider all aspects of MNM which have (or can have) a role in exposure and hazard. The project, therefore, specifically focuses on the influence of MNM aggregation/agglomeration (AA) and size distribution, two important aspects of the current EU definition of MNM, on their toxic activity. This project is sponsored by BRAIN-be (Belgian Research Action through Interdisciplinary Networks) and has started in March 2016.

3DNano Traceable three-dimensional nanometrology

In the framework of the European Metrology Program for Innovation and Research (EMPIR) a 3 year, 2 M€, project aimed at establishing the traceability of nanometre scale measurements in 3D with uncertainty less than 1 nm started on October 1st 2016. The Belgian National metrology Institute (FPS Economy, Service of metrology, National Standards) is partner of this project and will test reference nanoparticles with different materials, shape and/or size for the calibration of 3D-nanometrology measurements that target nanoparticles relevant for regulatory bodies. Probe/sample interaction, nonspherical particles and particles with different agglomeration behaviour will be selected. Reference spherical nanoparticles will also be selected in order to test the data fusion and hybrid metrology methods.

Further information on the project 15SIB09 3DNano Traceable three-dimensional nanometrology will be available on the website:

http://www.euramet.org/research-innovation/research-empir/empir-calls-andprojects/

Implementation and validation of an analytical methodology to assess engineered nanomaterials in food additives

This project aims to develop and validate a methodology for the screening, detection and physico-chemical characterization of nanoparticles in food additives. The methodology is based on the "Nanotechnologies – Guidance on detection and identification of nano-objects in complex matrices" (TC 352 WI 00352012.5) that is being developed in the context of CEN/TC 352. In agreement with this document, the selected detection and identification methods are based on a combination of size classification and chemical composition analysis. The proposed methodology includes physical characterization by electron microscopy-based techniques, such as TEM, SEM and HAADF-STEM, with chemical characterization by spectroscopic techniques, such as EDX, ICP-MS and SP-ICP-MS.

NanoStreeM - Nanomaterials: Strategies for safety Assessment in advanced Integrated Circuits Manufacturing

Belgium is participating in the EU funded project NanoStreeM. The ambition of this project is

- better understanding of the occupational hazards related to the use of nanomaterials

- better governance of the risks related to of the manipulation of nanomaterials on the workers and environment using the semiconductor industry as an example
- intensification of the international cooperation in the areas of standardization and risk governance related to nanomaterial use
- promotion of public knowledge in the understanding of the occupational hazards related to the use of nanomaterials

More information can be found via the website http://www.nanostreem.eu/the-project/

1.4. Canada

1.4.1. National developments on human health and safety

In 2015, Canada initiated work to address nanoscale forms of substances on the Domestic Substances List (DSL); this work aims to identify, prioritize and when warranted, assess nanomaterials which are considered to be in commerce in Canada. Fifty-three (53) substances previously identified as being manufactured and/or imported at the nanoscale in Canada are being prioritized."

A risk assessment framework is currently under development, which will be used to guide environmental and human health risk assessment of prioritized nanomaterials in commerce. Expert consultations on the draft framework are planned for 2018.

Risk assessment decisions, including the type of: (a) nanomaterials assessed; (b) testing recommended; and (c) outcomes of the assessment

Four nano-related substances, two organic and two inorganic, were notified to the program since WPMN17. In addition, two pre-notification consultations (PNCs) were initiated for nano-related substances. PNCs provide clarity on regulatory requirements prior to submission under the New Substances Notification Regulations (NSNR).

Development related to exposure measurement and exposure mitigation

In 2016, Canada and the US EPA co-led an analysis of the responses received from SG-08 member countries on the survey *Consumer and Environmental Exposures to Manufactured Nanomaterials*. Analysis of the survey results identified a need for projects that relate to the development and use of exposure models for manufactured nanomaterials. Canada submitted a proposal for a project entitled *Compilation of Available Tools and Models Used for Assessing Environmental and Consumer Exposure to manufactured Nanomaterials and Evaluation of their Applicability in Exposure Assessments*. The proposal was accepted and the project is planned to be completed in 2019. Results from Objective 1 of the project and the draft proposal for Objective 2 will be presented at WPMN-18.

1.4.2. Developments related to good practice documents

Canada's health department is contributing to the World Health Organization (WHO) Chemical Risk Assessment Network through participation in a collaborative project coordinated by the National Institute of Public Health and the Environment, RIVM, Netherlands, under the auspices of the Network, to develop a guideline document on principles and methods for assessing immunotoxicity following exposure to nanomaterials. This initiative has developed an Environmental Health Criteria Document

on Principles and Methods to Assess the Risk of Immunotoxicity Associated with Exposure to Nanomaterials.

Canada's health department is also contributing to an EU USA Nanoinformatics Roadmap 2030, which is a compilation of state-of-art commentaries from various interconnecting scientific fields combined with issues involving nanomaterial risk assessment and governance.

Canada's health department is also contributing to EU H2020 nano research programme projects that are focused on developing smart toxicological tools for nanomaterial toxicity and risk assessment, and establishing strategies for risk governance.

1.4.3. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

Canada's health and environment departments are co-leading a proposal 'Advancing Adverse Outcome Pathway (AOP) Development for Nanomaterial Risk Assessment and Categorization' that was submitted and approved by OECD WPMN in 2017. An expert group involving Netherlands (RIVM and Dutch Technical University), South Africa, National Institute Occupational Health), Switzerland (Federal Office of Public Health, NanoCASE GmbH), United Kingdom (University of Birmingham), United States (National Institute for Occupational Safety and Health) and Vireo Advisors, LLC has been convened. This project aims to support the development of AOP frameworks that have the greatest potential to inform categorization and risk assessments of nanomaterials. The project progress (completion of Objective 1) will be presented at WPMN-18.

Canada's health department is also contributing to the development of two individual Adverse Outcome Pathways (AOPs) for nanomaterials – "Increased substance interaction with the resident cell membrane components leading to lung fibrosis" and "Increased substance interaction with the resident cell membrane components leading to lung emphysema". The full AOPs are being developed and one of them has been submitted for OECD EAGMS committee internal review in January 2018. Two individual manuscripts describing the AOPs and their relevance to nanomaterial risk assessment have been published (Nikota et al., Part Fibre Toxicol, 2017, 14(1): 37; Labib et al., Part Fibre Toxicol, 2016, 13(1): 15).

1.4.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Scientific research

Canada's health department completed a comprehensive study involving investigation of pulmonary toxicity responses induced by OECD-provided titanium dioxide nanoparticles of different sizes, surface modifications and crystalline structures (Rahman et al., Mutagenesis, 2017, 32(1): 59-76). Canada's health department has also completed a study that investigated dissolution rate constants, half-lives, and static dissolution (solubility) at gastric pH (1.5) and neutral lung pH for nano zinc oxide, nano-anatase, nano-rutile and their bulk analogues (Avramescu et al., Environ Sci Pollut Res, 2017, 24: 1553).

Canada's environment department continues to fund research that assesses the fate and toxicity of engineered nanoparticles released from commercial products. Research

completed in December 2017 focused specifically on silver nanoparticles released from sports socks due to physical and chemical weathering. The study evaluated the fate and toxicity of "worn" silver nanoparticles in agricultural soil and wetland mesocosms.

National Research Council Canada, Measurement Science and Standards (NRC-MSS) has completed a study in collaboration with Canada's health department in which surface area and surface functional group content were measured for a set of 20 silica nanoparticles with different sizes and surface chemistries. This work used a protocol for quantification of silica surface groups developed in collaboration with Canada's environment department. The results provide some of the basic characterization data needed in order to make meaningful comparisons of the results of bio-assays for these materials with previous investigations.

Canada has published multiple studies pertaining to the safety aspects of nanomaterials:

Canada's health department has recently published a peer-reviewed publication on the *in vitro* toxicity of OECD-representative silver nanoparticles (Nguyen et al., Toxicol in vitro, 2016, 33:163-173).

In addition, Canada's health department has published a study that investigates the underlying mechanisms of carcinogenic effects of carbon nanotubes in mice (Rahman et al., Mutat Res Gen Tox En, 2017, 823: 28-44).

Canada's health department continues to develop strategies to use toxicological data derived using novel alternative methods in support of identifying mode of action of nanomaterials and to derive critical effect levels. Advancements in these research projects have been outlined in recent publications (Labib et al., Part Fibre Toxicol, 2016, 13(1): 15; Nikota et al., Part Fibre Toxicol, 2016, 13(1): 25; William and Halappanavar, Data Brief, 2017, 15: 933-940).

NRC-MSS has published a study on the cytotoxicity of graphene oxide (GO), an important emerging nanomaterial with applications for electronics, membranes for filtration, drug carriers. The results demonstrate that careful control of variables including cell line and GO dose and properties may help to resolve conflicting literature reports on GO toxicity (Gies and Zou, Toxicol Res, 2018, Advance Article).

1.5. Chile

Nanoseguridad at CEDENNA

CEDENNA is the main Center for Nanoscience and Nanotechnology in Chile. It comprises researchers from the main universities of the country, and it is led by the University of Santiago de Chile.

Safe working conditions are important when manipulating conventional hazardous chemicals. With nanometric materials, the levels of risk and the need for control and safeguarding, make the subject of nanosafety and occupational health a main area addressed by the Center, which is dedicated to creating knowledge and innovation at this scale of size. Accordingly, CEDENNA intends to become the leading institution in Chile on nanoscience, nanotechnology and nanosafety related issues.

As such, the objectives of CEDENNA have been established as follows:

- Achieve the highest national and international standards in nanosafety;

- Ensure the adoption of best work practices, while minimizing the impacts on the environment and society; and
- Make CEDENNA a national benchmark in nanosafety with the capacity to support government actions and initiatives on these issues.

To achieve these objectives, CEDENNA established the Nanosafety Commission whit the aim to:

- Assess the current nanosafety conditions in CEDENNA;
- Provide official information to all members on topics related to nanosafety, corresponding to instructions, regulations, resolutions and laws at both the National and International levels;
- Propose the creation and application of new Institutional regulations on Nanosecurity and Occupational Health; and
- Propose lines of action of short medium and long term.

As a first step, the Commission proceeded to survey all members and members of CEDENNA, permanent and occasional, covering both researchers and undergraduate and graduate students, administrative officials and visitors of the Center. The survey was done using the Nanorisk App developed by Pastrana and collaborators[2].

The results of the survey were used to create a database that allowed a global analysis of the nanosecurity situation of all members of CEDENNA. The survey included the level of risk (associated with the danger of the material to which each person is exposed), as well as the level of exposure (associated with the time of exposure to hazardous material). Expanding this analysis to other areas, would allow to have overarching assessment or to have target reviews by research line or at the personal level.

The analysis allowed, measuring the limited information that CEDENNA's personnel have on the material they are working with. This has been improved by informing workers on existing national safety regulations as well as international standards. At the present time, each CEDENNA employee is given an information folder containing the regulations, the informed consent letter, the survey (mandatory for all CEDENNA members) and the delivery of a leaflet with basic instructions on nanosafety, including emergency contacts. All the material is delivered in Spanish and English.

Given that the scenario is essentially changing over time (change of members, modification of a research line, modification of the material used) this survey will be carried out in a massive way twice a year.

To ensure adequate working conditions for all CEDENNA members who are continuously or occasionally in contact with nanomaterials, a "Safety Panel" has been installed in all laboratories that are supervised by CEDENNA. The Safety Panel includes an acrylic panel (approximate size 75% the size of a normal door) with boxes containing all personal protection barriers. The Safety Panel have been tailored according to the risk and personal exposure idneitfied by the survey, and following relevant regulatory measures. The safety materials and their maintenance are the responsibility of the center and the line manager of each area is responsible for its maintenance. Compliance with

[2] Pastrana, F., Avila, A., Muñoz, F. 2015, Nanorisk App. Retrieved from https://nanoseguridad.uniandes.edu.co/nano en / indexeng.html

this CEDENNA regulation will be safeguarded through at least two unannounced annual visits to each laboratory, its non-compliance will have effects on the budget that CEDENNA delivers to each section/ Laboratory.

Beyond implementing conditions that guarantee the right to information of each member of CEDENNA and the availability of personal security elements, the center is also focus to ensure the proper implementation of the engineering barriers necessary for the particular condition of dangerousness of the material of work of each line or of any of its members. Thus, in addition to the safety conditions according to any laboratory that works with hazardous chemicals, CEDENNA is looking to implement a laboratory with the highest existing measures for occasional work in conditions of risk that exceed the usual of a chemical or biological laboratory .

All the nanosafety measures implemented in CEDENNA are complemented by periodic training and induction to new CEDENNA members in all areas (researchers, students, officials), the implementation of internal procedures and regulations and the establishment of a continuous quality system.

1.6. Denmark

T**he Danish Nanoproduct register w**as established in 2014[3]. After three years of registrations, the following information is publicly available.

	2014-2015	2015-2016	2016-2017
Number of registrants	8	6	4
Number of products registered	117	100	32
Number of nanomaterials registered (differing in chemical composition)	10	9	6

As a part of an evaluation of the nanoproduct register, the Danish Minister for Food and Environment has decided to follow a recommendation from the Danish Implementation board to run a neighbour check of how neighbour countries are following the use of nanomaterials on their national markets. The results of this study are expected to be publicly available in the beginning of 2018.

One significant activity on nanomaterials in Denmark is the Danish Nanosafety Centre[4], which contributes with new knowledge necessary for all stages of a risk assessment of

[3] The statutory order is available on: https://www.retsinformation.dk/Forms/R0710.aspx?id=163367 (in Danish) and as an unofficial translation on the following link: http://mst.dk/media/mst/9500743/Bekendtg%C3%B8relse%20English%20unoff%20translation%20final.docx

[4] http://nanosafety.dk

nanoparticles in the workplace has funded with 30 mio. (4 mio. €) Danish kroner during the years 2016-2018.

Via researchers in the Danish Nanosafety Centre, Denmark is contributing to the OECD work on nanosafety by leading two OECD project related to the development of work relevant to the safety testing of manufactured nanomaterials. One project is addressing Solubility/dissolution, and the second one is focused on Surface chemistry. The latter is been done in collaboration with Germany.

1.7. France

1.7.1. Highlight Actions

INRA TOXALIM (Research Centre in Food Toxicology) has conducted toxicological studies under the NANOGUT project (French national funding / ANSES) and the NANOFOOD project (French national funding / INRA Division of Nutrition, Chemical Food Safety and Consumer Behaviour) on the fate and effects of nanomaterials (Titanium dioxide - TiO2) and food additive-containing nanomaterials (TiO2, referenced as E171 in EU) in the gut, after acute and chronic oral exposure, using rat and mice animal models. These projects were devoted to the influence of the nanoscale fraction present in food additives on the inflammatory risk in the intestinal mucosae and the susceptibility to develop preneoplastic lesions in the colon. Main results have shown that the food-grade TiO2 E171 is able to disrupt intestinal and systemic immune system homeostasis, with development of low-grade inflammation in the colonic mucosa, as well as the initiation and promotion of aberrant crypt foci in the colon. These studies were conducted in relation with the **CEA, ANSES**, Synchrotron **SOLEIL** and **LIST-LU**.

These results were published (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5247795) and were evaluated by **ANSES** on request from **French ministries**, pointing out that INRA highlighted new effects, specifically potential promoting effects for colorectal carcinogenesis (https://www.anses.fr/fr/system/files/ERCA2017SA0020.pdf).

SCL (Service Commun des Laboratoires) develops an analytical strategy for detecting nanomaterials used in everyday consumer products (cosmetics, food). This method aims to verify the compliance with the European requirements for labeling and consumer information. The SCL takes into account the complexity of the matrix (food or cosmetic), the nature of the nanomaterials (organic, inorganic), as well as the cost and the performance of different methods in order to verify the conformity of the products. A recent communication was made by the government on this method and its applicability:

https://www.economie.gouv.fr/files/files/directions_services/dgccrf/presse/communique/2018/cp-298-Bruno-Le-Maire-reuni-cnc.pdf

INERIS is conducting since several years studies on the development of nanomaterial guidance values for human toxicology (inhalation, ingestion) and environmental toxicology. Following previous work on the methodology and a first guidance value on human toxicity for TiO2, in 2017 we have published guidance values on human toxicology for CeO2 and have conducted a review document for nano-silver. In 2018, studies will be conducted on guidance value for NTC and guidance values on environmental toxicology for the above-mentioned nanomaterials (https://www.ineris.fr/fr/proposition-dun-repere-toxicologique-pour-loxyde-de-titane-nanometrique-pour-des-expositions).

ANSES is in charge of the Substance Evaluation process for titanium dioxide as part of the CoRap list for 2018 for REACh. The SEv process will start in March 2018.

ANSES has published an opinion concerning food exposure to titanium dioxide (published in april 2017). Review of Bettini et al. Sci Rep. 2017, 7:40373.

1.7.2. National developments on human health and environmental safety

SPF - EpiNano - The Ministries of Health and of Labour entrusted the French Public Health Institute to implement an ongoing surveillance system of labourers in the industry potentially exposed to engineered nanomaterials (ENMs) released during their synthesis or incorporation in solid/liquid matrices or packaging. This system, denominated EpiNano, was launched in 2014. Exposed labourers will be included and followed up by Santé publique France using auto-questionnaires and will be paired to information available through national databases (health insurance; national causes of death registry). Unexposed workers recruited in similar cohorts will serve as controls for comparisons of diseases rates. The surveillance incorporates a methodology for the traceability of occupational exposures to nanomaterials, based on control-banding methods (notably the Stoffenmanager nano tool). Currently, four families of nanomaterials (titanium/silicium dioxyde, carbon nanotubes, carbon black) were selected among those listed by the OECD. This list could be extended to other families depending on the scientific and industrial context.

SPF - Ev@lutil database : open access in French and English to data related to the characterization of occupational exposure to Nanoparticles (NP). The database was recently developed but it already contains more than 420 measurements and synthesis analysis coming from 370 scientific articles. About 80% of the scientific articles have information on particles concentration and especially in number which is the metric most frequently addressed, and 90%, on physicochemical characteristics (chemical species, size distribution, morphology). http://exppro.fr or https://ssl2.isped.u-bordeaux2.fr/eva_003.

1.7.3. Activities been initiated to implement the OECD Council Recommendation (e.g. regulatory changes, guidance, voluntary, etc.)

CEA has gathered experience on the use of the OECD harmonized tiered approach (ENV/JM/MONO(2015)19) for occupational exposure assessment in laboratories, SMEs and industries.

1.7.4. Developments related to good practice documents

INERIS, CEA, LNE, INRS have contributed to the design and the building of the MALTA project aiming to support the finalisation of OECD Guidance Document and Test Guidelines of reliance for REACH and CLP registration. A mapping of French organisations capabilities was notably built and several French organisations are already identified as active contributors to the Malta project, notably on Dustiness, SSA, Toxicokinetic, environmental fate and Solubility. INERIS has also contributed to several OECD documents such as the "Guidance Document on Aquatic (and Sediment) Toxicology Testing of Nanomaterials", the "Test Guideline on Dispersion stability of nanomaterials in simulated environmental media" published in October 2017, but also the on-going projects on "Physicochemical characterization decision framework", "Preliminary draft of the guiding principles for measurement and reporting for

nanomaterials", as well as the WPRPW project on "Nanomaterials in Waste Streams Current Knowledge on Risks and Impacts".

France & Denmark, **through INERIS & NRCWE** and with the support of **INRS & LNE**, had proposed a project for a new test guideline on the "Determination of the Dustiness of Manufactured Nanomaterials", to be discussed during the 18th WPMN and aiming to submit an SPSF in Nov 2018.

France (INERIS), The Netherland (RIVM) and BIAC had proposed a project « Moving forward to 'Safe-by-Design' for sustainable innovation in nanomaterials and nano-enabled products: Overview of existing risk assessment tools, framework & applicabilities in industrial innovations », to be endorsed by the WPMN.

INERIS and member of the French standardization body **AFNOR** have engaged in 2017 an initiative aiming to enhance traceability in the Business to Business value chain as a lever for Business to consumer labelling. Key point identified are notably on vocabulary and terminology as well as tools available (document such as MSDS as well as technical tools such as chemical, physical of nuclear tracers).

CEA has contributed to the development of a guide for risk assessment (NanoStream project). The identification of relevant exposure scenarios in the microelectronic industry was performed. Tools and methods to conduct occupational exposure assessment were adapted to the specificities of the microelectronic sector. CEA, within FutureNanoNeeds project and in collaboration with IUTA and TNO, had developed a Manual on best practice for safe nanotechnology action plan. The goal of this document is to prepare a FutureNanoNeeds approach on best practices for ensuring safety of the next generations of nanomaterials being developed for industrial applications. CEA was the lead author of guidelines and risk minimization procedures for nanopowders handling and processing adapted to the ten NanoLeap pilot lines producing nanomaterials and nanoenabled products for the construction industry. The goal of this document was to provide guidance, EHS advices and recommendations to pilot plants owners and their users (open access). A brochure summarizing the report will be prepared and distributed to a large public mid 2018.

Ministry for an ecological and solidary transition has developed and put in place a good practices guidance for industries producing or using manufactured nanomaterials. This document gives an overview of practices on process effluents treatment as well as guidance on storage and waste management. Information available on the website http://www.ecologique-solidaire.gouv.fr/nanomateriaux

1.7.5. Information on any developments related to Integrated Approaches to Testing and Assessment

ANSES is following its work concerning the development and investigation on exposure scenarios for the general population to a few manufactured nanomaterials contained in a sample of products placed on the market. The Agency issued an internal request to develop a pragmatic risk assessment methodology adapted to nanomaterials. The proposed evaluation method applies to a finished product initially containing one or more manufactured nanomaterials for a given scenario of the use of the nano-product under consideration. This method was published in 2015.

INERIS & UCO, within the NanoReg2 project and in collaboration with other organisations (INIA-SP), have conduction studies on the grouping methodology of NPs according to ecotoxicity.

INERIS, as coordinator of Nanoreg2 project on Safe By Design development (based on grouping and intelligent testing strategies) and industrial demonstration (7 case studies), together with the OECD on-going project on « Physicochemical characterisation decision framework » under **Canada, The Netherland and BIAC** co-leadership, have launched an OECD-NanoReg2 conference initiative devoted to physical and chemical descriptors and their relevance for Hazard and behavior assessment as well as their links to functionality or property descriptors. This initiative will be discussed during the 18th WPMN.

CEREGE, as coordinator of the LABEX SERENADE on Safe-by-Design having funded several projects involving industrial partners, has been designated as EU interface with the US for establishing a transatlantic alliance for establishing a database on exposure and hazard of engineered NMs. This project is notably examining the aging of consumer products (paints, cosmetics, food packaging…) through 7 case studies involving both academia and industrial partners to generate safer next generation of nano-enabled products.

University Paris Diderot is involved in H2020 BioRiMa project which just started to develop an Integrated Risk Management (IRM) framework for NanoBiomaterials used in Advanced Therapy Medicinal Products or Medical Devices. The BIORIMA IRM framework is a structure upon which the validated tools and methods for materials, exposure, hazard and risk identification/assessment and management are allocated plus a rationale for selecting and using them to manage and reduce the risk for specific biomaterials.

1.7.6. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

INRS had conducted studies on inhalation toxicology, using a dedicated nose-only inhalation system for rats. The work was devoted to the influence of agglomeration rate on the inflammation and the toxicokinetic, for the case of TiO2 nanomaterials. This work is conducted in relation with studies conducted on neuro-inflammatory studies, in collaboration with **CEA & Orsay University**, within the NanoTransBrain project. INRS is also contributing to the SmartNanoTox project (with **UC Dublin** as coordinator) aiming to develop prediction tools for toxicity.

INSERM - Institut Mondor de Recherche Biomédicale (IMRB) is conducting studies aimed to understand consequences of respiratory exposure to nanomaterials of anthropic origin (mainly carbon nanotubes, metal nanoparticles such as TiO2, CeO2, Ag, FexOy), as a function of their physico-chemical properties. This work is conducted in cells in vitro, after animal oropharyngeal exposure (adult or pregnant mice) and in human samples occupationally exposed to nanomaterials. Studies have been also initiated to decipher if (early) exposure to anthropic nanomaterials could represent a susceptibility factor to develop lung pathologies at adult age.

INSERM-EMSE (Ecole des Mines de St Etienne) has conducted studies on the biological monitoring of inhaled nanoparticles in bronchoalveolar lavage fluids (clinical trial), in an appealing approach to study causal link between human respiratory pathology and exposure to nanoparticles. INSERM-EMSE has also conducted studies on the relationship between nanoparticles physico-chemical parameters and their toxicity for nanoparticle hazard ranking in a context of industrial nanotoxicology.

LNE has conducted studies on the impact of fire degradation on phys-chem properties and toxicity of released nanoobjects used in EVA matrix (boehmite, silica, alumina with different coatings and shapes) within the NANOTOX'IN project (French national funding / **ADEME**) and has started studies on the impact of ageing on nanoobjects' release by thermal degradation of nanocomposites (containing nanomaterials as flame retardants). LNE has also started a study on of manufactured nanoobjects' release according to ageing of nanocomposite materials used for building applications (TiO2 in paint) under the EMANE project (French national funding / **ADEME**): and is also contributing to the study of the potential impact on brain functions of released (nano)particles from nanocomposite materials (paint with TiO2) under use (ageing, wear, UV) under the Nanotox project (French national funding / **ANSES**). Finally, LNE has started studies on the identification of useful parameters to discriminate manufactured nanomaterials from natural ones in the environment (Seine water / Ag, TiO2, CeO2) tracking through element ratios and study of different typical catchments (3 types = industrial, forestry and urban).

INRA TOXALIM is partner of the npSCOPE project funded by the European Commission H2020 (**LIST-LU** as coordinator) developing a new integrated and optimized instrument being able to provide a comprehensive physico-chemical characterisation of NPs in their original form or incorporated into complex matrices such as biological tissues, foodstuffs, cosmetics.

IRSN is conducting studies since several years on the mechanisms of transport of uranium particles from the nasal cavity to the brain via the so called "olfactory route" in the context of inhalation exposure. A specific experimental platform using nose-only inhalation chambers has been used on a rodent model (rat). In 2017, IRSN has demonstrated that in situ localization of inhaled uranium particles is consistent with a transport via the olfactory nerve using high resolution microscopy techniques in rat. This project is in line with the radioprotection concerns of IRSN and maybe more in the margins of studies on the safety of manufactured nanomaterials. But, active discussions are on-going at IRSN in order to develop new projects on different metal nano and microparticles. These discussions are conducted with the strong intention to collaborate with other institutes or laboratories working on the toxicity of inhaled particles."

University Paris Diderot, within ERA-NET SIINN project NanOxiMet, has developed methods to characterize the oxidative potential of nanomaterials to be used as a metric to allow grouping of nanomaterials and prediction of human health effects. SOPs related to the different acellular and cellular assays have been produced. University Paris Diderot, has also started studies on the combined effects of nanoparticles and organic compounds under the BarBaPAhr project (French national funding / ANSES). It extends a previous project with BASF aiming to characterize the long term effect of repeated exposures to nanoparticles using in vitro models of human bronchial epithelial cells by comparison to rat inhalation studies (PhD co-funding Ademe- BASF). In vitro chronic toxicity studies with this 3D culture model as well as co-cultures are planned in a starting H2020 project (BioRiMa) concerning biomaterials to be used in nanomedicine. Finally, University Paris Diderot, within the TiSiTrans project (French national funding / ANSES) has developed a model of human bronchial epithelial barrier to characterize the translocation of nanoparticles. University Paris Diderot now starts studies within the ANR project AlveolusMimics to develop a biomimetic alveoli.

LNE, Mines ParisTech and CEA have conducted a three year project, NanoMET which ended in 2017, on the development of reference methods to guarantee the accuracy and

comparability of measurement on nanomaterials. One goal of the project was to facilitate and promote the transfer of the characterization methods to SMEs.

CSTB has conducted and coordinated two research projects on the nanomaterials used for building applications:

- "Release study of manufactured nano-objects under aging from building nanocomposite materials" (EMANE project, French national funding / ADEME) in collaboration with **LNE**. The project ended in 2017 and has provided new scientific data and knowledge on the behavior of photocatalytic nanomaterials used for building applications (TiO2 nano-additived paints) to estimate the exposure of the consumers to manufactured nanoparticles. This project has contributed to improve the knowledge on the emissivity of nano-objects under aging and weathering conditions encountered in indoor environments (humidity, temperature, oxidation, cleaning and mechanical solicitation).
- "Impact on the nervous system of particles released from nanocomposite materials under stress use" (Release NanoTox project, French national funding / ANSES) in collaboration with **ANSES, LNE** and CarMen. This on-going project is aiming to evaluate the potential neurotoxicity of aerosols released from mechanical stress of nano-additived paints with TiO2 nanoparticles.

1.7.7. Information on research or strategies on life cycle aspects of nanomaterials, as well as positive and negative impacts on environment and health of nano-enabled applications

INERIS & UCO, within NanoReg2 project, has conducted actions in collaboration with industrial partners and other organisations (INIA-SP, Gaiker IK4-SP), to implement a safer by design testing strategy for environmental toxicity, following a life cycle analysis and using vivo assay and HTS based on marine and freshwater cells and/or organisms and mesocosm platform. UCO has developed notably adapted NANoREG SOPs for in vitro testing on marine organisms and had developed together with CEREGE mesocosm platform and notably a Marine platform mimicking tidal cycles, with controlled physico-chemical parameters. INERIS has adapted OECD tests guidelines on µalgae and daphnia and has conducted assays on industrial relevant nanomaterials.

INERIS, in collaboration **with Ecole des Mines de Nantes** and **an industrial partner**, in the framework of the ADEME NanoWET project, have engaged studies on incineration of waste of nanomaterials. This project, more devoted to high Temperature incineration route, in following a previous project NanoFlueGas devoted to urban waste incineration route.

CIRIMAT (UMR CNRS 5085) & **ECOLAB** (UMR CNRS 5245) are actually involved in the Graphene Flagship, which is a Future and Emerging Technology Flagship by the European Commission, devoted to graphene and related materials (graphene oxide, reduced graphene oxide, few-layer graphene, etc.). CIRIMAT and ECOLAB are involved in Work Package 4, dedicated to Health and Environmental issues, developing different approaches to assess the ecotoxicity of few-layer graphene, graphene oxide and reduced-graphene oxide on the aquatic compartment, in particular with amphibian models and lab-scale mesocosms.

ANSES is involved since several years on the measurement of TiO2 nanoparticles in biological matrices notably through the NANOGENOTOX project and the Equipex NANOID. 2 projects were recently submitted or engaged, together with INRA, on the

effect of respectively TiO2 and gold nanoparticles on the feto-placental development. ANSES is also currently involved in the above mentioned project Release Nanotox (French national funding / ANSES) coordinated by CSTB, in collaboration with LNE, aiming to study the potential impact on brain functions of released (nano)particles from nanocomposite materials (paint with TiO2) under use. ANSES has coordinated a French/German (BfR and university of Leipzig) ANR project dealing with the fate and the effects of inert nanoparticles (two rutile TiO2) and potentially soluble nanoparticles (Al0 and Al2O3) after ingestion focusing on intestine and liver.

CEA is conducting studies on the implementation and effectiveness of Safer-by-Design approaches under the frame of NanoLeap project (agglomerated particles and coatings). For this purpose, dustiness testing, aging and mechanical solicitation experiments are currently being performed.

1.7.8. Information on development related to exposure measurement and exposure mitigation

INERIS, in collaboration with **CEREGE, University of Strasbourg** and **an industrial partner**, in the framework of a project founded by the **ADEME**, have conducted field campaigns aiming to evaluate the environmental fate of manufactured Nanomaterial (in air, soil, water and sediments compartments) around an industrial production facility. Specific studies were done on sampling strategy and quantification issues.

LNE had conducted developments of an aerosol generation system with well controlled properties (number concentration, size range, stability over time…) useful for inhalation toxicity testing and calibration of airborne measuring analytical devices.

LNE has participated to an inter-laboratory comparison in the frame of BIPM/CCQM (Consultative Committee for Amount of Substance: Metrology in Chemistry and Biology) aiming at characterizing surface area of non porous silica through BET measurement (Russia lead) as well as number concentration of nanoparticles through sp ICP-MS and DMA measurements (UK lead / link to a VAMAS initiative and EMPIR InnanoPart project).

INRS is conducting since several years on collective or personal protection unit, notably using numerical aerologic tools, considering the specificity of nanomaterials to adapt protocols used to evaluate their efficiency and to support industries in the choice of their equipment. In 2017, work was notably conducted on respiratory apparatus, in collaboration with the CNRS-LRGP, conducting studies on those having a high protection ratio.

INRS and LNE have conducted studies on the evaluation of on-line instruments, evaluating results obtained by different instruments based on SPMS Scanning mobility particle sizer spectrometer) principle. INRS has also conducted studies on:

- Pre-normative studies on number concentration and its link with other mesurands such as mass and specific surface area. This work was conducted within NanoCEN project.
- The development of the NECID database in collaboration with TNO-NL and IFA-DE. This work was conducted within the PEROSH network.
- The optimisation of sampling tools based on impaction principle, for metal based nanomaterial.

- The development of European harmonized dustiness methods as well as dustiness indexes for workplace exposure evaluation. This work was conducted within NanoCEN project.
- On the full characterization of metal based ultrafine particles in collaboration with EMD (Ecole des Mines de Douai).

CEA through the recently started EnDurCrete project will conduct field measurements, occupational exposure assessments along with release studies on building and infrastructure case studies.

CSTB has developed an aerosol generation system for inhalation toxicity which is reproducing mechanical abrasion process of nanomaterial. CSTB has also developed experimental setup and protocols to characterize the emissivity of nano-objects under aging and weathering scenarios representative of environmental and use conditions encountered in indoor environments (humidity, temperature, oxidation, cleaning and mechanical solicitation).

1.7.9. Additional Information

ICAM of LILLE, IPL, LNE and Forum NanoRESP have co-organized 2 workshops devoted to the "condition of trust" in the development of manufactured nanomaterials as well as on the main stakes and needs in each of the relevant scientific fields of sustainable development of manufactured nanomaterials and nano-enabled products. CEREGE, INERIS, LNE and research organisations were invited to give keynote addresses.

CEA, INERIS & INRS have co-organised the annual workshop involving 50 attendees from most of French research organisation on metrology, hazard assessment (human and environmental toxicology) and life cycle assessment of aspects of nanomaterials. A session was devoted to the launch of a national structuration scheme on hazard and risk assessment knowledge and capabilities, that can be of high relevance to contribute to OECD WPMN and WPRPW issues.

LNE has organised a technical Workshop on nanomaterials applications in food (regulations, insights regarding on-going R&D activities on toxicity assessment for food additives, characterization methodologies to verify labelling requirements …).

INERIS, within the NanoReg2 project involving more than 40 partners, had co-organized with **JRC-EC** and **RIVM-NL**, a workshop involving more than 50 attendees from most of regulation bodies and dedicated to the regulatory preparedness for a safe innovation. Incentives and barriers to regulatory preparedness were notably identified as well as some recent initiatives in this field, to be further studied.

SPF - EpiNano: a scientific committee is being set up in order to validate the methodology of implementation of this surveillance system. Applications can be sent to Public Health France until 15 February. http://www.santepubliquefrance.fr/Actualites/Appel-a-candidatures-pour-la-constitution-d-un-Conseil-scientifique-pour-le-dispositif-EpiNano.

INRA TOXALIM has co-organized with the **SFN-French Nutrition Society** a Symposium devoted to "Nanoparticles and human food" at the SFN Annual Nutrition Congress (Journées Francophones de Nutrition, Nantes) dedicated to nutritionists, physicians and researchers.

ANSES is in charge of the French registry on nanomaterials R-nano. The mandatory reporting of nanomaterials has been introduced in January 2013, enabling the collection

of a significant amount of data. As defined in the application decree, ANSES, is in charge, of the management of the dedicated application and the data collected. The information collected will be used to describe the use of nanomaterials in several industrial sectors and to document the related exposition. ANSES, following the referral to the public authorities, has undertaking a expertise on the risks associated with the use of nanomaterials in the context of food, including the risks for professionals involved in the sector.

CEA has organised the "Ateliers de la Nanosécurité" in Grenoble, France involving 40 attendees from start-up companies, SMEs and industry. The workshop was aiming at providing guidance to promote a responsible development of nanomaterials.

1.8. Germany

Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety (BMUB)

The NanoDialogue of the Federal Government was continued with the second ExpertDialogue of the 5th dialogue phase on "Opportunities and risks of the application of nanotechnologies in the automotive sector".

The results of all dialogues are published as thematic reports at the homepage of the BMUB. The recent one at **www.bmub.bund.de/N54417-1.**

Federal Ministry of Education and Research (BMBF)

Highlights

The new national BMBF funding activity "NanoCare4.0 – material innovation for safe application" within the frame of the German funding programme "From Material to Innovation" (2015-2025) has been published on September 8th 2017. The topics are:

1. Safety-relevant effects and nano-effects in the whole system of materials

Nanomaterials and innovative materials with probable environmental or health-damaging potential should be fully investigated in terms of their human and/or ecotoxicological effects. The specific effects of the overall system of the synthetic nano-and microscale materials should be considered within their natural background. These specific effects include in particular:

- Release and transformation (materials with critical morphology; cumulative exposition and combined effects with respect of the toxicological potential)
- Toxicological effects (end of life; interaction between cells and NM in dynamic systems; long-term effects, low-dose-effects; green-design criteria

2. Prediction and modelling of toxicological effects

- Special focus on approaches for classification, grouping and read-across, including certified reference materials
- Development of models (for dose-response-relationship; for assessment of health risks)
- Prediction on changes of environmental-dependent materials properties (for example after oral intake of NM)

3. Further development of intelligent test strategies and quantitative measurement methods

- Nano-specific measuring methods for characterizing and assessing the risks of materials innovation
- Advancement of toxicological test strategies
- Development of screening methods of health and environmental effects of innovative materials (high-throughput technologies, innovative *in-vitro* test methods)

Deadline for the submission of proposals is January 31, 2018, respectively. (https://www.bmbf.de/foerderungen/bekanntmachung-1432.html)

Germany intensifies its cooperation with Israel and Greece in industry-led research and development. The countries aim to pursue their innovation dialogue and agreed on joint R&D programmes that focus on nanotechnology including aspects of nanosafety. The collaborative projects should enhance the overall competitiveness and innovation potential of both countries. Particular attention will be paid to the involvement of young researchers.

- The funding scheme of the Greek-German Partnership comprises different research areas (health, energy, materials etc.). The topic "Materials" focuses on nano-carbons and applications in membranes and porous materials (https://www.bmbf.de/foerderungen/bekanntmachung-1282.html).
- The collaboration with Israel is intended to strengthen technology transfer in the field of applied nanotechnology, too (e.g. bio-medical technologies, nano devices for sensors, nano-based energy resources and so on, see https://www.bmbf.de/foerderungen/bekanntmachung-1271.html).

The projects with Israel started on the 1st of January 2018; the projects with Greece are being planned.

1.8.1. National developments on human health and environmental safety

Federal Environment Agency (Umweltbundesamt, UBA) and Federal Institute for Risk Assessment (BfR)

In 2017 the German Environment Agency (UBA) together with the German Federal Institute for risk assessment (BfR) started a substance evaluation of zinc oxide, in particular the nanoforms of zinc oxide under the European Chemicals legislation REACH:
https://echa.europa.eu/de/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table

Federal Environment Agency (Umweltbundesamt, UBA)

A Scientific Stakeholder Meeting on Nanomaterials in the Environment took place on the 10th and 11th October 2017 at the headquarters of the German Environment Agency (UBA) in Dessau-Rosslau, Germany. The meeting was hosted by UBA and financed by the German Federal Ministry for the Environment, Nature Conservation, Building and Nuclear Safety. The meeting focused on regulatory relevant results of German and European research projects on nanomaterials in the environment which are carried out or finalised in the current years. By this, it gave a forum to present the state of the knowledge on environmental nanosafety in a regulatory context as well as to discuss the scientific results and their regulatory relevance between affected stakeholders. Therefore, the meeting particularly addressed representatives of science, industry, risk

assessors, regulatory experts, and NGOs. It included key note talks, invited platform presentations as well as poster presentations. A Knowledge Café provided the opportunity to discuss selected topics with regard to environmental safety of nanomaterials in smaller groups. The meeting was closed with a discussion on the lessons learned highlighting the outcomes of the meeting by the views of different stakeholders.

The meeting report and available presentations is published at the workshop webpage: https://www.umweltbundesamt.de/en/scientific-stakeholder-meeting-on-nanomaterials-in.

The report is available on the UBA webpage on nanotechnology: https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/good-to-know.

1.8.2. Activities been initiated to implement the OECD Council Recommendation (e.g. regulatory changes, guidance, voluntary, etc.)

Federal Environment Agency (Umweltbundesamt, UBA)

The OECD Test Guideline (TG) 318 ("Dispersion stability of nanomaterials in simulated environmental media") which was developed under the lead of Germany was published in October 2017. It features the first standardized test method particular for nanomaterials adopted by OECD. The method determines the dispersion stability of nanomaterials in aqueous media in dependence of varying environmental conditions. The TG was developed by the Department of Environmental Geosciences at the University of Vienna on behalf of the German Environment Agency and financed by the German Federal Ministry for the Environment, Nature Conversation, building and Nuclear Safety. It is available for download at the webpage on the OECD Guidelines for the Testing of Chemicals:

http://www.oecd-ilibrary.org/environment/test-no-318-dispersion-stability-of-nanomaterials-in-simulated-environmental-media_9789264284142-en

UBA launched a new research project for supporting the development of a new OECD Guidance Document on interpretation of data regarding dissolution rate and dispersion stability of nanomaterials in the environment. This GD is aimed as an overarching and accompanying GD to the OECD Test Guideline for dissolution rate of nanomaterials (currently under development by US) and the currently published OECD TG on dispersions stability of nanomaterials in simulated environmental media (TG 318), which was developed under the lead of Germany. The activity to develop such a GD is already included in the WNT POW. The project started in autumn 2017 and will run until 2019/2020. Aim of the GD under development is to serve as support tool for both the Test Guideline on dispersion stability (OECD TG 318) and the developing OECD TG for dissolution rate of nanomaterials in the environment by providing guidance on the influence of various experimental conditions and materials on the performance and outcomes of these tests and to give support for the interpretation of results towards further fate and eco-toxicological testing or modelling. A project related expert group was founded which will support the development of the document.

Federal Institute for Occupational Safety and Health (BAuA), Federal Institute for Materials Research and Testing (BAM) and Federal Environment Agency (Umweltbundesamt, UBA)

In April 2017, a new research project was launched on appropriate measurement techniques and concepts of particle size and particle size distribution of nanomaterials. This project addresses the endpoint of particle size and particle size distribution which was a still open activity mentioned in the work plan of the WPMN. The project will run from 2017 to 2020. A project related expert group was founded which will support the development of a new Test Guideline. In November 2017, a SPSF describing the objectives and procedures of the activity was submitted to OECD WNT.

In this context BAuA and BAM have started a research project sponsored by BMUB titled **"Development of a specific OECD Guideline to determine the particle size and number size distribution of nanomaterials"**. Goal of the project is the "Development of a specific OECD Guideline to determine the particle size and number size distribution of nanomaterials". The guideline to be drafted is closely related to the OECD Test Guideline 110 ("Particle Size Distribution / Fibre Length and Diameter Distributions") and is supposed to summarise methods being capable of measuring reproducibly primary particle size distributions as well as size distributions of fibres including nanofibers (determination of diameter and length per fibre and the distribution). This may be done as an extension of TG110 or in a separate document dependent also on the decision of the WPMN. The draft work program of the OECD-WPMN for 2017-2020 foresees the review of the OECD Test Guideline 110. The OECD has published a document listing the principally available methods for particle size measurements in the submicrometer range down to 1 nm. These methods will be examined and assessed in theory and experiment under the aspects of practicability, reproducibility and validity. The assessment will indicate if a method needs or can be used without further adaptions. These first assessed methods will be further tested in an international Round-Robin test which is one prerequisite for a draft guideline to be accepted. The results of the project are basis for drafting a guideline document for size distributions of primary particles and fibres in the size range of around 1-1000 nm. This document is foreseen to be submitted to the OECD via the German delegation. The project will be finished in 2020.

Federal Institute for Risk Assessment (BfR)

BfR is represented in the expert panel for the revision process of OECD Guidance Documents for inhalation toxicology, such as GD 39. In this context, the eligibility of optional BAL parameters for inhalation toxicology testing of nanomaterials is currently reviewed.

1.8.3. Developments related to good practice documents

Within a series of publication stemming from the ProSafe Project two open access articles investigating the regulatory readiness of recent developments related to nanomaterial exposure and in-vivo-effects have been recently published.

Kuhlbusch, T.A.J., Wijnhoven, S.W.P., Haase, A., Nanomaterial exposures for worker, consumer and the general public, NanoImpact, Volume 10, 2018, Pages 11-25.

Oberdörster, G., Kuhlbusch, T.A.J., In vivo effects: Methodologies and biokinetics of inhaled nanomaterials, In NanoImpact, Volume 10, 2018, Pages 38-60.

1.8.4. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

Federal Institute for Risk Assessment (BfR)

The National Metrology Institute (PTB) and the BfR intend to investigate on nanofibers with special emphasis on fiber rigidity in their research program. The focus shall be on characterization, exposure assessment and inhalation toxicology.

1.8.5. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Federal Ministry of Education and Research (BMBF)

The BMBF research priority "NanoCare - Safe handling of Manufactured Nanomaterials – Studying the effects on humans and the environment" is continued to be funded within the frame of the German funding programme "From Material to Innovation" (2015-2025).

Current projects are:

- CaNTser - Investigation of the toxic potency of carbon nanotubes following long time inhalation
- NanoBEL - Biological Elimination of Complex Diagnostic Nanoparticles
- nanoGRAVUR - Grouping of nanostructured materials for protection of workers, consumers, the environment and risk minimisation
- ProCycle-Analysis and toxicological evaluation of dusts from recycling and recycling processes of nanocomposites and strategies for risk minimisation

In the frame of the ERA-NET SIINN (Safe Implementation of Innovative Nanoscience and Nanotechnologies; coordinated by Germany, completed 2015) a total of 15 joint transnational projects are granted. German companies and institutes are involved in twelve projects, funded by the BMBF. All three projects of the first SIINN Call have been completed 2016 (see below). All other projects are ongoing and are still governed by the SIINN Call Office. The projects are also presented on the DaNa Platform (see below). The acronyms of the SIINN funded projects (underlined: with German participation) are:

First SIINN Call 2012: nanoIndEx, nanOxiMet, NANOHETER

Second SIINN Call 2013: FENOMENO, NanoToxClass, NANO_SAFE_LEATHER, NanoGeCo, PLATOX Third SIINN Call 2014: NANO-Transfer, FATENANO, ICONS, CERASAFE, NanoWIR2ES, NANOaers, nanoFARM

The projects of the first ERA-NET SIINN Call „nanoIndEx - Assessment of Individual Exposure to manufactured nanomaterials by means of personal monitors and samplers" and "nanOxiMet - **Oxi**dant generating capacity as a **met**ric to allow grouping of **nan**omaterials and prediction of human health effects" have been completed in 2016. The results of the projects have been published (www.nanoximet.eu; www.nanoindex.eu). Standard Operation Procedures (SOPs) from nanoIndEx regarding the proper use of the personal monitors and samplers and the performance of field studies have been written. Numerous field studies have been conducted and a data collection and evaluation protocol has been developed. All applicable data have been uploaded to the international Nano Exposure and Contextual Information Database (NECID). A 49- page Guidance Document "Assessment of Personal Exposure to Airborne Nanomaterials – a guidance

document, NanoIndEx Consortium 2016" on the assessment of personal exposure to airborne nanomaterials has been written, printed and disseminated (see www.nanoobject.info).

The web-based knowledge and data platform 'DaNa – The Knowledge Platform on Nanomaterials' is continued to be funded by BMBF (www.nanopartikel.info; www.nanoobject.info). The web presence illustrates the research results on safety aspects from the German funding projects in nanosafety.

The Cluster-Meeting of the two BMBF funding initiatives NanoCare & ERA-Net SIINN will take place from September 17th-18th 2018 in the Dorint Hotel Neuss, Germany, shortly before the international NanoTox2018. There, the latest results of the funding projects will be presented in the plenary sessions and as poster contributions.

Additionally, selected results will be presented on the NanoTox2018, 9th International Conference on Nanotoxicology, September 18th -21th 2018, at the Dorint Hotel Neuss, Germany.

The new national BMBF funding activity "NanoCare4.0 – material innovation for safe application" has been published on September 8th 2017 (see above).

Germany intensifies its cooperation with Israel and Greece in industry-led research and development. Two calls for collaborative projects have been published (see above).

Federal Environment Agency (Umweltbundesamt, UBA)

A research project on the relationship of nanomaterials physical-chemical properties and aquatic toxicity for the purpose of grouping which was conducted on behalf of UBA was finalised. The project objective was to correlate physical-chemical data with ecotoxicological effects for selected nanomaterials and to define reference parameters which can serve as a basis for grouping. The report presents the development of concepts for grouping of nanomaterials with regard to their ecotoxicological effects with focus on aquatic ecotoxicity. The final report with the title "Considerations about the relationship of nanomaterial's physical-chemical properties and aquatic toxicity for the purpose of grouping" is available for download: https://www.umweltbundesamt.de/en/publikationen/considerations-about-the-relationship-of.

The research project launched on behalf of UBA to support the development of the new OECD TG on dispersion stability on nanomaterials in simulated environmental media (OECD TG No. 318, published by OECD in October 2017) was finalized. Aim of the project was the development of the test set up to determine dispersibility and dispersion stability of nanomaterials in environmentally relevant media For this objective, both conceptual and experimental work was conducted and an international round robin was initiated and executed within this project to validate the proposed test setup regarding reliability and reproducibility. The final report summarizes the experimental work performed to develop the OECD Test Guideline. It is available for download: https://www.umweltbundesamt.de/publikationen/clarification-of-methodical-questions-regarding-the.

Federal Institute for Materials Research and Testing (BAM)

The large EU/FP7 project NanoDefine 'Development of methods and standards supporting the implementation of the Commission recommendation for a definition of

nanomaterial' with BAM lead of the work package 'Evaluation and selection of techniques and methodologies' has finished on October 31st, 2017 after 48 months duration. Two public workshops have been organized by NanoDefine:

- Final NanoDefine Outreach Event, Brussels, 19-20 September 2017: Classification of nanomaterials according to the EU definition – for regulatory bodies (including EC), s. http://www.nanodefine.eu/index.php/nanodefine-meetings/125-final-outreach-event-2017
- Second NanoDefine industry-focused workshop, DECHEMA/Frankfurt, 24 October 2017: "Measurement and classification of nanomaterials according to the EU definition" – for European industry, s. http://www.nanodefine.eu/index.php/nanodefine-meetings/128-nanodefine-frankfurt-workshop-october-2017.

A consistent framework of guidance for nanomaterial identification according to the EC Definition Recommendation has been issued in form of the NanoDefiner e-tool (https://labs.inf.fh-dortmund.de/NanoDefiner), with a transparent decision flow scheme and an extensive user manual, which are just being made publicly available. Also specific recommendations on a revision of the EC recommendation for a definition of nanomaterial based on the analytical possibilities as found within NanoDefine has been prepared for EC.

http://www.nanodefine.eu/index.php/nanodefine-publications/nanodefine-technical-reports

The EMPIR project INNANOPART, started in May 2015, combines expertises from several National Metrology Institutes and Designated National Metrology Institute to assess method for the determination of the size, thickness of surface shells, and concentration of nanoparticles in dispersion. Work package 3 focusing on different methods for surface group analysis and the determination of surface shell thicknesses is lead by division Biophotonics (BAM 1.2) with strong contributions from division Surface Analysis (BAM 6.1). Results from this project will contribute to written standards developed in ISO TC229 Nanotechnologies.

Federal Institute for Risk Assessment (BfR)

BfR is currently involved in the following activities:

- The EU Horizon 2020 Infrastructure Project nanoCommons will start in January 2018 and deals with the establishment of a European nanoinformatics infrastructure, including topics of harmonization of databases and ontologies as well as developing (modelling) tools for data analysis. BfR is a partner in nanoCommons.
- The EU Horizon 2020 project GRACIOUS (Grouping, Read-Across, CharacterIsation and classificatiOn framework for regUlatory risk assessment of manufactured nanomaterials and Safer design of nano-enabled products) will start in January 2018. BfR is a partner in GRACIOUS.

Federal Institute for Occupational Safety and Health (BAuA)

BAuA has started a research project sponsored by BMUB titled " **Investigations on the Detectability of possible Emissions of Carbon Nanofibres in Exhaust Gases from Combustion Processes".** For the detection of possibly increased concentrations of airborne nanofibers at workplaces handling such materials, it is necessary to know the

background concentration of nanoscale fibres in the environment. Possible emission sources of carbon nanofibers are combustion processes. The project develops methods for collecting, purifying and analysing exhaust gas samples, with the aim of investigating and optimizing the distinguishability and separate quantifiability of soot particles and carbon nanofibers. Exhaust gas samples are expected to contain predominantly soot particles and only a few carbon nanofibers. For this reason, oxidation processes for the selective removal of soot-like carbon structures are tested. They are supplemented by spectroscopic methods, from which additional information on a fibre identity is expected if morphological electron microscopic analyses fail for samples that are particle-dominated. The project will be finished in 2018.

In 2017 BAuA has finished its contribution **"Occupational safety aspects during manufacture and use of high-cycle fatigue performance resins for energy storage applications"** to the project "ELSE" funded by the German Ministry for Economic Affairs and Energy. The aim of the project is the development of rotational storage devices with reduced flywheel mass that absorb a large amount of energy in short time and release it again. For this purpose, a high static and dynamic strength of the flywheels is required, which in the moment is only accessible by using carbon fibre reinforced plastics. By adding carbon nanotubes to the resin system the resulting plastics show high form stability and long lifetime. The selection of nanoscale, fibrous additives for the production of load cycle resistant carbon fiber composites was accompanied in the project by BAuA in terms of materials science and the transfer of aspects of application safety. Five variants of carbon nanotubes (CNTs) were quantified, characterized and evaluated and prioritized in terms of their propensity to release dust and aerosol morphology.

Unexpectedly, BAuA workplace measurements during the mechanical processing of test pieces and their tensile testing revealed a release of high concentrations of alveolar fibrous objects. In machining operations, workplace concentrations of around 1,000,000 such objects per cubic metre were determined in accordance with the WHO criteria for critical fibres.

As a source of the fibrous emissions, BAuA's laboratory tests were able to identify fibrous fracture behaviour of the microscaled pitch-based carbon fibres used in the CF composite by systematically investigating methods of mechanical processing of CF composites in a test chamber. For this purpose, a new test chamber was set up at the BAuA and adapted to be used for abrasion experiments with the formation of potentially hazardous dusts.

BAuA has also finished the project **"Building blocks for a safe handling of nano materials at the workplace - memorandum for application of the EU precautionary principle"**

Within the scope of this umbrella project on BAuA's research activities on application safety for nanomaterials and advanced materials, the scientific basis for occupational exposure limits and protective measures, toxicological grouping and the adaptation of occupational safety and chemicals legislation was prepared and successfully implemented within the framework of policy advice. This concerns in particular Announcement 527 "Manufactured Nanomaterials" of the Hazardous Substances Committee (2013), the generic occupational exposure limit for respirable granular biopersistent dust in the technical rule TRGS 900 (2014) and the evidence-based guideline of the World Health Organization on protecting workers from potential risks of manufactured nanomaterials (2017). In addition to statements and position papers on regulatory issues and the continuation of a joint research strategy with other higher federal authorities in Germany,

a concept for assessing the regulatory maturity of R&D projects in risk and safety research is developed. Regulatory Readiness Levels (RRL) are an instrument to illustrate the status of governance-related R&D activities and needs for further risk and safety research in the field of technological innovations. They are set up parallel to the Technology Readiness Levels (TRL) for R&D in Key Enabling Technologies (KETs) used for Horizon 2020 by the European Commission. Governance-related R&D covers the development of tools, e.g. for risk assessment in different fields, as well as the adaption or the development of testing methods to be used for regulatory purposes, which range from soft to hard regulation.

For Regulatory Readiness Levels (RRL) the following levels are currently discussed:

- RRL 1 regulatory needs / adaption requirements observed
- RRL 2 regulatory concept and corresponding tools / testing methods formulated
- RRL 3 experimental design of tool / testing method ("prototype")
- RRL 4 prototype of tool / testing method validated "in lab"
- RRL 5 tool prototype validated in relevant environment / pre-validation of testing method
- RRL 6 tool prototype demonstrated in relevant environment / validation of testing method
- RRL 7 tool prototype / testing method demonstrated for regulatory concept (implementation)
- RRL 8 regulatory concept implemented
- RRL 9 adapted regulation proven in operational environment (evaluation)

1.9. Italy

1.9.1. National developments on human health and environmental safety

Italy participated to the revision of REACH Annexes for substances with nanoforms. The draft regulation is being discussed prior to the adoption and relevant information requirements for nanoforms are going to be addressed in the amendment (e.g. dissolution rate, dustiness, agglomeration, long-term ecotox. studies).

1.9.2. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials.

In the framework of NanoInnovation 2017 Conference (Rome, 26-29 September 2017), the Italian National Institute of Health (ISS) organized the session “The RInnovareNano project: new insight into regulations and research of nanomaterials”. During the session were described the relevant updates on normative requirements for the use of nanomaterials in chemicals, biomed and agri-food sectors, and some specific results achieved in RInnovareNano project.

Two technical workshops have been also organized by ISS for Lazio industries. The former examined methodologies for physical-chemical characterization of NMs while in the latter regulatory improvements in the light of evolving scientific knowledge have been discussed.

ISS participate to the EU2020 NanoReg2 project, WP1 - Regulatory orientated activities. Project activities are focused on: a) establishing a framework of grouping approaches, in which current and prospective regulatory requirements for NMs risk assessment are identified; b) developing and applied grouping concepts for NMs; c) implementing technically oriented instruments and QSARS methods in order to build a general Intelligent Testing strategy (ITS) suitable to identify/develop risk assessment models.

A novel approach for risk management and communication of nanomaterials in R&D labs have been developed within the project Nano-lab (www.nano-lab.it), funded by the Italian Workers Compensation Authority (INAIL). The approach is based on a combination of modelling activities (control banding tools for nanomaterials), and multi-parameters exposure measurements in the labs. Safety data sheets, visuals and pictograms specific for each of the research process and the different expertise of the R&D personnel in the lab have been designed for risk communication.

1.9.3. Developments related to good practice documents

The RinnovareNano project, coordinated by ISS, has published a public web-platform to make available to all stakeholders information on the safety of nanomaterials, SOPs for safety testing, and updates in the regulation of nanomaterials.

The platform is now available on-line: https://nanotecnologie.iss.it

1.9.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

The Scientific Committee on Nanomaterial Workers' Health of the International Commission on Occupational Health, (ICOH), chaired by an Italian representative, is conducting a survey to collect information about the occupational safety and health in the engineered nanomaterials-related industries. The information gathered will be used to enhance its understanding of how its efforts related to engineered nanomaterial is influencing occupational safety and health across a range of nanomaterial-related businesses.

The survey (https://goo.gl/forms/U9SUMllfjAwzfdhT2) will be open until Summer 2018.

1.10. Japan

1.10.1. National developments on human health and environmental safety

The Ministry of Economy, Trade and Industry (METI) publicised information on safety test data and management methods of manufactured nanomaterials, on METI's website[5] firstly in 2010 (only in Japanese). Such information was voluntarily provided and annually updated by the manufacturers. METI publicised the updated information in 2017.

In March 2017, a committee established by the Ministry of Health, Labour and Welfare (MHLW) launched the discussion for the prevention of impairment of workers' health caused by exposure to TiO2 in nanoscale and non-nanoscale.

[5] http://www.meti.go.jp/policy/chemical_management/other/nano_program.html

1.10.2. Developments related to good practice documents

The Japanese Industrial Standards Committee (JISC), which is the national member body participating as a P-member in ISO/TC229 (Nanotechnologies), nominated the Convenor and Secretary of TC229/JWG2 (Measurement and characterisation). In TC229/JWG2, JISC jointly (with ANSI, the American National Standards Institute) leads a project group 22 "Particle size and shape distribution measurement using transmission electron microscopy" (IS 21363), and also jointly (with ANSI) leads a project group 21 "Measurements of particle size and shape distributions by scanning electron microscopy" (IS 19749), and leads a project group 23 "Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation" (TS 21362), and leads a project group 25 "Characterization of individualized cellulose nanofibril samples" (TS 21346). In TC229/WG3 (Health, Safety and Environmental Aspects of Nanotechnologies), JISC leads a New Work Item Proposal " Method for quantification of cellular uptake of carbon nanomaterials by using optical absorption measurement" (TS 23034).

The National Institute of Advanced Industrial Science and Technology (AIST), as a member of the Technology Research Association for Single Wall Carbon Nanotubes (TASC), released the English edition of "General procedures for safety tests on carbon nanomaterials: Procedures for sample preparation, characterization, in vitro cell-based assays, and animal tests on carbon nanomaterials" in October 2017 that is available on the AIST-RISS website[6].

1.10.3. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

METI proposed a WPMN project of feasibility study on in vivo short-term exposure methods for inhalation toxicity testing of manufactured nanomaterials in collaboration with BIAC at WPMN 17 in 2017. The proposal was revised according to the comments SGTA members. A domestic inter-laboratory comparison study on the procedure of intratracheal instillation is currently underway.

METI launched a new three-year project "Development of Safety Assessment Methods for Cellulose Nanofibers (CNFs)" (JFY 2017-2019) that is commissioned by the New Energy and Industrial Technology Development Organization and implemented by AIST and four CNF-manufacturing companies. In this project, methods for the analysis, hazard assessment, and emission/exposure assessment of CNFs are developed. Based on obtained results, guidance documents and case study reports will be published to support voluntary safety assessment in CNF-related companies.

MHLW has promoted research on the human health aspect of several nanomaterials since 2003 through the Health and Labour Sciences Research Grants. In JFY 2017, four research projects, including a basic research on development of methods for evaluating hazard and disposition of nanomaterials on human health, are progressing.

The Japan Bioassay Research Center has promoted the carcinogenicity test of the nanomaterials, commissioned by MHLW, which focused on the worker's health. Thirteen week inhalation study in rats and four week inhalation study in mouse were carried out in 2016 as the preliminary studies for inhalation carcinogenicity study of TiO2. Inhalation carcinogenicity study of TiO2 is on going in JFY 2016-2020.

[6] https://en.aist-riss.jp/assessment/6226/

From JFY 2011 the Ministry of the Environment (MOE) has been focusing their efforts on environmental risk of manufactured nanomaterials via understanding of their environmental fate and ecotoxicity. In JFY 2017 MOE continued collecting and reviewing existing literature on ecotoxicity of manufactured nanomaterials such as TiO2, silver and CNTs to identify any harmful effects attributed to their particle sizes.

For the purpose of developing methodologies for measurement of manufactured nanomaterials in the environment (i.e. , ambient air and surface water), in addition to its attempts for measuring nanoscale TiO2 in a closed system and then in the open air outside of some waste shredders until JFY 2014, another attempts to CNTs in the ambient air was conducted in JFY 2015-17. In JFY 2017, experimental attempts are being conducted to determine the lower limit to distinguish CNTs from background carbons in the ambient air by integrating the information from carbon analyzer, Raman spectroscopy, and SEM.

1.11. Korea

1.11.1. National developments on human health and environmental safety

The Ministry of Environment (MOE) has added nanomaterials to the list for hazard evaluation prescribed in 'Act on Registration and Evaluation, etc of Chemical Substances'

1.11.2. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

KATS(Korea Agency for Technology and Standards)is developing 4 international standards in the ISO/TC 229 (Nanotechnologies) relevant to nanomaterial safety testing "Aerosol generation for NOAA (Nano-objects, and their aggregates and agglomerates) air exposure studies and Electron spin resonance (ESR) as a method for measuring reactive oxygen species (ROS) generated by metal oxide nanomaterials", "Aquatic Toxicity Assessment of Nanomaterials using Artemia sp.", "Materials specification - Antibacterial silver nanoparticles", and "Materials specification – Nanostructured Layer for Enhanced Electrochemical Bio-sensing Applications: Characteristics and measurements" These standard documents will complement the work of the OECD WPMN and other related framework documents.

The 20th ISO TC229 Nanotechnologies was held in Seoul, South Korea from Nov. 13rd 2017 to Nov. 17th 2017. More than 150 experts from UK, US, Japan, Germany, France etc. were attended in the meeting. In ISO TC229-WG3 (Health, Safety and Environment), 11 projects which are related with the method developments for nanosafety evaluation were discussed and 3 new proposals (PWI) were introduced during the meeting.

KATS(Korea Agency for Technology and Standards)is developing 4 projects; 1. Aquatic toxicity assessment of manufactured nanomaterials in salt water lakes using *Artemia* sp. nauplii, 2. Photocatalytic activity assay for nanoparticles in aqueous suspension, 3. In vivo toxicity assessment of nanomaterials using dechorionated zebrafish embryo, 4. High throughput screening method for nanoparticles toxicity using 3D cells. KATS suggested 3 new proposals in the meeting; 1. To standardize new test method for nanoparticle release from composite containing nanomaterial, 2. To standardize CNF(Carbon Nano Fiber) aerosol generation system for inhalation study, 3. CNT(Carbon Nano Tube) and CNF aerosol characterization for inhalation exposure studies.

1.11.3. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Based on the policy and research infrastructures developed from the 2nd National Nano-safety Master Plan(2017-2021) at inter-ministerial levels(including Korea Ministry of Environment, Ministry of Trade, Industry and Energy, and Ministry of Food and Drug Safety), the Korean government has been established the goal, vision, and implementation for research programmes of nanomaterials.

NIFDS (National Institute of Food and Drug Safety Evaluation) conducted a research project on the CFE assay extended application in 2017. The SOPs of CFE assay were established for 3 cell lines (hepatocytes, alveolar cells and kidney cells) and 5 nanomaterials (TiO2, CuO, CeO2, GNP, Fe2O3). In 2018, Korea (MFDS) would participate in the project on development of new test guidelines on toxicokinetics (or amendments to OECD TG 417(Toxicokinetics)) to accommodate nanomaterials which is led by Netherland. An expert meeting would be held and conceptual development would be followed to develop an SPSF.

In the field of food packaging materials, we conducted to examine the possibility of nanomaterial leaching from food packaging materials into food simulants from 2015 to 2017. The results were published in journals such as polymer composites, etc. In the field of nanofood, we have conducted the study on absorption evaluation system for nano based foods using by non-animal model.

Development of 3rd National NanoTechnology Roadmap was launched on Sept. 22, 2017. Based on accumulated nanotechnology competence, Korea government tries to develop 3rd National Nanotechnology Roadmap to promote the convergence of nanotechnology and secure leading technologies for promising industries in the future. In the Roadmap, we will suggest future technologies that are attributed by nanotechnologies to establish the foundation of 4th industrial revolution. In addition, the Roadmap will include some core nanotechnologies to solve nanosafety issues that are related with human health and environmental safety aspects of nano-products. Eventually, this Roadmap will be used to develop national R&D strategies for human and environmental nanosafety.

Tier 3 project (2015-2017) called “Development of safety evaluation based technology for nanoproduct to promote commercialization” that is supported by Ministry of Trade, Industry and Energy (MOTIE) was recently terminated (Sep. 2017). In this project, MOTIE in collaboration with several research organizations investigated the exposure and toxicity (human and environment) assessments of graphene and carbon nanofiber. In this project, MOTIE has developed graphene and carbon nanofiber aerosol generating devices for inhalation toxicity as well as suggested occupational exposure limits (OEL) of graphene and carbon nanofiber.

1.12. Netherlands

The Dutch Ministry of Infrastructure and Water Management in close collaboration with RIVM will organise a policy conference to establish a common EU agenda on how to create a future-proof approach to nanomaterials, based on the recommendations of the ProSafe White Paper and related ongoing or new initiatives in the field of nanosafety with an emphasis on the regulatory context.

1.12.1. National developments on human health and environmental safety

The ProSafe project ended on 30 April 2017. Following the example of the NANoREG project, all results have been made available in the ProSafe Results Repository.

One of the key outcomes, the ProSafe White Paper, has been published in September 2017. The subtitle of this document: 'towards a more effective and efficient governance and regulation of nanomaterials', summarises in a nutshell the aim of the document.

Also notable is the special issue of NanoImpact, 'Reliability of Methods and Data for Regulatory Assessment of Nanomaterial Risks', presenting a series of publications as follow-up for the very successful OECD – ProSafe scientific conference in November 2016 in Paris.

On 17-18 April 2018 the Dutch Ministry of Infrastructure and Water Management in close collaboration with RIVM will organise a policy conference to establish a common EU agenda based on shared views and agreements on how to create a future-proof approach to nanomaterials. During the Policy Conference, the ProSafe White Paper will be presented to EU policy makers, the European Commission and other international bodies and stakeholders. The aim of the conference is to discuss the recommendations of the White Paper and related ongoing or new initiatives in the field of nanosafety with an emphasis on the regulatory context.

Participation is by invitation only.

The NanoReg2 project (http://www.nanoreg2.eu/), built around the challenge of coupling Safe by Design to the regulatory process, will demonstrate and establish new principles and ideas based on data from value chain implementation studies to establish Safe by Design as a fundamental pillar in the validation of a novel manufactured nanomaterial. The project contributed to further implementation of the Safe by Design and Regulatory Preparedness concept, starting with awareness raising activities among innovators and regulators. In addition, some tools are being developed which support Safe by Design. Furthermore, a workshop on the topic 'Regulatory Preparedness' was organised to openly discuss with various regulatory bodies the regulatory challenges posed by nanotechnology innovations.

1.12.2. Developments related to good practice documents

In May 2017 the inaugural meeting of a project group (ISOTC229 WG3PG27) on toxicokinetics of nanomaterials took place. This project group led by the Netherlands will provide an overview of the existing knowledge on toxicokinetics of nanomaterials. The format of the document (**ISO TR 22019**) was discussed at two meetings (Berlin and Seoul). This document can subsequently be used as a basis for adaptation of the OECD test guideline document on performing toxicokinetic studies.

RIVM is partner in the EU project "Performance testing, calibration & implementation of a next generation system-of-systems risk governance framework for nanomaterials" (**caLIBRAte**). The caLIBRAte project (http://www.nanocalibrate.eu) aims to establish a state-of-the-art risk governance framework for assessment and management of human and environmental risks of manufactured nanomaterials and nano-enabled products. The framework will be a web-based "system-of-systems" (SoS) linking different tested calibrated models and methods for screening of apparent and perceived risks, for control banding, decision support tools, and risk surveillance, risk management and risk guidance documents. After selection of models in the first year of the project, testing and

calibration of these models is planned for the coming year, using available environmental health and safety data as well as data generated in the project. By engaging stakeholders caLIBRAte will develop an up-to-date, user-friendly and reliable risk governance framework.

1.12.3. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

The main goal of the new EU project **GRACIOUS** (start date January 1st, 2018) is to generate a science-based framework to enable practical application of grouping and read-across of nanomaterials. The project will work continuously with stakeholders to ensure that the framework effectively meets the needs of both regulators and industry. The GRACIOUS Framework will be underpinned by scientific hypotheses identifying endpoints relevant to grouping and read-across. Application of the Framework will allow movement away from the case-by-case risk assessment paradigm, thereby improving the efficiency of risk analysis and decision making for safer design of quality nanomaterials. RIVM is a main partner in this project, as work package lead and playing a crucial role in the development of the Framework and engagement of stakeholders.

The EU project **REFINE** had its the kick-off meeting in December 2017 and will deliver a regulatory framework for the risk benefit analysis of nanomedicinal products. The framework will be built upon the Decision Support System as developed within the previous SUN project. The Decision Support System will be used to identify the most efficient way to deliver the data required by regulation by the best fitting methods for registration of nanomedicinal products. The decision tree will explicate the product's specific regulatory challenges and the priorities of both missing data and missing methods to match these challenges. It will thus allow planning a cost-and time efficient strategy both for necessary measurements and for the advancement of methods. Within REFINE special emphasis will be on kinetic modelling at cellular and organ level to potentially replace or limit animal testing. In addition, assays needed to identify specific nano-associated risk will be implemented and if not available newly developed.

The EU-project NanoFASE (http://www.nanofase.eu/) aims to deliver an integrated Exposure Assessment Framework (protocols, models, parameter values, guidance ...) with the ambition to reach a level of fate and exposure assessment for nanomaterials that is at least comparable with that for conventional chemicals. Within the project Wageningen University and Research (WUR) is leading the work package on biota uptake of nanomaterials where exposure and uptake studies have been initiated in earthworms (WUR) and in in vitro models for the human gastrointestinal tract (RIKILT). RIVM is working on updating the SimpleBox4nano model using the output from the project. This update is aimed at direct application in regulatory frameworks. Recently the environmental exposure tools from NanoFase were presented and their regulatory relevance discussed at ECHA's Nanomaterial Expert Group.

1.12.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

The aim of the new EU project **PATROLS** (start date January 1st, 2018) is to establish and standardize methods for the next generation of advanced, physiologically anchored, hazard assessment tools. The ambition is to accurately predict adverse effects caused by long-term (chronic), low dose engineered nanomaterial exposure in humans and environmental systems to support regulatory risk decision making. PATROLS will

deliver: 1) more realistic and predictive, in vitro three dimensional lung, gastrointestinal tract and liver models for mechanism-based hazard assessment; 2) cross-species models linking human and environmental systems; 3) innovative methods for sub-lethal hazard endpoints in ecologically relevant test systems and organisms, selected according to their position in the food chain; 4) robust in silico methods for exposure and dosimetry modelling, as well as hazard prediction.

The **Nanosolutions** project ended in 2017 and aimed to further build on the SimpleBox4Nano model that includes nanospecific parameters which determine the distribution of nanomaterials over the several environmental compartments. SimpleBox4nano did, however, not include the effect of the nanomaterials on the human population and the environment. USEtox, which is used to derive life cycle assessment (LCA) characterisation factors for human health and the environment, lacked the nanospecific parameters and the idea rose to let SimpleBox4Nano deliver input for USEtox. Differences have been mapped and work has been performed to 'tweak' SimpleBox4Nano so that at least the compartments are comparable. Effect factors for specific Nanosolutions nanoparticles (including different types of MWCNTs, nanosilver, and nanotitania) have been derived, and compared with the results of the predictive tool they has been developed. In addition, much effort was devoted to deriving health effect factors for CdTe as CdTe QD based ink was chosen as a case study for a full life-cycle assessment in the project.

Within the **EC4SafeNano** project, 15 well known European institutes build a virtual institute to assist governments and industries with their nanosafety issues. TNO leads WP1, in which the needs related to nanosafety experienced by governments, industries and other stakeholders are mapped. Simultaneously, the resources to answer to these needs are mapped and collected. Within the mapping and collection of resources TNO is responsible for coordinating the inventory of tools or methods, trainings, standards, SOPs and Guidance or Best practice documents. Through the participation of TNO, also the Dutch Nanocentre (http://www.nanocentre.nl/) is connected to this European initiative, as an example of a national nanosafety platform. In addition, TNO leads the technological innovation (related to nanomaterials) network. In 2017, first steps were made to 1) set up the legal mechanisms to operate the centre after the end of the project, addressing the contractual relations, IPR issues, governance; and to 2) build a business model and to design a business plan for a sustainable centre.

The **FutureNanoNeeds** project (FNN, http://www.fnn.eu/) was finalised by 31 December 2017. The project focused on "new" risks that may arise from the development of more advanced and more complex nanostructures (e.g. nanostars, nanoflowers, nanocurls).

The most important finding of the FNN project is that the acute toxicity of nanoparticles in themselves is low or absent. Chronic effects were observed and these effects could partly be attributed to subtle uptake and effect mechanisms that are influenced by particle properties such as size, shape, and chemical composition. During the last year, FNN completed best practices for the safe nanotechnology action plan, which considers the different life cycle stages and hierarchy of control in the workplace, partly based on potential hotspots for nanomaterial release along the value chains. Project results are currently being implemented in the adaptation/development of nanospecific (guidance for) OECD test guidelines.

The FP7 project **NanoDefine** (http://www.nanodefine.eu), coordinated by Research institute RIKILT, ended on 30 October 2017 with a number of international presentations of the results. Different analytical techniques were improved or developed to determine

whether a material, as used in commercial products (e.g. sunscreen, toothpaste) is a nanomaterial. A flow scheme was developed to identify the best technique for a certain material, and a NanoDefiner eTool was developed to process analytical data and decide whether a material is a nanomaterial according to European definition. NanoDefine also addressed issues on the availability of suitable measuring techniques, reference materials, validated methods, acceptability for all stakeholders (authorities, policy makers, industry). During the project a close international cooperation and networking between academia, concerned industries and standardization bodies was achieved. In the summer of 2017 a summer school was organised to provide information and training on a number of analytical techniques and the use of the NanoDefiner eTool.

Research institute RIKILT is partner in the EU project **ACEnano** (http://www.acenano-project.eu/). Based on results from other EU projects (e.g. NanoDefine, NANoREG, NanoReg2, NanoFASE), the project will create a "conceptual toolbox" including a tiered approach to cost efficient nanomaterials analysis that will facilitate decision-making in choice of techniques and SOPs, linked to a characterisation ontology framework for grouping and risk assessment.

Under auspices of WHO/IPCS an expert group was installed that is preparing an Environmental Health Criteria Document Principles and Methods of Assessing the **Risk of Immunotoxicity Associated with Exposure to Nanomaterials**. Henk van Loveren (Maastricht University, formerly RIVM) has been appointed as the chair of this expert group. A scoping meeting and a subsequent workshop were organized in 2015 and 2016 respectively. The document " Principles and methods to assess the risk of immunotoxicity associated with exposure to nanomaterials" was published for a consultation and review period in 2017. In October 2017 the WHO organized a meeting at Bilthoven, The Netherlands, to discuss the comments received during the consultation/review period. The document is currently being prepared for final editing and publication (foreseen for mid-2018) as part of the Environmental Health Criteria Series of WHO. OECD is involved in this endeavour as an observer.

Maastricht University (Department of Toxicogenomics), in collaboration with the National Autonomous University of Mexico, are performing collaborative research into the effects of titanium dioxide nanoparticles as component of food additives. Based on the classification of **titanium dioxide as a possible inhalatory carcinogen** (IARC, category 2B), studies were undertaken to investigate effects of oral uptake of the food additive E171 on the development of colon cancer. E171 comprises titanium dioxide particles, including nanoparticles. In a mouse model, facilitation of colon tumour formation was noted and toxicogenomic approaches revealed different potentially underlying pathways, e.g. immune, inflammation, signal transduction pathways. A thesis on this subject is foreseen end 2018. A next step is finding resources for a human intervention study to investigate if similar biomarkers (regulated genes or pathways) as those seen in animal and in vitro studies can be found in humans after exposure. This has partly been achieved METC permission has been granted. The study will be initiated early 2018.

The EU **NanoSafety Cluster** (NSC, https://www.nanosafetycluster.eu/) maximizes the synergies between European research projects addressing the safety of materials and technologies enabled by the use of nanoparticles. The studied aspects include (eco)toxicology, exposure and risk. The NSC also functions as an open platform for dialogue and exchange of information among researchers, regulators, administrators, industry, civil society representatives etc. The cluster has been reorganized in 2017 with

more emphasis on establishing task forces that allow creating a rapid answer to emerging issues, for example responding to classification proposals of nanomaterials. The extensive knowledge available through the NSC could support OECD in its development/adaptations of technical guidelines and guidance documents.

1.12.5. Additional Information

The EU project **nTRACK**, which started in October 2017, aims to develop a safe and highly sensitive agent for stem cell tracking and whole body biodistribution. In addition nTRACK will provide information on cell (long-term) viability using a combination of currently available imaging techniques. The synthesis of nTRACK nanoparticles and cellular labelling processes will be scaled up, while ensuring good manufacturing practice (GMP) requirements. A second goal is to establish a predictive model for early assessment of treatment effectiveness, based on short-term evaluation of the typical migration and biodistribution patterns of the stem cells. RIVM is leading the work package on regulatory issues of nTRACK with the goal to achieve regulatory preparedness and safe innovation

1.13. Sweden

The Swedish Chemicals Agency is introducing a new requirement whereby companies reporting products to the Agency's Products Register must also state whether these products contain nanomaterials. The new regulations came into force on 1 January 2018. This means that information on nanomaterials will be reported for the first time in the Products Register in February 2019.

There has been a long-standing requirement in Sweden for companies to register the content of their chemical products in the Swedish Chemicals Agency's Products Register. The new regulations mean that companies reporting products to the Products Register must also state whether these products contain nanomaterials that have been deliberately added.

The purpose of the new reporting requirement is to obtain information on the quantities and types of nanomaterials used in Sweden. This information can provide a basis on which to make changes to legislation or take other measures in the future regarding nanomaterials.

The new regulations on nanomaterials are based on a report produced by the Swedish Chemicals Agency on behalf of the Government in 2015. Companies with a turnover of less than SEK 5 million per year are exempted from the new reporting requirement on nanomaterials.

Articles are outside scope of registration as well as waste, food, animal feed, medicinal products, cosmetics and tattoo inks which are regulated under other legislations.

The new rules are being incorporated in the Swedish Chemicals Agency's new basic regulations (KIFS 2017:7) on Chemical Products and Biotechnical Organisms, which has replaced the old basic regulations KIFS 2008:2

SweNanoSafe, the Swedish National Platform for Nanosafety at Swetox, was established in 2016. Its goal is to facilitate knowledge and information exchange between academia, authorities, industry, NGOs and other stakeholders with an interest in nanosafety. One of

the main tasks is to identify hindrances to safe use and handling of nanomaterials. The platform has an Expert Panel covering different research disciplines within the field of nanosafety, and a Cooperation Council with stakeholder representatives.

Since its establishment, the platform has continued to develop its organisation, approaches and tools to promote interdisciplinary dialogue between the various actors. During 2017, SweNanoSafe arranged three major events in collaboration with the Swedish Chemicals agency and/or the Swedish partners of the EU-funded project NANoREG, the Swedish Mistra Environmental Nanosafety Programme, the Swedish Work Environment Authority and SwedNanoTech;

1) a nanosafety conference "From Research to regulation", March 28th 2017,
2) a stakeholder workshop, "Nanosafety - How do we secure future nanotechnology?", September 5th 2017,
3) a focus meeting, "Nanomaterials in the work environment", October 24th 2017.

Reports from all three events have been published and are currently available on the SweNanoSafe web page under Swetox. The report from the nanosafety conference is in English, and the other two are in Swedish but include summaries in English.

A new web-based information and knowledge resource, the SweNanoSafe web portal, will be launched the first quarter 2018 at www.swenanosafe.se. The aim of this portal is to improve knowledge transfer and facilitate interaction between stakeholders within the field of nanosafety. Information about guidelines, legislation and research reports will be published together with topical news, events, reports, Q&A etc.

In addition, experts within the platform have commented on public consultations. The platform has also initiated the mapping of research and educational activities within the nanosafety field in Sweden. During 2018, the work will focus on increasing the knowledge on hindrances to safe use and handling of nanomaterials and how these hindrances can be addressed.

SwedNanoTech, an umbrella organization for the Swedish nanotechnology actors, has published an investigation of academic nanoscience and its members have agreed on a roadmap regarding assets and needs for creating the next industrial generation, regarding advanced materials science, infrastructure and other building blocks.

1.14. United Kingdom

A draft Guidance Document (GD) **'Assessing the Apparent Accumulation Potential of Nanomaterials'** has been produced by Professor Richard Handy of Plymouth University in a project co-led by the UK and Spain. The GD presents a testing strategy to determine the bioaccumulation potential of nanomaterials using *in silico*, *in vitro* and *ex vivo* approaches. It also provides guidance on applying TG305 (bioaccumulation in fish) to nanomaterials using a dietary approach, if *in vivo* testing is considered necessary. A paper has been submitted to a peer reviewed scientific journal that can support this testing strategy. Spain is continuing to perform additional experiments to show in a systematic way that nanomaterials can be easily added to feed pellets and that they can be successfully administered to fish and allow the calculation of a biomagnification factor. These experiments will be subject to a second scientific paper supporting any additional modifications to the GD required for conducting TG305 in testing of nanomaterials. A

progress report will be presented at the 18th Meeting of the Working Party on Manufactured Nanomaterials in February 2018.

Staff from the UK Health and Safety Laboratory participated in the development of standards for the ISO Technical Committee 229 and the European Committee for Standardisation:

Phys-chem characterisation of nanomaterials (ISO TC229)

- ISO/TS 12025:2012 – Nanomaterials – Quantification of nano-object release from powders by generation of aerosols
- PWI 21361 Nanotechnologies – Identification and quantification of airborne nano-objects in a mixed dust industrial environment.

Hazard evaluation – Human Health (ISO TC229)

- ISO/TS 12025:2012 Nanomaterials – Quantification of nano-object release from powders by generation of aerosols.
- ISO/TR 13014:2012 Nanotechnologies – Guidance on physico-chemical characterization of engineered nanoscale materials for toxicologic assessment.

Exposure assessment (CEN TC137)

- EN 16897:2017 – Workplace exposure – Characterization of ultrafine aerosols/nanoaerosols – Determination of number concentration using condensation particle counters.
- prEN 16966:2016 – Workplace exposure – Metrics to be used for the measurements of exposure to inhaled nanoparticles (nano-objects and nanostructured materials) such as mass concentration, number concentration and surface area concentration. Publication expected early 2018.
- prEN 17199-1-2-3-4-5 – Workplace exposure – Measurement of dustiness of bulk materials that contain nano-objects and their aggregates and agglomerates. The current status is: Under Drafting
- prEN 17058 – Workplace exposure – Assessment of inhalation exposure to nano-objects and their agglomerates and aggregates. Publication expected early 2018.

Exposure assessment (ISO TG229)

- ISO/AWI TR 22293 – Evaluation of methods for assessing the release of nanomaterials from commercial, nanomaterial-containing polymer composites.
- ISO/AWI TR 21386 – Nanotechnologies – Considerations for the measurement of nano-objects, and their aggregates and agglomerates (NOAA) in the environment.
- ISO/AWI TS 21361 – Nanotechnologies – Quantification of airborne nanoscale carbon black and amorphous silica in a manufacturing environment.
- ISO/AWI TS 19805 – Nanotechnologies – Guidelines for collection and sample preparation of airborne nanoparticles for microscopy techniques.

Risk assessment (ISO TG229)

- ISO/TR 13121:2011 –Nanotechnologies – Nanomaterial risk evaluation.
- ISO/TS 12901-1:2012 – Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 1: Principles and approaches.

- ISO/TS 12901-2:2014 – Nanotechnologies – Occupational risk management applied to engineered nanomaterials – Part 2: Use of the control banding approach.

Guidance or good practice documents for registrants and stakeholders (ISO TG229)

- ISO/TR 12885:2008 - Nanotechnologies - Health and safety practices in occupational settings relevant to nanotechnologies.
- ISO/TR 13329:2012 - Nanomaterials - Preparation of material safety data sheet (MSDS).

Guidance or good practice documents for registrants and stakeholders (CEN TC352)

- Nanotechnologies – Guidelines for Life Cycle Assessment – Application of EN ISO 14044:2006 to Manufactured Nanomaterials. The current status is: Under Drafting
- Nanotechnologies – Guidelines for the management and disposal of waste from the manufacturing and processing of manufactured nano-objects. The current status is: Under Drafting.

1.14.1. Relevant new research projects or strategies on nanomaterials

Swansea University has published several papers this year that have highlighted good practice and future developments required to support standardisation of *in vitro* approaches:

- Burden N, Aschberger K, Chaudhry Q, Clift, MJD, Fowler P, Johnston H, Landsiedel R, Rowland J, Stone V, Doak SH (2017). Aligning nanotoxicology with the 3Rs: What is needed to realise the short, medium and long-term opportunities? *Reg Toxicol Pharmacol*, 91, 257-266.
- Burden N, Aschberger K, Chaudhry Q, Clift, MJD, Doak SH, Fowler P, Johnston H, Landsiedel R, Rowland J, Stone V (2017). The 3Rs as a framework to support a 21st century approach for nanosafety assessment. *Nano Today*, 12, 10-13.
- Wills JW, Summers HD, Hondow N, Sooresh A, Meissner KE, White PA, Rees P, Brown AP, Doak SH (2017) Characterising Nanoparticles in Biological Matrices: Tipping Points in Agglomeration State and Cellular Delivery *In Vitro*. *ACS Nano*, in press (DOI: 10.1021/acsnano.7b03708).

1.14.2. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

The UK Public Health England (PHE) has an ongoing nanotoxicology programme, which is focussed on research into the effects of inhaled nanoparticles on public health. It includes *in vivo* and *in vitro* studies and associated biophysical investigations of interactions between nanomaterials and lung surfactant. Research is focussed on the deposition, clearance, biodistribution and biological effects of inhaled nanomaterials in normal and compromised (e.g. asthma) lungs. Nanomaterials currently being investigated include ceria, iron oxides, silver and carbon nanotubes. Some of the work is supported by external funding, including EU FP7 and UK NIHR (National Institute for Health Research). A study to explore individual exposures to engineered nanomaterials in consumer products is also currently being undertaken. Recent papers include published studies on translocation of nanoparticles and review on asthma and nanoparticles:

- Buckley A, Warren J, Hodgson A, Marczylo T, Ignatyev K, Guo C, Smith R. (2017) Slow clearance and limited translocation of four sizes of inhaled iridium nanoparticles. *Particle and Fibre Toxicology* 14:5.
- Meldrum, K, Guo C, Marczylo EL, Gant TW, Smith R., Leonard MO (2017) Mechanistic insight into the impact of nanomaterials on asthma and allergic airway disease. *Particle and Fibre Toxicology* 14:45

The H2020 project **TRANSAT** (TRANSversal Actions for Tritium) started September 2017. This is primarily a fission/fusion related project focussed on tritium management, but as part of this PHE will be undertaking *in vivo* inhalation studies using nanosized metallic particles (some tritiated) relevant to the fission/fusion cycle and other partners (including CEA) will be undertaking *in vitro* studies, primarily focussed on genotoxicity.

The H2020 project **PATROLS** (Physiologically Anchored Tools for Realistic nanOmateriaL hazard aSsessment) started on 1st Jan 2018. The project is led by Professor Shareen Doak at Swansea University, UK and includes a total of 24 partners. The project aims to establish and standardise a battery of next generation physiologically anchored, hazard assessment tools that more accurately predict adverse human health and environmental effects caused by long-term, low dose ENM exposure to support regulatory risk decision-making. PATROLS will develop: 1) more realistic *in vitro* 3D lung, gastrointestinal tract and liver models for mechanism-based hazard assessment, which will be anchored against chronic *in vivo* exposure outcomes and will report on mechanistic endpoints linked to adverse outcome pathways (AOPs). 2) Novel methods to evaluate long-term exposure hazard endpoints in ecologically relevant test systems and organisms, selected according to their position in the food chain; these endpoints will be based on key events associated with AOPs. 3) Robust *in silico* methods for exposure and dosimetry modelling, as well as *in vitro*-to-*in vivo* extrapolation (IVIVE) and hazard prediction.

The **in3 project** (An integrated interdisciplinary approach to animal-free nanomaterial and chemical safety assessment) is funded by the EU's Marie Skłodowska-Curie Action - Innovative Training Network. This aims to drive the synergistic development and utilisation of *in vitro* and *in silico* tools for human chemical and nanomaterial (NM) safety assessment. Thirteen collaborating institutes are involved, including PHE, and it is led by Professor Paul Jennings (Medizinische Universität Innsbruck, Austria). The project will focus on differentiation of human induced Pluripotent Stem Cells (hiPSC) to toxicologically relevant target tissues including; brain, lung, liver and kidney. Data generated will be used to develop safety assessment approaches by integrating cheminformatics, mechanistic toxicology and biokinetics into computational models. Ultimately to create a unified expandable integrated testing strategy for chemical and NM safety assessment. The project will hire 15 PhD students to carry out these activities in a coordinated and highly collaborative fashion.

The H2020 project **ACEnano** started on the 1st Feb 2017 and is led by Professor Éva Valsami-Jones at the University of Birmingham, UK. The project includes a total of 26 partners and aims to introduce confidence, adaptability and clarity into nanomaterial risk assessment by developing a widely implementable and robust tiered approach to physico-chemical characterisation that will simplify and facilitate contextual (hazard or exposure) description and its transcription into a reliable NMs grouping framework. ACEnano addresses the challenge of reliable and reproducible characterisation of nanomaterials particularly in complex environments, such as within different biological, environmental and technological compartments. Two key approaches are proposed: 1) the development

of a holistic framework for reproducible NM characterisation, spanning from initial needs assessment through method selection to data interpretation and storage; the framework encompasses both new analytical techniques and assays as well as optimised existing methods; and 2) the embedding of this framework in an operational, linked-up ontological regime to allow identification of causal relationships between NMs properties, and biological, (eco)toxicological or health impacts.

The fate and transport of metals and metallic oxide engineered nanoparticles are undergoing research at Cranfield University through a Commonwealth Scholarship Commission award and a NERC research grant **TINE** (Transatlantic Initiative for Nanotechnology and the Environment). This is led by Professors Bruce Jefferson and Frederic Coulon. Collectively their research here has improved understanding of the environmental fate of engineered nanoparticles as a non-dissolved pollutant and on how ENPs interact in complex functioning ecosystems such as wastewater treatment and anaerobic digestion plants. To date, Coulon and Jefferson have provided the most complete assessment of engineered nanoparticles on wastewater treatment at pilot scale, enabling revised design guidance to be established for associated technologies (Eduok et al., 2015). Such knowledge is critical to our understanding of the resilience of these systems to ENPs as environmental hazards. The work will enable improved management strategies and models to be developed to better cope with the impacts and fate of engineered nanoparticles in the environment.

- Eduok S, Ferguson R, Jefferson B, Villa R, Coulon F. 2017. Aged-engineered nanoparticles effect on sludge anaerobic digestion performance and associated microbial communities. *Science of the Total Environment*. 609: 232-241
- Eduok S, Coulon F. 2017. Engineered nanoparticles in the environment: interactions with microbial systems and microbial activity. Part II Concepts and Case studies, Chapter 5. In *Microbial Ecotoxicology*, Cravo-Laureau C., Cagnon C., Lauga B., Duran R. (eds), Springer International Publishing . DOI 10.1007/978-3-319-61795-4, pp 63-108
- Eduok S. and Coulon F. 2017. Microbiological toxicity of nanoparticles. Chapter 6. In: *Emerging Nanotechnologies in Food Science*, A volume in Micro and Nano Technologies, 1st edition, Busquets R. (ed), Elsevier; https://doi.org/10.1016/B978-0-323-42980-1.00006-6; pp 97-117.
- Eduok S., Hendry C., Ferguson R., Martin B., Villa R., Jefferson B., Coulon F. 2015. Insights into the effect of mixed engineered nanoparticles on activated sludge performance. *FEMS Microbiology Ecology*. 91: 1-9

1.15. United States

1.15.1. National developments on human health and environmental safety

Risk assessment decisions, including the type of: (a) nanomaterials assessed; (b) testing recommended; and (c) outcomes of the assessment

Under section 5 of the Toxic Substances Control Act (TSCA), the U.S. Environmental Protection Agency (EPA) reviewed TSCA premanufacture notices for 4 quantum dots and a single-walled carbon nanotube. Based on potential risk findings to human health and the environment, EPA issued consent orders and/or significant new use rules (SNURs) for all of these materials. See details in #1c for risk management approaches and #4 for required testing. EPA also reviewed low volume exemptions for 5 quantum

dots and 4 nanodiamond substances. EPA allowed the exemptions under conditions that limited human and environmental exposures to prevent unreasonable risks.

On September 21, 2017, EPA issued final SNURs on a carbon nanotube and nanocarbon. On October 3, 2017, EPA issued a final SNUR on single-walled carbon nanotubes, a bimodal mixture of multi-walled and other classes of carbon nanotubes, following a notice and comment proposed rule. On October 17, 2017, EPA issued final SNURs on multi-walled carbon nanotubes.

The U. S. National Institute for Occupational Safety and Health (NIOSH) published two sentinel documents addressing the toxicology of a nanomaterial along its life cycle: Bishop L., et al. An In-Vivo Toxicity Assessment of Occupational Components of the Carbon Nanotube Life Cycle to Provide Context to Potential Health Effects, ACS Nano, 2017, 11(9), pp. 8849-8863; and describing a quantitative framework for categorizing nanomaterials by hazard potency: Drew N.M., et al. A quantitative framework to group nanoscale and microscale particles by hazard potency to derive occupational exposure limits: Proof of concept evaluation, Reg. Tox Pharm., 2017, 89, pp. 253-267.

Development related to exposure measurement and exposure mitigation

NIOSH published a new chapter in the NIOSH Manual of Analytical Methods, 5th edition: Analysis of Carbon Nanotubes and Nanofibers on Mixed Cellulose Ester Filters by Transmission Electron Microscopy (https://www.cdc.gov/niosh/nmam/pdf/chapter-cn.pdf) and contributed to the ISO/TR 19057:2017 Nanotechnologies -- Use and application of acellular in vitro tests and methodologies to assess nanomaterial biodurability.

Risk management approaches

U.S. Environmental Protection Agency

On January 12, 2017, EPA issued a final regulation requiring reporting of existing exposure and health and safety information on nanoscale chemical substances in commerce pursuant to its authority under TSCA section 8(a). This rule requires companies that manufacture, import, or process certain chemical substances already in commerce as nanoscale materials notify EPA of certain information, including specific chemical identity; production volume; methods of manufacture; processing, use, exposure and release information; and available health and safety data.

On May 12, 2017, EPA extended the effective date of the January rule to August 14, 2017. On May 16, 2017 EPA issued a draft question and answer guidance that would be used to assist with complying with the rule. After reviewing comments on the proposed guidance, EPA made revisions and additions to the guidance and posted it on the EPA website for the rule. EPA notes in the guidance that it intends to add further questions/answers and revisions based on questions identified by persons who may be subject to the rule. EPA has received one notification under the rule. The deadline for reporting existing nanoscale materials in commerce is August 14, 2018.

Since January 2005, EPA has received and reviewed more than 210 new chemical notices for nanoscale materials under TSCA including fullerenes, quantum dots, and carbon nanotubes. EPA has issued consent orders and SNURs regulating new chemical submissions of these nanoscale materials permitting manufacture under limited conditions. A manufacturer or processor wishing to engage in a designated significant new use identified in a SNUR must submit a Significant New Use Notice (SNUN) to

EPA at least 90 days before engaging in the new use. A sanitized version (i.e., without confidential business information) of such a consent order is available. Because of confidential business information claims by submitters, EPA may not be allowed to reveal to the public the chemical substance as a nanoscale material in every new chemical SNUR it issues for nanoscale materials. EPA will continue to issue SNURs and consent orders for new chemical nanoscale materials in the coming year.

Because of limited data to assess nanomaterials, the consent orders and SNURS contain requirements to limit exposure to workers through the use of personal protective equipment, limit environmental exposure by not allowing releases to surface waters or direct releases to air, and limit the specific applications/uses to those described in the new chemical notification.

U.S. Food and Drug Administration

The U.S. Food and Drug Administration (FDA) has announced the availability for public comment a draft guidance on Drug Products, Including Biological Products, that Contain Nanomaterials. Nanotechnology can be used in a broad array of FDA-regulated products, such as human drug products, including those that are biological products. The draft guidance provides recommendations to industry engaged in developing human drug products in which a nanomaterial is present in the finished dosage form, including recommendations regarding investigational, premarket, and postmarket submissions for these products. Nanomaterials in drug products may perform a variety of functions, for example, as active ingredients, carriers loaded with an active ingredient, or inactive ingredients. This draft guidance describes a risk-based approach to the regulation of these products, focusing on the characteristics of the nanomaterial, its intended use and application, and evaluating how its attributes may relate to product quality, safety, and efficacy. FDA is seeking comment on the draft guidance including on the terminology used in the document. To comment on the draft guidance, please go to http://www.regulations.gov and insert docket number: FDA-2017-D-0759.

Any updates, including proposals, or modifications to previous regulatory decision

No, the approaches used given the level of available information are consistent with previous regulatory decisions.

New regulatory challenge(s) with respect to any action for nanomaterials

Standards/methods for differentiating between different forms of the same chemical substance that is a nanomaterial.

Standardized testing for the physical properties that could be used to characterize/identify nanomaterials.

Differentiation between genuinely new nanoscale materials introduced in commerce and existing products which have been in commerce for decades or centuries.

1.15.2. Activities been initiated to implement the OECD Council Recommendation (e.g. regulatory changes, guidance, voluntary, etc.)

A final regulation requiring reporting of existing exposure and health and safety information on nanoscale chemical substances in commerce pursuant to its authority under TSCA.

Regulation of new chemical substances that are nanomaterials with consent orders and SNURs.

1.15.3. Developments related to good practice documents

NIOSH led the development of the World Health Organization's guidelines on nanomaterial safety in the workplace and was actively involved in all aspects of this effort: conducting one of systematic reviews, developing recommendations and providing critical expert review (https://blogs.cdc.gov/niosh-science-blog/2017/12/15/who-nano/).

1.15.4. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

Consent orders and SNURs for carbon nanotubes and other nanomaterials typically contain required or recommended testing for a 90-day inhalation study and pchem properties such as particle size/ distribution, morphology, surface area, crystallinity, surface charge and surface chemistry. The 90-day study typically has at least a 90-day post-exposure observation period and evaluation of the broncoalveolar fluid. For carbon nanotubes blood and plasma endpoints indicative of cardiotoxicity are monitored.

U.S. federal agencies, including the Environmental Protection Agency, the Army Corps of Engineers, and the National Institute of Standards and Technology, are leading and/or participating in nanomaterials-related OECD test guidelines projects and other activities, such as the "Evaluation of in vitro methods for human hazard assessment applied in the Organisation for Economic Cooperation and Development's (OECD's) Working Party on Manufactured Nanomaterials (WPMN) Sponsorship Programme.

1.15.5. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

The National Nanotechnology Initiative 2011 EHS Research Strategy provides guidance to the Federal agencies that produce the scientific information for risk management, regulatory decision-making, product use, research planning, and public outreach. Participating agencies adaptive manage the strategy under the auspices of the interagency Nanotechnology Environmental and Health Implications working group of the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee. URL: http://nano.gov/about-nni/working-groups/nehi

The US Army Engineer Research and Development Center Environmental Laboratory (ERDC-EL) developed the Nano Guidance for Risk Informed Deployment (NanoGRID) tool, designed to guide users through a tiered testing framework (Collier et al 2015) to more consistently characterize the durability, degradation, potential for nano-scale material release and environmental health and safety considerations of nano-enabled products. The tool offers guidance on when testing may be necessary/unnecessary, testing design, test selection, hazard screening and decision documentation. The tool is a framework and is not currently intended to provide a direct risk decision or a full life cycle approach. The beta version of the NanoGRID tool is available at: https://nano.el.erdc.dren.mil/tools.html.

1.15.6. Additional Information

The U.S. National Nanotechnology Coordination Office (NNCO) holds webinars periodically to share information with the general public and the nanotechnology research

and development community. Recent topics include "The Utility of Alternative Testing Strategies in Nanotechnology, Health, and Safety Evaluations"; "An Introduction to Voluntary Standards"; and "Water Sustainability through Nanotechnology." URL: https://www.nano.gov/PublicWebinars

1.16. European Union

1.16.1. National developments on human health and environmental safety

Regulatory development:

- Work has progressed on the modification of technical Annexes to REACH to (better) address nanomaterials. The Commission proposal that has also been been notified under WTO and subject to 4 week public feedback (comments available at link) is currently discussed with the Member States in the REACH committee, with the adoption envisioned later in 2018. Transition arrangement regarding its full application by 2020 are also discussed.
- Following the review of the Commission Recommendation on the definition of nanomaterial (2011/696/EU) minor revision of the recommendation is anticipated. Public consultation on the considered changes is expected to be launched in spring 2018. After consideration of the feedback, the adoption is planned later in 2018. The recommendation (as potentially revised) will be providing basis for the update of the nanomaterial definitions in EU regulations (REACH, food, cosmetics, biocides, medical devices).
- In 2017, Regulations (EU) No 2017/745 on medical devices and (EU) No 2017/746 on in vitro diagnostic medical replaced existing European Directives on the subject. They will start to apply in spring 2020 and 2022, respectively. In the new regulation, references to nanomaterials (defined as per the Recommendation 2011/696/EU) are made to ensure that adequate assessment is performed. Specific rule on the classification of medical devices incorporating or consisting of nanomaterial is also applied.

Implementation:

- European Food Safety Authority (EFSA) EFSA presently (until 4 March 2018) runs a public consultation on its draft guidance for the risk assessment of nanoscience and nanotechnology applications in the food and feed chain. The guidance covers the relevant areas within EFSA's remit, such as novel foods, food contact materials, food and feed additives, and pesticides. The new document takes account of scientific developments that have taken place since publication of the previous guidance in 2011, particularly studies that offer new insights into exposure assessment and hazard characterisation of nanomaterials. It also considers nanospecific considerations relating to in vivo/in vitro toxicological studies and outlines a tiered framework for toxicological testing, and proposes ways to carry out risk characterisation and uncertainty analysis.
- REACH: further ECHA board of appeal decision regarding ECHA evaluation decision has been issued on silicon dioxide substance evaluation case A-014-2015. All nanomaterial-related decisions can be found at https://www.echa.europa.eu/about-us/who-we-are/board-of-appeal/decisions
- Cosmetics: certain groups of substances, i.e. colourants, preservatives and UV-filters, including those that are nanomaterials, must be authorised by the European Commission prior to their use in cosmetic products. An opinion from the SCCS,

which reviews submitted toxicological data, precedes authorisation of nanomaterials for cosmetic use in the EU. Up until now, the Commission has authorised 3 UV-filters as nanomaterials: titanium dioxide, zinc oxide and tris-biphenyl triazine. It has also allowed carbon black (nano) for use as a colourant in cosmetic products. Follow the link more information on nanomaterials in cosmetic, including the requirement for the Comission to publish a catalogue of nanomaterials used in cosmetic products placed on the market.

1.16.2. Developments related to good practice documents

NANoREG Framework and ToolBox available on-line in JRC Science Hub

Data, information and tools addressing nanoEHS aspects, which were generated and/or evaluated during the project and in relevant scientific literature, formed the knowledge basis to develop the NANoREG Framework for the Safety Assessment of NMs and the related Toolbox. They are the result of a collective, project-wide and consensual effort under JRC's leadership. The NANoREG Framework is the project's proposal for a common understanding in the field of nanoEHS under the current European regulatory framework, focused on the REACH Regulation (EC) No. 1907/2006. The Framework serves as an overarching structure that indicates where and how to apply the tools collected in the NANoREG Toolbox – about 540 unique tools as of December 2017. The Toolbox assembles instruments from within NANoREG and several other initiatives – in Europe and beyond –, aimed to implement NM safety assessment under REACH and those three proposed strategies. It is an inventory of 'functional tools' (user-ready and publicly available) and also contains 'prospective tools' (not fully developed yet, but expected to become available in the short to medium term). While it focuses on REACH, this unique and large categorised collection is useful in the frame of other EU/non-EU legislation for NMs. The Framework (DOI: 10.2760/245972) and Toolbox (DOI: 10.2760/332209; URI: http://data.jrc.ec.europa.eu/dataset/jrc-nano-ehs-ring-nanoreg-tb) were published in 2017.

NanoReg2 Project news

NanoReg2 (Coordinated by INERIS , FR) concentrates its efforts on tailoring, implementing and testing the Safe-by-Design (SbD) concept proposed by the EU NANoREG project and further complemented within the EU ProSafe project. The SbD concept aims at reducing uncertainties and risks to humans and the environment starting at an early phase of the innovation process. SbD considerations enable the evaluation of the life-cycle safety aspects for humans and the environment already in the design phase of a Manufactured Nano Material (MNM) or a MNM-containing product.

Within NanoReg2, the SbD concept is combined with Regulatory Preparedness (RP) (regulators being prepared for innovation) into the NanoReg2 Safe Innovation Approach (SIA), to be seen as a process for strengthening the innovation management of new nanotechnology-related initiatives.

The regulatory authorities need to anticipate new materials and products appearing on the market that may be insufficiently, or not at all, covered by present legislation and guidelines. The present pace of innovation makes it challenging for regulators to anticipate such developments. NanoReg2 aims to improve the foresight of regulators and thus facilitate the development of adaptable (safety) legislation that can keep up with the pace of knowledge generation and innovation in the field of nanotechnology. The

NanoReg2 project organised a dedicated Workshop on Regulatory Preparedness (5–6 October 2017) at the JRC (Ispra), led by the JRC (organisation and scientific programme) and RIVM (scientific programme) to stimulate the discussion on how regulators can better prepare themselves for the assessment of new and emerging nanotechnologies. During the workshop, more than 50 regulators form EU and US, representatives of industry and stakeholders discussed how regulators currently deal with innovation, the needs of regulatory risk assessors to be prepared for addressing innovations, the tools available and needed to support RP and possible practical barriers for RP. Proactive and systematic communication between industry, regulators and other stakeholders in trusted environments all along the innovation process is essential to enable regulators to address the challenges posed by quickly developing technologies, such as nanotechnology. A full report is currently in preparation.

Publication by JRC and NIST (USA) on the use of reference materials in characterisation of nanomaterials: 'Reference nanomaterials to improve the reliability of nanoscale measurements', G. Roebben, V. Hackley, H. Emons, in 'Metrology and standardization for nanotechnology: protocols and industrial innovations', eds E. Mansfield, D. L. Kaiser, D. Fujita, M. Van de Voorde, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, ISBN 978-3-527-34039-2, 2016.

Release by JRC of a new certified reference material for nanoparticle size characterisation: 'The certification of equivalent diameters of silica nanoparticles in aqueous solution: ERM-FD101b', Y. Ramaye, V. Kestens, A. Braun, T. Linsinger, A. Held, G. Roebben, Report EUR 28362 EN, European Union, Luxembourg, ISBN 978-92-79-64637-9, 2017..

Publication by JRC on the validation of the PTA method for nanoparticle size analysis: 'Validation of a particle tracking analysis method for the size determination of nano- and microparticles, V. Kestens, V. Bozatzidis, P.-J. De Temmerman, Y. Ramaye, G. Roebben, J. Nanoparticle Research , Vol. 19:271, DOI 10.1007/s11051-017-3966-8 (2017)

Publication by JRC, NMIA (Australia), NPL (UK) and LUM (Germany) on the reliability of the CLS method for nanoparticle size analysis: 'Improved metrological traceability of particle size values measured with line-start incremental centrifugal liquid sedimentation, V. Kestens, V. Coleman, P.-J. De Temmerman, C. Minelli, H. Woehlecke, G. Roebben, Langmuir, Vol. 33, 8213−8224, DOI: 10.1021/acs.langmuir.7b01714 (2017)

While the information is probably coming also from other sources, it is worth noting that **WHO** recently published **Guidelines on protecting workers from potential risks of manufactured nanomaterials** that can be downloaded as a pdf file from the WHO website at http://apps.who.int/iris/bitstream/10665/259671/1/9789241550048-eng.pdf

1.16.3. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Two projects selected under the Horizon 2020 Research Framework Programme (H2020) – NMBP have started on 1/1/2018:

- GRACIOUS - Framework and strategies for nanomaterial characterisation, classification, grouping and read-across for risk analysis
- PATROLS - Advanced and realistic models and assays for nanomaterial hazard assessment

Two projects are running under H2020 relevant for management of data related to safety of nanomaterials.

- OpenRiskNet: Open e-Infrastructure to Support Data Sharing, Knowledge Integration and in silico Analysis and Modelling in Risk Assessment; started 1/12/2016 (Call: EINFRA-22-2016 - User-driven e-infrastructure innovation)
- NanoCommons: The European Nanotechnology Community Informatics Platform: Bridging data and disciplinary gaps for industry and regulators; started 1/1/2018 (Call INFRAIA-02-2017 - Integrating Activities for Starting Communities)

There are two running Horizon 2020 – NMBP calls for research proposals for 2018 (first stage):

- NMBP-13-2018: Risk Governance of nanotechnology (RIA)
- NMBP-14-2018: Nanoinformatics: from materials models to predictive toxicology and ecotoxicology (RIA)

More information on these calls can be found here:

Other developments in EU research:

- The ProSafe/NANOREG white paper is completed and put for the consideration of OECD-WPMN. Results are publicly available.
- DG RTD NMP initiative EU Nanosafety cluster continues their activities. More details at: www.nanosafetycluster.eu. The 2017 edition of the "Compendium of Projects in the European NanoSafety Cluster" is available: https://www.nanosafetycluster.eu/uploads/files/pdf/2017_NSC_Compendium.pdf
- The US-NNCO and European Commission DG Research and Innovation are fostering research cooperation on EHS issues of nanomaterials through joint workshops and the establishment of EU-US Communities of Research. More on http://us-eu.org. The sixth workshop was held in Birmingham, UK in September 2017.
- An EU research experts group visited Iran in November 2017 to discuss initiation of cooperation in nanosafety. The workshop was attended by members of the Asian Forum from Thailand, Taiwan, Korea and Russia.
- An EU nanosafety experts group visited South Africa in December 2017 to foster cooperation.
- A workshop was organised between Korea and EU experts in January 2018 to strengthen cooperation in nanosafety.
- DG RTD prepares for assisting the elaboration of OECD Technical Guidelines and Guidance Documents for nanomaterials testing through additional funding of 2M€ under the risk governance call topic and a specific topic of 3M€ to be published end 2018; the "Malta" project.

1.16.4. Additional Information

The EUON (EU Observatory on Nanomaterials) was launched in June 2017. The observatory aims at collecting information on the safety of nanomaterials and making it available to the public. In addition, a microsite targeted at the general public on nanomaterials will be launched in March 2018. ECHA is working on the development of new content and databases to the EUON.

1.17. Thailand

1.17.1. Any national developments on human health and environmental safety

Collaboration with Thailand Industrial Standard Institute (TISI)

Completed 7 industrial standardization manuals related to nanotechnology:

Propose to initiate 5 additional industrial standardization manuals related to nanotechnology by 2021:

- Guidance on voluntary labelling for consumer products containing manufactured nano-objects
- Standard Guide for Size Measurement of Nanoparticles Using Atomic Force Microscopy)
- Preparation of Material Safety Data Sheet (MSDS) For nanomaterials
- Occupational risk management applied to engineered nanomaterials -- Part 1: Principles and approaches
- Occupational risk management applied to engineered nanomaterials Part 2: Use of the control banding approach)

1.17.2. Activities been initiated to implement the OECD Council Recommendation (e.g. regulatory changes, guidance, voluntary, etc.)

Since the NanoQ label inception in 2012, several companies have received the label in areas related to anti-bacteria coating properties for color, plastic, and fabric sector. There is also an interest to issue NanoQ for cosmetic products. However, this is yet to be decided by the nanotechnology association due to concerns. In addition, NanoQ technical group is also looking at possibly issuing NanoQ for companies that import raw materials that have nano properties and are re-selling the raw materials. Nano Mark (Taiwan) have stated their interest to work with NanoQ for goods being imported between the two countries. Discussion is still on going.

On-going collaboration with the 4 NANO Plus+ Centers) and the Training of Trainers on Nanotechnology (TTN) members to include aspects of nanosafety in their workshop programs. This year 4 workshops on aspects of nanosafety have been conducted in which over 300 participants included students, community representatives, and local administration officials have attended. Plans are being drawn up to start moving the TTN members to the next phase and that is to become SMART Nano Safety Experts and to focus their knowledge and training capabilities towards nanosafety topics.

Co-organized the NanoSafety Seminar 2016 on November 28 at Greenery Resort Khao Yai as part of the NanoThailand 2016 conference. Speakers from Indonesia, Japan, Korea, Malaysia, Singapore, Switzerland, Taiwan, and Thailand participated in giving presentations from country report to specific research projects.

We conducted a Public Hearing session on the Nanosafety and Ethics Strategic Plan 2017-2021 on December 22 at Thailand Science Park Convention Centre. The plan will focus on 3 strategies: Knowledge Management (accessibility to information), regulation and standards, public engagement. The plan was finally approved by the Deputy Prime Minister on……..

1.17.3. Developments related to good practice documents

The National Advanced Nano-characterization Center (NANC) is completed and research activities have begun. The Nano Characterization Lab (NCL) and Nano Safety and Risk Assessment Lab have been incorporated to NANC.

The 2nd Thailand Meeting on Alternative Methods to Animal Testing is being organized at Thailand Science Park by Thailand Center of Excellence for Life Sciences (TCELS) and NANOTEC, with collaboration from EPISKIN Academy of France (Mr. Alain Alonso, Sales & Marketing Director and Dr. Christian Pellevoisin, Scientific Director). The three day workshop included a one day lecture session by Dr. Christian on the topic of "EPISKIN, at the heart of tissue engineering for 25 years" followed by two days of hands-on session which was held at Nano Safety and Risk Assessment Lab (SRA) at NANOTEC Thailand Science Park facility.

1.17.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials; (e.g. government, national labs, academic, industry)

Published Papers:

(Research paper) Interaction evaluation of silver and dithizone complexes using DFTcalculations and NMR analysis.

(Research paper) Human primary erythroid cells as a more sensitive alternative in vitro hematological model for nanotoxicity studies: toxicological effects of silver

2. Current Activities in Other Organisations Related to Nanotechnologies/ Nanomaterials

2.1. The Business and Industry Advisory Committee to the OECD (BIAC)

2.1.1. National developments on human health and environmental safety

CEFIC (European Chemical Industry Council)

Cefic has been actively involved in the discussions related to the amendments of the REACH Regulation Annexes to adapt them for nanomaterials, contributing in the Competent Authorities subgroup on Nanomaterials organized by the EU Commission, submitting comments and cooperating with the EU authorities in the development of the new text. Regarding the European review of the definition of Nanomaterials, Cefic has made available a list of their position on the future definition proposal.

NIA (Nanotechnology Industries Association)

The Nanotechnology Industries Association (NIA) and its members have been actively engaged with European Regulators during the development of e.g. the draft modifications or the EU REACH Annexes and is closely following the development of the revised European Commission recommendation for a nanomaterial definition. NIA has also provided feedback to various OECD Member consultations, e.g. to the Swedish notification scheme. In general, NIA is concerned about the various and often non-harmonised regulatory requirements put forward by regulators.

VCI (German Chemical Industry Association)

The German Chemical Industry Association (VCI) and its member companies are engaged in the process of implementing the REACH regulation, in sector specific legislations addressing nanomaterials, in the safe handling of nanomaterials throughout the value chain (workplace safety), and in updating and prioritizing the agenda on safety research on nanomaterials together with the federal government. The chemical industry is deeply engaged in research projects on the safety of nanomaterials.

VCI is engaged in the political discussion on the EU definition of nanomaterials and is, in close co-operation with its sector groups, supportive in the establishment of suitable analytical methods for this definition by engagement in R&D-projects and discussion to the political outreach.

VCI keeps supporting independent scientific literature reviews on the safety of nanomaterials concerning toxicology, health effects, emission, fate and behaviour in the environment, and ecotoxicological effects and has taken up efforts to leverage the use of the scientific data. On the basis of this project several peer reviewed scientific papers

have been published [7] [8]. The results of these activities have been presented on behalf of the Business and Industry Advisory Committee (BIAC) to the OECD Working Party on Manufactured Nanomaterials (WPMN) in September 2016 in order to help to prioritise the WPMN working plan.

ACC (American Chemistry Council)

The ACC Nanotechnology Panel has provided comments to the European Commission, the Korean Ministry of Environment, and Australia's National Industrial Chemicals Notification and Assessment Scheme on their respective proposals for considering manufactured nanomaterials in their chemical regulatory frameworks. The Panel's comments identified issues and concepts requiring clarification in each of the proposals. The Panel's comments are available on request.

2.1.2. Developments related to good practice documents

VCI (German Chemical Industry Association)

The German chemical industry is committed to a responsible production and use of nanomaterials. To support member companies, and customer companies in the value chain, to manage the health, safety and environmental aspects of nanomaterials throughout the life cycle, the German Chemical Industry Association VCI has – over the years - issued a series of documents. They provide guidance on all aspects of a good product stewardship on nanomaterials.

Key documents:

- Implementing Responsible Care® for a Responsible Production and Use of Nanomaterials

Regulatory documents:

- Requirements of the REACH Regulation on Substances which are Manufactured or Imported also as Nanomaterials
- Guidance for a Tiered Gathering of Hazard Information for the Risk Assessment of Nanomaterials
- Guidance for Handling and Use of Nanomaterials at the Workplace
- Guidance for the Passing on of Information along the Supply Chain in the Handling of Nanomaterials via Safety Data Sheets
- Guidance for Safe Recovery and Disposal of Waste containing nanomaterials

These documents have been discussed with the public as well as with national and European authorities, and were also communicated to the OECD WPMN.

[7] Harald Krug: "Nanosafety Research — Are We on the Right Track?", http://dx.doi.org/10.1002/anie.201403367; Stephan Wagner, Andreas Gondikas, Elisabeth Neubauer, Thilo Hofmann und Frank von der Kammer: „Spot the Difference: Engineered and Natural Nanoparticles in the Environment — Release, Behavior, and Fate", http://dx.doi.org/10.1002/anie.201405050;

Lars Michael Skjolding, PhD; Sara Nørgaard Sørensen, MSc; Nanna Bloch Hartmann, PhD; Rune Hjorth, MSc; Steffen Foss Hansen, PhD; Anders Baun, PhD: "A Critical Review of Aquatic Ecotoxicity Testing of Nanoparticles – The Quest for Disclosing Nanoparticle Effects", (Correspondence Author: Prof. Anders Baun), Applied Chemistry (International Edition) http://dx.doi.org/10.1002/anie.201604964

[8] The paper "Conclusions and recommendations from the project „Health assessment, exposure and environmental effectsof nanomaterials: literature review and assessment" is available on the website of VCI: http://www.vci.de.

The Association of the Laquer-Producers VdL within VCI have published "Examinations concerning release and exposure from nanostructured paints and coatings" in 2017 describing a series of high sophisticated experimental setups to analyse potential emissions of nanoparticles out of complex matrices like nanomaterial enhanced plastics or paints in different steps of industrial processing and environmental conditions.

The Joint Research Centre (JRC) of the European Commission and the European Association of pigment producers (Eurocolour) have published a joint report of "Basic comparison of particle size distribution measurements of pigments and fillers using commonly available industrial methods" in November 2014 [9]. On the basis of this report and on current research projects a tiered measurement strategy for the implementation of the recommendation for a nanomaterial definition of the European Commission is in discussion.

The Association of Pigment-Producers VdMi within VCI and VCI have commonly developed and brought into the regulatory process "A tiered measurement strategy to implement the EC recommendation for a nanomaterial definition". This measurement strategy is directed to contribute to industries need for a quick and unique measuring method based on commercially available and widespread used measuring instruments, designed to measure existing commercial products to clearly define nanomaterials and non-nanomaterials according to the Recommendation of the European Commission.

Developments related to voluntary or stewardship schemes: The German chemical industry is still deeply engaged and contributing in the German "Nano-Dialog" initiated by the German government and led by the German Federal Ministry of Environment (BMUB).

2.1.3. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

NIA (Nanotechnology Industries Association)

NIA is actively participating in several EU funded projects (e.g. NanoReg2, PATROLS) that are promoting IATA.

2.1.4. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

CEFIC (European Chemical Industry Council)

Cefic contributes to the Nanosafety cluster through its members.

NIA (Nanotechnology Industries Association)

NIA is involved in several EU funded projects addressing EHS aspects (e.g. NanoReg2, PATROLS) and are involved in the NanoSafetyCluster activities.

JCIA (Japan Chemical Industry Association)

The chemical industries in Japan, the United States and Europe have jointly promoted the LRI program as per the initiative of the International Council of Chemical Associations in

[9] http://publications.jrc.ec.europa.eu/repository/handle/JRC92531

order to provide long-term support for research on the effects of chemical substances on human health and the environment. Following theme which JCIA had supported in Japan was completed by Feb 2017; “Construction of the novel in vitro evaluation systems based on the genotoxic mechanisms of nanomaterials” by National Cancer Centre Research Institute. As results, /a novel in vitro genotoxicity assay model to assess lung toxicity using a co-culture system, and / a novel in vitro assay model to assess skin toxicity using 3D human skin reconstitution models were obtained. JCIA is supporting another theme of “Establishment of mechanism based assay protocol for hasard and carcinogenic risk of carbon based nanomaterisals” by Nanotoxicology Project, Nagoya City University since Mar 2017.

VCI (German Chemical Industry Association)

Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Research projects on the safety of nanomaterials are conducted by the VCI member companies. The German chemical industry is engaged in several projects of the Framework Programme Horizon 2020 of the European Commission (e.g. NanoReg, Marina, SINN, Nanosafe II, Nanoderm, IMPART, NEST Particle Risk, NanoDefine) and the German Federal Ministries (e.g. NanoCare, NanoNature, NanoGEM, TRACER, NanoGRAVUR and projects that have determined the emission of nanoparticles from endproducts in typicle life cycle stages).

The German chemical industry, VCI together with the scientific chemical associations continuously review and analyse safety research needs and is therefore in permanent dialogue with the German Federal Ministry of Research (BMBF), the German Federal Ministry of Economy and Energy (BMWi), and federal authorities to derive programs on nanomaterials safety research.

Documents on safety research:

- Roadmap for Safety Research on Nanomaterials
- Environmental Aspects of Nanoparticles
- 10 Years of Research: Risk Assessment, Human and Environmental Toxicology of Nanomaterials
- Conclusions and recommendations from the project „Health assessment, exposure and environmental effects of nanomaterials: literature review and assessment" (continuously updated)

Information on research or strategies on life cycle aspects of nanomaterials, as well as positive and negative impacts on environment and health of nano-enabled applications

The German chemical industry is engaged in the review process on research and strategies on life cycle aspects of nanomaterials within the OECD WPMN SG 9.

VCI is engaged within the OECD Working Party of Resource Productivity and Waste (WPRPW) to discuss the know-how of the chemical industry on waste containing nanomaterials and to contribute to coordinate the efforts of the WPRPW and WPMN via concept papers on the scientific state of knowledge concerning the treatment of waste containing nanomaterials.

On national level several industry and federally sponsored research projects with industry engagement with a focus on the incineration process of waste containing nanomaterials have been successfully conducted. Several follow-up projects on the fate of nanoparticles within the waste treatment process are worked on or will be established with industry engagement as well.

Information on any development related to exposure measurement and exposure mitigation.

A special focus is given on workplace safety. On the basis of the "Tiered Approach to an Exposure Measurement and Assessment of Nanoscale Aerosols Released from Engineered Nanomaterials in Workplace Operations" of VCI, the German Federal Institute of Occupational safety and health (BAuA), the German Social Accident Insurance Institution for the Raw Materials and Chemical Industry (BG RCI), and the Federal Institute for Occupational Safety and Health (IFA) of the German Social Accident Insurance (DGUV) a guidance of the Committee on Hazardous Substances (AGS) at BAuA worked out a publication in 2013 aiming at deriving best practices for exposition measurement and is currently communicated at scientific and political level that is also the basis for the BIAC sponsored SG 8 project that already has been endorsed by the WPMN. On national expert level the discussion of the possibility to deduct of exposure limits of airborne nanoscale particles at work places is still going on.

ACC (American Chemistry Council)

The ACC Nanotechnology Panel continues to support a project of ISO Technical Committee 229 (TC/229) through the American National Standards Institute (ANSI) to develop an ISO technical report titled "Considerations for the Measurement of Nano-objects and Their Aggregates and Agglomerates (NOAA) in the Environment." The latest draft of the report was discussed at the TC/229 plenary meeting in Seoul, and the Panel anticipates completion of the project in the second half of 2018.

2.1.5. Additional Information

NIA

NIA has recently initiated (end 2017) a Global Regulatory Working Group supporting industries in their work at a global level of nano regulations. The Global Regulatory Working Group has identified several focus issues of global relevance to industries. The outcome is expected to be made available later in 2018.

2.2. The International Council on Animal Protection in OECD Programmes (ICAPO)

2.2.1. Information on any developments related to Integrated Approaches to Testing and Assessment (IATA)

- The PETA International Science Consortium Ltd., a member of the International Council on Animal Protection in OECD Programmes (ICAPO), is working with Health Canada on the development of an adverse outcome pathway (AOP) for lung fibrosis titled 'Secretion of inflammatory cytokines leading to lung fibrosis' (AOP 173: https://aopwiki.org/wiki/index.php/Aop:173). A publication on this work is expected to be submitted for publication in 2018.

2.2.2. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

- The PETA International Science Consortium is funding the development of a three-dimensional *in vitro* system to predict the potential of manufactured nanomaterials to cause lung fibrosis in humans. The project is led by Professor Dr. Barbara Rothen-Rutishauser of the Adolphe Merkle Institute at the University of Fribourg and MatTek Corporation. The results of the project were presented in 2017 at several international conferences including the Society of Toxicology, EUROTOX, and the 10th World Congress on Alternatives and Animal Use in the Life Sciences. A manuscript focusing on the dose and dose metrics of nanomaterials used in the study was recently submitted to a peer-reviewed journal, and another publication is expected to be submitted in 2018. The progression of this project can be followed on our website: http://www.piscltd.org.uk/nanoworkshop/
- The PETA International Science Consortium awarded VITROCELL® systems to four international laboratories:
  - ScitoVation (United States)
  - VITO NV (Belgium)
  - Professor Vicki Stone at Heriot-Watt University (Edinburgh)
  - Institute for In Vitro Sciences (United States)

  More details can be found on our website: http://www.piscltd.org.uk/vitrocell-prize/
- In September 2016, the PETA International Science Consortium co-hosted a webinar series and workshop with the US NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), focusing on the use of alternative methods for acute inhalation toxicity testing. To implement recommendations from the workshop, four working groups were formed, each focussing on a specific area: 1) developing a database of existing acute inhalation toxicity data; 2) preparing a state-of-the-science review on mechanisms, dosimetry considerations, and assays for acute inhalation toxicity; 3) developing *in silico* models; and 4) conducting a proof-of-concept study to optimize an integrated approach comprised of *in vitro* and *in silico* methods. Updates from the work were presented in 2017 at EUROTOX, the American Society for Cellular and Computational Toxicology, and the 10th World Congress on Alternatives and Animal Use in the Life Sciences. The workshop report has been published in *Toxicology In Vitro* (available here: https://www.ncbi.nlm.nih.gov/pubmed/29277654) and another review article is in preparation. More information regarding this work is available on our website: http://www.piscltd.org.uk/acute-inhalation-toxicity/

2.2.3. Additional Information

- The PETA International Science Consortium's Director is the Guest Editor of a special issue of *Applied In Vitro Toxicology* on 'Implementing Alternative Approaches for Inhalation Toxicity Testing'. The issue will cover topics relevant to the risk management of nanomaterials and other substances including *in vitro* test methods, non-testing methods (e.g., quantitative structure activity relationships, grouping, or read-across), AOP development and dosimetry considerations.

2.3. Environmental NGOs

2.3.1. ReLANS Latinamerica ongoing research projects

- The Latin American Nanotechnology & Society Network (ReLANS — www.relans.org) is working on two parallel research projects aimed at identifying the advance of nanotechnologies in Latin America and the Caribbean. One of the projects compares the public policies to spur R&D in nanotechnologies in some Latin American countries, and follows the methodology used by an OECD Policy Survey carried out in 2008. -advances to date are available by request at relans2010@gmail.com. Another research project is aimed at identifying companies that manipulate nanotechnologies in Latin America and their location according to the economic sector and place in a production chain (initial results are available at http://micrositios.cinvestav.mx/nano). Partial results will appear in a March, 2018, book published by the University of the Andes in Colombia, entitled Cadenas de producción de las nanotecnologías en América Latina: Argentina, Brasil, Colombia y México (Production chains of nanotechnologies in Latin America: Argentina, Brazil, Colombia and Mexico), freely available in digital format.
- In Brazil, 122 companies that have been financed by the government to develop innovative projects were analyzed; in Mexico, 53; in Argentina, 37; and in Colombia, eight. The limited presence of companies producing tools and equipment to measure or manipulate nanotechnology is evident, leading to a regional dependence on large producer consortia to acquire sophisticated microscopes and other equipment for the evaluation, measurement and processing of nanoparticles and structures. This calls into question the quality and safety procedures of nanomaterials in the region. Regarding the production of raw nano-material, which is the first step in the production chain, the field is uneven. In Brazil, where the research focused only on those companies that have received financial support from the federation, 16% of the projects lie in this initial production stage; in Mexico, 15%; in Argentina, 16%; and in Colombia, 25%. The second step is the production of nano-intermediaries, that is to say, nanotechnology products already functionalized or aimed at certain purposes or productive chains. The distribution is as follows: in Brazil, 43%; in Mexico, 17%; in Argentina, 35%. Colombia does not have companies working at this stage. The third step is the creation of end-products, that is, those that do not undergo subsequent nanotechnological transformations.
- The ongoing research intends to analyze in depth the production chain of some of these companies, with the purpose of identifying the degree of vertical integration of nanotechnologies.

2.4. International Organisation for Standardization (ISO)

ISO TC229 introduction

Standardization in the field of nanotechnologies that includes either or both of the following:

a. Understanding and control of matter and processes at the nanoscale, typically, but not exclusively, below 100 nanometres in one or more dimensions where the onset of size-dependent phenomena usually enables novel applications,
b. Utilizing the properties of nanoscale materials that differ from the properties of individual atoms, molecules, and bulk matter, to create improved materials, devices, and systems that exploit these new properties.

Specific tasks include developing standards for: terminology and nomenclature; metrology and instrumentation, including specifications for reference materials; test methodologies; modelling and simulations; and science-based health, safety, and environmental practices.

Some statistics:

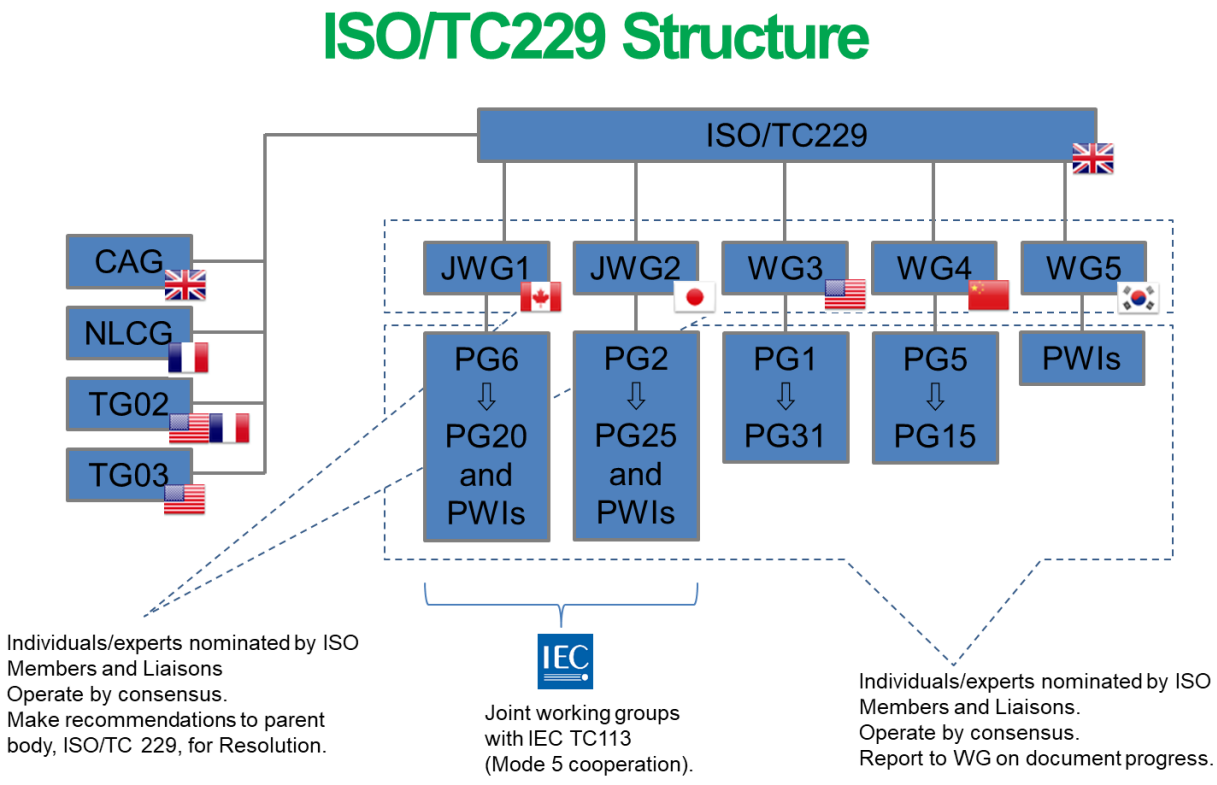
63 published ISO standards under the direct responsibility of ISO/TC 229

38 ISO standards under development under the direct responsibility of ISO/TC 229

36 Participating members

15 Observing members

150-200 expert attendance at plenaries



ISO/TC 229/JWG 1 - Terminology and nomenclature Working group

ISO/TC 229/JWG 2 - Measurement and characterization Working group

ISO/TC 229/WG 3 - Health, Safety and Environmental Aspects of Nanotechnologies Working group

ISO/TC 229/WG 4 - Material specifications Working group

ISO/TC 229/WG 5 - Products and Applications

ISO/TC 229/TG 2 - Consumer and societal dimensions of nanotechnologies Task group (does not draft standards)

ISO/TC 229/TG 3 - Nanotechnologies and sustainability Task group (does not draft standards)

ISO/TC 229/CAG - Chairman Advisory Group

[PG: Project Group, PWI: Preliminary Work Item]

The most relevant to OECD WPMN work is done a JWG2 and WG3. The following is a selected list of a few workitems under development. This list and descriptions of the workitems are followed by a comprehensive list of documents under development in JWG2 and WG3. These documents are at various stages of development requiring input from experts working in these areas. Close cooperation of ISO TC229 and OECD aims to ensure transparent commenting on ISO documents from OECD experts.

ISO works with a number of external organisations through a Liaison interaction:

Organization	Title
ANEC	European Association for the Co-ordination of Consumer Representation in Standardization
ANF	Asia Nano Forum
EC	European Commission
ECOS	European Environmental Citizens Organisation for Standardisation
ETUI	European Trade Union Institute
IUPAC	International Union of Pure and Applied Chemistry
NIA	Nanotechnology Industries Association
OECD	Organisation for Economic Co-operation and Development
VAMAS	Versailles Project on Advanced Materials and Standards

2.4.1. Developments related to good practice documents

Selected list of relevant documents:

[TS: Technical Specification TR: Technical Report]

Document	Title
TS 80004-6 (Revision of ISO/TS 80004-6:2013)	Nanotechnologies -- Vocabulary -- Part 6: Nano-object characterization *Note: Standard is under revision. Contributions are welcomed*
TS 19590:2017	Nanotechnologies -- Size distribution and concentration of inorganic nanoparticles in aqueous media via single particle inductively coupled plasma mass spectrometry *Note: this document is published*
TS 21362	Nanotechnologies -- Application of field flow fractionation for characterization of nanomaterial contents *Note: This document is approved for publication and is already planned for an upgrade into a full international standard (IS)*
ISO 21363	Nanotechnologies -- Protocol for particle size distribution by transmission electron microscopy *Note: This document is under development. Contributions are welcomed*
ISO 19749	Determination of size and size distribution of nano-objects by scanning electron microscopy *Note: This document is under development, Contributions are welcomed*
TS 16195 (Revision of ISO/TS 16195:2013)	Nanotechnologies -- Guidance for developing representative test materials consisting of nano-objects in dry powder form *Note: This document is under revision. Contributions are welcomed*
TS 12025 (Revision of ISO/TS 12025:2012)	Nanomaterials -- Quantification of nano-object release from powders by generation of aerosols *Note: This document is under revision. Contributions are welcomed*
TR 20489	Separation and size fractionation for the characterisation of metal-based nanoparticles in water samples
TS 21361	Nanotechnologies -- Quantification of airborne nanoscale carbon black and amorphous silica in a manufacturing environment
PWI 21357	Nanotechnologies -- Measurement of average nanoparticle size and assessment of agglomeration state by static multiple light scattering (SMLS) in concentrated media
PWI 23151	Nanotechnologies – Particle size distribution for cellulose nanocrystals
TR 12885 (Revision of ISO/TR 12885:2008)	Nanotechnologies – Health and safety practices in occupational settings relevant to nanotechnologies
ISO 19007	Nanotechnologies – In vitro MTS assay for measuring the cytotoxic effect of nanoparticles
TS 20787:2017	Nanotechnologies -- Aquatic toxicity assessment of nanomaterials using Artemia sp *Note: This document is published*
ISO 20814	Nanotechnologies -- Photocatalytic activity assay for nanoparticles in aqueous suspension
TR 21386	Nanotechnologies -- Considerations for the measurement of nano-objects, and their aggregates and agglomerates (NOAA) in the environment
TR 21624	Considerations for in vitro studies of airborne engineered nanomaterials

TS 21633	Label-free impedance technology to assess the toxicity of nanomaterials in vitro
TR 22019	Considerations in performing toxicokinetic studies of nanomaterials
TS 22082	Nanotechnologies --- In vivo toxicity assessment of nanomaterials using dechorionated zebrafish embryo
TR 22293	Evaluation of methods for assessing the release of nanomaterials from commercial, nanomaterial-containing polymer composites
TR 22455	High throughput screening method for nanoparticles toxicity using 3D cells
ISO/NP TS 23034	Nanotechnologies -- Method for quantification of cellular uptake of carbon nanomaterials by using optical absorption measurement

Comprehensive list of documents under development.

This is a full list of the ISO TC229 programme of work. It includes the documents listed in the previous section. This list includes the working groups the relevant documents are developed at.

Document	Title	Working Group/Lead
IEC/AWI 62607-6-3	Nanomanufacturing -- Key control characteristics -- Graphene - Characterization of graphene domains and defects -- Part 6-3:	ISO/TC 229
ISO/FDIS 19007	Nanotechnologies -- In vitro MTS assay for measuring the cytotoxic effect of nanoparticles	ISO/TC 229/WG3
ISO/NP TS 22801	Nanotechnologies -- Specification of nanoclays used for gas barrier films	ISO/TC 229/WG 4
ISO/NP TS 22292	Nanotechnologies -- 3D image reconstruction of nano-objects using transmission electron microscopy	ISO/TC 229/JWG 2
ISO/NP TS 23302	Nanotechnologies -- Guidance on measurands for characterising nano-objects and materials that contain them	ISO/TC 229/JWG 2
ISO/NP TR 19733	Matrix of characterization and measurement methods for graphene	ISO/TC 229/ JWG2
ISO/WD 19749	Nanotechnologies -- Measurements of particle size and shape distributions by scanning electron microscopy	ISO/TC 229/JWG 2
ISO/WD 21363	Nanotechnologies -- Protocol for particle size distribution by transmission electron microscopy	ISO/TC 229/JWG 2
ISO/AWI 20814	Nanotechnologies -- Photocatalytic activity assay for nanoparticles in aqueous suspension	ISO/TC 229/ WG3
ISO/AWI TS 19808	Nanotechnology - Specifications for Carbon Nanotube Suspension: characteristics and test methods	ISO/TC 229/WG 4
ISO/NP TS 80004-4	Nanotechnologies -- Vocabulary -- Part 4: Nanostructured materials	ISO/TC 229/JWG 1
ISO/NP TS 21236	Nanotechnologies -- Nanoclays -- Characteristics and measurements	ISO/TC 229/WG 4
ISO/NP TS 21237	Nanotechnologies -- Nano-enhanced air filter media using nanofibres -- Characteristics, performance and measurement methods	ISO/TC 229/WG 4
ISO/AWI TR 20489	Separation and size fractionation for the characterisation of metal-based nanoparticles in water samples	ISO/TC 229/ JWG2
ISO/AWI TS 21412	Nanotechnologies -- Nanostructured layers for enhanced electrochemical bio-sensing applications -- Characteristics and measurements	ISO/TC 229/WG 4

ISO/AWI TR 21386	Nanotechnologies -- Considerations for the measurement of nano-objects, and their aggregates and agglomerates (NOAA) in the environment	ISO/TC 229/WG 3
ISO/DTS 19807	Nanotechnology -- Liquid suspension of magnetic nanoparticles -- Characteristics and measurements	ISO/TC 229/WG 4
ISO/NP TS 11308	Nanotechnologies -- Characterization of carbon nanotubes using thermogravimetric analysis	ISO/TC 229/JWG 2
ISO/NP TS 10798	Nanotechnologies -- Characterization of carbon nanotubes using scanning electron microscopy and energy dispersive X-ray spectrometry	ISO/TC 229/JWG 2
ISO/AWI TS 21633	Label-free impedance technology to assess the toxicity of nanomaterials in Vitro	ISO/TC 229/WG 3
ISO/PRF TS 21362	Nanotechnologies - Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation	ISO/TC 229/JWG 2
ISO/AWI TS 21975	Nanotechnologies -- Polymeric nanocomposite films for food packaging -- Barrier properties: characteristics and measurement methods	ISO/TC 229/WG 4
ISO/NP TS 12025	Nanomaterials -- Quantification of nano-object release from powders by generation of aerosols	ISO/TC 229/JWG 2
ISO/NP TS 17200	Nanotechnology -- Nanoparticles in powder form -- Characteristics and measurements	ISO/TC 229/WG 4
ISO/NP TS 16195	Nanotechnologies -- Guidance for developing representative test materials consisting of nano-objects in dry powder form	ISO/TC 229/JWG 2
ISO/NP TS 22082	Nanotechnologies --- In vivo toxicity assessment of nanomaterials using dechorionated zebrafish embryo	ISO/TC 229/WG 3
ISO/NP TS 10867	Nanotechnologies -- Characterization of single-wall carbon nanotubes using near infrared photoluminescence spectroscopy	ISO/TC 229/JWG 2
ISO/NP TS 11251	Nanotechnologies -- Characterization of volatile components in single-wall carbon nanotube samples using evolved gas analysis/gas chromatograph-mass spectrometry	ISO/TC 229/JWG 2
ISO/NP TS 80004-3	Nanotechnologies -- Vocabulary -- Part 3: Carbon nano-objects	ISO/TC 229/JWG 1
ISO/AWI TR 22455	High throughput screening method for	ISO/TC 229/WG

	nanoparticles toxicity using 3D cells	3
ISO/AWI TR 22293	Evaluation of methods for assessing the release of nanomaterials from commercial, nanomaterial-containing polymer composites	ISO/TC 229/WG 3
ISO/AWI TS 21361	Nanotechnologies -- Quantification of airborne nanoscale carbon black and amorphous silica in a manufacturing environment	ISO/TC 229/JWG 2
ISO/NP TS 80004-8	Nanotechnologies -- Vocabulary -- Part 8: Nanomanufacturing processes	ISO/TC 229/JWG 1
ISO/NP TS 80004-6	Nanotechnologies -- Vocabulary -- Part 6: Nano-object characterization	ISO/TC 229/JWG 1
ISO/AWI TS 21346	Nanotechnologies - Characterization of individualized cellulose nanofibril samples	ISO/TC 229/JWG 2
ISO/AWI TS 23034	Method to estimate cellular uptake of carbon nanomaterials using optical absorption	ISO/TC 229/WG 3
ISO/PWI 21356	Nanotechnologies -- Structural characterization of graphene	ISO/TC 229/JWG 2
ISO/PWI 23362	Nanostructured porous alumina as catalyst support for vehicle exhaust emissioncontrol -- Material specification	ISO/TC 229/WG 4
ISO/AWI TR 21624	Considerations for in vitro studies of airborne engineered nanomaterials	ISO/TC 229/WG 3
ISO/PWI 23361	Nanotechnologies -- Crystallinity of cellulose nanomaterials by powder X-ray diffraction (Ruland-Rietveld analysis)	ISO/TC 229/JWG 2
ISO/PWI 21357	Nanotechnologies -- Measurement of average nanoparticle size and assessment of agglomeration state by static multiple light scattering (SMLS) in concentrated media	ISO/TC 229/JWG 2
ISO/PWI 22761	Nanotechnologies -- Specification for superparamagnetic beads composed of nanoparticles for circulating tumor DNA extraction	ISO/TC 229/WG 4
ISO/PWI 23366	Nanotechnologies -- Performance evaluation of quantification methods of biomolecules using fluorescent nano-particles	ISO/TC 229/WG 5
ISO/PWI 23367-1	Nanotechnologies -- Performance evaluation of nanobio-sensor using electrochemical method for DNA identification -- Part 1: DNA hybridization	ISO/TC 229/WG 5
ISO/PWI TS 80004-10	Nanotechnologies -- Vocabulary -- Part 10:	ISO/TC 229/JWG1
ISO/AWI TR 22019	Nanotechnologies -- Considerations in performing toxicokinetic studies of	ISO/TC 229/WG 3

	nanomaterials	
ISO/PWI 22802	Nanofluids for heat transfer applications -- Specification of characteristics, performance and measurement methods	ISO/TC 229/WG 4
ISO/PWI 23151	Nanotechnologies -- Particle size distribution for cellulose nanocrystals	ISO/TC 229/JWG 2
ISO/PWI 23359	Nanotechnologies -- Chemical characterisation for graphene in powders and suspensions	ISO/TC 229/JWG 2
IEC/CD 62565-3-1	Nanomanufacturing -- Material specifications -- Part 3-1: Graphene -- Blank detail specification	ISO/TC 229
ISO/DTR 12885	Nanotechnologies -- Health and safety practices in occupational settings relevant to nanotechnologies	ISO/TC 229/WG3
ISO/DTS 20660	Nanotechnologies -- Materials specification -- Antibacterial silver nanoparticles	ISO/TC 229/WG4
ISO/TS 10797	Nanotechnologies -- Characterization of single-wall carbon nanotubes using transmission electron microscopy	ISO/TC 229/JWG2