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

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Series on the Safety of Manufactured Nanomaterials

No. 89

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

IOMC

INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

Environment Directorate

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris, 2019

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The Environment, Health and Safety Division publishes free-of-charge documents in 12 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; Safety of Manufactured Nanomaterials**, and **Adverse Outcome Pathways**. 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.

This publication is available electronically, at no charge.

**For this and many other Environment,
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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 19th WPMN meeting (February 2019). 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 the Working Party on Chemicals, Pesticides and Biotechnology of the OECD.

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

1.1. Australia

1.1.1. National developments on human health and environmental safety

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

No new nanomaterial risk assessments have recently been completed by NICNAS. To date, NICNAS has assessed four nanoscale materials.

- b. 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.

In September 2018 NICNAS consulted on the details of the types of information that will be required when applying to introduce a new chemical into Australia under the proposed new scheme, the Australian Industrial Chemicals Introduction Scheme. This detail included a proposal for dealing with chemicals at the nanoscale. Details can be found on the NICNAS website: https://www.nicnas.gov.au/_data/assets/pdf_file/0020/83261/Applications-for-certificates-under-reforms.pdf

1.1.2. Activities initiated to implement the OECD Council Recommendation¹ (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](#)

1.2. Austria

1.2.1. Highlight of developments

- Austria plans to work on **Guidance development regarding Environmental abiotic transformation of nanomaterials** - a proposal for this project has been sent to WNT. The work is under the auspices 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). The scientific work is funded by the EU Horizon 2020 Project Gov4Nano.
- 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. In the most recent call two projects (NanoAdd & NANA CYCLE) are funded dealing with the role of nanomaterials and “advanced materials” in the circular economy (project duration 2018 – 2019). 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.
- The **International Conference for Environmental Effects of Nanomaterials and Nanoparticles - ICEENN 2019** will be held in Vienna from 01.09. - 04.09.2019 (at University of Vienna, Department for Environmental Geosciences; <https://nano2019.univie.ac.at/>).
- The “**2nd EU-Asia Dialogue on Nanosafety**”, Oct 29th, 2018, Vienna, has been organized by BioNanoNet (contact: Andreas Falk) together with the Ministry for Transport, Innovation and Technology (contact: Alexander Pogany), the EU NanoSafety Cluster, and the Asia Nano Forum. The 2nd EU-Asia Dialogue on Nanosafety, which brought together Asian and European nanosafety experts, enabled insights on actual and future human and environmental nanosafety research and discussions on the progress towards thematic collaboration (<https://www.bionanonet.at/events/upcoming-events/1631>). This dialogue forum will be further developed and extended towards a global dialogue on Nanosafety. The next dialogue forum will be held in March 2019 in Thailand.

1.2.2. National developments on human health and environmental safety

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 opportunities 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. 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>

On behalf of the Ministry of Labour, Social Affairs, Health and Consumer Protection a survey was done on “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 it. Although nanoparticles can be composed of two or more materials, current rules concerning labelling 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.oew.ac.at/ita/nanotrust-dossiers>).

1.2.3. Developments related to good practice documents

The central labour inspectorate (part of the Federal Ministry of Labour, Social Affairs, Health 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 is intended to 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. Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials

Projects funded by the national NANO Environment Health and Safety programme
(<http://www.ffg.at/nano-ehs>)

- In the framework of the project **NanoAdd** (project duration 2018 – 2019), the role of "Advanced Nanocomposites" in the circular economy of plastics and their impact on the recyclability of the products will be investigated. The project is coordinated by University of Natural Resources and Life Sciences, project partner are Mag. Sabine Grebler, POLYMERWERKSTATT GmbH and BRIMATECH Services GmbH.
- In the project **NANO CYCLE** (project duration 2018 – 2019), manufactured nanomaterials (MNM) and advanced materials (AM) in waste streams shall be quantified and effects of MNM and AM on the recycling process analysed. The exposure of MNM and AM in a circular economy will be described and visualised, and methods for recycling of MNM and AM are tested. The project is led by AIT Austrian Institute of Technology (contact: Manuela Kienegger), partners are Environment Agency Austria and Austrian Society for Environment and Technology (ÖGUT).

- The project **SbD-AT** (project duration 2017 – 2018), coordinated by BRIMATECH Services GmbH with the partners BioNanoNet Forschungsgesellschaft mbH and University of Vienna, Department for Environmental Geosciences aimed at identifying and analyzing perceived advantages and disadvantages, risk awareness and acceptance barriers of the Safe by Design (SbD) concept from the company perspective (potential user of the SbD concept).
- In the project **Nano EHS SWOT SbD** (project duration 2017 – 2018) by AIT Austrian Institute of Technology GmbH based on an operationalization of the Safe by Design (SbD) concept for stakeholder consultations, the strengths and weaknesses of the concept were analyzed in the exchange with potential users.
- The project **SafeNanoKap** (project duration 2017 – 2018) led by 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>) aimed 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. The strengths and weaknesses of the SbD concept were identified and summarised using the example of nanomaterial-containing coffee capsules.

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 like CuO. The project covers characterisation in environmental media, transformation and transport, plant uptake and trophic transfer as well as ecotoxicological effects.

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.

In the project **NANO-IMMUNOTOX** human peripheral blood mononuclear cells (PBMC) are used to investigate immunomodulatory effects of nano compounds and materials in vitro. The project is led by Medical University Innsbruck, Biochemical Immunotoxicology Group (contact: Johanna Gostner and Dietmar Fuchs) with partners from SPAM-LFP, French Atomic Energy Commission within the nanoLINEN consortium established in the ERANET initiative.

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 Ehmoser) 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 project **NanoTrust**, funded by the Austrian Federal Ministry for Transport, Innovation and Technology (BMVIT), the Federal Ministry of Labour, Social Affairs, Health and Consumer Protection, and the Austrian Federal Ministry of Sustainability and Tourism 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>, last publication 2018 regarding Nanotechnological Applications for Food Contact Materials.

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 <https://us-eu.org/communities-of-research/>

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 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 **H2020 project NanoCommons** (start: January 2018) **BioNanoNet** (Andreas Falk) and **University of Salzburg** (Albert Duschl) are partners 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 (<https://www.nanocommons.eu/>).

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 **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 named “compilation of resources and tools to support nanotoxicology, risk & safety testing” was published in September 2018. See: <https://www.bionanonet.at/index.php/about-nanotoxicology/> (contact: Andreas Falk).

In the **H2020 pilot-projects Inspired** (<http://www.nano-inspired.eu/>), **R2R-Biofluidics** (<http://www.r2r-biofluidics.eu/>), **Hi-Response** (<http://hi-responseh2020.eu/>) 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).

The EU funded **H2020 Research and Innovation action BIORIMA** (Biomaterial Risk Management; start: November 2017). The project aims to develop an integrated risk management framework for nano-biomaterials used in advanced therapeutic medicinal products and medical devices. BioNanoNet (contact: Andreas Falk) and Joanneum Research Department HEALTH (Thomas Birngruber) are part of the BIORIMA consortium.

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).

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.

1.3. Canada

1.3.1. 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. A risk assessment framework is currently under development, which will be used to guide environmental and human health risk assessment of nanomaterials in commerce. A generalized draft risk assessment framework is expected to be completed by spring 2019. In addition, expert consultations on the high-level framework will be planned for a later date.

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

Two nano-related substances, both inorganic, were notified to the program since WPMN18. In addition, one pre-notification consultation (PNC) was initiated for a potential nano-related substance. PNCs provide clarity on regulatory requirements prior to submission under the New Substances Notification Regulations (NSNR).

- b. Development related to exposure measurement and exposure mitigation;

Responding to a need identified through the survey *Consumer and Environmental Exposures to Manufactured Nanomaterials*, Canada has been working on 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* (approved by the OECD WPMN in 2017). Objective 1 of the project, which involved generating an inventory of available models/tools for assessing environmental and consumer exposure to manufactured nanomaterials, has been completed. Objective 2, now underway, involves evaluating the models/tools gathered in Objective 1 for their applicability to regulatory nanomaterial exposure assessment.

Canada hosted a WPMN Expert Meeting on Exposure Measurement and Exposure Mitigation of Nanomaterials in Ottawa, Canada. The meeting discussed progress on current projects under the Steering Group of Exposure Measurement and Exposure Mitigation (SG8) within the OECD WPMN, including the *Compilation of Available Tools and Models Used for Assessing Environmental and Consumer Exposure to Manufactured Nanomaterials and Evaluation of their Applicability in Exposure Assessments* project led by Canada and the *Assessing the global readiness of regulatory and non-regulatory models for assessing occupational exposure to MNs* project led by Denmark. In addition, projects under other international organizations related to

exposure modelling of nanomaterials and the state of the art regarding international and national activities relevant to the work of the OECD WPMN SG8 were discussed.

c. risk management approaches;

In response to a New Substance Notification submitted under Schedule 1 (Research & Development), a ministerial condition was enforced to support the research initiative and to collect monitoring data on the substance's fate in the environment. Ministerial conditions are control measures used to minimize risk to the environment or human health when a new substance is suspected to be toxic under the Canadian Environmental Protection Act, 1999.

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

Canada's health and environment departments are co-leading a project 'Advancing Adverse Outcome Pathway (AOP) Development for Nanomaterial Risk Assessment and Categorization' that was submitted to and approved by OECD WPMN in 2017. An expert group involving Netherlands (RIVM and Dutch Technical University), South Africa (National Institute of 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 was convened to support the development of AOP frameworks that have the greatest potential to inform categorization and risk assessment of nanomaterials by examining a key event (KE) as a case study. Objective 1, completed in January 2018, involved mining a curated database to generate a list of potential key events relevant for manufactured nanomaterials for case study development. Toward Objective 2, project partners selected the tissue injury KE for case study development and are currently completing literature evaluations (using study quality criteria crafted under Objective 1) to develop a high-quality dataset and knowledge base for the case study. Objective 3 is to gather expert input on the current status, use, and future needs for AOPs as tools for the categorisation and risk assessment of MNs. Toward Objective 3, the project team collaborated with the Horizon 2020 SmartNanoTox project to convene an expert workshop during the 2018 International Nanotoxicology Conference in Neuss, Germany titled "Advancing Adverse Outcome Pathway (AOP) Development for Nanomaterial Risk Assessment and Categorisation (NanoAOP workshop)." The project progress (completion of Objective 1; efforts on Objectives 2 and 3) will be presented at WPMN-19.

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

Canada's health department has initiated a project attempting to create quantitative and semi-quantitative predictive models for hazard endpoints using machine learning approaches. To date, this project has established a curated database of peer-reviewed toxicological studies on priority nanomaterials which will serve as a test platform to train models and attempt to predict hazard outcomes based on physical-chemical characteristics of nanomaterials. This work will serve to enable justified read-across for nanomaterial hazard assessment where data gaps would otherwise impede conclusion

Scientific research

Canada's health department recently 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). This solubility research has been expanded to investigate the relationship between dissolution behaviour and toxicity of eight metal oxide nanomaterials that are currently in commerce in Canada. The team found it necessary to optimize the sonication protocol separately for each individual metal oxide, based on the finding that the critical delivered sonication energy is material-specific. The team reported their findings at the NanoSAFE 2018 conference in Grenoble. This study also demonstrated that the composition and purity of engineered nanopowders purchased from suppliers must be independently confirmed by researchers, as the team found that two out of the eight metal oxide products did not meet the manufacturer's claims.

Canada's health department has conducted integrated in vitro toxicity testing for single and multi-walled carbon nanotubes and their oxidized forms using multiple cell lines and their atmospherically transformed products, and have addressed the issue of methodological interferences arising during in vitro toxicity testing with these nanomaterials. Relative in vitro potencies of amorphous nanosilica as well as pristine and surface modified (-COOH both short and long chain) mesoporous silica nanomaterials were analysed. Toxicoproteomic analyses were used in determining relative potencies of these well-characterized nanomaterials. Association between the toxicity of these nanomaterials and their physicochemical properties were assessed in these studies. The findings are published. (Kumarathasn et al. *Curr Top Biochem Res.* 2012, 14(1):15-27; Das et al. *J Nanomaterials.* Vol 2014; Kumarathasn et al. *Nanotoxicology.* 2015, 9(2):148-61; Breznan et al. *Toxicol In Vitro.* 2015, 29(1):142-7; Liu et al. *Environ Sci Technol.* 2015, 49(5): 2806-14; Breznan et al. *Nanotoxicology.* 2017, 11(2): 223-235. Breznan et al. *ACS Nano.* 2018 (in press)). There are studies currently underway on toxicity testing of amorphous pristine and surface-modified as well as atmospherically transformed silica nanoparticles.

Canada's health department is analysing mouse exposure data to understand the synergistic toxicity of repeated ingestion of antibiotics with OECD-approved silver nanoparticles. The effects of exposure on the gut microbiota and immune system balance are being investigated.

Canada's health department is participating in round robin tests that will be used to validate the methods within a new OECD test guideline on particle size and particle size distribution for manufactured nanomaterials.

Canada's environment department funded research that assessed the fate and toxicity of engineered nanoparticles released from commercial products. Research was completed by the Royal Military College of Canada in September 2018. The research 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. The results of this research will soon be published in scientific literature.

Canada's environment department continues to fund research that evaluates the environmental risks of nanoparticle release from nano-enabled materials in the Canadian environment. In particular, the research compares the physicochemical properties, environmental fate and toxicity of pristine nanoparticles with those released from paints and paperboard due to weathering. The results of this research will soon be published in scientific literature.

National Research Council (NRC) Canada, Metrology Research Centre has published initial work on development of a quantitative NMR protocol for measuring functional group content on silica nanoparticles (Kunc et al. *Anal Chem.* 2018, 90 (22): 13322–13330). This project was undertaken in collaboration with Environment and Climate Change Canada. This work is currently being extended to a wider range of methods including thermogravimetric analysis, colorimetric assays

and X-ray photoelectron spectroscopy. A related project with Health Canada is aimed at characterizing a number of commercial metal oxide nanoparticles that will be used for cytotoxicity assays.

The effects of human serum albumin on stability and cytotoxicity of 20 nm silver nanoparticles have been examined, demonstrating enhanced stability and lower cell uptake (Kennedy et al. *Environ Sci: Nano*. 2018, 5: 863-867).

Previously NRC-Metrology has published studies on cytotoxicity of graphene oxide (GO), an important emerging nanomaterial that has shown promise for biotechnology applications such as drug delivery, biosensors and anti-microbial devices. Chemically and physically processed GO materials are often used in order to achieve ideal properties for different applications. Detailed characterization of morphology, sizes and chemical compositions of processed GO materials were evaluated and correlated with cytotoxicity in multiple cell lines. (Gies et al. *Nanoscale Advances*, 2019, DOI:10.1039/c8na00178b.)

1.4. Denmark

1.4.1. Activities initiated to implement the OECD Council Recommendation

In November 2018 Denmark (lead) and Germany submitted two SPSFs for developing Guidance on ‘Determination of solubility and dissolution rate of NMs in water and relevant synthetic biological media’ and ‘Identification and quantification of the surface chemistry and coatings on nano- and microscale materials’ to the WNT for review and eventual inclusion in the TGP work plan.

The work is being conducted by experts from the Danish National Research Centre for the Working Environment (NRCWE) and the German Federal Institute for Risk Assessment, (BfR).

France (lead) and Denmark submitted a SPSF to the WNT for a new test guideline on the “Determination of the Dustiness of Manufactured Nanomaterials”. This work is being conducted by experts from France (INERIS) and from the Danish National Research Centre for the Working Environment (NRCWE).

The projects will be discussed during the 31st WNT meeting in April 2019.

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

The Danish National Research Centre for the Working Environment (NRCWE) is a partner in several EU projects including GRACIOUS <https://www.h2020gracious.eu/>; NanoReg2 (www.nanoreg2.eu) and Gov4Nano <https://www.gov4nano.eu/>.

Furthermore, the Danish research institutions NRCWE and DTU are partners in the EU project “Performance testing, calibration & implementation of a next generation system-of-systems risk governance framework for nanomaterials” (caLIBRAte) (www.nanocalibrate.eu).

1.5. European Union

1.5.1. National developments on human health and environmental safety

The Changes to technical Annexes to REACH to (better) address nanomaterials have been [adopted](#), with a transition arrangement for its full application by 1 January 2020. ECHA guidance is being updated in the first half of 2019 to facilitate implementation of the updated provisions. The changes include the requirement to document characterisation of the nanoforms of substances registered under REACH, and ensure the relevant information in the registration dossier on hazard and risk can be associated with these different forms. Related update to the Safety Data Sheet requirements (REACH Annex II) is currently in progress.

Following the review of the Commission Recommendation on the definition of nanomaterial (2011/696/EU) minor revision of the recommendation was anticipated, so a public consultation on the considered changes has been planned but its launch has been delayed. The launch may take place later in 2019, at which time the further planning will also be made available. Until any change, the existing Commission Recommendation 2011/696/EU should be used. The definition from the Recommendation has been used also in the changes to REACH (see above) and can be altered under REACH only by the same formal changes of the REACH Annexes. Such change is not expected at least until 1 January 2020.

1.5.2. Activities initiated to implement the OECD Council Recommendation

No specific individual measures to address the Recommendation in particular, but impact assessment supporting regulatory changes under REACH explicitly indicated the Recommendation as one of the drivers for change.

1.5.3. Developments related to good practice documents

Joint Research Centre of the European Commission (JRC) has published the following reports:

"Workshop on Regulatory Preparedness for Innovation in Nanotechnology"

Editors: Paula JANTUNEN, Agnieszka MECH and Kirsten RASMUSSEN

Authors: Paula JANTUNEN, Kirsten RASMUSSEN, Agnieszka MECH, Juan RIEGO SINTES, Stefania GOTTARDO, Cornelle Noorlander, Lya Soeteman-Hernández, Adriëne Sips, Monique Groenewold, Susan Dekkers et al.

Publications Office of the European Union (2018). ISBN 978-92-79-94163-4 (online), 978-92-79-94164-1 (print). DOI 10.2760/278827 (online); 10.2760/102066 (print)

"Physicochemical characterisation of gold, silica and silver nanoparticles in water and in serum-containing cell culture media"

Drewes C.C , Ojea Jiménez I., Mehn D., Colpo P., Gioria S., Bogni S., Ponti J., Kinsner-Ovaskainen A., Gilliland D., Riego Sintes J., , EUR 29054 EN, *Publications Office of the European Union, Luxembourg*, 2018, ISBN 978-92-79-77705-9, doi 10.2760/818663, PUBSY No. JRC110379

["An overview of concepts and terms used in the European Commission's definition of nanomaterial"](#)

H. Rauscher, G. Roebben, A. Mech, N. Gibson, V. Kestens, T. P. J. Linsinger, J. Riego Sintes, JRC Science for Policy report EUR 29647 EN, ISBN 978-92-79-99660-3 ISSN 1831-9424 doi:10.2760/459136

and papers:

"Physico-chemical Properties of Manufactured Nanomaterials - Characterisation and Relevant Methods. An outlook based on the OECD Testing Programme"

Kirsten Rasmussen, Hubert Rauscher; Agnieszka Mech, Juan Riego Sintes, Douglas Gilliland, Mar Gonzalez, Peter William Edward Kearns, Kenneth Moss, Maake Visser, Monke Groenewold, Erik A. J. Bleeker. *Regulatory Toxicology and Pharmacology*. 92, 8-28. (2018). DOI: 10.1016/j.yrtph. ISSN 0273-2300

"An inventory of ready-to-use and publicly available tools for the safety assessment of nanomaterials"

JANTUNEN Anna Paula; GOTTARDO Stefania; RASMUSSEN Kirsten; CRUTZEN Hugues *Nanoimpact*, 12, 18-28 (2018). DOI 10.1016/j.impact.2018.08.007

"Insights into possibilities for Grouping and Read-Across for Nanomaterials in EU Chemicals Legislation"

Mech A. et al
Nanotoxicology DOI 10.1080/17435390.2018.1513092

"Direct quantification of nanoparticle surface hydrophobicity"

Valaesia A. et al
Communications Chemistry. DOI 10.1038/s42004-018-0054-7 (online)

"Introducing a new standardized nanomaterial environmental toxicity screening testing procedure, ISO TS/20787: aquatic toxicity assessment of manufactured nanomaterials in saltwater lakes using Artemia sp. Nauplii"

JOHARI Seyed Ali; RASMUSSEN Kirsten; GULUMIAN Mary; GHAZI-KHANSARI Mahmoud; TETARAZAKO Norihisa; KASHIWADA Shosaku; ASGHARI Saba; PARK Jun Woo; YU Il Je
Toxicology Mechanisms and Methods. DOI 10.1080/15376516.2018.1512695 (online)

"Developing OECD Test Guidelines for Regulatory Testing of Nanomaterials to ensure mutual acceptance of test data"

Kirsten Rasmussen, Hubert Rauscher; Mar Gonzalez, Peter William Edward Kearns, Juan Riego Sintes
Accepted in *Regulatory Toxicology and Pharmacology*

JRC has also organised the following meetings:

"Meeting of an "Expert Group for the development of a New OECD Test Guideline on the Determination of the (Volume) Specific Surface Area of Manufactured Nanomaterials".

European Commission's Joint Research Centre, Ispra, Italy. 25-26 October 2018

"Expert meeting on the Development of the Guidance Document on the Adaptation of the "In Vitro micronucleus assay (OECD TG 487) TGs for Testing of Manufactured Nanomaterials". European Commission's Joint Research Centre, Ispra, Italy 29-30 January 2019

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

There were several projects launched in 2018 with significant relevance to the work of WPMN. For comprehensive information on ongoing and launched projects, calls and meetings, including the **Malta initiative**, go to [Nanosafety Cluster](#) website, but there are further details below:

Based on the call [NMBP-13-2018 - Risk Governance of nanotechnology \(RIA\)](#)) three projects were launched:

1. **Nanorigo** = Establishing a Nanotechnology Risk Governance Framework: <https://cordis.europa.eu/project/rcn/220129/factsheet/en>
2. **Riskgone** = Risk Governance of Nanotechnology : <https://cordis.europa.eu/project/rcn/220127/factsheet/en>
3. **Gov4nano** = Implementation of Risk Governance: meeting the needs of nanotechnology: <https://cordis.europa.eu/project/rcn/220380/factsheet/en>

Two projects were launched within the call [NMBP-14-2018 - Nanoinformatics: from materials models to predictive toxicology and ecotoxicology \(RIA\)](#) :

4. **Nanoinformatix** = Development and Implementation of a Sustainable Modelling Platform for NanoInformatics: <https://cordis.europa.eu/project/rcn/220833/factsheet/en>
5. **Nanosolveit** = Innovative Nanoinformatics models and tools: towards a Solid, verified and Integrated Approach to Predictive (eco)Toxicology: <https://cordis.europa.eu/project/rcn/219995/factsheet/en>

There are three research calls which fit with **Malta Initiative**: already closed NMBP-15-2019: Safe by design, from science to regulation: metrics and main sectors (RIA), proposals currently under evaluation, NMBP-16-2020: Safe by design, from science to regulation: multi-component nanomaterials (RIA), and NMBP-34-2019: In support of documentary standards (CSA) – so called **Malta II**: <https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/topic-details/nmbp-34-2019>

In addition, two upcoming calls have been announced that might be of interest: DT-NMBP-04-2020: Open Innovation Test Beds for nano-enabled bio-based materials (IA)DT-NMBP-06-2020: Open Innovation Test Beds for nano-pharmaceuticals production (IA)

*Acronyms for the [type of the project](#): RIA-Research and Innovation Actions;IA-Innovation Actions, RIA-, CSA-Coordination and Support Actions

1.5.5. Additional Information

The [EUON](#) (EU Observatory on Nanomaterials) was launched already in June 2017 but has in 2018 received very important upgrades, in particular integration of the NanoData nanotechnology knowledge base dataset, and the partial integration of the eNanoMapper, the platform with data and tools for nanomaterial risk assessment. The observatory aims at collecting information on the safety of nanomaterials and making it available to the public. ECHA is continuously working on the development of new content and databases to the EUON.

1.6. Finland

1.6.1. National developments on human health and environmental safety

Finland is a member of the EU and accordingly follows the EU regulations. Finnish Safety and Chemicals Agency (Tukes) as a Competent Authority for chemicals (REACH, CLP) and biocides regulations takes part in the nanomaterial expert working group of the European Chemicals Agency.

The Ministry of Health and Social Affairs coordinates since 2011 an official discussion forum on nanotechnology in order to follow and participate in the national and international discussions.

Finland as a member of the UN ECOSOC Sub-Committee of Experts on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) has actively participated in a task regarding the applicability of GHS to nanomaterials. In order to directly examine the applicability of the existing GHS criteria to nanomaterials using available data, a project on 'The applicability of the GHS classification criteria to nanomaterials' is currently ongoing. The project is conducted under the Nordic Chemical Group (a working group operating under the auspices of the Nordic Council of Ministers). The aims of the project are to i) evaluate data from the WPMN dossiers and other sources (e.g. the NanoReg project, the NanoSafety Cluster project and REACH registrations) for four selected nanomaterials (single-walled carbon nanotubes, zinc oxide, silicon dioxide and silver), ii) to assess the (non-) applicability of the current GHS classification criteria for the data and to iii) discuss whether the criteria for classification are fulfilled for the specific human health hazard classes. The scope of the project is to support the work of the GHS Sub-committee with regard to making review of the applicability of the GHS classification criteria to manufactured nanomaterials. The findings from this project are planned to be assessed and reported to the GHS Sub-Committee in 2019.

1.6.2. Activities initiated to implement the OECD Council Recommendation

The Finnish Institute of Occupational Health (FIOH) is engaged in a new project proposal launched by Poland (Nofer Institute of Occupational Medicine, NIOM) for the development of a Guidance Document on the adaptation of the OECD TG 474 Mammalian Erythrocyte Micronucleus assay for nanomaterials. The new proposal was submitted to the OECD WPMN by December 2018, and was discussed at the WPMN meeting in Paris, on February 2019. Thereafter, FIOH has supported NIOM in modifying the proposal according to the comments received. The proposal has been resubmitted to the OECD WPMN.

FIOH has also positively responded to the invitation launched by the Joint Research Centre (JRC) to take part in the development of the Guidance Document on the adaptation of the in vitro micronucleus assay (based on the current OECD TG 487). This activity is included within the OECD project 4.95 (Guidance Document on the Adaptation of In Vitro Mammalian Cell Based Genotoxicity TGs for Testing of Manufactured Nanomaterials) led by JRC. FIOH attended the Expert Workshop organized by JRC in Ispra on January 2019, has become a member of the following-up management team, and has taken part on a video conference organized in March 2019.

1.6.3. Developments related to good practice documents

FIOH is a member in CEN standardization committee TC 137, Assessment of workplace exposure to chemical and biological agents. The standardization work in the working group 3 (WG3 Particulate matter) has been very active in the field of assessing the safety of nano related work. Recently, some new standards have already been published, and currently several standards and technical specifications are under construction in the field of nano safety.

VTT (Technical Research Centre of Finland) is contributing as an expert to the new work items in ISO TC 229 WG2, where guidance for characterizing cellulose nanocrystals and nanofibrils are currently being prepared.

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

FIOH takes part in the following research programmes:

- The EU funded H2020-project **EC4SafeNano** (No. 723623) aims at developing a distributed centre for the risk management and safe innovation for nanomaterials and nanotechnologies. The objectives are to understand the needs of the different stakeholders and to identify the resources of the service providers, provide solutions and finally develop a business plan for the self-sufficient centre. In this project, FIOH is especially responsible for the work aiming at addressing the stakeholder needs, and in the development of international cooperation. Duration of the project Nov 2016-Oct 2019.
- The EU funded H2020-project **NECOMADA** (No. 720897) aims at developing nano-enabled conductive materials compatible with volume manufacture of hybrid and large area electronics. FIOH is responsible for chemical safety issues, mainly related to nanomaterials, of the development process, to ensure workers health and safety. FIOH will also provide guidance for legislation involving the utilization of nanomaterials. The duration of the project is Jan 2017-Dec 2019.
- The EU funded H2020-project **caLIBRAte** “Performance testing, calibration and implementation of next generation System-of-systems Risk Governance Framework for nanomaterials” (No: 686239) will establish a versatile next-generation nano-risk governance framework for assessment and management of human and environmental risks of manufactured nanomaterials (MN) and MN-enabled products. FIOH participates in the identification and evaluation of human risk assessment models at the different stages of innovation process. Moreover, FIOH has been involved in gathering, evaluating and generating hazard and exposure data required for the performance testing, demonstration and use of the nano-risk governance framework.
- FIOH has also continued working in the EU-funded H2020 project **SmartNanoTox**, where our task has been to the pulmonary study toxic effects of nanomaterials.
- Throughout 2018, FIOH has proceeded with its research activities on the toxicological assessment of **different types of nanocelluloses** within a project funded by The Finnish Work Environment Fund (Työsuojelurahasto, TSR). A new TSR-funded project focused on the identification of the cancer risk of nanomaterials, concentrating on carbon nanotubes, started in January 2018.

- From the beginning of 2019, FIOH is involved in two new EU H2020 projects, **NANORIGO** and **NanoInformaTIX**, focused on the development of a European Risk Governance Framework for Engineered Nanomaterials, and a Sustainable Informatics Framework for the risk assessment of nanomaterials, respectively.

VTT takes part in the following research programmes:

- VTT coordinates the EU funded H2020-project **NanoTextSurf** (No. 760601), where cellulose nanomaterials are used to create nanotextured or nanostructured surface on substrates by thin surface treatment for membranes, protective textiles, friction pads and abrasive materials. As part of sustainability tasks, consortium partners will make exposure measurements and evaluate occupational safety risks at VTT's and industrial partners' pilot facilities, where nanocelluloses are used as different coating formulations. Duration of the project Nov 2017-Oct 2020.
- VTT works in the EU funded H2020-project **INN PAPER** (No. 760876). Nanocelluloses are studied in paper-based electronics, which are targeted to replace plastic material in sensors and to be used in the food, security and medical sectors. The food and medical sector applications are sensors in the packages without any contact to food or medicines. Sustainability studies included in the project are focused on environmental management of electronic waste and re-use issues. Duration of the project Jan 2018-June 2021.

1.6.5. Additional information

As part of the next EUROTOX 2019 meeting, FIOH will organize an EC4SafeNano-sponsored symposium on *Promotion of safe nanotechnology through global networking* (<http://eurotox-congress.com/2019/>).

FIOH will also organize a national seminar on nanosafety, which will be held in September 2019 in Helsinki, Finland. The seminar will be open for all the stakeholders related to engineered nanomaterials.

1.7. France

1.7.1. National developments on human health and environmental safety

ANSES: Investigation of new approaches for a reliable testing of the absorption of nanomaterials *in vitro* across epithelial barriers (activity not included in a funded project).

HCSP (Haut Conseil de Santé Publique): Opinion regarding the management measures to be implemented for populations living near sites producing and handling nanoparticulate titanium dioxide (NPs TiO₂) as well as towards workers (<https://www.hcsp.fr/Explore.cgi/AvisRapportsDomaine?clefr=663>).

The HCSP made the following recommendations:

- Protection and medical monitoring of workers handling nanomaterials, in particular pregnant women and women of childbearing age

- Application of workplace good prevention practices concerning the production, handling storage, conditioning, transportation and integration of TiO₂ NPs in end-product, as well as for end of life process.
- Protection of residents around industrial sites (TiO₂ NPs production and handling)
- Development of measurement and monitoring of occupational and environment exposures
- Elaboration of occupational and environmental exposure limit values for TiO₂ NPs
- Extension of the mandatory declaration in the R-Nano database to all products containing nanoscale substances with a minimum number of 10% as NPs, and accessibility of this database for all agencies that assess risks of nanomaterial;
- That manufacturers and importers of TiO₂ NPs include studies on their reprotoxic potency to document their dossier in the framework of the REACH procedure;
- Strengthening of prevention agencies (INRS, Santé Publique France, INERIS, ANSES) regarding their expertise on NPs.
- Supporting research on mutagenesis, carcinogenesis and reprotoxicity of TiO₂ NPs.

INRS: Ongoing studies are dedicated to the prevention of occupational risks associated with manufactured nanomaterials:

- Five toxicological studies (mainly conducted by inhalation in animals),
- Five studies on the characterization of occupational exposures,
- A study on collective protection devices (filtration).

In 2019, INRS is also going to start a major epidemiological study: a study of biomarkers of early effects related to occupational exposure to amorphous nanostructured silicas.

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 contains now more than 1173 measurements and synthesis analysis coming from 750 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.

INERIS & UCO, within the NanoReg2 project and in collaboration with INIA(Spain), have conducted studies on the grouping methodology of NPs for ecotoxicity endpoints (Algae, daphnia, mussel, fish cell lines). The data are currently being evaluated.

Ministry for an Ecological and Solidary Transition has developed and put in place a good practices guidance for classified installations producing or using manufactured nanomaterials where operators are expected to use the best available technology at an economically and technically viable cost on their sites to reduce impacts and forestall risks related to their facilities. This document is aiming to give an overview of practices on process effluents treatment as well as guidance on storage and waste management. This guidance, having more than 2 years of feedback in its use, was translated in English with the support of the OECD WPMN secretariat. This guidance is now circulating among WPMN delegates for expression of interest in developing an OECD guidance document for operators of classified installations for environmental protection which are producing or using nanomaterials.

1.7.2. Activities initiated to implement the OECD Council Recommendation

LNE registered as participant for the OECD test guideline on particle size distribution for 5 techniques (AFM, SEM, DLS, sp ICP-MS and ESI-DMA).

INERIS: Following the submission of the project in 2018 to the WPMN and its support, France with Denmark had proposed a SPSF to the WNT for a new test guideline on the “Determination of the Dustiness of Manufactured Nanomaterials”. The project is currently being evaluated by National Coordinators and will be discussed during the 31st WNT meeting

France (INERIS) and Spain had proposed a project on the “Adaptation of OECD Test Guidelines 201, 202 and 203 for the determination of the ecotoxicity of Manufactured Nanomaterials (MNs)”, to be discussed during the 19th WPMN. This project aims at completing the draft “GD on aquatic and sediment toxicological testing of MNs” under development and to describe pragmatic and validated protocols that ensure the relevance of the results obtained. Simultaneously, a technical proposal has been made under the Malta 2 project to support the experimental work and the validation exercise linked to this project.

1.7.3. Developments related to good practice documents

initiative aiming to develop a guidance document to determine the nanofraction of additive integrated in food product by using electron microscopy (EM) and sp ICP-MS as complementary techniques. E551, E171, E172, E174, E175 additives are more particularly targeted and a focus will be made on the sample preparation step (extraction of additives from the food matrices).

LNE with its European partners (BAM, PTB, LGC, VSL, SMD) launched the nPSize EMPIR project which aims to assess the performances of various measurement techniques (SEM, SAXS...), deliver to users reference materials and develop methods and models to improve the metrological traceability chain and comparability of nanoobjects size distribution characterization. Methodologies will be transferred in 2021 to European standardization body CEN/TC 352 Nanotechnologies.

France (INERIS), The Netherland (RIVM) and BIAC are involved in the 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 », developed under the auspices of the WPMN. The objectives of this project are to:

- develop a working definition for a safer innovation approach concept, including the Safer-by-Design concept;
- develop inventories of risk assessment tools and frameworks to a) help industry implement a ‘Safer Innovation Approach’ for NMs and nano-enabled products and b) to help regulators anticipate regulatory challenges posed by innovations such as NMs and nano-enabled products.

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

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 initiated the NanoDeTox project (French national funding / ADEME) to examine characteristics and toxicity of nanoparticles that remains within combustion residue after thermal degradation of

nanocomposites. LNE continues its study on the impact of ageing on nanoobjects' release by thermal degradation of nanocomposites (containing nanomaterials as flame retardants) and contributed also 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 Release_Nanotox project (French national funding / ANSES). LNE concluded a study initiated three years ago on the identification of useful parameters to discriminate manufactured nanomaterials from natural ones in the environment (Seine water / Ag, TiO₂, CeO₂) by using element ratios tracking and study of different typical catchments (3 types = industrial, forestry and urban). Finally, LNE initiated a new project with IGFL regarding the development of a stable and validated aerosol generation system to support *in vivo* toxicity study of nano-pesticides (Paraquat + TiO₂) by the inhalation route.

LNE has launched a new project aiming to assess metrological performances and compare results provided by different techniques (SEM, SAXS, DLS, XRD) to characterize size parameters of nanoparticles in complex media (biological sample, consumer products, soot).

LNE has initiated an inter-laboratory comparison at the French national level in the frame of the Club nanoMétrologie (network, which gathers almost 400 members coming from academics and industry to share issues on nanomaterials characterization/metrology and launch different initiatives to help its members to progress on this topic / www.club-nanometrologie.fr). Around 30 participants using 10 different techniques are involved in this ILC on nanoparticles size characterization (ERM-FD304, E171, SiO₂ with two populations and different ratios). LNE is also participating to the ILC organized by RIKILT for the characterization of Au nanoparticles by A4F in the frame of the Horizon 2020 ACEnano project. Finally, LNE launched a new topic on nanoaerosol characterization and metrology issues within the Club nanoMétrologie with INRS, IRSN and CEA.

LNE put in place with NPL (UK) and University of Saragossa (SP) the *Validation Service* within the Graphene Flagship in order to offer industry high metrological quality services regarding characterization of graphene features and behaviour (in particular ageing and released during the life cycle of product).

ANSES: The unit of Toxicology of contaminants (ANSES Fougères) is involved in the H2020 project Riskgone on governance of nanomaterials, especially on *in vitro* genotoxicity and high throughput methods. Anses has a long experience on *in vitro* and *in vivo* genotoxicity assays with different types of substances including nanomaterials.

1.7.5. Additional Information

LNE organized in Paris on 29 March 2018 a Technical Workshop on nanomaterials applications in cosmetics (regulations, insights regarding on-going R&D activities on toxicity assessment and environmental exposure for cosmetics additives, characterization methodologies to verify labelling requirements...). LNE organized also the first session of a training aiming to help industry choosing the most suitable characterization technique to determine number size distribution of particles and be able therefore to answer regulatory requirements (labelling, REACH, French R-Nano register) on the basis of improved quality data.

LNE is participating in the NanoResp forum, a French initiative which aims to get all the different parties (industry, civil society, NGO, public institutions) around the table and discuss about the nanomaterials topic (performances, risk, metrology...). Three open meetings have been organized on 2018 (nano and food, graphene, occupational exposure) and a dedicated initiative on nano in food has been launched in order to find conditions for mutual trust. Additives producers and users, NGO, toxicologist, national metrology institute... are involved in this NanoAlim working group. LNE was invited to participate to the 2ND WORKSHOP 'NANO IN BELGIUM' 2018: OCCUPATIONAL HEALTH PROTECTION (1ST OCTOBER 2018) to stress the importance of metrology to address occupational issues on the basis of reliable data.

LNE joined the EC4SafeNano Center as an Associated Member.

INERIS is involved in the assessment of the environmental impregnation near industrial production facilities potentially emitting manufactured nanoparticles. In 2018, INERIS has conducted field campaigns around three incineration plants.

1.8. Germany

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

The Federal Ministry for the Environment, Nature Conservation and Nuclear Safety (BMU) continues the national stakeholder dialog – The NanoDialog of the Federal Government. In 2022, the BMU plans an international conference in cooperation with the OECD.

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 (<https://www.bmbf.de/foerderungen/bekanntmachung-1432.html>). The evaluation of the pre-proposals has been completed and the consortia were invited to submit full proposals. The first projects are intended to start on the first of January 2019.

Germany intensifies its collaboration 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 focus of the Greek-German collaboration (<https://www.bmbf.de/foerderungen/bekanntmachung-1282.html>) lies on nano-carbons and applications in membranes and porous materials. The collaboration with Israel is intended to strengthen the technology transfer in the field of applied nanotechnology (e.g. bio-medical technologies, nano devices for sensors, nano-based energy resources, see <https://www.bmbf.de/foerderungen/bekanntmachung-1271.html>). Six projects have already started in the first half of 2018.

The cluster meeting of the two BMBF funding initiatives NanoCare & ERA-Net SIINN has taken place in the Dorint Hotel Neuss, Germany on the 17th and 18th of September 2018, just before the international conference NanoTox2018. During this meeting and the NanoTox2018 the latest results of the funded projects were presented as talks and as posters.

In August 2018 the BMBF published selected results on the effects of synthetic nanomaterials on humans, *Nanomaterialien im Alltag* (“Nanomaterials in Daily Life”). Also interviews with project managers from finished projects were added to this publication. Extensive information and a realistic assessment of the possible risks of nanomaterials for the general public have summarised www.bmbf.de/pub/Nanomaterialien_im_Alltag.pdf

1.8.1. National developments on human health and environmental safety

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

In 2018 the substance evaluation of the nanoforms of zinc oxide under the European Chemicals legislation REACH, evaluated by the German Environment Agency (UBA) together with the German Federal Institute for risk assessment (BfR) in 2017, was continued. <https://echa.europa.eu/de/information-on-chemicals/evaluation/community-rolling-action-plan/corap-table>

- a risk assessment decisions, including the type of: (a) nanomaterials assessed ; (b) testing recommended; and (c) outcomes of the assessment;
- BfR prepared a Draft Decision within the Substance Evaluation process under EU REACH for zinc oxide in nanoform due to human health concerns
- BfR prepared a Proposal for Harmonised Classification under EU CLP for fibre-like multi-walled carbon(nano)tubes as respiratory carcinogen

1.8.2. Activities initiated to implement the OECD Council Recommendation² (e.g. regulatory changes, guidance, voluntary, etc.)

Federal Environment Agency (Umweltbundesamt, UBA)

The German Environment Agency (UBA) held an Expert Workshop for the harmonized development of OECD TGs and GDs for Nanomaterials behaviour and fate in the environment at the 23rd-24th of August 2018.

Aim of this core expert meeting was to technically discuss synergies and overlaps for the ongoing and planned TG/GDs development on solubility and dissolution, dispersion stability and transformation in the environment and to promote harmonisation of these activities by enhanced cooperation and communication.

At the meeting project leading experts of the OECD TG No. 318, the (Draft) TG on Dissolution Rate in Aquatic Media (led by US), the (Draft) GD on Dissolution and Dispersion Stability in Environmental Media (led by DE), and the planned OECD TG on aquatic (environmental) transformation of NM (led by AT) were present or took part via video conference. Furthermore, the scope and timeline of the planned OECD TG on solubility and dissolution rate of NM in water and relevant synthetic biologically media (led by DK) was presented.

² [Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials](#)

Central results of the workshop were recommendations for a possible adjustment of the upcoming validation test for the draft TG on Dissolution Rate in Aquatic Media and the finalisation of the draft. It was also proposed to develop in longer term a standardised method for the determining dissolution rate for environmental media in a dynamic system in addition. For the draft GD on Dissolution and Dispersion Stability in Environmental Media it was noted which aspects need to be further addressed and who could deliver input: e.g. interpretation and presentation of data for risk assessment and test strategies, mid-term guidance for the determination of dissolution via dynamic method, hetero-agglomeration, derivation of attachment coefficient, data use for exposure modelling.

1.8.3. Developments related to good practice documents

Two standardization projects ‘ISO/DIS 21363 Nanotechnologies -- Measurements of particle size and shape distributions by transmission electron microscopy’ and ‘ISO/DIS 19749 Nanotechnologies -- Measurements of particle size and shape distributions by scanning electron microscopy’ with significant contributions of BAM, PTB and large-scale German nanoparticle manufacturers are in the final phase of development under ISO/TC 229 Nanotechnologies.

1.8.4. 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” will continue to be funded within the frame of the German funding programme “From Material to Innovation” (2015-2025). Selected results of the projects were presented on the international conference NanoTox2018 (9th International Conference on Nanotoxicology) at the Dorint Hotel Neuss, Germany between the 18th and 21st of September 2018.

The projects of the new national BMBF funding activity “NanoCare4.0 – material innovation for safe application” are intended to start in the beginning of 2019.

In the frame of the ERA-NET SIINN (Safe Implementation of Innovative Nanoscience and Nanotechnologies; coordinated by Germany, completed 2015) the projects of the second and third call are still ongoing and are continuously governed by the SIINN Call Office. The projects are also presented on the DaNa platform (see below).

Here, two projects are given as examples:

- The multidisciplinary project “FENOMENO - Fate and effect of wastewater-borne manufactured nanomaterials in aquatic ecosystems” investigates the impact of end-of-life manufactured nanomaterials (MNM) on aquatic ecosystems in a realistic scenario (Lake Mondsee) and in several laboratory studies to develop and provide an early warning system and a robust risk assessment for the safe implementation of MNMs.
- The project “NanoToxClass - Establishing nanomaterial grouping / classification strategies according to toxicity and biological effects for supporting risk assessment” (www.nanotoxclass.eu) aims to establish nanomaterials (NM) grouping approaches with a focus on NM inhalation. NMs can be produced in numerous different variants by modifying for instance size, charge or surface coating. For regulatory purposes, each variant has to be

tested individually, rendering the assessment time and cost intense. Thus, the establishment of NM grouping approaches has gained huge interest recently.

The web-based knowledge and data platform ‘DaNa – The Knowledge Platform on Nanomaterials’ will continue to be funded by BMBF (www.nanopartikel.info; www.nanoobject.info). The website shows the research results from the German funded projects on safety with a special emphasis on nanosafety.

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

Federal Environment Agency (Umweltbundesamt, UBA)

A research project UBA entitled “Development of a method for the investigation of bioaccumulation of manufactured nanomaterials in filtering organisms” conducted on behalf of UBA was finalised. The project was a follow up activity to the “Horizontal Meeting on ecotoxicity and environmental fate of nanomaterials” of OECD WPMN (Berlin, 2013) at which experts recommended to explore the relevance and potential of alternative test organisms to investigate the potential of bioaccumulation of nanomaterials next to fish. Filtering and sediment organisms were identified as potential target organisms. The aim of the project therefore was to develop a robust, relevant and reliable test method for determining the bioaccumulation of nanomaterials in mussels (*Corbicula fluminea*). Applying the new method, the bioaccumulative potential of nanomaterials of differing chemical nature was investigated (Ag, TiO₂, polystyrene). Limitations and strengths of the methods for determining bioaccumulation endpoints were investigated and relevant analytical data and methods for accurate data interpretation were identified. A protocol for test conduction was drafted and the further steps for improvement and verification for applicability were evaluated. The final report will be available for download at: <https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/research-development-projects>

In summer 2018 UBA launched a new research project to accompany the development of a potentially new OECD Test Guideline for the determination of bioaccumulation in *Hyalella azteca*. Within the CEFIC-LRI Project ECO 40 (Investigations on the bioconcentrations of xenobiotics in the freshwater amphipod *Hyalella azteca* and inter-laboratory comparison of a new BCF test protocol) a test protocol for testing of bioaccumulation in crustacea *Hyalella azteca* was developed on the basis of five lipophilic substances and a validation ring test will be performed. The UBA project will investigate the applicability, resilience, and limitation of this non-vertebrate test method for highly lipophilic organic substances and nanomaterials. If the method is applicable, a proposal will be prepared on how the method can be applied to these substances and, if relevant, which adaptations are needed. A draft test guideline will be developed.

<https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/research-development-projects>

Also in summer 2018 UBA launched a survey on relevant **studies and research projects regarding the detection of nanomaterials in different environmental compartments and deduction of need for action regarding method development**. Content of the survey is the analyses of recent scientific studies, research projects and relevant activities of standardization boards regarding the availability and development of suitable detection and analysis methods for nanomaterials in the different environmental compartments. Based on this analysis, the survey will

provide a gap analysis and deduce short term, midterm and long term actions required for method development and standardization. The survey will be finalized in April 2019 and it is intended to publish the report on <https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/research-development-projects>

In 2019, UBA will launch a new research project aiming to promote the knowledge on **advanced materials on the European market and their relevance for the risk assessment in the context of chemical safety regulations**. Initially within this project, a survey on advanced materials on the European market and its (future) application will be conducted providing information for following topic conferences. In the topic conferences stakeholders will discuss in order to address the following objectives: to identify advanced materials and their (future) applications, to identify challenges for appropriate risk assessment and safe use in the framework of chemical safety and to deduce recommendations for actions to assure safety of human and environment in the framework of chemical safety. The project is intended to start in May 2019 with a duration of 29 months. Topic conference are scheduled for autumn/winter 2019, summer 2020 and spring 2021.

In 2019, UBA also intends to launch a research project focusing on the **development of a static and a dynamic standard method to determine solubility and dissolution rate of nanomaterials in environmental media**. Both methods are intended for inclusion in an OECD Test Guideline. The activity will be closely related to the WNT project 3.9 (lead: DE) and 3.10 (lead: US) as well as the proposed WNT project on a GD/TG on solubility and dissolution rate of nanomaterials in water and biological relevant media (lead DK, co-lead DE) as well as the proposed WNT project on a GD/TG on transformation of nanomaterials in aquatic environment (lead: AT). Therefore, a close cooperation for harmonized development is envisaged with the aim for a meaningful integration into the mentioned activities. However, if necessary, also an update of the draft GD on dissolution and dispersion stability in environmental media will be necessary based on the outcomes of this activity.

Within the project, a proof of principle of well-established methods with 3-4 nanomaterials in environmental relevant media is intended. The final test protocols for both methods will be validated in an international round robin and the draft and final versions of the test protocol for inclusion in a TG will be developed based on the inputs from WPMN and WNT. The project is intended to start in October 2019 with a duration of approx. 3 years.

Federal Institute for Materials Research and Testing (BAM)

The EMPIR nPSize project '*Improved traceability chain of nanoparticle size measurements*' with BAM, LNE, LGC, PTB, SMD, VSL, CEA, DIN, Pollen and University of Turin as partners has started on 1st of May 2018 under the coordination of BAM, for a period of three years. This project will develop measurements procedures, reference nano-materials and data modelling to improve the traceability chain, comparability and compatibility of nanoparticle size and shape measurements by electron microscopy (SEM, TSEM and TEM), atomic force microscopy (AFM) and small-angle X-ray scattering (SAXS). nPSize will eventually contribute to standardisation

within the framework of CEN/TC 352 “Nanotechnologies”, ISO/TC 229 ‘Nanotechnologies’, ISO/TC 24/SC 4 ‘Particle characterization’ and ISO/TC 201/SC 9 ‘Scanning probe microscopy’.

1.8.5. Additional Information

Federal Environment Agency (Umweltbundesamt, UBA)

UBA publishes data sheets of applications of nanomaterials for which benefit for the environment are expected. The data sheets focus on the description of application and potential impact on environment and human health. Already published Fact Sheets are available at the UBA website: <https://www.umweltbundesamt.de/en/topics/chemicals/nanotechnology/good-to-know>

A new Fact Sheet dealing with the use of nanomaterials in plastic packaging was published in August 2018 („Einsatz von Nanomaterialien in Kunststoffverpackungen”, <https://www.umweltbundesamt.de/publikationen/einsatz-von-nanomaterialien-in>). This Fact Sheet is currently available in German only, however a version translated to English is under preparation and will be available at the above mentioned webpage once finalised.

Federal Institute for Materials Research and Testing (BAM)

On 14th and 15th of May 2018 the ‘Nano-Workshop on Reference Nanomaterials – Current situation and needs: development, measurement, standardization’ has been organized by BAM and PTB in Berlin Adlershof. The scope of the workshop was to provide a forum for discussion on progress in development, characterization and application of reference nanomaterials. Results of recently finished national and international research projects have been presented and the need for future developments has been addressed by more than 50 contributions from 11 countries, see <https://www.ptb.de/cms/en/ptb/fachabteilungen/abt5/dates/nanoworkshop2018.html>.

1.9. Italy

1.9.1. National developments on human health and environmental safety

ISS attended the ECHA-NMEG-12 meeting and the back to back “Workshop on supporting the implementation of the REACH information requirements for nanomaterials” discussing and providing an update on scientific and technical issues related to ECHA’s preliminary proposal on how to implement the concept of nanoform and sets of nanoforms and on how to fulfil the characterisation requirements of REACH Annex VI (Information to submitted for general registration purpose).

1.9.2. Developments related to good practice documents

The Italian Workers Compensation Authority (INAIL) has recently published the volume “Nanomaterials exposure in the workplace” (Italian language). It describes an innovative methodology based on a semi-quantitative and multi-parametric approach for assessment, management, and communication of risk in work environments (as research laboratories, production areas) using nanomaterials. The volume represents one of the main input of the project NanoLab (www.nano-lab.it). English version of the volume is planned.

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

A “Multidisciplinary Unit on Nanotechnologies and Nanomaterials” has been established at the Italian National Institute of Health (ISS), coordinated by the Environment and Health Department. This Unit involves different expertise to better identify the potential risks and benefits for human health and environment related to the use of nanomaterials. The final goal will be to realize a National network in cooperation with the Ministry of Health, and involving different stakeholders.

As partner of the NaNoReg2 consortium, Italy actively participated to the Joint Scientific Conference on Grouping of Nanomaterials and to the Expert Meeting on Physico-Chemical Parameters hosted by OECD in September 2018.

The Italian web platform on Nanotechnologies (<https://nanotecnologie.iss.it>), realised at ISS in the framework of RInnovaReNano project as a guide and a focal point concerning regulatory and safety aspects of nanomaterials, has been presented during the EC4SafeNano Day held in Grenoble in November 2018.

Italy is partner of the EU H2020 project Gov4nano “Implementation of Risk Governance: meeting the needs of nanotechnology” started the 1st of January 2019. The project is aimed to develop the first implementation of a future-proof operational Nano Risk Governance Model addressing the needs of the transdisciplinary field and innovative (and key enabling) character of nanotechnology. Italy is also partner of the EU H2020 project RiskGone “Risk Governance of Nanotechnology”.

The Italian Ministry of Health funded a preliminary study for the development of a Guidance Document on “Integrated *in vitro* approach for intestinal fate of orally ingested nanomaterials”. This project proposal has been presented by Italian delegation during the 19th WPMN (ENV/CHEM/NANO(2019)5/ADD1). ISS is in charge of the study.

In the framework of NanoLab project, AIRI (Italian Association for Industrial Research) realised a survey providing an updated overview on R&D figures, nanomaterials, research, application, and market areas as well as main priorities for responsible development of nanomaterials and nanotechnologies. This survey verify the applicability in several context of the methodological approach developed by the NanoLab project.

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 firstly in 2010 (only in Japanese). Such information was voluntarily provided and annually updated by the manufacturers. METI publicised the updated information in 2018.

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 now DIS voting was approved. JISC also jointly (with ANSI) leads a project group 21 “Measurements of particle size and shape distributions by scanning electron microscopy” (IS 19749), and now DIS voting was also approved. JISC leads “Analysis of nano-objects using asymmetrical-flow and centrifugal field-flow fractionation” and now this was published. JISC 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 "Guide to Evaluating Emission and Exposure of Carbon Nanomaterials (carbon nanotubes and graphenes)" in April 2018 that is available on the website: <https://en.aist-riss.jp/assessment/6315/>.

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

- 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;
- Current or future activities on nanotechnologies on a multilateral basis, including with non-OECD countries.

METI completed a domestic inter-laboratory comparison study on the procedure of intratracheal instillation which AIST and five laboratories participated in. Reproducibility of the distribution of instilled nanomaterials to the lung lobes and short-term inflammatory responses was examined. Regarding the formerly-proposed feasibility study on in vivo short-term exposure methods for inhalation toxicity testing of manufactured nanomaterials, the scope of project is under reconsideration.

METI leads a 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 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 2018, four research projects, including a basic research on development of methods for evaluating hazard and disposition of nanomaterials on human health, are progressing.

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 2018 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), experimental attempts are being conducted in JFY 2017-18 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

With the enforcement of Consumer Chemical Products and Biocides Safety Act in January 2019, the Ministry of Environment (MOE) has prescribed in its Ordinance to submit evaluation reports on impacts of nanomaterials contained in biocidal products on humans, animals and the environment. In case of biocidal products containing nanomaterials, the name of a substance should be labelled with the word ‘nano’ in brackets before the name of a substance.

1.11.2. Activities initiated to implement the OECD Council Recommendation³ (e.g. regulatory changes, guidance, voluntary, etc.)

Korea Research Institute of Standards and Science has conducted relevant researches as follows:

- a. OECD test guideline development for particle size and size distribution of nanomaterials (TG110)
 - KRISS (Korea Research Institute of Standards and Science) provide two types of CRM silica nanoparticles (20 nm & 50 nm size) and their results of XPS and XRD. KRISS will participate in round robin test for determination of size and size distribution of fibres and particles using SEM, TEM, DLS and DMAS. This round robin test will take place in winter 2018 – spring 2019.
- b. OECD TG 442E: In vitro skin sensitisation (In Vitro Skin Sensitisation assays addressing the Key Event on activation of dendritic cells on the Adverse Outcome Pathway for Skin Sensitisation)
 - KRISS will participate in this project.
- c. OECD test guideline development for determination of the (volume) specific surface area of manufactured nanomaterials
 - KRISS will participate in round robin test using the BET technique.

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 established the goal, vision, and implementation for research programmes of nanomaterials.

³ [Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials](#)

The Ministry of Environment has been participating in the OECD frame project on physico-chemical properties, and presented the lifecycle assessment results of nanomaterials in titanium dioxide-containing products as a case study. In particular, in September 2018 when the OECD WPMN expert meeting on physico-chemical parameters framework for the risk assessment of nanomaterials and the scientific workshop on grouping of nanomaterials were jointly held, we demonstrated study outcomes on grouping for read-across outcomes for the hazard assessment of 1,500 manufactured nanomaterials and exchanged opinions with participating experts.

Occupational Safety and Health Research Institute, affiliated body of Korea Occupational Safety and Health Agency has conducted relevant researches as follows:

- a. Research on exposure assessment of nanomaterials generating nanoparticles in the laboratory (II)
 - Study about the accuracy comparison and limitations of various instrument nano particles in laboratory such as particle counts, TEM analysis
- b. Study on providing the toxicity information about the carbon based nanomaterials
 - Provide up-to-date information about the classification, characterization, read-across study, national/international regulation status, and tools for risk assessment of carbon-based nanomaterials
- c. Ultrafine particle, chemical and metal concentration from 3D printers in real 3D printing sites
 - The purpose of the study is that we measure emitted UFPs, VOCs, and metal from rear 3D printers (FDM, SLA, DLP, SLS, etc) in rear sites
- d. Study on the generation and characterization of metal oxide aerosols
 - Nano-sized and micro-sized metal oxides (Al₂O₃, TiO₂, SiO₂) were generated mists or dusts and compared the characterization of the aerosols.

Ministry of Food and Drug Safety (MFDS) has conducted safety studies on manufactured nanomaterials since 2005. We focused on providing toxicity data to evaluate safety of nano materials. Research areas encompassed a wide range of safety issues related to nanomaterials, such as ZnO and SiO₂, including toxicological evaluation, ADME (absorption, distribution, metabolism and excretion), kinetics, and physico-chemical properties. Moreover, MFDS participated in the joint interlaboratory study on CFE (Colony Forming Efficiency) assay. MFDS conducted research on the effect of ionization on toxicity of nanomaterials and recently conducted further study on domestic application of CFE assay. MFDS is currently conducting skin sensitization research on nanomaterials including NiO based on the OECD 442D guideline in 2018. Further research on additional nanomaterials is also planned in 2019.

In the field of nanofood, MFDS has conducted the study on absorption evaluation system for nano based foods using non-animal model.

1.12. Malaysia

1.12.1. National developments on human health and environmental safety

National Nanotechnology Centre (NNC) under the Ministry of Energy, Science, Technology, Environment and Climate Change (MESTECC) serves as the National Focal Point for the coordination of research, development and all related activities including awareness of nanotechnology in Malaysia. NanoMalaysia Berhad was incorporated as a company limited by

guarantee (CLG) by the government to act as a business entity entrusted with nanotechnology commercialisation activities.

1.12.2. Activities initiated to implement the OECD Council Recommendation

Malaysia being full adherent to the OECD MAD system acknowledges the inclusion of nanomaterials in the scope. Test facilities have been made aware on some of the existing OECD Test Guidelines which may need to be adapted to take into account the specific properties of nanomaterials.

1.12.3. Developments related to good practice documents

Department of Occupational Safety and Health, under the Ministry of Human Resource Malaysia has published a Guideline on Control and Safe Handling of Nanomaterial. This guideline provides information and recommendations on handling of nanomaterials at workplace.

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

Current or future activities on nanotechnologies on a multilateral basis, including with non-OECD countries

- i. On 10-16 April 2018, NNC participated in the 1st International Nanotechnology Olympiad hosted by the Iran Nanotechnology Innovation Council at Pardis Technology Park, Tehran. Malaysian team won a gold medal for the ‘Science and Technology’ category.
- ii. On 29 October to 2 November 2018, NNC participated in the ISO/TC229 Nanotechnologies’ 21st Plenary Meeting and Related Meetings hosted by Standards Malaysia in Kuala Lumpur.
- iii. On 12-16 November 2018, NNC and UNITAR organized a Nanosafety Course based on UNITAR’s e-Learning module in Putrajaya, Malaysia. Dr Vladimir Murashov (NIOSH US) and Dr Peter Kearns (OECD) were the invited speakers. Dr George Kaarlaganis (UNITAR) delivered his presentations via Skype. A total of 60 participants from Malaysia, Thailand, Philippines and Vietnam attended the course.

1.13. Netherlands

- On 17-18 April 2018 the Netherlands organised a policy conference to establish EU agreements on how to create a future-proof approach to nanomaterials.
- The new EU research project GOV4nano will design and establish a well-positioned and broadly supported Nano Risk Governance Council. The project includes contributions to the work of the OECD via the Malta Initiative.

1.13.1. National developments on human health and environmental safety

On 17-18 April 2018 the Dutch Ministry of Infrastructure and Water Management in close collaboration with RIVM organised 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. Information on the speakers, reports and outcomes of this conference can be found at the ProSafe Results Repository [subpages](#).

The **NanoReg2** project (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, such as the Safe by Design scenarios and an overview of safety information needs. Furthermore, a workshop on the topic 'Regulatory Preparedness' was organised to openly discuss with various regulatory bodies the regulatory challenges posed by nanotechnology innovations. The workshop report can be found [here](#).

In 2014, the Netherlands started a **substance evaluation** of silver within the REACH process. The focus in this evaluation was on the environmental fate and toxicity of the nanoforms of silver in relation to ionic silver (silver nitrate). On 6 July 2016 the final decision on this substance evaluation was published on ECHA's website. In this decision further comparative testing was requested on nanoforms of silver and silver nitrate. The test results provided by Industry in response to the decision show that silver nitrate can be seen as a 'worst case' for the risk assessment of nanoforms of silver. On 14 December 2018 the conclusion document by the Netherlands has been published by ECHA on their website.

1.13.2. Developments related to good practice documents

In October 2018 the Technical Report (ISO TR 22019) "Considerations in performing **toxicokinetic studies** of nanomaterials" completed balloting. The last comments were resolved at the ISO TC229 meeting in Kuala Lumpur and the document will be submitted for publication in the beginning of 2019. A project group led by the Netherlands prepared this document. It provides an overview of the existing knowledge on toxicokinetics of nanomaterials. This document will be used as a basis for adaptation of OECD Test Guideline 417 (Toxicokinetics).

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 (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-portal linking different tested and 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 currently performed, 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 Nano Risk Governance Framework.

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

The main goal of the EU project **GRACIOUS** (January 2018 until June 2021) is to generate a science-based framework to enable practical application of grouping and read-across of nanomaterials. The project has developed a draft framework that has been presented at a workshop at the OECD and discussed with regulatory (ECHA, EFSA, OECD delegations), industrial and academic stakeholders. The comments are used to adapt the framework and target further research. The project will continue to seek input from 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** (refine-nanomed.com) had its 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. In the first year (2018) of the project a start was made for a white paper on regulatory aspects and needs, and safety testing of nanomedicinal products. A licence for the performance of animal toxicokinetic studies was obtained, and a “starter set” of assays for nanomedicine characterisation and determination of potential immunotoxicity was developed. Preliminary work was done on kinetic modelling at cellular and organ level to potentially replace or limit animal testing.

The EU-project **NanoFASE** (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 contributes to development of algorithms for quantifying the fate of nanomaterials in the aquatic environment, and is working on an update of 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 (ECHA-NMEG). The project results will also be input to the current efforts in nanospecific modification of the OECD guidance documents on testing of chemicals.

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

The new EU research project **GOV4nano** (start date January 1st, 2019) will design and establish a well-positioned and broadly supported Nano Risk Governance Council (NRGC). GOV4nano is coordinated by the RIVM (Dutch Institute for Public Health & the Environment). Partners from Europe (28 partners) and other regions (Korea, South Africa, US) are participating. Organising, connecting and engaging are key activities in Gov4Nano and its creation of a sustainable NRGC. Gov4nano will develop an *operational* trans-disciplinary Nano Risk Governance Model (NRGM) for nanotechnologies, building on an established governance framework developed by the International Risk Governance Council (IRGC). Engaging stakeholders (including regulators) to proactively address nanospecific safety and seek dialogue for joint activities. In order to support these activities, NRGC and its precursor project Gov4nano will engage with the broad variety of stakeholders across all relevant nano-disciplines (chemical, biocides, food and feed, pharma and medical devices and materials development) and draft a review on our knowledge progress over the last decade whilst initiating dialogue. To boost the quality of the dialogue it will create a platform for dialogues between stakeholders in a “trusted environment”, inclusive of civil society.

The NRG core business is to coordinate, guide and harmonise in order to overcome the fragmentation of current knowledge, information and needs over various sectors and disciplines (workers, consumers/patients, environmental safety) and to prepare the transfer of this knowledge. To that end, the NRG will be equipped with a self-sustainable NanoSafety Governance Portal (NSGP) consolidating state-of-the-art and progressive nanosafety governance tools including ones for dialogues and measuring risk perception. Major efforts will be towards requirements for data harmonisation and data curation to be defined and laid down in guidance on obtaining harmonised and standardised quality-scored data collections promoting a big data approach for nanotoxicology. Research activities will be initiated for regulatory sound knowledge in support of harmonised (OECD) guidance for characterisation and testing of nanomaterials.

An important part of the project contributes to the work of the OECD via the **Malta Initiative**. This work will focus on research and experimental work needed to adapt specific test guidelines for nanomaterials:

- Scientific basis for dissolution testing of nanomaterials (based on TG105) (TG)
- Identification and quantification of the surface chemistry (GD)
- Measuring the volume specific surface area (VSSA) of nanomaterials (TG)
- Evaluating the applicability of TG 442D in testing nanomaterials for skin sensitisation (TG)
- Dustiness testing for exposure and industrial risks (TG)
- Abiotic transformation of nanomaterials in environmental aquatic media (GD)
- Evaluating the applicability of TG 305 in testing the bioaccumulation of nanomaterials in fish (TG)

The Malta Initiative is aligned with procedures as determined by OECD. At WPMN 18 project proposals for the above mentioned GD/TG were approved by the WPMN.

The aim of the EU project **PATROLS** (www.patrols-h2020.eu, January 2018 until June 2021) is to establish and standardise 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. A workshop organised by the RIVM on the development of standard operating procedures was held on the 12-13 June 2018 in collaboration with GRACIOUS and under the umbrella of the NanoSafety Cluster WG C: Exposure & Hazard Assessment. A short report on the goal and results of the workshop has been published in the [NanoSafety Cluster Newsletter](#).

Within the **EC4SafeNano** project (ec4safenano.eu) 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 (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 set up the legal mechanisms to operate the centre after the end of the project, addressing the contractual relations, IPR issues, governance. In parallel initial steps were taken to build a business model and to design a business plan for a sustainable centre.

Research institute RIKILT is partner in the EU project **ACEnano** (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. 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 organised a meeting at Bilthoven, the Netherlands, to discuss and address the comments received during the consultation/review period. The document will be published as part of the [Environmental Health Criteria Series of WHO](#). OECD is involved in this endeavour as an observer. Publication of the document (expected in 2018) was delayed. Early 2018 the document was corrected by a WHO editor. In October and November 2018 the final editing and check of the document was done by a core group of the expert group led by Henk van Loveren. The document is now expected to be published early in 2019.

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 inhalation studies, IARC classified titanium dioxide as a possible human carcinogen (Group 2B, [IARC 2010](#)⁴). For the researchers this raised questions on potential effects after oral uptake, in particular 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 was published on November 2018 (H.A.A. Proquin: [Beyond the white: effects of the titanium dioxide food additive E171 on the development of colorectal cancer](#)). The next step is to investigate whether similar biomarkers (regulated genes or pathways) as those seen in the animal and *in vitro* studies can be found in humans after exposure to E171 or titanium dioxide nanoparticles. METC permission has been granted for performing an epidemiological intervention study. So far, funding has not yet been accomplished.

The EU **NanoSafety Cluster** (NSC, www.nanosafetycluster.eu) maximises 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

⁴ This is in line with developments within the EU, i.e. the proposal by RAC to classify TiO₂ as....

reorganised 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 NSC has developed activities to offer the extensive knowledge available for the Malta Initiative. The latter being an initiative by several European member states to support the OECD in its development/adaptations of technical guidelines and guidance documents to accommodate testing of nanomaterials.

1.13.5. Additional Information

The EU project **nTRACK** (www.n-track.eu), 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. RIVM is leading the work package on regulatory issues of nTRACK with the aim to achieve regulatory preparedness and safe innovation approaches for these types of innovative products.

At 12 months into the project, nanoparticles with the desired properties for imaging have been developed on lab scale and the project is working on a process to upscale the production. In addition, a meeting with the [Innovative Task Force of the European Medicines Agency](#) was held with the purpose to discuss, amongst other issues, the most appropriate regulatory classification (medical device or medicinal product) for these nanoparticles. The conclusion of this meeting was that the product could be classified as a medical device. The next step will be to contact a Notified Body and Competent Authority to decide on the required safety and performance studies.

1.14. Sweden

1.14.1. SweNanoSafe – the Swedish National Platform for Nanosafety

During 2018, the national platform SweNanoSafe has further developed possibilities for communication and interaction between stakeholders with an interest in nanosafety. Discussions have focused on the identification of hindrances and on suggestions for concrete actions for safe use and handling of nanomaterials.

The web portal swenanosafe.se was launched in March 2018. It contains up-to-date information on research as well as regulatory issues, together with basic knowledge on regulations, guidelines, and current research. Furthermore, the portal manages Q&A's and presents news on conferences and courses in nanosafety. The portal has been built in collaboration with the members of the expert panel and the cooperation council at SweNanoSafe. SweNanoSafe also uses twitter for dissemination of information.

The cooperation council at SweNanoSafe has been expanded to about 30 representatives during 2018. At a joint meeting in March various stakeholder from Swedish authorities, industry, NGO's and academia openly discussed current knowledge gaps and needs among stakeholders.

The expert panel of the SweNanoSafe platform, chaired by Prof. Bengt Fadeel at Karolinska Institutet, was involved in the organization of the inaugural meeting of the nanosafety research network, and provided expert comments on various documents including the EFSA guidance documents on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain, as well as the EU-US Roadmap on Nanoinformatics 2030 developed by the EU Nanosafety Cluster.

In June, SweNanoSafe organised a workshop on research and education within nanosafety. The discussions focussed on strengths and needs in Swedish nanosafety research and how research results more effectively can be implemented to meet societal needs. The workshop was also the start of a new research network within nanosafety. The purpose of the network is to promote interdisciplinary collaborative research in nanosafety, but also increase access to expert knowledge for authorities and other stakeholders. The network currently includes about 75 participants from 13 Swedish universities and research institutes of which about 50 participated in the workshop.

In collaboration with the Swedish Chemicals Agency and the national research network at SweNanoSafe, six Swedish experts have been nominated to aid various WPMN projects at OECD (Maria Huffman, Mohammed Toprak, Inger Odnevall Wallinder, Yolanda Hedberg, Julián Gallego, Joydeep Dutta, and Ulrika Carlander).

1.14.2. Nanotoxicology Report from Institute of Environmental Medicine

The Institute of Environmental Medicine (IMM), a department at Karolinska Institutet, is an interdisciplinary research organization in the field of environmental medicine. At IMM, research is conducted in toxicology, environmental medicine, and epidemiology. Additionally, IMM provides environmental risk assessments to governmental agencies. IMM has played an important role in the field of nanotoxicology in the past decade, with participation in numerous EU-funded projects, including FP7-NANOREG, as well as national projects, eg., MISTRA Environmental Nanosafety. IN 2018, researchers at IMM have compiled a comprehensive report on the state-of-the-art of nanotoxicology along with an outlook with regards to future research needs. The report is available at the homepage of IMM and is also linked to the EUON webpage at ECHA (<https://euon.echa.europa.eu/safety>). The IMM report provides an overview of each of the fundamental aspects of nanosafety including material characterization, exposure assessment, hazard assessment, and risk assessment. The report includes a detailed evaluation of the potential hazards posed by engineered nanomaterials (ENMs) including effects on key organ systems such as the pulmonary system, cardiovascular system, skin, gastro-intestinal system, immune system, and central nervous system, and discusses developmental and reproductive effects as well as carcinogenic properties of ENMs. Furthermore, the report discusses the implementation of advanced *in vitro* and *in silico* approaches to evaluate ENMs including systems toxicology methods. The report, edited by Prof. Bengt Fadeel, concludes with future research challenges related to the four main areas, material characterization, exposure assessment, hazard assessment, and risk assessment.

1.14.3. Environmental Health Criteria Document on Toxicity Testing

Since 2015, the WHO has been developing an Environmental Health Criteria Document (EHC) on principles and methods to assess the risk of immunotoxicity associated with exposure to nanomaterials. Prof. Bengt Fadeel and Prof. Harri Alenius, both at Institute of Environmental Medicine at Karolinska Institutet, have been actively involved in this work. The work was coordinated by the RIVM in The Netherlands. The EHC document was recently released for public consultation (<http://www.who.int/ipcs/Immunonano/en/>) and it is due to be published soon.

1.14.4. MISTRA Environmental Nanosafety – a large national consortium

The Swedish foundation for strategic environmental research (MISTRA) supports research of strategic importance for a good living environment and sustainable development. The MISTRA Environmental Nanosafety project (<http://www.mistraenvironmentalnanosafety.org/>) was

launched in 2014 and the project will run until December 2018. The consortium is comprised of 5 Swedish universities (Chalmers Technical University, Gothenburg University, Lund University, Royal Institute of Technology-KTH, and Karolinska Institutet) and AkzoNobel, the world's largest producer of nanosilica, and it is coordinated by Chalmers Technical University. The project budget is 40 MSEK, making this the largest nanosafety project in Sweden to date. The project has covered both experimental (eco)toxicological studies as well as risk analysis, life cycle analysis, and stakeholder awareness (Larsson S., et al. Attitudes towards nanomaterials and nanotechnology among Swedish expert stakeholders: Risk, benefit, and regulation. GRI 2017:2). The MISTRA Environmental Nanosafety project organized a scientific conference and a stakeholder workshop in November, and Prof. Mark Wiesner from Duke University delivered the keynote lecture in which he presented some of the lessons learned during the past 20 years (refer to project webpage for a summary).

1.14.5. Swedish Participation in EU-funded research projects in H2020

The Horizon2020 project BIORIMA (<https://www.biorima.eu/>) aims to develop an integrated risk management (IRM) framework for nanobiomaterials (NBM) used in advanced therapy medical products (ATMP) and medical devices (MD). The BIORIMA IRM framework is a structure upon which validated tools and methods for materials, exposure, hazard and risk identification/assessment and management are allocated along with a rationale for selecting and using them to manage and reduce the risk for specific NBMs used in ATMP and MD. The hazard workpackage in BIORIMA which comprises both toxicology and ecotoxicology is coordinated by Prof. Bengt Fadeel, Karolinska Institutet. One of the main objectives of the work is to 'test the tests' with regards to the applicability of existing OECD and other test guidelines for the evaluation of NBMs. BIORIMA is coordinated by IOM in the UK.

The Horizon2020 project CALIBRATE (www.nanocalibrate.eu/) is focused on risk governance of nanomaterials and aims to develop a 'system of systems', based on a suite of tested and calibrated manufactured nano-specific risk prioritization and control banding tools. The work will leverage more than a decade of nanosafety research and resources to develop models for next generation nano-risk governance framework. Prof. Roland Grafström at Karolinska Institutet and his team are partners in CALIBRATE and provide expertise and knowledge on advanced computational analysis tools for integrating high-throughput screening (HTS) and high content analysis (HCA) data into the development of grouping approaches and the risk banding tool. Grafström and colleagues recently published an original article in *Nature Communications* in which they utilized a 'big data compacting and data fusion' concept to capture diverse adverse outcomes on cellular and organismal levels, creating a 'predictive toxicogenomics space' (PTGS) tool. In the paper, the authors showed that the PTGS tool predicts chemically induced pathological states in the liver of rats, and also predicts human drug-induced liver injury from hepatocyte experiments (Kohonen P, Parkkinen JA, Willighagen EL, Ceder R, Wennerberg K, Kaski S, Grafström RC. [A transcriptomics data-driven gene space accurately predicts liver cytopathology and drug-induced liver injury](#). Nat Commun. 2017;8:15932).

The GRAPHENE FLAGSHIP is a Future Emerging Technologies (FET) Flagship Project funded by the European Commission (<https://graphene-flagship.eu/>). The Graphene Flagship is tasked with bringing together academic and industrial researchers to take graphene from the realm of academic laboratories into European society in the space of 10 years, thus generating economic growth, new jobs and new opportunities. The consortium consists of over 150 academic and industrial research groups in more than countries and the project is coordinated by Chalmers Technical University in Gothenburg, Sweden. Researchers at Karolinska Institutet are engaged in

the workpackage dealing with health & environment, and they have recently coordinated a comprehensive review on safety assessment of graphene-based materials to mark the first 5 years of this 10-year effort (Fadeel B., et al. [Safety assessment of graphene-based materials: focus on human health and the environment](#). ACS Nano. 2018 Nov 12. doi: 10.1021/acsnano.8b04758. [Epub ahead of print]).

The EU Nanosafety Cluster (<https://www.nanosafetycluster.eu/>) provides a forum for European Commission funded nanosafety projects in FP7 and H2020. In 2018, Prof. Bengt Fadeel, Karolinska Institutet, coordinated and published a perspective article in *Nature Nanotechnology* in collaboration with several other coordinators of recent FP7 projects including FP7-NANOSOLUTIONS and FP7-eNANOMAPPER including Prof. Kai Savolainen (FIOH, Helsinki), former coordinator of the EU Nanosafety Cluster. The authors focused on recent advances in hazard and risk assessment of engineered nanomaterials and the development of novel tools including systems biology and high-throughput screening (HTS) based tools with which to evaluate ENMs across their life cycle. The authors pointed out that uncertainty regarding the hazards and risks of ENMs for human health and the environment may hamper the exploitation and use of such materials. Moreover, regulatory uncertainty may increase the cost and time needed for the development of new products. The authors also opined that adaptation of traditional assays used for testing of chemicals is not sufficient; it is also necessary to speed up testing of ENMs using validated *in vitro* assays based on relevant end-points, i.e., end-points that adequately mirror *in vivo* outcomes of exposure to ENMs. To this end, HTS and omics based approaches may provide a meaningful way forward (Fadeel B, Farcas L, Hardy B, Vázquez-Campos S, Hristozov D, Marcomini A, Lynch I, Valsami-Jones E, Alenius H, Savolainen K. [Advanced tools for the safety assessment of nanomaterials](#). Nat Nanotechnol. 2018;13(7):537-543).

1.15. Switzerland

1.15.1. National developments on human health and environmental safety

- The Swiss precautionary matrix (PCM) has been updated and revised according to new information about the effect potential of nanomaterials.
- The Swiss chemicals ordinance was amended. Nanomaterials, which specifically contain biopersistent fibres or tubes exceeding 5µm in length, have to be reported within 3 months after first placing them on the market.

1.16. Thailand

1.16.1. National developments on human health and environmental safety

The Food and Drug Agency (FDA) is starting to seriously look at product certification that have nanoparticles. They have seek the assistance of NANOTEC to implement awareness training for their staff on nanoparticles and labels. The Thai FDA have indicated that they would like to initiate a collaborative working agreement with NANOTEC to promote nanosafety awareness.

1.16.2. Developments related to good practice documents

Submitted 2 industrial standards manuals for approval by Thai Industrial Standards Institute (TISI). An additional manual is expected to be completed in 2019 and also to be submitted to TISI.

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

1. Our NanoEHS team has expertise on intestinal cell culture (Caco-2 cells and 3D-intestinal model developed from intestinal organoid) and transport study. NanoEHS would like to have opportunities to join EU project in vitro approach for intestinal fate of orally ingested nanomaterials
2. NANOTECH can support EU project that relate to development and validation of Enzyme-linked in vitro comet assay, since we have the facility for performing comet assay (Comet software and electrophoresis).
3. Info on assessing the global readiness of regulatory and non-regulatory models for assessing occupational exposure to manufacture NMs (trend and guideline for assessing occupational exposure to manufacture NMs,)
4. Development of novel predictive models for assessment both human health and ecological effects of nanomaterials.
 - Completed an easy to read version of the approved 7 industrial standards manuals related to nanotechnology and will use for workers' training program.
 - Organized the Nanosafety Technical Forum 2018 during NanoThailand 2018 on 12 Dec at Thailand Science Park. A total of 5 overseas speakers were invited to give technical presentations.
 - Working with Nanotechnology Association of Thailand to conduct nanosafety course related to occupational health hazard by nanomaterials
 - Collaborating with Asia Nano Forum (ANF) and Nanotechnology Association of Thailand to organize the 3rd EU-Asia Dialogue on Nanosafety: Occupational Exposures to Manufactured Nanomaterials (MNM) and Waste Disposal during ASEAN Next 2019 in Bangkok on 18 March 2019

1.16.4. Additional Information

Nanosafety awareness initiative by NANOTECH will put more emphasis on occupational safety as we see the workers as the frontline group to be exposed to nanoparticles. We will need to work more with the ministry of industry to conduct trainings and seminars, etc. We foresee additional collaboration with experts from EU with regards to awareness program for occupational safety of nanomaterials.

1.17. United Kingdom

1.17.1. Activities initiated to implement the OECD Council Recommendation⁵ (e.g. regulatory changes, guidance, voluntary, etc.)

In January 2018 the UK Government published its 25 Year Environment Plan - 'A Green Future: Our 25 Year Plan to Improve the Environment', which sets out what we will do to improve the

⁵ [Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials](#)

environment, within a generation. This contains a series of actions that we will take on chemicals including:

“Working internationally to strengthen the standardisation of methods that assess chemical safety in support of the mutual acceptance of data to identify and share information on emerging concerns and new approaches to risk assessments.”

In this context, and to prepare for the recently adopted revision of the REACH information requirements for nanomaterials, the UK continues to actively engage internationally within the WPMN to adapt OECD test guidelines for assessment of nanomaterials, including through the Malta Initiative. We have attached representatives to WPMN expert groups and are actively reviewing proposals. In addition, UK led H2020 research projects are ready to cooperate directly with other active projects, such as Gov4Nano, to contribute expertise and data to support test guidelines development.

The UK is co-leading the WPMN project to develop/or revise the current Toxicokinetic Test Guideline to address nanomaterials. During this year the Ad Hoc Expert Group was established and the first teleconference held. UK representatives also joined the WPMN meeting on Environmental Fate and Ecotoxicity of Nanomaterials in December 2018 to discuss the progress of test guidelines work on nanomaterials, in particular the guidance document on assessing the apparent accumulation potential for nanomaterials for TG305 for which we are the co-lead with Spain. Aquatic bioaccumulation testing of nanomaterials is of particular interest to us at the current time since log K_{ow} may not be applicable to predicting bioaccumulation potential of nanomaterials, leaving risk assessment reliant on the TG305 bioaccumulation in fish test. We are therefore exploring the development of a tiered approach to bioaccumulation assessment to ensure that only appropriate nanomaterials are tested in the fish to minimise animals in testing and to deliver cost savings to industry whilst maintaining a high level of environmental protection. We are submitting a project proposal to the WPMN for consideration so that we can work together to develop an internationally harmonised approach.

RiskGone

The 23 partner H2020 project coordinated by NILU in Norway will begin in the first quarter of 2019 with Swansea University and the University of Birmingham as work package leads in human hazard assessment (Prof Shareen Doak) and ecotoxicity (Prof Isuelt Lynch) respectively. The overarching goals of RiskGone are: (1) to establish a transparent, self-sustained and science-based Risk Governance Council composed of representatives of EU member states and European stakeholders (e.g., regulatory agencies, public bodies, industry, NGOs, etc.); (2) to contribute to the strengthening of EU safety governance of nanomaterials through the development of the Risk Governance Cloud Platform, which will facilitate the dynamic integration of scientific evidence as it evolves over time, and advance the handling of scientific uncertainty in the regulatory risk assessment of nanomaterials; and (3) to provide state-of-the-art decision-making tools and support risk communication to relevant stakeholders, including industry, regulators, insurance companies, and especially to the general public. The project will support the standardization and validation process for nanomaterials by evaluating, optimizing and pre-validating Standard Operating Procedures and OECD Test Guidelines and integrating them into a framework for risk governance. Rather than producing assays and methods ex novo, this will be achieved through Round Robin exercises and multimodal testing of OECD TGs and ECHA methods supporting the implementation of Malta-Initiative funded under Gov4Nano.

1.17.2. Developments related to good practice documents

Nanoparticle Concentration Inter-laboratory studies

The Versailles Project on Advanced Materials and Standards (VAMAS) Project 10 on nanoparticle concentration has completed the data collection phase from laboratories participating in an inter-laboratory study. The National Physical Laboratory (NPL) led study has more than 86 participants from laboratories all over the world. NPL also contributed to the LGC-led BIPM-CCQM-P194 inter-laboratory comparison on colloidal concentration using UV-Visible spectroscopy. They are also leading an ISO technical report on all of the methods to measure nanoparticle concentration, which is planned to be developed and funded via an EU EMPIR support for impact project.

Surface Chemical Analysis

ISO 20579-4:2018 on Surface chemical analysis -- Guidelines to sample handling, preparation and mounting -- Part 4: Reporting information related to the history, preparation, handling and mounting of nano-objects prior to surface analysis has been published recently. The work was US led with technical experts from NPL involved in the drafting. The standard identifies information to be reported in a datasheet, certificate of analysis, report or other publication regarding the handling of nano-objects in preparation for surface chemical analysis. This information is needed to ensure reliability and reproducibility of analyses needed to advance research and technology using these materials, and for obtaining appropriate understanding of potential nano-object environmental and biological impacts. Such information is in addition to other details associated with specimen synthesis, processing history and characterization, and should become part of the data record (sometimes identified as provenance information) regarding the source of the material and changes that have taken place since it was originated. It also includes informative annexes that summarize challenges associated with nano-objects that highlight the need for increased documentation and reporting in a material data record.

Graphene standardisation

NPL are leading the development of five ISO standards on the measurement of graphene. These are on structural characterisation of graphene flakes, chemical characterisation of graphene flakes and structural characterisation of CVD grown graphene.

Genotoxicity

Swansea University was involved in a large international review exercise to establish good practice for genotoxicity evaluation of nanomaterials, leading the aspect of work that focused on the *in vitro* micronucleus assay. The work has been published in the journal *Toxicological Sciences*:

Elespuru, R.K. et al. (2018) Genotoxicity assessment of nanomaterials: recommendations on best practices, assays and methods. Tox Sci, 164:391-416.

NanoCommons

The [NanoCommons](#) H2020 research infrastructure project started in 2018 and is coordinated by the University of Birmingham (Prof Iseult Lynch). It is working on a range of initiatives to promote good practice in nanosafety evaluation, focusing on developing best practice in data and knowledge management. A key output will be facilitation of community adoption of **electronic notebooks** from the experimental design phase of experimental and computational research, linked

to community developed and agreed ontologies and protocols, and directly intergratable with relevant databases. The overall goals are to: (1) increase the overall quality of the data through curation at the point of generation and annotation-based integration into the databases; (2) enhancing the FAIRness (Findability, Accessibility, Interoperability and Re-usability) of the datasets by supporting the community to make their data available and comparable to other datasets as well as maintain the datasets beyond project lifetimes.

As a research e-infrastructure project, NanoCommons will directly support users in the adoption and implementation of best practice in data management for nanosafety through provision of funded access to the tools development and expertise to implement them locally. Utilisation of the data lifecycle management approach, via the electronic notebooks, has already been demonstrated for a research group (via a local area network), for support of international inter-laboratory comparison activities (supporting the H2020 ACEnano project), and with multi-partner long-term nanomaterials transformations in the environment and uptake experiments such as mesocosms supporting the H2020 NanoFASE project) as exemplar case studies. These, and the best practice guidelines are currently being prepared for publication to support the first call for Transnational Access planned for early 2019. NanoCommons is happy to support other current or ended EU and national projects with sizable datasets, or indeed the datasets being collated and utilised to support the Malta Initiative's revision of OECD test guidelines for nanomaterials, through annotation of datasets.

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

GRACIOUS

The H2020 funded [GRACIOUS](#) project led by Heriot-Watt University aims to develop a framework that groups nanoforms together based on similarity for risk assessment. The justification for whether a grouping hypotheses applies to a specific (group of) (nano)form(s) is tested by a tailored IATA. The IATA guides the user through identification of relevant existing information and the work needed to obtain new information to justify the proposed grouping. The level of detail provided by the IATA, and the level of similarity required for justification, depend upon the purpose, with more extensive testing and assessment required for regulatory purposes. In this manner, the GRACIOUS framework aims to facilitate scientifically sound risk decision making for nanoforms, while minimising case-by-case testing.

The draft GRACIOUS framework has been discussed with stakeholders via an on-line consultation, one-to-one interviews and via a stakeholder workshop at the OEC D. The original framework draft has now been adapted according to the feedback, primarily by improving clarity. During the course of the project it will continue to be tested and refined with ongoing engagement with stakeholders. The consortium is currently building the decision trees and IATAs that will constitute the bulk of the framework. Case studies will be essential to test the validity of the IATAs and will be conducted. The IATA's will also be used to generate the blueprints for software development of an online tool for GRACIOUS and its guidance document. The final framework will be launched in 2021 and the framework, decision trees and IATA's will be published in the peer reviewed literature.

NanoSolveIT

This project is coordinated by Novamechanics, with the University of Birmingham (Prof Iseult Lynch) as Deputy Coordinator. This will develop and deliver a validated, sustainable, multi-scale nanoinformatics IATA, tested and demonstrated at TLR6 via OECD style IATA case studies, serving the needs of diverse stakeholders at each stage of the NMs value chain, for assessment of potential adverse effects of NM on human health and the environment. The innovative nanomaterial fingerprint approach developed in NanoSolveIT will be the core of the model integration, supporting the IATA by linking laboratory characterization data, computational characteristics, biological signatures, image analysis, artificial intelligence predictions, and functional effects. Case studies utilising the OECD IATA Case studies approach will be used to demonstrate the utility/functionality of the training, modelling, virtual experiments, and documentation, thereby raising the models from TRL4 to TRL 6, establishing Safer-by-Design principles and increasing the confidence of industry and regulators in the tools and IATA. NanoSolveIT will undertake 4 case studies, 3 building on existing OECD case studies, and one overarching one utilising NanoSolveIt data, as follows:

1. Prioritization of chemicals using Integrated Approaches for Testing and Assessment (IATA)-based Ecological Risk Classification (Prioritization of chemicals / Ecotoxicity) – **NanoSolveIT will adapt this for NMs**
2. Case study on grouping & read-across for nanomaterials genotoxicity of nano-TiO₂ (Grouping / Genotoxicity) – **NanoSolveIT will assess the ability of our models / IATA to reproduce (improve on) the findings**
3. A Case Study on Use of IATA for Sub-Chronic Repeated-Dose Toxicity of Simple Aryl Alcohol Alkyl Carboxylic Esters: Read-Across (Grouping (Read-across) / Repeated dose toxicity) – **NanoSolveIT will adapt this for NMs.**
4. The final demonstration case study will integration datasets compiled and generated within NanoSolveIT, via a **Case study for immunotoxic effects of non-soluble NMs.**

RiskGone

RiskGone will develop regulatory-relevant guidance, addressing both human and environmental health and prioritising *in vitro* methods, based on an IATA framework. The University of Birmingham will support the translations of *in vitro* approaches (including the lab-on-a-chip biomimetic micro/nanofluidic platforms for high throughput testing, and interference-free endpoint testing that relates to AOPs to ensure the mechanistic relevance of the bioassays) into ecotoxicological species. They will establish a *Daphnia magna* gut model and dynamic flow model exposure systems to more realistically represent the *in vivo* exposure system *in vitro* and enhance the throughput of ecotoxicity testing. A strong focus on functional assays to support building of AOPs will be implemented.

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

ACENano

The [ACENano](#) project led by the University of Birmingham (Prof Éva Valsami-Jones) has progressed well and successfully completed its first periodic review. This 26-partner H2020 project aims to introduce confidence, adaptability and clarity into nanomaterial risk assessment by

developing a widely implementable and robust tiered approach to physicochemical characterisation that will facilitate contextual (hazard or exposure) description and its transcription into a reliable nanomaterial grouping framework.

Selected progress highlights in the first year of the project include:

- Hyphenation of AF4 and ICP-ToF-MS, which makes multi-element analysis possible, along with measuring the concentration of challenging nanomaterials, such as SiO₂, as well as the possibility of working with samples of unknown composition (which traditional ICP-MS cannot do) and complex samples such as soils or sediments.
- Development of a dynamic nanomaterial dissolution assay based on SP-ICP-MS approach and linked to OECD TG318.
- Optimisation of different capillary electrophoresis separation methods for different NM surface chemistries / charges & for corona (large & small molecule) analysis.
- Development of a prototype air-liquid interface benchtop instrument.
- Adaptation of ToF-SIMS to nanomaterial characterization, specifically optimising both sample prep and performance (mass & lateral (spatial /localization) resolution) in complex matrices – cryofixation to avoid chemical modification of sample and preserve live cells.

Additionally, ACEnano has made good progress in terms of a number of inter-laboratory comparison studies for e.g. DLS, NTA and BET, developing its libraries of analytical protocols and generating the project's knowledge warehouse, which will form the basis for the development of a nanomaterials characterisation decision tree.

HISENTS

The H2020 project [HISENTS](#) led by the University of Leeds (Prof Andrew Nelson) has been running since 1st April 2016 and is now at the peak of its activity. The project aims to revolutionise the toxicity testing of nanomaterials by developing a third generation screening platform composed of flow modules containing individual organelle and tissue sensor elements (on-chip) of increasing complexity embedded in a microfluidic flow system. The global device mirrors the human physiology and is underwritten by a custom designed physiologically based pharmacokinetic (PBPK) *in silico* model. The biomembrane toxicity sensing platform has now been automated and rationalised and is now operating at Technology Readiness Level 4-5. Flow modules at four other labs have been configured, each with different cell and tissue sensor elements together with the optical and electrochemical instrumentation for driving and interrogating these modules. A comprehensive study on nanomaterials screening using the device has shown how important the HISENTS concept of screening at the point of production (SPoP) is in the safety management of nanomaterials.

EC4SafeNano

The H2020 project [EC4SafeNano](#) aims to build an open collaborative network gathering expertise in risk management of nanotechnologies. The University of Birmingham is participating to support the integration of science and research developments, as well as developing approaches to overcome the barriers to data sharing.

In3

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 Public Health England (PHE), and it is led by Professor Paul Jennings (Medizinische Universität Innsbruck, Austria). The project focuses 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 nanomaterial safety assessment. The project has hired 15 PhD students to carry out these activities in a coordinated and highly collaborative fashion. One of the UK based students is progressing the development of lung cell cultures and using this to test a panel of materials including cerium dioxide nanoparticles.

NanoGenTools

The H2020 project [NanoGenTools](#) aims to develop fast *in vitro* high throughput assays, with molecular based computational models for better understanding of the molecular fundamentals of nanotoxicity, and will initiate the development of online nanosafety assays for use by SMEs during product development. The University of Birmingham is participating and working mainly on aspects of biophysical techniques and mathematical models for accurate and fast nanotoxicity prediction linked to safety-by-design concepts.

NanoInformaTIX

The H2020 project lead by CSIC in Spain begins in the first quarter of 2019 with Swansea University as a partner organisation. This aims to create a comprehensive, sustainable, multi-scale modelling framework for exposure and (eco)-toxicity of nanomaterials to facilitate cost-effective risk assessment, less reliant on animal testing, and to support the design of safer materials and products. The approach integrates several relevant EU/US databases with validated nanoinformatics models covering: Materials, Exposure, Physiologically-Based Pharmacokinetics (PBPK), Quantitative-Structure-Activity Relations (QSAR) and Systems Biology modelling and *in vitro/in vivo* extrapolation to support the prediction of biological effects and exposure of ENM at various stages of their life cycle and product development. The NanoInformaTIX modelling framework will be a web-based platform with a user-friendly interface tailored to the needs of different stakeholders.

PATROLS

The 24 partner H2020 project [PATROLS](#) started on 1st Jan 2018 is led by Swansea University (Prof Shareen Doak). This 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 nanomaterial 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.

Public Health England's Nanotoxicology Programme

Public Health England's programme is focused 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 under the Health Impacts of Environmental Hazards Health Protection Research Unit (HPRU) (<http://hih.hpru.nihr.ac.uk/>) funded by the National Institute for Health Research. A study to explore individual exposures to engineered nanomaterials in consumer products is also currently being undertaken under the HPRU. Recent papers include:

Guo et al (2018). The small airway epithelium as a target for the adverse pulmonary effects of silver nanoparticle inhalation, Nanotoxicology, DOI: 10.1080/17435390.2018.1465140.

Meldrum et al (2018). Cerium dioxide nanoparticles exacerbate house dust mite induced type II airway inflammation. Particle and Fibre Toxicology 15:24. <https://doi.org/10.1186/s12989-018-0261-5>.

Guo et al (2018). Pulmonary toxicity of inhaled nano-sized cerium oxide aerosols in Sprague-Dawley rats. Nanotoxicology, DOI: 10.1080/17435390.2018.1554751.

TRANSAT

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 steel particles (some tritiated) relevant to the fission/fusion cycle. Non tritiated particles have been provided and work is progressing to produce and characterise aerosols for the study.

1.17.5. Additional Information

Nanotechnology and Medical Applications

Nanomaterials have the potential to form the basis of many new medical applications. A new White Paper "[Nanotechnology: What does the future look like for the medical devices industry?](#)" published by the British Standards Institution gives a snapshot of the main areas of activity for many aspects of future healthcare along with some of the regulatory and standards issues. Nanoparticles can be introduced into the body for enhancing many methods of medical imaging. They can also be used to carry approved drugs to particular organs or parts of the body and allow for triggered release via special functional coatings on their surface. There is growing evidence of their utility in generating free radicals, or local heating effects to destroy cancer cells or viruses and microbes. A very promising application is in sensors for detecting biomolecules that are physiologically important, and these, because they are used outside of the body have less restrictive regulatory issues. All of this adds up to improvements in healthcare and opportunities for new business.

1.18. United States

1.18.1. National developments on human health and environmental safety

- a. *risk assessment decisions, including: the type of nanomaterials assessed; testing recommended; and outcomes of the assessment;*

The U.S. Environmental Protection Agency (EPA) completed review of low volume exemptions for 5 quantum dots and a metal oxide substance. EPA allowed the exemptions under conditions that limited human and environmental exposures to prevent unreasonable risks.

The U. S. National Institute for Occupational Safety and Health (NIOSH) released for public review a revised Draft Current Intelligence Bulletin: Health Effects of Occupational Exposure to Silver Nanomaterials in September 2018 (available at <https://www.regulations.gov/document?D=CDC-2016-0001-0026>)

- b. *development related to exposure measurement and exposure mitigation;*

NIOSH published three workplace design solutions for nanotechnology in March 2018 and a poster on Controlling Health Hazards When Working with Nanomaterials in February 2018 (all four publications are available at <https://www.cdc.gov/niosh/topics/nanotech/pubs.html>)

- c. *risk management approaches;*

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 the U.S. Toxic Substances Control Act (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. The deadline for reporting existing nanoscale materials in commerce was August 14, 2018.

As of November 2018, EPA had received notification for 67 nanoscale chemical substances that met reporting criteria. Reporting criteria exempted nanoscale chemical substances already reported as new chemicals under TSCA and those nanoscale chemical substances that did not have unique or novel properties. Most reporting was for metals or metal oxides.

Since January 2005, EPA has received and reviewed more than 220 new chemical notices for nanoscale materials under TSCA including fullerenes, quantum dots, and carbon nanotubes. EPA has issued consent orders and Significant New Use Rules (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.

EPA completed review of low volume exemptions for 5 quantum dots and a metal oxide substance. EPA allowed the exemptions under conditions that limited human and environmental exposures to prevent unreasonable risks.

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.

- d. any updates, including proposals, or modifications to previous regulatory decisions; and/or*

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

- e. 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.

1.18.2. Activities initiated to implement the OECD Council Recommendation

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.

1.18.3. Developments related to good practice documents

In 2018, NIOSH led the update of the International Organization for Standardization (ISO) Technical Report 12885 on nanomaterial safety in the workplace (<https://www.iso.org/standard/67446.html>) and is supporting the implementation of the World Health Organization's guidelines on nanomaterial safety in the workplace (http://www.who.int/occupational_health/topics/nanotechnologies/en/).

NIOSH published three workplace design solutions for nanotechnology in March 2018 and a poster on Controlling Health Hazards When Working with Nanomaterials in February 2018 (all four publications are available at <https://www.cdc.gov/niosh/topics/nanotech/pubs.html>).

1.18.4. 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 bronchoalveolar fluid. For carbon nanotubes blood and plasma endpoints indicative of cardiotoxicity are monitored.

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

- 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;
- Current or future activities on nanotechnologies on a multilateral basis, including with non-OECD countries.

The National Nanotechnology Initiative (NNI) 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 adaptively 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/neh>

NIOSH released for public review a draft NIOSH Nanotechnology Research Plan for 2018-2025 in February 2018.

https://www.cdc.gov/niosh/docket/review/docket312/pdfs/NTRC-Strategic-Plan-2018-2025_February-2018.pdf

1.18.6. Additional Information

The U.S. National Nanotechnology Coordination Office (NNCO) holds webinars periodically to share information with the public and the nanotechnology research and development community. On September 19, 2018, the NNCO held a webinar on “Technology Pathways Toward Commercializing Nanotechnology.” Previous webinars include “NanoEHS and Nanomedicine: Similarities and Synergisms,” “The National Nanotechnology Coordinated Infrastructure (NNCI) Nodes and Environmental Research: Examples from the Field,” “The Utility of Alternative Testing Strategies in Nanotechnology, Health, and Safety Evaluations”; “An Introduction to Voluntary Standards”; and “Water Sustainability through Nanotechnology.” The webinars are archived at URL: <https://www.nano.gov/PublicWebinars>

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

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

2.1.1. 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), has produced a series of webinars on alternative approaches for testing the toxicity of inhaled substances. The 21 pre-recorded webinars feature international experts from industry, government, and non-profit organizations presenting on *in silico* models, *in vitro* test systems, and integrated approaches to testing and assessment. The webinars are available at <https://www.piscltd.org.uk/inhalation-webinars/>.

The PETA International Science Consortium is collaborating with Health Canada to develop an adverse outcome pathway (AOP) for lung fibrosis. The AOP entitled ‘Secretion of inflammatory cytokines leading to lung fibrosis’ is available on the AOPwiki (AOP 173: <https://aopwiki.org/wiki/index.php/Aop:173>). A manuscript on this work is currently under preparation.

The PETA International Science Consortium is funding the development of an advanced, three-dimensional *in vitro* system to predict the potential of manufactured nanomaterials to cause lung fibrosis in humans. The highlights of the project were presented this year at the 57th Society of Toxicology meeting, NanoTox 2018 – the 9th International Conference on Nanotoxicology, and 20th International Congress on *In Vitro* Toxicology (ESTIV2018). As part of this project, MatTek Corporation has developed a model of the lower respiratory tract (EpiAlveolar™); the model is currently available for beta-testing and should be commercially available in the coming year. The progression of this project can be followed on our website: <http://www.piscltd.org.uk/nanoworkshop/>.

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. The most recent article published from this work is available here: <https://www.ncbi.nlm.nih.gov/pubmed/29908304>. The decision tree presented in the article is being used as the basis to design a testing strategy. A proof-of-concept study to demonstrate the utility of the non-animal testing strategy to predict the acute toxicity of inhaled substances is expected to commence in the coming months.

The PETA International Science Consortium’s Director was Guest Editor of a special June 2018 issue of *Applied In Vitro Toxicology* on ‘Implementing Alternative Approaches for Inhalation Toxicity Testing’. The issue covered 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. It is available to read here: <https://www.liebertpub.com/toc/aivt/4/2>.

The PETA International Science Consortium and Epithelix announced an award to provide an opportunity for researchers worldwide to win three-dimensional reconstructed human respiratory tissues from Epithelix. The awardee will receive a \$5,000 award redeemable for Epithelix MucilAir™ or SmallAir™ tissues. The award winner(s) will be selected based on their proposal's scientific merit and potential to replace animal testing. More details on this award can be found here: <https://www.piscltd.org.uk/epithelix-award/>.

2.2. Business and Industry Advisory Committee to the OECD

2.2.1. National developments on human health and environmental safety

VCI

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 still deeply engaged in research projects on the safety of nanomaterials.

The engagement of VCI in the political discussion on the EU definition of nanomaterials and, in close co-operation with its sector groups is still going on. The discussion to further adapt analytical methods to determine nanomaterials according to the EU definition of nanomaterials is also ongoing. Further engagement in R&D-projects and discussion to the political outreach still seems to be necessary.

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).

2.2.2. Activities initiated to implement the OECD Council Recommendation⁶ (e.g. regulatory changes, guidance, voluntary, etc.)

NIA

NIA is a partner of the EU project Gov4Nano and work package 2 ‘the Malta Initiative’ that will start in January 2019. WP2 tasks will work on several potential updates to OECD TG and GD and NIA will ensure appropriate and relevant industry input to these discussions.

⁶ [Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials](#)

2.2.3. Developments related to good practice documents

ACC

The ACC Panel has supported the development of an ISO technical report titled “Nanotechnologies -- Considerations for the measurement of nano-objects and their aggregates and agglomerates (NOAA) in environmental matrices.” The report was finalized at the ISO Technical Committee 229 (TC 229) global meeting in Kuala Lumpur, Malaysia (October 29-November 2, 2018) and should be available from ISO during the first half of 2019.

The ACC Panel continues to support the development of another ISO technical report, “Evaluation of methods for assessing the release nanomaterials from commercial, nanomaterial-containing polymer composites.” The project team aims to have a new review draft available in mid-January and will host two webinars to present their work and receive feedback prior to the ISO TC 229 meeting in Sydney, Australia, in May 2019.

ACC Nanotechnology Panel is contributing its expertise to all ISO TC 229 work groups, and in particular the work groups focusing on terminology, metrology, EHS considerations, and performance-based standards for nanotechnology applications.

VCI

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

Documents on measurement methods

- Assessment of the results of the NanoDefine project with regard to the concrete use of (real life) pigments and fillers and other comparable particulate substances

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

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 2014.⁷ 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. In August 2018 VdMi and VCI have jointly published an assessment of the core project to develop measurement methods to apply the EU nanomaterial definition according to regulatory requirements, the NanoDefine project.

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

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

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 order to provide long-term support for research on the effects of chemical substances on human health and the environment.

JCIA

JCIA is supporting a theme of “Establishment of mechanism based assay protocol for hazard and carcinogenic risk of carbon based nanomaterials” by Nanotoxicology Project, Nagoya City University since Mar 2017. The purpose of the research is to establish for toxicity and carcinogenicity testing using Trans-tracheal Intra-pulmonary Spraying (TIPS). To examine the usefulness of the TIPS methods for practical use, the study has been conducted for MWCNT-7 (a known carcinogen composed of 40 layers of graphene) and Double-Walled Carbon Nanotubes (DWCNT) (2 layers).

VCI

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

⁷ <http://publications.jrc.ec.europa.eu/repository/handle/JRC92531>

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 typical life cycle stages). The Federal Ministry of research has just launched the project NanoCare 4.0 in which member companies of VCI and cooperating universities are engaged

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)

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.^{8,9}

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. VCI, its member companies and federal authorities and universities applied for a project to establish a database for toxicological findings on substances in the nanoscale by the German Federal Ministry of Research (BMBF).

⁸ 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>

⁹ The paper "Conclusions and recommendations from the project „Health assessment, exposure and environmental effects of nanomaterials: literature review and assessment" is available on the website of VCI: <http://www.vci.de>.

2.2.6. Additional Information

ACC

ACC Nanotechnology Panel members spoke at and participated in the 2nd Quantifying Exposure to Engineered Nanomaterials from Manufactured Products (QEEN II) Workshop sponsored by the U.S. Consumer Product Safety Commission, Occupational Safety and Health Administration, and the National Nanotechnology Initiative. The workshop focused on new research, tools and methods to characterize and quantify effective population exposures and the potential release of nanomaterials. More information is available at <https://www.nano.gov/queen2>.

In a letter to the White House Office of Management and Budget, the ACC Nanotechnology Panel contributed suggestions for additional cooperative work on nanomaterial assessment under the U.S.-Canada Regulatory Cooperation Council.

NIA

NIA co-authored an EC report as part of the NanoData project which ended in 2017. The 350 page report is a comprehensive insight into the scientific, policy and commercial ecosystem for the support and performance of nanotechnologies and materials.¹⁰

The NanoReg2 project, of which NIA is a partner, has published a comprehensive review of EU legislation addressing chemical substances and the potential for Grouping and Read Across in nanomaterials. 'Insights into possibilities for grouping and read-across for nanomaterials in EU chemicals legislation' is published with open access in *Nanotoxicology*.¹¹

VCI

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 has been engaged in the review process on research and strategies on life cycle aspects of nanomaterials within the OECD WPMN SG 9.

VCI has been 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 currently established with industry engagement as well.

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

¹⁰ http://nanotechia.org/sites/default/files/nanodata_landscape_compilation_2018.en.pdf

¹¹ <https://www.tandfonline.com/doi/full/10.1080/17435390.2018.1513092>

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 a WPMN 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.