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

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

Environment Directorate
ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT
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Also published in the Series of Safety of Manufactured Nanomaterials:

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No. 40, *Ecotoxicology and Environmental Fate of Manufactured Nanomaterials: Test Guidelines (2014)*

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No.42, *Report of the questionnaire on regulatory regimes for manufactured nanomaterials 2010-2011 (2014)*

No.43, *Genotoxicity of Manufactured Nanomaterials: Report of the OECD expert meeting (2014)*

Nos. 44-54, These items are the dossiers derived from the Testing Programme on Manufactured Nanomaterials which are located at:
http://www.oecd.org/chemicalsafety/nanosafety/testing-programme-manufactured-nanomaterials.htm

No.55, *Harmonized Tiered Approach to Measure and Assess the Potential Exposure to Airbone Emissions of Engineered Nano-objects and their Agglomerates and Aggregates at Workplaces. (2015)*

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

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

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

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FOREWORD

The OECD Joint Meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology (the Joint Meeting) held a Special Session on the Potential Implications of Manufactured Nanomaterials for Human Health and Environmental Safety (June 2005). This was the first opportunity for OECD member countries, together with observers and invited experts, to begin to identify human health and environmental safety related aspects of manufactured nanomaterials. The scope of this session was intended to address the chemicals sector.

As a follow-up, the Joint Meeting decided to hold a Workshop on the Safety of Manufactured Nanomaterials in December 2005, in Washington, D.C. The main objective was to determine the "state of the art" for the safety assessment of manufactured nanomaterials with a particular focus on identifying future needs for risk assessment within a regulatory context.

Based on the conclusions and recommendations of the Workshop [ENV/JM/MONO(2006)19] it was recognised as essential to ensure the efficient assessment of manufactured nanomaterials so as to avoid adverse effects from the use of these materials in the short, medium and longer term. With this in mind, the OECD Council established the OECD Working Party on Manufactured Nanomaterials (WPMN) as a subsidiary body of the OECD Chemicals Committee in September 2006. 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. This programme 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 is published under the responsibility of the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, pesticides and Biotechnology of the OECD.

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EXECUTIVE SUMMARY

This document compiles information, provided by delegations including the European Commission (EC), together with other organisations, on current developments on the safety of manufactured nanomaterials. This document is to provide background information on activities related to manufactured nanomaterials at the national and international level.

Background

The purpose of the information exchange is to facilitate delegations to share their experiences and preoccupations with respect to safety, and serve as the basis to identify opportunities for future co-operation and co-ordination.

The OECD Working Party on Manufactured Nanomaterials (WPMN) agreed that these reports were informative and recommended that they are made available publicly. The information provided in this document captures activities that occurred in delegations **before September 2015**.

Headings for the Tour de Table

Delegations were invited to prepare a short written paper and to organise, where possible, under the headings identified below. Nevertheless it is recognised that not all delegations would be able to supply information under each heading.

With this in mind, submissions are organised around the following topics:

- Highlight of developments
- Work completed, underway or planned
    - Regulatory developments on human health and environmental safety including recommendations or discussions related to adapting existing regulatory systems or the drafting of laws/ regulations/ guidance materials;
    - Developments related to voluntary or stewardship schemes;
    - Information on risk assessment decisions;
    - Developments related to good practice documents;
    - Developments related to Integrated Testing Strategies and/or Alternative test methods
    - Research programmes or strategies designed to address human health and/ or environmental safety aspects of nanomaterials;
    - Information on public/ stakeholder consultation;
    - Research programmes or strategies which focus on life cycle aspects of nanomaterials
    - Development related to exposure measurement and exposure mitigation
- Additional Information (i.e. any consideration on the benefits of nanotechnologies; consideration of ethical implications; and Information on past, current or future activities on nanotechnologies that are being done in countries in co-operation on a bilateral basis with non-OECD countries.

RESPONSES FROM DELEGATIONS

AUSTRIA

Highlight of developments

- The implementation report 2012 of the "Austrian Nanotechnology Action Plan" recommends to carry out coordinated enforcement of legislation which is relevant for nanomaterials (see http://nanoinformation.at/uploads/media/Umsetzungsbericht_2012_EN.PDF). In cooperation with European partners, enforcement activities in the field of REACH-regulation have been launched in year 2014 including checks of safety data sheets for nanomaterial-relevant information. The project is lead-managed by the Federal Ministry of Agriculture, Forestry, Environment and Water Management. Currently a report is compiled. Austria participates also in the Prosafe Joint Action Nantechnology and Cosmetics. Testing for nanomaterials content will be part of the project (cremes, liquides with TiO_2, SiO_2, AlO_2, ZnO_2 or mixtures thereof). The project is lead-managed by the Federal Ministry of Health. The results were presented in a Workshop in Brussels in February 2015 and will be made available in the first quarter of 2015 on http://nanoinformation.at/.

- As another measure of implementation of the Austrian Nanotechnology Action plan five projects from three calls of the national **NANO Environment Health and Safety** programme (http://www.ffg.at/nano-ehs) are or have been conducted (see bullet 9). This EHS programme is owned by the Federal Ministry of Agriculture, Forestry, Environment and Water Management and Federal Ministry of Federal Ministry for Transport, Innovation and Technology and is handled by the FFG - Austrian Research Promotion Agency. The programme is going to be prolonged.

- The 10th anniversary of the International Conference on the Environmental Effects of Nanoparticles and Nanomaterials (**ICEENN 2015**) will be held in Vienna, Austria, September 6-10, 2015 (see: . http://nanoenvironment2015.univie.ac.at/home/

National regulatory developments on human health and environmental safety including recommendations or discussions related to adapting existing regulatory systems or the drafting of laws/ regulations/ guidance materials;

No national laws/regulations are planned at the time being.

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 Federal Ministry of Agriculture, Forestry, Environment and Water Management (BMLFUW, contact: renate.paumann@bmlfuw.gv.at) and elaborated based on a broad stakeholder involvement (see also chapter 7). The implementation report on the Austrian Nanotechnology Action plan including an English translation has been finalised after a public consultation see http://nanoinformation.at/oesterreichischer-aktionsplan/umsetzungsbericht-2012.html

Developments related to good practice documents

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

In the **committee 052 „Occupational health, ergonomics, safety techniques"** the **working group 052.73** with the titel "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).

The Workers' Compensation Board in co-operation with the central labour inspectorate developed a document in German language: Merkblatt M 310 Nanotechnologien Arbeits- und Gesundheitsschutz: https://www.sozialversicherung.at/portal27/portal/auvaportal/content/contentWindow?action=2&viewmode=content&contentid=10007.672853.

Developments related to Integrated Testing Strategies and/or Alternative test methods

At Medical University of Graz, **nanotoxicology studies** (cytotoxicity, genotoxicity, impact on macrophage function, intracellular accumulation in lysosoms and cellular effects after long-term exposure; in-vitro model for exposure to nanoparticles in aerosols generated from suspensions) regarding **CNT (SW + MW),** and polystyrene are performed (contact: Eleonore Fröhlich). Lanthanide-doped nanocrystals as imaging agents to improve the sensitivity and reliability of fluorescence-based technologies are evaluated for biocompatibility in the frame of the COST action **CM1403** The **European Upconversion Network**: From the **Design of Photon-upconverting Nanomaterials to (Biomedical) Applications** (contact: Eleonore Fröhlich).

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

The FP7 project **NanoDefine** develops analytical tools and methods for the categorization of materials according to the recommendation for a definition of nanomaterials. The methods and decision support tools shall enable the grouping of materials as being nano or not. The Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer) is involved in several workpackages. The central workpackage on confirmatory methods is lead by UNIVIE.

The project Development of a Decision Support Tool for the Investigation of the Environmental Behavior of Nanomaterials on the Basis of their Dispersion Stability and Solubility as a Function of Enviromental Conditions funded by the German Environmental Protection Agency and aims at developing the scientific basis and experimental methods to determine the dispersability and dispersion stability in the context of the OECD WPNM testing framework. This project is lead by the Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer).

NanoTOES (Nanotechnology: Training Of Experts in Safety), a Network of Initial Training (ITN) in the framework of FP7 coordinated by Albert Duschl from the University of Salzburg aims at development and validation of methods for examination of possible nanorisks for health and environment coupled with research for a better understanding of the involved mechanisms. Furthermore it will focus on the education of young academics in the field of nanosafety and will be a European best practice" example in this respect. University of Salzburg´s main specialist work will be research on the effects of nanomaterials on the immune system.

In the FP7 project **NanoValid** Albert Duschl (University of Salzburg) is partner and work package leader for case studies (www.nanovalid.eu). The efforts led by University of Salzburg aim to apply methods and techniques developed in research laboratories for samples collected on-site in real or modelled working place environments.

In the FP7 project **MARINA** Austrian partners from University of Salzburg (contact: Christian Huber) and from Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer) are involved in several workpackages. UNIVIE is involved in material characterization and developing analytical methods for the **quantification of ENPs in environmental samples**. University of Salzburg plans to investigate nanoparticle **effects on the proteome level**.

In the FP7 project **NanoLyse** the Department for Environmental Geosciences, University Vienna (UNIVIE, contact: Frank von der Kammer) is leading the workpackage for the **sample preparation and quantification of inorganic nanoparticles in food**. UNIVIE is responsible member of the project management board and also involved in the development of organic nanoparticle analysis (www.nanolyse.eu).

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. See: http://www.euro-nanotox.eu/

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

The FP7 CSA NanoEIS (www.nanoeis.eu) is coordinated by University of Salzburg. The focus lies on enhancement of education in Europe including nanosafety.

In the FP7 project **NANoREG** Austrian partners from BioNanoNet (contact: Andreas Falk, national coordinator) and from AIT - Austrian Institute of Technology GmbH (contact: Mats-Olof Mattsson) are involved in several workpackages. Alexander Pogany from Austrian Federal Ministry for Transport, Innovation and Technology is national advisor. The project deals with regulatory testing of nanomaterials (www.nanoreg.eu). Furthermore, within NANoREG-project one of the Value Chain Case Studies (VCCS) with focus on TiO2 coating will be done with Austrian industry and scientific partners.

In the H2020 projects **Inspired** (project started on January, 1st, 2015), **R2R-Biofluidics** (project will start on February, 1st, 2015), and **Hi-Response** (will start on March, 1st, 2015) Austrian partner BioNanoNet is responsible for the nano-related safety-tasks (contact: Andreas Falk).

Information on public/ stakeholder consultations

As a measure of implementation of the Austrian Nanotechnology Action plan the Austrian **Nanoinformation Commission** was founded by the federal Minister of Health to provide expertise regarding nanotechnology for consumers and decision makers. This commission comprises representatives from several ministries, agencies, NGOs, research institutions, industry and other experts. This work also includes the update of the **website on nanotechnology for the public** including chances and risks of nanomaterials: http://www.nanoinformation.at

A **platform ("Österreichische Nanotechnologie-Plattform")** consisting of representatives of relevant ministries, agencies, NGOs, occupational health organisations, the Austrian Chamber of Commerce (WKO) and research institutions lead-managed by the Federal Ministry of Agriculture, Forestry, Environment and Water Management (BMLFUW) exchange information and discuss specific nanomaterial related topics.

ZSI, the centre for Social Innovation in Vienna coordinated the **NanOpinion project** which terminated in October 2014. It was a 30 month FP 7 project to investigate how opinion on nanotechnologies is shaped, and how to inform public debate, especially among hard to reach groups, and enhance education. The results inform recommendations about future discussion and regulation of NT (available at: http://results.nanopinion.eu/)

BioNanoNet is partner in **NanoDiode** (www.nanodiode.eu) project focussing on educational activities specialising in the knowledge transfer of relevant nanotech information on several educational levels (secondary schools, universities, research facilities, etc). BioNanoNet will organize several citizen dialogues and in-depth interviews to reach the goal of developing an innovative outreach and dialogue on responsible nanotechnologies in EU civil society (Contact: Sonja Hartl).

Research or strategies on life cycle aspects of nanomaterials

The FP7 project **SUN - Sustainable Nanotechnologies** develops strategies and tools for a combined risk assessment and life cycle assessment to develop a user-friendly, versatile software-based decision support system (DSS) for practical use by industries and regulators. The Department for Environmental Geosciences, University Vienna (contact: Frank von der Kammer) is involved in the development of techniques to detect and analyse nanoparticles released from products and investigation on the life cycle induced modifications of nanoparticles and how these changes affect their environmental behaviour.

University of Vienna (contact: Thilo Hofmann) is WP leader in FP7 **NANOREM**: Taking NANOtechnological REMediation Processes from Lab Scale to End User Applications for the Restoration of a Clean Environment.

Austria (BMVIT and AIT) is partner of the **ERA-net SIINN** ("Safe implementation of innovative Nanoscience and Nanotechnolgies") and leader of WP3 ("Risk assessment and life cycle validation"). The ERA-Net will coordinate European activities in the area of Nano-EHS and has published three joint calls for research projects.

The project "**NanoSan - Application of nanoscale zero-valent iron (nZVI)** for in situ remediation of groundwater contaminated by chlorinated solvents" focuses on improving nZVI particles properties with respect to sufficient longevity, reactivity, and in-depth understanding of their mobility under hydrogeological conditions typically accounted in coarse-grained, alpine, highly productive porous aquifers and under corresponding water chemical conditions. The project is led by the Department for

Environmental Geosciences, University of Vienna (project partner: Austrian Institute of Technology GmbH (AIT),Health&Environment Department) and funded by the Federal Ministry of Agriculture, Forestry, Environment and Water Management (BMLFUW). Management by Kommunalkredit Public Consulting GmbH.

Development related to exposure measurement and exposure mitigation.

The project **DetectNano** –aims at the development of quantification methods for nano-metal oxides (TiO2, CeO2) in surface water. The project is conducted by University of Vienna (contact: Frank von der Kammer) and sponsored by the national research program NANO Environment, Health and Safety.

"Nanoproducts - Identification and Exposure" (**NanoProdEx**) is a research project (lead: BioNanoNet Forschungsgesellschaft; partners: Environment Agency Austria, Montanuniversität Leoben, Mondi Uncoated Kraft & Fine Paper GmbH) within the national research program NANO Environment, Health and Safety: In this project, consumer goods that are produced or used in Austria have been investigated in terms of the nanomaterials they contain. A questionnaire and face-to-face-interviews have been conducted in order to prepare realistic exposure scenarios, which also take the chemical´s legislation REACH into account. The final report (language German; additionally, an English summary is available) of the project is available in the "download"-section following this link: http://www.bionanonet.at/projects/nanoprodex

The project "**Nano-Metals in food contact materials**" (lead: Austrian Agency for Health and Food Safety (AGES), partner University of Vienna, sponsored by the national research program NANO Environment, Health and Safety) aimed at developing methods for detection and quantification of nano-metals extruded into or sputtered on the surface of polymer materials (polypropylene or polyethylene) using food simulants.

In summary the release of nanoparticles was negligible low under the given test conditions. The smaller the silver nanoparticles the higher is the solubility and therefore the concentration in the food simulant. The type of polymer (polyethylene or polypropylene) as well as the applied stress tests did not influence the release behavior. Silver mainly dissolves in aqueous surrounding and therefore really migrates, palladium migrates neither dissolved nor is released particulate in significant amounts. Nevertheless single particles were always detectable in the used food simulants.

In the project **Nano-DESTINARA** research on sewage treatment plants regarding nanoparticles (TiO_2, CeO_2, Ag, fullerenes) was performed by Environment Agency Austria and Vienna University of Technology (sponsored by the national research program NANO Environment, Health and Safety): In acute as well as in chronic tests no inhibition of carbon respiration or nitrification were detected. More than 90% of the nanoparticles were retained in the sewage sludge. No fullerenes were measurable in the inlet or sludge of real sewage treatment plants.

In the project **NanoMIA** conducted by the Institute für Waste Management of the University of Natural Resources and Life Sciences, Vienna, and the Institute of Technology Assessment oft he Austrian Academy of Sciences an existing Austrian database for nanoproducts will be updated. Based on this database six consumer products will be chosen to develop material flow oriented disposal and release scenarios. These scenarios aim exemplarily to review the environmental fate of nanoproducts at their end-of-life and to evaluate the waste legislation as well as the surveillance mechanisms in waste management (sponsored by the national research program NANO Environment, Health and Safety).

University of Vienna (contact: Frank von der Kammer): WG-4- partener in "Engineered Nanoparticles in the Environment" of the **NORMAN Network** (Network of reference laboratories for

monitoring of emerging substances) and participation in **COST Action ES1205**: The transfer of engineered nanomaterials from wastewater treatment & stormwater to rivers.

BELGIUM

National regulatory developments on human health and environmental safety including recommendations or discussions related to adapting existing regulatory systems or the drafting of laws/ regulations/ guidance materials

The Royal Decree concerning the placing on the BE market of substances produced in nanoparticular state has been signed, and published on 24th September 2014.

The Decree involves nanoscale substances and mixtures that contain one or more of these substances as well as articles or complex objects in which nanoscale particles have been incorporated.

Existing substances have to be registered before 1st January 2016, existing mixtures before 1st January 2017. Substances, resp.mixtures placed on the market after these dates, have to be registered before they are actually placed on the market.

The web based tool for registration will be available from 1st September 2015 onwards. Registrants interested will have the opportunity to test the tool during June - July – August.

Developments related to good practice documents;

Three BE partners are involved in the FP7 research project NANoREG (NMP.2012.1.3-3; Regulatory testing of nanomaterials). This in both characterization of nanomaterials (including SOPs development) as well as in advancement of regulatory risk assessment and testing (development of solubility testing procedures, the relevance of barriers, in vitro toxicity assays). The Federal Public Service Health, Food Chain Safety and Environment acts as a National Coordinator. In March 2015, a national mid-term meeting is foreseen to present and discuss the current progress status.

CANADA

Highlights of Developments

National regulatory developments on human health and environmental safety

International Cooperation

- Canada participated in the WPMN workshops on physical-chemical methods and categories (Washington D.C.) in 2014.

- As a follow-up to the United States-Canada-European Chemicals Agency (ECHA) tri-lateral discussion on nanomaterial regulatory frameworks, all three parties continue to discuss how best to leverage ongoing activities and lessons learned.

- Canada and the United States have developed a joint pre-notification consultation process, i.e., a dialogue (e.g., technical, regulatory) between industry and the two programs prior to substance pre-market notification. The aim of this process is to increase alignment and leverage expertise between the two countries. Both countries conducted their first pre-notification consultation in the fall of 2014 and found it to be very useful by all parties involved. Industry is invited to continue using this joint process.

Information on any Risk Assessment Decisions.

Industrial or commercial chemicals: In line with the 2013 OECD Council Recommendation, Canada is using its existing chemical regulatory framework to manage nanomaterials, making adaptations where necessary to take into account the specific properties of nanomaterials. As such, industrial nanomaterials are assessed and managed by the New Substances Program, under the *New Substances Notification Regulations (Chemicals and Polymers)* of the *Canadian Environmental Protection Act, 1999* (CEPA 1999). Canada has recently published an Advisory Note to clarify when engineered nanomaterials require notification and under which circumstances the Program will request additional nano-specific information in addition to what is required under the current regulations (https://www.ec.gc.ca/subsnouvelles-newsubs/53527F9D-10F7-4390-A498-7AB54777DA52/Advisory%20Note%202014-02_EN.pdf).

In addition, Canada (Environment Canada and Health Canada) is developing an approach to assess nanomaterials that are currently in Canadian commerce and do not require notification under the New Substances Program because their Chemical Abstract Service (CAS) number is already listed on Canada's domestic chemicals inventory (i.e. the Domestic Substances List).

Information on any Developments Related to Good Practice Documents.

A. The Canadian Standards Association (CSA) has published a national standard, CSA Z5100 "Cellulosic Nanomaterials – Test Methods for Characterization". This standard is intended to build on Canada's leading role in nanocellulose production and R&D.

B. Canada submitted a New Work Item Proposal (NWIP) for a technical report on "Characterization of Cellulose Nanocrystals" which was approved by ballot to member countries of ISO/TC229 in April 2014. This technical report will provide a basis for moving forward with standards in the emerging area of cellulosic nanomaterials. To support this activity, National Research Council (NRC) Measurement Science and Standards is working with partners to develop a second generation cellulose nanocrystal (CNC) reference material that will be used for an inter-laboratory comparison for selected measurands.

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

Scientific research

Health Canada continues its research to investigate the effects of surface-modified silica nanoparticles. The aims of these projects are to: (1) study the importance of size and surface functionalization; and (2) to provide a genotoxic profile and to identify mechanistic relationships of particle properties to elicited toxic responses. A first manuscript reporting the synthesis of the

nanoparticles and their physico-chemical characterization has been published in a peer-reviewed journal and three additional manuscripts reporting the toxicity results obtained to date are in preparation.

Environment Canada continues to support various academic research projects. This research has to date included studying fate and effects of nanomaterials in the aquatic, sediment, and soil compartments. New projects supported in fiscal 2014-15 are aimed at studying sub-surface transportation, and determining key physical-chemical parameters to predict ecotoxicity. This research is meant to directly feed into risk assessments of nanomaterials by: (1) informing on fate and behaviour in soils; and (2) informing on the development of predictive models by using a key base-set of physical-chemical parameters.

Environment Canada has also continued to foster excellence within its own department by conducting research on the fate of nanomaterials in aquatic, soil, sediment, and air compartments. This includes a research project, conducted with academic partners and Health Canada, which currently studies transformations of carbon nanotubes in the atmosphere. The objective of this study is to link observed physical and chemical changes to these nanotubes as a result of atmospheric processes, to broad changes in human and aquatic toxicity.

NRC Measurement Science and Standards is developing techniques for the measurement of mass concentration of airborne nanomaterials, concentrating on nanocarbon materials, but also applicable to metal oxides, metals, and possibly boron nitride nanomaterials. Further, a method for the calibration of real-time nanoaerosol mass concentration instruments selective to nanocarbon has been developed, and a traceable method for the calibration of real-time nanoaerosol mass concentration instruments (selective and nonselective) is under development. These methods may be useful for monitoring in manufacturing environments and for atmospheric monitoring.

Developments related to Integrated Testing Strategies and/or Alternative test methods.

Canada participated at the meeting on Alternative Testing Strategies (ATS) held back-to-back with the OECD WPMN Categories meeting in Washington D.C in September, 2014. This project supports the ongoing project on ATS within SG-AP. Outcomes from this workshop will feed into the final report to the WPMN and will also be published in a series of scientific publications.

Research programmes or strategies which focus on life cycle aspects of nanomaterials

Canada, along with Government agencies in the United States, Non-Governmental Organizations and Industry, is engaged in a project led by the International Life Sciences Institute (ILSI) to look at releases of nanomaterials from industrial consumer matrices (e.g., coatings). The objectives of this project are to develop information on different test methodologies and nanomaterials used to study releases from matrices, and to develop standard methodologies (validated through interlaboratory testing) to quantify releases of nanomaterials from a matrix. At present, Technical Groups have published two of the three white papers (the third paper is planned to be submitted shortly for peer-review) to inform on the present state pertaining to multi-walled carbon nanotubes (MWCNTs) in polymer matrices. In addition, a state of the science report is being drafted to provide recommendations and direction for the laboratory testing stage. After selecting the nanomaterial system and relevant test methods/protocols, the lab testing is currently being initiated. Health Canada and NRC are working on the sample characterization. Additional information can be found at

http://www.ilsi.org/ResearchFoundation/Pages/NanoRelease1.aspx.

Under the OECD Working Party on Resource Productivity and Waste (WPRPW), the expert group on waste containing nanomaterials has developed four reflection papers on the fate of nanomaterials in waste treatment operations. Canada is preparing the paper on the fate of nanomaterials in landfills; Switzerland on the recycling of waste containing nanomaterials; Germany on the incineration of waste containing nanomaterials; and France on nanomaterials in wastewater treatment sludge. The purpose of these papers is to provide an overview of the existing knowledge on the behaviour of nanomaterials during disposal operations and identify the information gaps. At the fourth meeting of the WPRPW that took place on 12-14 November 2013, three of the four reflection papers were considered by members. Canada's paper was presented and discussed at the fifth meeting of the WPRPRW that took place on 8-10 December 2014. Once the four papers are finalized, the plan is to draw these papers together into a publication in 2015. During the upcoming meeting, delegates will also discuss possible further work in this area in 2015-16.

Development related to exposure measurement and exposure mitigation.

Canada and Netherlands are currently developing a draft of the SG8 report "Strategy for distinguishing CNTs from background aerosols". Canada will present on this project in June 2015.

DENMARK

National regulatory developments on human health and environmental safety

In 2011 the Danish Government has allocated funding (approx 3,2 mio € from 2012-15) for establishing activities aimed at gaining clarity about the consequences for consumers and the environment due to the use of nanomaterials. The activities include the establishment of a database on products with nanomaterials. In October 2012 an Amendment Act to the Danish Chemicals Act was proposed with the purpose of establishing the necessary legislation for a mandatory national nano product database. After a public hearing, this proposal was presented in the national parliament in December 2012 and the first debate took place in the parliament on 29th of January. The amendment entered into force on the 12th of March 2013.

Following this amendment a proposal for a statutory order on a national register of mixtures and articles that contain nanomaterials as well as the requirement for manufacturers and importers to report to the register was submitted for public hearing in June 2013. An updated version taking comments from the public hearing into consideration was notified to the EU-commission in accordance with Directive 98/34/EF. The register entered into force in June 2014[1]. The first registration year is expected to be from 30th of August 2014 to 30th of August 2015. A guidance for importers and producers of nanoproducts in relation to the register has been published in Danish[2] and in English[3] and a help-desk service has been established[4].

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

[2] Link to the guidance in Danish: http://www2.mst.dk/Udgiv/publikationer/2014/06/978-87-93178-67-0.pdf

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

The Danish Environmental Protection Agency (DK-EPA) is responsible for implementing the initiatives under the National action plan for getting better control of nanomaterials (2012-15). Under this activity, a range of projects are currently being developed. These projects cover:

- General knowledge status and identification of knowledge gaps in relation to fate and effects of nanomaterials.
- Research oriented projects addressing important knowledge gaps (Dermal absorption of nanomaterials)
- Nanomaterials and waste
- Surveys and risk evaluations of specific uses of nanomaterials (aerosol projects, nanopigments, anatase titanium-dioxide)
- Overall assessment of environment and human risk in relation to nanomaterials in Denmark
- Support to WPMN-activities (in 2015, DK is financing researchers from the Technical University of Denmark who is contributing to project no. 3.8 in the OECD-test guidelines programme, the New TG on dissolution rate of nanomaterials in aquatic environment)

Since WPMN13 the Danish Environmental Protection Agency has published the following reports published under this initiative:

- Supplementary survey of products on the Danish market containing nanomaterials. Environmental project no. 1581, 2014[5].
- Environmental fate and behaviour of nanomaterials. Environmental project no. 1594, 2014[6].
- Nanomaterials in waste - Issues and new knowledge. Environmental Project no. 1608, 2014[7]

Further, as a part of these activities 10-15 reports will be prepared over the next years.

[3] Link to the guidance in English:
http://mst.dk/service/publikationer/publikationsarkiv/2014/aug/guideline-for-the-danish-inventory-of-nanoproducts/

[4] Link to the help-desk:
http://mst.dk/virksomhed-myndighed/kemikalier/miljoestyrelsens-nanoindsats/nanoproduktregistret/

[5] http://www2.mst.dk/Udgiv/publications/2014/06/978-87-93178-66-3.pdf

[6] http://www2.mst.dk/Udgiv/publications/2014/08/978-87-93178-87-8.pdf

[7] http://www2.mst.dk/Udgiv/publications/2014/10/978-87-93283-10-7.pdf

FINLAND

National regulatory developments on human health and environmental safety

Finland is a member of the EU and accordingly follows the EU regulations. Finland and Finnish Safety and Chemicals Agency (Tukes) as Competent Authority for chemicals, plant production products and biocides is actively participating in REACH competent authority (CARACAL) subgroup on nanomaterials (CASG-nano) and also ECHA Working Group for nanomaterials including GAARN work on already registered NMs, Tukes had been involved in the development of technical guidance how to apply the regulation on nanomaterials.. Similarly the work on novel foods and cosmetics is followed at EU level.

The Ministry of Health and Social Affairs has established 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. Specifically, Finland has contributed to the work of the GHS Sub-Committee informal correspondence group on nanomaterials by conducting a classification exercise on aquatic environmental hazards of selected nanomaterials. Finland has also coordinated a Nordic stakeholder survey to identify possible challenges concerning classification and labelling of nanomaterials. The project was carried out under the auspices of the Nordic Council of Ministers and the project report is available at http://norden.diva-portal.org/smash/record.jsf?pid=diva2%3A769053&dswid=-7596,.

Developments Related to Good Practice Documents

The Finnish Institute of Occupational Health has prepared practical guidance on the use of nanomaterials at working places. The first edition was published 2013.

Developments related to Integrated Testing Strategies and/or Alternative test methods

The alternative in vitro test methods are used in the several research projects among the in vivo tests.

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

Tukes (as National Coordinator) and **Finnish Institute of Occupational Health** together with industry partners **UPM Kymmene** and **Stora Enso** are participating in the FP7 project NANoREG by testing and assessing nanofibril cellulose, and regulatory issues.

The University of Technology, **VTT Finland** and **UPM Kymmene** have established The Finnish Centre for Nanocellulosic Technologies with 40 researchers concentrating on innovations but also on safety assessment of nanocellulose applications. The activities of the virtual Centre ended on December 31st 2013 as agreed in the contracts at the beginning of the co-operation. The targets set for the Centre were fulfilled.

Forestcluster LTD (a public-partnership for science, technology and innovations) had run a EffNet (Efficient Networking towards Novel Products and Processes, 2010 – 2013) program that focused, on one hand, on developing radically new energy and resource efficient web production technologies and, on the

other hand, reengineering the product concept of fiber based products with nanocellulose[8]. The E15 million program develops and demonstrates new types of products, but carries out also safety assessment of nanocellulose applications and studies their life-cycle. The EffNet programme ended in June 2013. The project results have been published in a public report[9] . In addition, a review on the safety assessment of bio-based nanomaterials will be published in Handbook of Green Materials in June[10] and a paper containing results on toxicity testing of nanocellulose was published in Cellulose in September.[11]

VTT is or has been involved in several research projects related to nanomaterial safety:

- EffTech/EffNet as described above
- MARINA - Managing Risks of Nanomaterials (EU-FP7, 2011-2015). "Standardised" measurement strategies and characterisation methods for nanoparticles and nanomaterials to be used in risk management of nanomaterials.
- Nanosafe 2 - Safe production and use of Nanomaterials (EU FP6).
- Nanosolutions (EUFP7, 2013-)
- NanoSustain – Development of sustainable solutions for nanotechnology-based products based on hazard characterization and LCA (EU-FP7, 2010-2013).
- Nanoturva - Nanoparticle detection and assessment of exposure in industrial facilities, part of the FinNano 2005-2010 (Finnish national nanosafety program) program funded by the Finnish Funding Agency for Innovation (TEKES).
- SUNPAP – Scaling up nanoparticles for modern papermaking (EUFP7, 2010-2012). VTT as coordinator
- INCOM – Industrial Production Processes for Nanoreinforced Composite (EU FP7, 2013-2017). VTT as coordinator.

Finnish Institute of Occupational Health and its Nanosafety Research Centre has been operational since January 1, 2011. The Centre has a staff of 25, and focuses on research on assessment of exposure to, and immuno- and genotoxic effects of engineered nanomaterials. The Centre also carries out research on nanoparticles characterization and risk assessment of engineered nanomaterials, and prepares guidance on safe use of engineered nanomaterials in workplaces.

Finnish Institute of Occupational Health (FIOH) is coordinating or participating several ongoing research projects on nanomaterials:

- Coordination of European Commission 7th Framework Programme project "NANOSOLUTIONS"
- European Commission 7th Framework project "QualityNano"
- European Commission 7th Framework project "Scaffold"
- European Commission 7th Framework project "MARINA"
- European Commission 7th Framework project "NANoREG"

[8] http://www.forestcluster.fi/d/content/efficient-networking-towards-novel-products-and-processes-2010-2013

[9] http://fibic.fi/wp-content/uploads/2012/07/EffNet_Ohjelmakirja_web.pdf

[10] http://www.worldscientific.com/worldscibooks/10.1142/8975

[11] Pitkänen, M., Kangas, H., Laitinen, O., Sneck, A., Lahtinen, P., Peresin, M.S. and Niinimäki, J. (2014) Characteristics and safety of nano-scale cellulose fibrils. Cellulose 21, 3871-3886. DOI 10.1007/s10570-014-0397-x

- European Commission 7th Framework project “GUIDEnano”
- European Commission COST action “MODENA”
- European Commission Marie Curie student exchange programme “Brasinoeu”
- Academy of Finland project "Carbon nanomaterial induced inflammatory effects "
- The Finnish Work Environment Fund is financing a project on nanomaterail assessment based on the proteinmodifications they cause. “*Nanomateriaalien ja niiden pintaominaisuuksien haitallisuuden määrittäminen proteiinimodifikaatioiden avulla*”
- The Finnish Work Environment Fund is financing a project on particle releases during 3-D printing.” *Materiaalia lisäävän valmistuksen (3D-tulostus) kaasu- ja hiukkaspäästöt eri työvaiheissa*
- In addition, FIOH is coordinating European NanoSafety Cluster which includes all the EU funded projects concerning nanosafety.

Finnish Environment Institute (SYKE) has started Academy of Finland project ”Nanosafety on trial(s): Understanding politics and potentials of product oriented environmental policies” that analyses how environmental and safety concerns are integrated into the development and design of nanocellulose products and production. The project aims to deepen our understanding of industry - government interaction and provides means to assess new regulatory approaches in the fields of nanotechnology and -materials and potentials of product-oriented environmental policy in general.

The SYKE laboratory has studied on aquatic exposure concentrating especially on nanomaterial characterization, fate and effects. The research has been funded by several national foundations.

The Ministry of Social Affairs and Health is a collaborator as the Finnish Institute of Occupational Health is an associated partner in the NanoGenotox project which is a Joint Action, and partly funded under the Commission's Second Health Programme focusing on Safety evaluation of manufactured nanomaterials by characterization of their potential genotoxic hazard.

The Finnish Food Safety Authority (Evira) is coordinating the work of a newly established Nordic Network on nanomaterials in Foodstuffs. The work is financed by The Council of Nordic Ministers.

The Finnish Food Safety Authority (Evira) and VTT Finland are participating in a European COST FA0904 project on “Eco-sustainable food packing base on polymer nanomaterials”.

FRANCE

National regulatory developments on human health and environmental safety

- Le Gouvernement français a rendu public le second bilan du dispositif de déclaration des substances à l'état nanoparticulaire fabriquées, distribuées ou importées sur le territoire national (http://www.developpement-durable.gouv.fr/IMG/pdf/rapport-nano-2014.pdf). Au 31 mai 2014, date limite pour déclarer les données 2013, plus de 1490 déclarants (670 en 2013) avaient réalisé plus de 10 400 déclarations (3 400 en 2013), représentant 400 000 tonnes de substances mises sur le marché en France en 2013 (500 000 tonnes en 2013). Le triplement du nombre de déclarations témoigne de la montée en puissance du dispositif auprès de l'ensemble des secteurs concernés. L'information relative aux quantités a pu être affinée.

- Les informations collectées sont mises à disposition d'organismes désignés par les textes en vigueur, dans le cadre de leurs travaux d'évaluation des risques et dans le respect des règles de confidentialité.

Developments related to good practice documents;

- L'ANSES (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail) vient de traduire en anglais son rapport et son avis d'avril 2014 relatifs à l'état des connaissances sur l'évaluation des risques associés aux nanomatériaux : https://www.anses.fr/sites/default/files/documents/AP2012sa0273RaEN.pdf

Developments related to Integrated Testing Strategies and/or Alternative test methods

- Dans le cadre du projet NanoREG (FP7), l'INERIS (Institut national de l'environnement industriel et des risques) a mené des tests d'exposition de cellules pulmonaires à des nanoparticules présentes dans l'air (interface air-liquide (ALI)) qui ont pu être comparés aux tests d'exposition, plus classiques, à des nanoparticules en suspension (conditions immergées). Pour un nanomatériau donné (TiO2 P25 NM105), les résultats ont montré que l'exposition ALI, plus représentative de l'inhalation *in vivo*, induisait des effets plus importants (cytotoxicité, inflammation) qu'en conditions immergées. Des tests sur d'autres nanomatériaux sont en cours (NM100, 101, 212 et 220) pour valider que le modèle ALI est bien représentatif des résultats obtenus dans les essais *in vivo*.

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

- Le Gouvernement français a adopté son 3ème Plan National « Santé-Environnement » qui couvre la période 2015-2019 (http://www.developpement-durable.gouv.fr/IMG/PNSE3(1).pdf). Celui-ci prévoit notamment les actions suivantes dans le domaine de la sécurité des nanomatériaux manufacturés :
    - l'évaluation de l'exposition aux nanomatériaux dans les denrées alimentaires ;
    - le soutien du renforcement du corpus réglementaire européen sur les nanomatériaux (modification des annexes de REACH et examen d'autres options comme un registre européen des nanomatériaux comparable au dispositif français) ;
    - l'incitation des parties prenantes à porter au niveau européen de demandes de classification harmonisée de familles de nanomatériaux pour lesquels il existe un faisceau de preuves significatif ;

- la réalisation de campagnes expérimentales de mesure à l'extérieur des sites de fabrication et, en fonction des résultats, l'objectif de fixer des valeurs limites dans les milieux ;
- l'étude du devenir des nanomatériaux (vieillissement, phase déchets) et l'acquisition de connaissances sur les déchets contenant des nanomatériaux et les déchets d'installations produisant des nanomatériaux ;
- la caractérisation des dangers des nanomatériaux, en particulier à faible dose, en exposition chronique ;
- la définition de priorités dans les projets de recherche dont la métrologie et la traçabilité des nanomatériaux dans les milieux et les produits de consommation.

- Le Gouvernement français a également publié sa feuille de route 2015 issue des travaux de la conférence environnementale de novembre 2014 associant l'ensemble des parties prenantes. Dans ce cadre, les autorités françaises ont proposé au Conseil Environnement de l'Union européenne du 17 décembre 2014 qu'une stratégie d'étiquetage des produits de consommation courante contenant des nanomatériaux et de restriction des produits dangereux en contact avec la peau (notamment avec les enfants et les femmes enceintes) soit mise en place au niveau européen. Un groupe de travail sera créé au niveau national pour préciser ces propositions au cours du premier semestre 2015. Les conclusions issues de ses travaux seront transmises par le gouvernement français à la Commission européenne et aux autres Etats membres.

- Une opération de prospective intitulée « Les nanomatériaux manufacturés à l'horizon 2030 : conséquences en santé et sécurité au travail dans les petites entreprises en France » a été menée en 2014 par l'INRS (Institut national de recherche et de sécurité) dans le cadre d'un groupe de travail pluridisciplinaire impliquant 7 organismes partenaires (ANSES, InVS, Institut Jean Lamour, Université de Bretagne-Sud, CARSAT Alsace-Moselle, SUVA, Ecole des Ponts ParisTech). Cet exercice a porté sur les évolutions probables du contexte, des risques et de la prévention associés aux nanomatériaux manufacturés à l'horizon 2030. Les rendus de ce projet sont disponibles sur demande.

- L'INERIS a engagé des études afin d'améliorer les connaissances sur les nanoparticules de TiO2 connues pour induire des tumeurs, des inflammations et une génotoxicité dans les poumons, le sang et le foie. Le résultat est que des doses importantes de TiO2 induisent des lésions de l'ADN dans les poumons et le foie indépendamment du temps de récupération. Il a également été montré que le TiO2 induisait des dommages à effet retardés sur l'ADN et des mutations chromosomiques dans les cellules sanguines même à des doses non-inflammatoires. A partir de ces données, il a été conclu que les comètes et les micronuclei du sang pouvaient être des biomarqueurs utiles dans les études épidémiologiques pour suivre la génotoxicité après exposition professionnelle.

Research or strategies on life cycle aspects of nanomaterials

- Le projet "NanoFlueGas", piloté par l'INERIS et soutenu par l'ADEME (Agence de l'environnement et de la maîtrise de l'énergie), est dédié à la compréhension : 1/ du comportement et du relargage des nanomatériaux lorsqu'ils sont incinérés, 2/ de la capacité des incinérateurs à filtrer les aérosols émis. Des bancs de mesure ont été développés et sont désormais disponibles pour étudier différents types de déchets.

- Dans le cadre d'un programme d'appui au Ministère de l'écologie, l'INERIS a mené des études sur le vieillissement de matériaux bruts et de revêtements, par action mécanique ou environnementale, et a produit dans ce cadre plusieurs articles scientifiques (ISI). En particulier, il a été démontré que des nanoparticules "libres" peuvent être émises à partir de nanoparticules intégrées dans une matrice, après exposition de celle-ci à des facteurs environnementaux. Cela confirme que les tests

ne doivent pas être menés uniquement sur les matériaux dans leur état d'origine mais aussi sur des matériaux vieillis.

Development related to exposure measurement and exposure mitigation.

- En décembre 2014, l'INERIS a inauguré sa plateforme de nanosécurité, S-NANO. Avec une surface de 400 m² divisée en 4 laboratoires, une zone de stockage et une zone de déchets, S-NANO est dédiée à la métrologie et à l'étude des caractéristiques physico-chimiques des nanomatériaux, la caractérisation de leur émissivité au cours de leur production et de leur usage, la gestion de la fin de vie des produits et la caractérisation des dangers, en particulier dans le cadre de la sécurité des procédés et des sites industriels comme l'inflammabilité, l'explosivité, la pulvérulence…

- Dans le cadre du projet SANOWORK (FP7), des campagnes d'évaluation sur le lieu de travail ont été conduites sur différents sites industriels. Cela a permis d'identifier des cas d'étude faisant l'objet d'approches « safe-by-design ». En particulier, il a été démontré la capacité à développer des nano-poudres présentant des propriétés commerciales équivalentes mais une pulvérulence moindre, améliorant ainsi le niveau de sécurité sur le lieu de travail (Le Bihan et al., 2014). Cette approche a été étendue à divers nanomatériaux manufacturés (NTCs, nanofibres de TiO2, ZrO2).

Additional Information

Consideration on the benefits of nanotechnologies

- L'INERIS travaille actuellement sur l'établissement d'un cadre méthodologique destiné à évaluer les coûts et bénéfices associés aux nanotechnologies. Une étude de cas a été développée autour de l'utilisation de revêtements photocatalytiques de nano-TiO2 pour empêcher l'encrassement de panneaux photovoltaïques. Cette technologie permet des économies d'énergie mais le nano-TiO2 pourrait présenter des effets toxiques pour la santé et l'environnement tout au long du cycle de vie du produit. Basé sur une caractérisation physico-chimique de 2 produits présents sur le marché et sur un état des connaissances sur les effets potentiels du TiO2 sur la santé et l'environnement, plusieurs variables économiques ont pu être définies comme (i) la monétisation des externalités environnementales liées à la mise en œuvre de cette technologie à l'échelle française, (ii) le bénéfice global attendu pour les possesseurs de tels panneaux, (iii) la rentabilité de la solution en terme de réduction des émissions de CO2.

GERMANY

Highlight of developments

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

Expert dialogue on nanomaterials: Nanomaterial in Waste

Representatives of the scientific community, industry, environmental associations, government and government agencies met on 28-29 October on the invitation of the BMUB. At the conference the discussion focused on chances and risks of nanotechnology in the field of waste and disposal of waste. The results will be published in a thematic report on the homepage of BMUB. http://www.bmub.bund.de/en/topics/health-chemical-safety-nanotechnology/nanotechnology/nanodialogue/

The conference on nanomaterials and the aquatic environment constitutes the continuation of the fourth phase of the NanoDialogue – a platform for the discussion of emerging issues with stakeholders starting in 2006. The emphasis of the dialogue workshops is based on the societal context of the respective topics. The main objective is to facilitate the exchange of views among the stakeholders.

Developments related to Integrated Testing Strategies and/or Alternative test methods

A. Federal Ministry of Education and Research (BMBF)

Standardisation efforts and OECD activities are being supported by national collaborative research projects funded under the "NanoCare" research priority within the WING Programme (see below).

B Federal Environment Agency (Umweltbundesamt, UBA)

On behalf of UBA a proposal for a test and environmental risk assessment strategy for engineered nanomaterials (ENM) addressing environmental fate and effect was developed within a research project. For the test strategy development both conventional and alternative endpoints were considered. Recommendations for the fate and effects testing were provided. The recommendations consider various levels of test complexity as they are commonly used in a tiered risk assessment scheme. The proposed test strategy on effects comprises of three sub-steps: Step 1: decision on ENM to be tested; Step 2: testing; Step 3: use of test results. Furthermore, in a comprehensive literature survey the usefulness of employing alternative endpoints within a regulatory framework was reviewed. The suggested test strategy was developed based on the knowledge of (inter)national publications and discussions. It also takes into account the conclusions made by the OECD WPMN Expert Meeting on ecotoxicity and environmental fate which met in Berlin in January 2013. The test strategy features an overarching/general approach to test and assess fate and effects of NM. However, it has to be noted that it is not yet specified to fulfil the information requirements of a certain legislation (e.g. plant protection act, biocide regulation, REACH). The project report ("Integrative test strategy for the environmental assessment of nanomterials") will be available on the web page of the Federal Environment Agency soon:

http://www.umweltbundesamt.de/publikationen

C Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR)

In close collaboration with the newly established Berlin-Brandenburg Research Platform and Graduate School BB3R the BfR will establish a test platform for systematic toxicity testing of nanomaterials in vitro.

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

A. Federal Ministry of Education and Research (BMBF)

The research priority "NanoCare - Safe Handling of Manufactured Nanomaterials – Investigating Impacts on Health and the Environment" is continued to be funded within the frame of the German funding programme "WING" (Materials Innovations for Industry and Society). Seven new projects started in 2014:

- DENANA - Design criteria for sustainable nanomaterials

- nanoCOLT - Long-term effect of modified carbon black nanoparticles on healthy and damaged lungs

- INHALT-90: 90 days inhalation testing with CeO_2 in the rat and subsequent analysis of gene expression profiles for the early detection of toxic / carcinogenic effects

- NANOMOBIL: Synthetic Silver Nanoparticles in the system Soil-Groundwater - mobility, effects on cohabitation and interaction between hydro-, pedo- and biosphere

- NanoBioDetect: Nanoparticles in the tissue: detection, quantification and presentation of biological effect markers

- NANOSUPPE - Behaviour of engineered nanoparticles in the pathway wastewater - sewage sludge - plant using the examples TiO_2, CeO_2, mwCNT and quantum dots

- NanoUmwelt - Risk analysis of engineered nanomaterials in the environment: identification, quantification and analysis of the human- and ecotoxicological effects

First results of the project „CarboTox" (toxicity of carbon nanotubes, CNT) funded by BMBF in the frame of the funding measure "NanoCare" have been published. Tailor-made multi-walled carbon nanotubes (mwCNTs) without functionalization were investigated in vivo in a two-year intraperitoneal carcinogenicity study in rats. Treatments induced tumors in all dose groups, most tumors were classified as malignant mesotheliomas. All tested mwCNT types caused mesotheliomas and showed fibre-typical carcinogenic effects. The rather straight mwCNT types cause earliest appearance of morbid mesothelioma after treatment, the more curved types of nanotubes lead to appearance of morbid mesothelioma at a later time in this two-year study. Besides aspect ratio, curvature seems to be an important parameter influencing the carcinogenicity of mwCNTs. Published online Nov 20, 2014: Particle and Fibre Toxicology, Part Fibre Toxicol. 2014; 11(1): 59. doi: 10.1186/s12989-014-0059-z

Germany is coordinating the European FP7 ERA-NET project "SIINN" (Safe Implementation of Innovative Nanoscience and Nanotechnology - www.siinn.eu) in which 20 ministries and national/regional funding organizations from 13 European countries/regions and Israel participate. The SIINN ERA-NET is bringing together today's fragmented research activities on the potential risks of engineered nanomaterials for the environment, human health and safety through networking and joint transnational calls.

The second SIINN Call was published in 2013 and resulted in five transnational projects (four of them with participation of Germany) which will start in early 2015.

The European Commission agreed to prolongate the ERA-NET SIINN by one year. SIINN will now end in July 2015. The major objective of this prolongation is the implementation of the third joint transnational SIINN Call which has been opened on the 1st of October for the submission of innovative transnational research proposals focusing on manufactured nanomaterials (MNMs) in the four topics listed below:

1. Exposure assessment
2. Toxicity mechanisms
3. Effects of MNMs on human health
4. Environmental impacts of MNMs

(Submission deadline: 16/01/2015, 12:00 am CET, 07:00 a.m. Washington D. C. Time; http://www.siinn.eu/en/joint-calls/2014-third-siinn-call/,161)

In the frame of the third SIINN call, seven funding agencies from European countries/regions (Austria, Belgium, Germany, Portugal, Region Nord-Pas de Calais (France), Romania, Spain) and three funding agencies from the USA (NSF, CPSC, NIEHS) have agreed to launch the first joint transatlantic funding programme on nanosafety research.

B Federal Environment Agency (Umweltbundesamt, UBA)

UBA launched a new project entitled "Categorization of nanomaterials aiming for a joint assessment of ecotoxicity for regulatory purposes". Aim of the project is to correlate physical chemical data of selected nanomaterials with their ecotoxic effects and to identify reference parameters which may serve a basis for categorization. A set of nanomaterials was selected which cover a variability of different physical chemical characteristics which are suspected to influence ecotoxicity of pristine nanomaterials. Based on this set of nanomaterials a preliminary categorization is created. The assumed categorization will be verified by experiments applying aquatic ecotoxicological standard tests according to OECD TG (OECD TG 201, 202, 236). Based on the experimental results the categorization will be modified and refined. The project is intended for finalization in spring 2017.In the context of the EU Research and Innovation Program Horizon 2020 UBA is engaged in a new joint activity called PROSAFE - Promoting the Implementation of Safe(r) by Design. The aim of this activity is to coordinate and support risk assessment, management and governance by streamlining data acquisition, collection and management on regulatory orientated toxicology testing of nanomaterials, exposure monitoring, LCA, and disposal and treatment of waste nanomaterials. Furthermore, PROSAFE aims to facilitate and promote the acceptance of Safe(r) by Design within the EU COM, its members and associated states. Within this activity, UBA will coordinate the liaisons to national partners as well as international bodies and will be involved in the organisation of conferences and workshops related to this activity.

UBA acts as (associated) partner in several new projects launched under the research priority "NanoCare - Safe Handling of Manufactured Nanomaterials – Investigating Impacts on Health and the Environment" of the Federal Ministry of Education and Research (BMBF). The different projects address fate and effects of manufactured nanomaterials on environment and human health with emphasis e.g. on safe(r) design (DENANA – Design criteria for sustainable nanomaterials), , higher tier tests for soil and groundwater (NanoMobil - Synthetic Silver Nanoparticles in the system Soil-Groundwater - mobility, effects on cohabitation and interaction between hydro-, pedo- and biosphere) as well as the investigation of residues of manufactured nanomaterials in biological tissues (NanoUmwelt - Risk analysis of engineered nanomaterials in the environment: identification, quantification and analysis of the human- and ecotoxicological effects). The projects are intended for a duration of three years and started in autumn this year or scheduled for early spring next year, respectively. Within these projects UBA will perform studies on environmental fate of manufactured nanomaterials in water and water saturated sandy sediments as well

as studies on acute and long term aquatic ecotoxicity. Furthermore, within these projects, UBA will act as interface for OECD and regulatory activities.

C Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR)

BfR is involved in a still ongoing BMBF project DENANA (Design criteria of sustainable nano materials). The project started in October 2014 and is funded under the "NanoCare" research priority within the WING Programme. The goal of DENANA is the development of criteria for the production of sustainable nano materials (NM) with focus on long-term effects under realistic environmental conditions. The project is focused on commercially important nano particles (NP) like SiO2, CeO2 and Ag. The commercial aspects will be observed exemplarily using a lubricant model on the basis of Silica dioxid-NP (SiO2NP). BfR will contribute to the project with the investigations of the fate, the alteration and the effects of the NP in plant and animal tissues, with the goal to identify early-warning indicators that may be transferred to other systems.

Additionally BfR is involved in a still ongoing EU FP7 Project NanoDefine, which focuses primarily on the development of an integrated approach based on validated and standardized methods to support the implementation of the EC recommendation for a definition of nanomaterial. The challenge consists in the development of methods that reliably identify, characterize and measure nanomaterials (NM) both as substance and in various products and matrices. One major outcome of the project will be the establishment of an integrated tiered approach including validated rapid screening methods (tier 1) and validated in depth methods (tier 2), with a user manual to guide end-users, such as manufacturers, regulatory bodies and contract laboratories, to implement the developed methodology. Furthermore we develop best practice SOP's by testing protocols for suitability and robustness in round robins and interlaboratory comparisons.

The BfR is involved in the French-German collaborative project "The toxicity in intestine and liver for nanoparticles used in food and packaging. Determining factors of the toxicity in intestine and liver for two similar sized nanoparticles used in food and packaging: In vitro and in vivo investigation on uptake and mechanisms involved (SolNanoTOX)".

Little is known concerning the toxicity of NMs following ingestion. Moreover, their size, morphology and state of agglomeration together with physiological modifications are likely to play a considerable role in the uptake and toxicity of these materials to humans. Actually, very little data is available concerning the toxic effects of NMs following oral exposure in vivo.

Among the properties of NMs, the solubilisation capacity is likely an important determinant of nanomaterial uptake and the initiation of specific pathways of toxicity. In the SolNanoTox project, representatives of two different classes of NMs will be investigated: titanium dioxide as an example for insoluble species due to its stability in water and aluminium representing the soluble category.

Information on public/ stakeholder consultation

A. Federal Ministry of Education and Research (BMBF)

The web-based knowledge and data platform 'DaNa – The Knowledge Platform on Nanomaterials' is continued to be funded by BMBF (www.nanopartikel.info; www.nanoobject.info). The aim of the web presence is to illustrate research results on safety aspects of nanomaterials to a broad audience – to experts as well as to lay people – well-structured and intelligible to all. The core of this website is the data base of nanomaterials in the domain 'nanoINFO', which concentrates the latest knowledge in this field.

The BMBF continues its series of dialogue events “citizens meet experts” to inform the interested public on chances, risks and perspectives of nanotechnology and to provide an opportunity for the participants to discuss with experts.

Research or strategies on life cycle aspects of nanomaterials

A Federal Environment Agency (Umweltbundesamt, UBA)

UBA publishes data sheets concerning nano-products. The data sheets focus on the description of application and on ecotoxicological and health aspects. So far, four fact sheets were published which are available on the UBA website:

- Use of nanoscale iron for the remediation of groundwater damages (http://www.umweltbundesamt.de/publikationen/use-of-nanoscale-iron-for-the-remediation-of)
- Nanotechnology-based lighting systems: organic light-emitting diode (OLED) (http://www.umweltbundesamt.de/publikationen/nanotechnology-based-lighting-systems-organic-light)
- Use of nanomaterials in textiles (http://www.umweltbundesamt.de/publikationen/use-of-nanomaterials-in-textiles)
- Use of nanomaterials in coatings (http://www.umweltbundesamt.de/en/publikationen/use-of-nanomaterials-in-coatings)

A further datasheet on use of nanomaterials in energy storage devices is underway.

Development related to exposure measurement and exposure mitigation

A Federal Institute for Risk Assessment (Bundesinstitut für Risikobewertung, BfR)

In an in-house research project the BfR systematically investigates the release of nanoparticles from consumer products. One of the main challenges is to determine the internal dose of nanoparticles. Therefore the BfR develops different methods suitable to study uptake and distribution of nanoparticles in vitro and in vivo, possibly even in a quantitative manner.

ITALY

Highlight of developments

National regulatory developments on human health and environmental safety

The activity on the National registry on nanomaterials is still in progress. The structure of the Italian nano-database is being set in collaboration with other EU Member States in order to harmonize the approach used to gather information on nanomaterials on the EU market.

Following the EU Commission 2nd regulatory review on nanomaterials publication, Italy has been involved in discussions among MSs on possible ways to adapt existing regulations on chemicals vs proposal on ad hoc regulation with nanospecific requirements.

Developments related to voluntary or stewardship schemes

A national Working Group on Nanomaterials under REACH Competent Authority technical committee was established to deal with regulatory issues related to REACH and CLP application to nanomaterials. The WG sees the participation of relevant institutions involved in REACH and CLP implementation and technical bodies, workers protection Agencies and main industrial associations, plus experts form research centers and industry. Main outcome of the WG activity is the set-up of a national registry on nanomaterials on the national market and R&D. The draft project is now under public consultation among national experts and stakeholders. The following main scientific and technical challenges of the current scheme designed to gather data on nanomaterials put on the market and used, also in R&D, are under discussion: definition, tonnage threshold, chemical-physical characterization methods, terminology, online submission of huge amount of data, IUCLID compatibility.

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

Nanosafety Cluster and Modena COST action organized in Italy a scientific conference focused on presentations of young scientists working in EU-funded nanosafety projects. The event, held in October 2014 in Syracuse (Sicily), was an open Forum for scientists involved in nanosafety researches; oral presentations from young scientists and forward-looking keynotes from senior investigations were planned. The goal was to exchange scientific information and visions between young and senior scientists.

CARIPLO foundation funded eight two-year research projects (2014-2016) addressed to the study of the impact of ultrafine particles and engineered nanoparticles on human health.

Activities related to the Sustainable Nanotechnologies (SUN) project are in progress. The project brings together 35 partners from 12 EU countries. It is coordinated by Venice University Ca' Foscari and it is based on the idea that the current knowledge on environmental and health risks of nanomaterials, while limited, can nevertheless guide nano-manufacturing to avoid liabilities if an integrated approach addressing the complete product lifecycle is applied.

Health and safety issues related to silica nanoparticles are under study in the project "Sviluppo di metodi validati e/o alternativi per la determinazione della dimensione, distribuzione, agglomerazione e citotossicità di nanomateriali utilizzati in diversi settori industriali" founded by Italian Ministry of Health. Results of the project, led by National Institute of Health (Istituto Superiore di Sanità, ISS), are expected in early 2015.

Results of the project Nanotox "*Toxicology of chronic exposure to engineered silver nanoparticles*", led by the University of Milan, will be make public during a workshop planned in March 2015 in Milan.

ISS experts participated to the OECD Horizontal Meeting on Categorization of Manufactured Nanomaterials (Washington, September 2014) and the Expert Meeting on the adaptation of the genotoxicity in vitro micronucleus assay (TG 487) for testing of NMs (Paris, October 2014).

Activities related to NANoREG project (NMP.2012.1.3-3 Regulatory testing of nanomaterials) are ongoing. The National coordinator of the project, Italian Ministry of Health, organized the Italian mid-term meeting in Rome (July 2014) in order to discuss the progress of the activities with partners and stakeholders.

Information on public/ stakeholder consultation

A survey to gather the opinion of European and Italian citizens on nanotechnology innovation priorities has been conducted in EU and Italy (March to September 2014), within the activities of the EU NMP NanoDiode Project (AIRI/Nanotec IT partner). More than 1500 people from Europe and 230 from Italy participated showing, overall, a positive view on nanotechnologies. Results will be published in January 2015 on the NanoDiode website.

On the Italian Ministry of Health website is still available the voluntary survey on the use of nanomaterials in cosmetics, including information on safety and labelling: http://www.salute.gov.it/portale/temi/p2_6.jsp?lingua=italiano&id=3104&area=cosmetici&menu=vuoto

In the framework of NanotechItaly 2014 Conference (26-28 November 2014), it has been held a User Committee on safety by design of nanosilver. It involved industry, research, authorities, and civil society organizations.

JAPAN

Highlight of developments

- Japan is positively participating in ISO/TC229 activities.
- Many of scientific research projects are still on going in Japan.

Developments related to voluntary or stewardship schemes

The Ministry of Economy, Trade and Industry (METI) calls on the industries to voluntarily report their safety data and management activities on the manufactured nanomaterials to METI. METI publicised each report on its website (see 5. for details).

Developments related to good practice documents

METI firstly publicised information on safety test data and management methods of manufactured nanomaterials, on METI's website[12] in 2010 (only in Japanese). Such information was voluntarily provided and annually updated by the manufacturers. METI publicised the updated information in 2014.

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

Since December 2011, a committee established by METI has discussed measuring methods of nanomaterials and some case studies on risk assessment of products containing nanomaterials. In June 2013, the committee issued an interim report on its discussion.

In April 2012, a committee established by the Ministry of Health, Labour and Welfare (MHLW) began consideration of risk assessment for the prevention of impairment of workers' health caused by exposure to TiO_2 in nanoscale. In addition, MHLW launched development of measurement methods for airborne nanomaterials, carbon black and SW/MWCNT.

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) and currently leads the development of a TC229 document (Technical Specification) in TC229/WG3 (Health, Safety and Environmental Aspects of Nanotechnologies) that is ISO/TS 19337 "Nanotechnologies -- Characterisation of working suspensions of nano-objects for *in vitro* assays to evaluate inherent nano-object toxicity." In TC229/JWG2, JISC leads the Study Group on Tiered Approach for Nano-object Identification within a Sample, and jointly (with ANSI, the American National Standards Institute) leads the Study Group on Particle Size Distribution by Transmission Electron Microscopy, and also jointly (with ANSI) leads a Preliminary Work Item "Determination of size and size distribution of nano-objects by scanning electron microscopy" (PWI 19749), and has been preparing a New Work Item Proposal "General framework of determination of reliable size distribution of particles in nanosuspension using pre-treatment/pre-fractionation and sizing methods.".

An expert committee, organised by the Ministry of the Environment (MOE) issued the "Guidelines for preventing the environmental impact of manufactured nanomaterials" to provide manufacturers with currently available information for the environmentally sound management of manufactured nanomaterials, in March 2009[13]. From 2011 JFY MOE has been focusing their efforts on environmental risk of manufactured nanomaterials via understanding of their environmental fate and ecotoxicity. Aiming at developing methodologies for measurement of manufactured nanomaterials in the environment (i.e., ambient air and surface water), MOE has initiated their attempts through measuring nano-scale TiO_2 in a closed system and then in the open air outside of the waste shredders. MOE has also been collecting and reviewing existing literature on ecotoxicity of manufactured nanomaterials such as TiO_2, silver and CNTs to identify any harmful effects attributed to their particle size.

Developments related to Integrated Testing Strategies and/or Alternative test methods

The National Institute of Advanced Industrial Science and Technology (AIST) participated in a WPMN interlaboratory comparison study on colony forming efficiency (CFE) assay led by the European Commission's Joint Research Centre (JRC), where Japan provided, as one of test samples, dispersions of SWCNT with a guarantee of two-month dispersion stability.

AIST, as a member of the Technology Research Association for SWCNT(TASC), released a document "The protocols of preparation, characterisation and *in vitro* cell based assays for safety testing of carbon nanotubes" that is available on the AIST-RISS website[14].

[13] http://www.env.go.jp/chemi/nanomaterial/eibs-conf/guideline_0903_enab.pdf
[14] http://en.aist-riss.jp/research/assessment/

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

METI launched a five-year programme for the "Development of Innovative Methodology for Safety Assessment of Industrial Nanomaterials" in 2011, which aims to develop fundamental hazard assessment methodology leading to a tiered risk assessment approach for industrial nanomaterials. The programme has two R&D themes: 1) establishment of equivalence criteria of nanomaterials and 2) establishment of an intratracheal administration method as low-cost and convenient method for hazard assessment to acquire basic hazard information, both of which are for regulatory purposes. A website http://www.aist-riss.jp/projects/meti-nano/en/ to introduce this programme was released in December 2013. Some results of the R&D theme 2) above were presented at a WPMN horizontal expert workshop on toxicokinetics of nanomaterials in February 2014. Preliminary results of the R&D theme 1) above were presented at a WPMN horizontal expert workshop on categorisation of nanomaterials in September 2014. Against a backdrop of the implementation of this programme, Japan leads a WPMN Risk Assessment Pilot Project "Survey on approaches to develop or use concepts of grouping, equivalence and read-across based on physical-chemical properties of nanomaterials for their human health and ecosystem hazard assessment in regulatory regimes" , whose preliminary results were also presented at the WPMN categorisation workshop.

METI also launched a five-year programme "Development of Innovation Carbon Nanotube Composite Materials for a Low Carbon Emission Society" in 2010. One of various R&D themes of the programme was "techniques suitable for voluntary safety management of CNTs by industries"[15], which focused on the development of toxicity testing and exposure assessment protocols for ensuring safety of CNTs and their applications, and whose results were released as the two documents described in 6. above and 10. below by AIST, as a member of TASC, in October 2013. The programme was converted into a three-year programme "Commercialising Carbon Nanomaterials for a Low Carbon Emission Society" starting in mid-2014. One of R&D themes of this successive programme is "to establish techniques for assessing release and exposure of carbon nanomaterials from their application products". Under this R&D theme, the following two documents (only in Japanese) regarding two types of SWCNTs[16] were released by AIST, as a member of TASC:

- "Safety data and introduction of a voluntary safety management regarding Super-growth single-wall carbon nanotubes" released in November 2014 and

- "Safety data and introduction of a voluntary safety management regarding eDIPS single-wall carbon nanotubes" released in December 2014.

MHLW has promoted research on the human health aspect of several nanomaterials since 2003 through the Health and Labour Sciences Research Grants, etc. In 2014 JFY, eight research projects, including a basic research on development of methods for evaluating hazard and disposition of nanomaterials on human health, are progressing.

The Japan Bioassay Research Center launched a "Research project on the potential hazards, etc. of nanomaterials", commissioned by MHLW, which focuses on carcinogenicity of nanomaterials used/manufactured in the workplace (six-year programme, 2009-2015). Two-year inhalation study of MWCNT is on-going now (2012-2015). In addition, in order to elucidate the carcinogenic mechanism, *in vitro* chromosome aberration and *in vivo* micronucleus tests have been carried out in 2015.

[15] http://tia-nano.jp/en/core/area/nano-material.html

[16] http://tia-nano.jp/en/core/area/carbon-nano.html

The National Institute of Occupational Safety and Health, Japan (JNIOSH) is currently conducting a three-year project study (2012-2014 JFY), "Toxicological Study on Ultrafine Particles of Metal Oxides". This project includes investigation on 1) genotoxicity, 2) neurotoxicity, and 3) reproductive toxicity of nano-sized TiO2 particle. Another three-year project (2013-2015 JFY), "Study on collection and analysis procedures of airborne particulate matters in nanomaterial-handling workplaces" can provide a practical procedure for exposure assessment of multi-dispersed particles by using real-time instruments and interpretation of different metrics of nanomaterials including (chemical) mass, and a continuous generating method of multi-dispersed particles simulating real workplace environment.

The National Institute for Environmental Studies (NIES) completed the 1st nanotoxicology programme (2006-2010 JFY) which included the interaction of MWCNTs with cell membranes and *in vitro* transepithelial and transpulmonary migration of polystyrene or gold nanoparticles. NIES has been undertaking the 2nd nanotoxicology programme (2011-2015 JFY) which includes *in vivo* toxicological studies of MWCNT, *in vitro* and *in vivo* toxicological study of silver nanoparticles in reference to dissolution of metal nanoparticles, toxicokinetics of fluorescence-labelled dendtrimers and ecotoxicological study of TiO_2 nanoparticles using embryo and sac-fry fish.

Development related to exposure measurement and exposure mitigation

AIST, as a member of TASC, released a document "Guide to measuring airborne carbon nanotubes in workplaces" that is available on the AIST-RISS website[17].

KOREA

National regulatory developments on human health and environmental safety

Ministry of Environment has developed the guidance on exposure assessment and safe management of manufactured nanomaterials.

Developments related to voluntary or stewardship schemes

Ministry of Environment has been conducting the project which is a voluntary survey on the production, use, import and export volumes and use patterns of manufactured nanomaterials from 2011.

Information on risk assessment decisions

The Korean government has implemented the research projects as elaborated below in #5 this year including risk assessment, but these are still in the initial stage.

[17] http://en.aist-riss.jp/research/assessment/

Developments related to good practice documents

The Korean government has implemented the projects related to good practice as following.

Developments related to Integrated Testing Strategies and/or Alternative test methods

KATS(Korea Agency for Technology and Standards)is developing 2 international standards in the ISO/TC 229 (Nanotechnologies) relevant to nanomaterial safety testing "Aerosol generation for NOAA (Nano-objects, and their aggregates andagglomerates) air exposure studies" and Electron spin resonance (ESR) as a method for measuring reactive oxygen species (ROS)generated by metal oxide nanomaterials". These standard documents will complement the work of the OECDWPMN and other related frameworkdocuments. KATS will revised KS A 6202:2009 "Guidance to safe handling of manufactured nanomaterials in workplace/laboratory" to update to include newly emerged information (2015).

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

The Korean government has well recognized the importance of potential risks of nanomaterials, and several projects are in progress, regarding human health and environmental safety issues of nanomaterials.

Ministry of Environment (MOE)

MOE implemented the projects such as 'Research on the most relevant dosing metric for the ecotoxicity management system of manufactured nanomaterials (2009~2012)' in order to identify the correlation between the dose metric and the risk assessment and 'Genomic studies of nanoparticles to rats, bacteria, yeast and fish' to develop alternative methods for nanotoxicity tests.

MOE and NIER (National Institute of Environmental Research, an affiliated body of MOE) have conducted the nanomaterials hazard assessment projects to review and adopt the OECD TGs on nanomaterials and cumulate the data related to physico-chemical properties, eco-toxicity, environmental fate and human-health in order to contribute to decision making since 2007. MOE and NIER launched the project for a survey on the production, use, import and export volumes, use pattern and the information on manufactured nanomaterials in order to establish inventory for nanomaterials. As a result, in December 2012, MOE conducted an inventory survey on nanomaterials and is performing a follow-up survey on four nanomaterials (CNT, ZnO, Ag, SiO_2) to investigate their states of lifecycle circulation and specific usages, etc. NIER is responsible for the Nanomaterial Risk Expert Committee that handles the nanomaterial safety issues, such as reviewing of the project planning on the nanomaterial safety assessment. Also, we are preparing a guideline on definitions of nanomaterials at an inter-ministerial level within 2014.

Furthermore, MOE and NIER take a key role in facilitating and conducting OECD sponsorship programme under close co-operation among ministries, academia, and industries.

Ministry of Trade, Industry and Energy (MOTIE)

MOTIE in collaboration with MSIP has initiated the programme "Strategy on Nano Convergence Industry Development" to strengthen research on the safety and social impact of nanomaterials. The MOTIE/KATS implemented "Risk Management Platform Technology for NanoProducts (2009-2013)" which provided an infrastructure for the certification of nanoproducts based on a risk management system including characterization, efficacy quality and safety assessment along with standard development. The project "Risk Management Platform Technology for NanoProducts (2009-2013)" was finished October,

2014. This project provided test reports of health effects and environmental effects for nanosilver, nanoTiO2 and MWCNT. The program tested 3 nanomaterials (Ag, TiO2, MWCNT) according to OECD test guidelines including acute to subchronic toxicity testing with various administration routes. In addition, skin and eye irritation test and genotoxicity tests were also conducted with OECD test guidelines. The project also provided foundation for developing nanomaterial exposure assessment and risk management technologies.To carry out the 'National Nano-safety Master Plan(2012-2016)', MOTIE launched Tier 2 project called "Development of safety evaluation based technology for nanoproduct to promote commercialization" was launched. The project lasts from 2013-2015. The project has 3 parts; Part 1(Establishment of database for product containing nanomaterials and inventory) includes nanomaterial/product safety inventory including safety data sheets for nanomaterials, and developing algorism for certification of nanoproduct safety. Part 2 (Nanoproduct safety assessment by case studies) includes *in vivo* and ecotoxicological safety data production for nanoproducts which have different physicochemical properties, ionization and biopersistence of antimicrobial nanomaterials and preparing recommendation of reference dose for products containing nanomaterials. Part 3 (Development of testing methods and standardization of nanomaterials and product containing nanomaterials) includes development of product chemistry methods for nanoproduct, development of exposure assessment from nanoproduct, development of testing methods for nanorelease from nanoproduct and international cooperation with ISO/TC 229, OECD WPMN, ILSI Nanorelease, and EU Nanosafety Cluster. In addition, MOTIE is planned to participate EU NanoReg project form 2015. The participating tasks are "data platform and data management", NanoReg instruments toolbox for regulators and legislators", "developing technologies for nanomaterial inhalation toxicology", and "developing methodologies on exposure assessment for products containing manufactured nanomaterials". KATS is developing 2 international standards in the ISO TC 229 (Nanotechnologies) relevant to nanomaterial safety testing "Aerosol generation for NOAA (Nano-objects, and their aggregates and agglomerates) air exposure studies" and Electron spin resonance (ESR) as a method for measuring reactive oxygen species (ROS) generated by metal oxide nanomaterials". These standard documents will complement the work of the OECD WPMN and other related framework documents.

Ministry of Food and Drug Safety (MFDS)

MFDS and NIFDS (National Institute of Food and Drug Safety Evaluation) have conducted the safety studies for manufactured nanomaterials in order to evaluate the safety of manufactured nanomaterials and nanoproducts since 2005. NIFDS has been operating the Nanotoxicology Project since 2007. The Nanotoxicology Project mainly focuses on providing toxicity data for preparing guidelines to evaluate safety and nano risk management associated with food, drugs, medical devices and cosmetics using nanoscaled materials. Research areas in the Nanotoxicology Project encompass a wide range of safety issues related to nanoscaled nanomaterials including toxicological evaluation, risk assessment, ADME (absorption, distribution, and metabolism, excretion), kinetics, and physico-chemical characterization behavior. Test materials such as SiO_2, silver, gold, ZnO, and nano-calcium etc. have been used for the safety evaluation. Effects of size, shape and surface properties of nanomaterials on general toxicity, genotoxicity, immune response, developmental and reproductive toxicity, brain uptake mechanism, interaction with biomaterials are investigating. NIFDS has also been participating in the joint interlab study for CFE (colony forming efficiency) assay. From 2010 to 2013, NIFDS mainly conducted studies on the selected nanomaterials, such as SiO_2, ZnO to get the information on physico-chemical properties, kinetics, and toxicity.

Information on public/ stakeholder consultations

The guidance for prevention of environmental impact by manufactured nanomaterials is under development by MOE.

THE NETHERLANDS

Highlights of developments

- The Netherlands were the evaluating member state of the first REACH substance evaluation that considers a nanomaterial. The decision on this substance was adopted in December 2014.
- The European NANoREG project has had its mid-term review and is mainly on track.
- The Dutch organisations of employers and employees joint forces in a pilot study regarding the pros and cons of exposure registration for working with synthetic nanomaterials.

National regulatory developments on human health and environmental safety

The European NANoREG project (www.nanoreg.eu) is The latter being the outcome of the mid-term review meeting with the EC Project Officer and the EC Project Technical Advisor. A few delays in the R&D work have been reported, which need to be absorbed during the next two years. After the reviewing, developing and evaluating of the standard operation procedures, etc., partners are now in the middle of 'testing the tests'. A selection of the first main results and new developments are summarised here:

- The majority of the results of the first exposure studies (biokinetic, oral, dermal and inhalation toxicity), with exception to the high-aspect-ratio-nanomaterials, show a low toxicity in contrast to the many *in vitro* effects reported on the substances tested.
- Regarding the *in vitro* testing and the work on "the relevance of barriers", preliminary work has been done in order to harmonise activities and to assure the reliability of the results. Suitable methods for solubility measurements have been tested.
- After the completion of Deliverable 3.1 (a gap analysis report, identifying the critical exposure scenarios within the key value chains), data gaps have been identified and exposure scenarios of potential highest exposure along the value chain of currently marketed engineered nanomaterials prioritised. Based on this deliverable the final selection of exposure scenarios to be examined did start.
- The work on safe-by-design resulted in a working document on a concept for safe innovation (including safe by design) and a draft report on lessons learned from drug development testing.
- The development of the regulatory framework on "how to address the safety of nanomaterials" and the creation of the NANoREG toolbox have just started.

As from November 1, 2014, 3 new beneficiaries from the Czech Republic entered the NANoREG Project. Collaboration Agreements with South Korea and Brazil have been signed and even more important, detailed work plans have been completed. On a bilateral basis, collaborations between NANoREG and several other (FP7) projects have been established.

Activities initiated to implement the OECD Council Recommendation

RIVM contributed to the SCENIHR "Opinion on the Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices", by providing the chair and an additional expert to the working group that drafted the document. The opinion is publicly available at the website of SCENIHR http://ec.europa.eu/health/scientific_committees/emerging/opinions.

Information on risk assessment decisions

In July 2014 a publication on "Novel insights into the risk assessment of the nanomaterial synthetic amorphous silica (SAS), additive E551, in food" (http://dx.doi.org/10.3109/17435390.2014.940408) was published online in the scientific journal Nanotoxicology (van Kesteren et al., 2014). SAS concentrations in human livers were estimated based on food intake and kinetic modelling, and compared to

concentrations of SAS in livers (measured or modelled) in toxicity studies. Estimates for human liver were similar to concentrations that resulted in effects in animals. Hence, this assessment suggests that SAS in food may pose a health risk. Yet, for this risk assessment, assumptions had to be made and several sources of uncertainty were identified that make it difficult to draw firm conclusions. Recommendations to fill in the remaining data gaps are discussed. More insight in the health risk of SAS in food is warranted considering the wide applications and these findings.

In 2012 the Netherlands started a substance evaluation of synthetic amorphous silica (SAS) within the REACH process. In their December 2014 meeting the Member State Committee agreed with the draft decision that the Netherlands prepared. The final decision includes requests to industry for further information on the physicochemical properties of each of the different forms of SAS (including surface treated forms). To fulfil this information request the potential use of a grouping approach is indicated. In addition, additional information on inhalation toxicity is requested. In 2014, the Netherlands has started a substance evaluation of silver. Here the focus is on the environmental fate and toxicity of the nanoforms of silver in relation to ionic silver. Currently, a first draft decision is in its final stages of drafting.

Developments related to good practice documents

As reported in an earlier stage within the NANoREG project 'The Guidance Document on Minimum Requirements and Data Logging' has been developed to set the working standards for the R&D work. This document has been further updated and completed with benchmark data, selected protocols and an annex with questions and answers.

Developments related to Integrated Testing Strategies and/or Alternative test methods

In November 2014 a workshop on the MARINA (www.marina-fp7.eu) Risk Assessment strategy was organised in Lisbon, Portugal. The workshop was organised in collaboration with NanoREG. Several aspects of the strategy were discussed in break-out groups. Besides representatives of the various work packages within MARINA, active contribution from other EU projects (NanoREG, GUIDEnano and SUN) resulted in vivid and interesting discussions. The outcome will be used in further development of the Risk Assessment strategy.

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

Several Dutch partners (RIVM, TNO, Utrecht University, GeoChem, and Think Works) are involved in the European GUIDEnano project (www.guidenano.eu). The project aims to develop new strategies and create a web-based guidance tool for nanotechnology industries to assess and mitigate nano-enabled product risks on human and environmental health in risk assessment. RIVM is leader of the work package that deals with the risk assessment strategy. Within the work package Hazard Assessment RIVM is responsible for the human health hazard testing strategy. In the past year, the knowledge behind the model has been developed and the first version of the tool - in which the release and exposure models are completed - will be released in April 2015. A first complete version of the tool including hazard and risk assessment will be developed during the rest of 2015 (release scheduled for January 2016).

The WHO Collaborating Centre for Immunotoxicology and Allergic Hypersensitivity, which is located at RIVM, will lead a project on the development of a WHO/IPCS Environmental Health Criteria Document on Principles and Methods to assess the risk of immunotoxicity associated with exposure to nanomaterials. The objective of this project is to present the current state of the art of testing for toxicity to the immune system of nanomaterials, and to design strategies for assessing the risk for immune mediated health effects. The project will start on 8-9 April 2015 with a WHO scoping meeting of a core group of scientists. This

core group will identify issues that need to be tackled in the document, produce a table of contents, and help to identify scientists who will contribute in producing texts covering issues indicated in the outline.

Information on public/ stakeholder consultations

In its strategic outlook towards 2020, RIVM expressed the ambition to enter dialogue with societal actors more frequently when it comes to complex (technical) environmental and health risks. Consequently, these dialogues may lead to increased understanding of the societal context in which RIVM operates, therefore strengthening RIVM products and research. RIVM organized two dialogues on nanotechnology; one involving stakeholders (June 2013), the other involving the general public (April 2014). The stakeholder dialogue included representatives from ministries, industry and research and focused on early phase information exchange between risk assessors and industry. In addition, eight member of the general public were asked to reflect on technological innovation and the roles of several stakeholders (including the general public) therein. During both dialogues the nanomaterial graphene was used as a practical example. For both sessions, the aim was to acquire the full spectrum of the participants' views and perspectives, instead of achieving consensus. Results include the findings that RIVM was seen to be in the right position to perform such exploratory dialogues and that the general public prefers to interact with RIVM at given moment, when research (e.g. graphene applied in consumer products) may affect citizens on an individual level.

The European NanoDiode project (www.nanodiode.eu), establishes an innovative, coordinated programme for outreach and dialogue throughout Europe so as to support the effective governance of nanotechnologies. The project integrates vital engagement activities along the innovation value chain, at the levels of research policy, research & development (R&D), and the use of nanotechnological innovations throughout society. The project is currently halfway. Many activities are taking place on upstream, midstream and downstream engagement of stakeholders in nanotechnologies. A recent workshop showed some preliminary conclusions from the Nanodiode project. These show that there is still confusion about nanotechnology, which is primarily seen as beneficial development, versus nanomaterials risks, and that such risk discussion are mainly focussing on 1st generation nanomaterials, whereas 2nd and 3rd generation nanomaterials are more and more under development. Furthermore, there are ongoing discussions on how to deal with transparency (in relation to nanoregistry activities by e.g. France and Belgium).

Research or strategies on life cycle aspects of nanomaterials

RIVM contributes to the EU-project FutureNanoNeeds (www.futurenanoneeds.eu). Currently, value chains are identified to be used as demonstrators for the novel framework to be developed in this project. These value chains include nanomaterial applications like energy harvesting, display technology, lubricants, batteries, thermoelectric applications and 3D printing inks. For these value chains the life cycle of the nanomaterials will be determined. In addition, as a first step, a framework is almost developed to assess the exposure of the nanomaterials during the life cycle. RIVM has performed a short-term inhalation toxicity test on nano-copper oxide. This test includes a 5 day exposure protocol with a recovery period of three weeks in which also the nanomaterial distribution throughout the body is determined. This data will serve as a case study for the decision support tool that is being developed in SUN.

Development related to exposure measurement and exposure mitigation

In the European MARINA project (www.marina-fp7.eu), TNO prepared a review of exposure models. The available nanospecific models are mostly qualitative / control banding / risk banding tools. They aim to be simple (for use by occupational safety and health practitioners), require few input parameters (which are

usually easily accessible) and claim to be conservative in their estimate of exposure by using the precautionary principle for unknown input parameters. The applicability domains of the various tools are different, and mainly focus on the use phases rather than the synthesis and end-of-life activities. All reviewed models consider the respiratory route of exposure. The dermal and oral routes of exposure are not considered. None of these qualitative (control banding) models have been validated, neither with nanomaterials, nor with other types of exposure data.

Within SUN (www.sun-fp7.eu), TNO will build on exposure and risk assessment knowledge gained in several European projects in order to:

- Establish a versatile 3-tier qualitative to quantitative inhalation, dermal and dermal-to-oral occupational and consumer exposure assessment tool
- Collate and generate an extensive set of high-quality, time-resolved occupational and consumer inhalation exposure measurements with detailed contextual information
- Collate and generate an extensive data library on process, product and article specific emission potentials and source strengths for key production, application, and consumer use scenarios
- Collate and generate high-quality data on in-use efficiencies and protection factors for engineered ventilation control and Personal Protective Equipment

All data will be stored in libraries for use in the 3-tier exposure assessment and management framework. All objectives will be addressed including data-generation and assessment for the selected SUN case-studies.

The Dutch organisations of employers and employees joint forces in a pilot study regarding the pros and cons of exposure registration for working with synthetic nanomaterials. Currently, the project is about halfway and showing good progress. Based on desk research six papers are being drafted, a concept scenario for exposure registration, an overview of scientific state-of-the-art on process generated nanoparticles (PGNPs), an overview of (European) registries of nanoproducts, an overview of existing forms of exposure registrations, a draft guidance "Working safely with nanomaterials (including exposure registration)", and a draft protocol for activities by companies. The draft guidance documents are tested in several industrial sectors (chemical, paints, cosmetics, rubber and plastics, metal, car repair, science and R&D, building/concrete). In some companies, measurements are carried out to determine presence of nanomaterials to further test the possibilities of exposure generations. The pilot is co-financed by the Netherlands Ministry of Social Affairs and Employment and will run from April 2014 until the end of 2015.

Consideration on the benefits of nanotechnologies

Within LICARA (www.licara.eu), TNO developed a structured life-cycle approach for nanomaterials in order to provide faster and greater insight into the effects of nanoproducts on environment, economy, society and health (www.tno.nl/licara/). The approach enables companies to weigh up the risks and benefits of using these products. The project is of particular interest to small and medium-sized enterprises (SMEs). TNO together with partners within LICARA developed Guidelines for the sustainable competitiveness of nanoproducts to support SMEs to make decisions about developing safe, sustainable nanoproducts by gathering relevant information to answer the pertinent questions. The guidelines are accompanied by the LICARA nanoSCAN, which is a tool that supports SMEs through their decision-making process. It does this by scanning both the benefits and risks over the nanoproduct's life time in comparison to a conventional product with a similar functionality. The LICARA nanoSCAN can be performed by SMEs themselves. In addition, a new approach for professionals was developed for an in-depth assessment to study the benefits and risks into more detail using quantitative data and state of the art assessment methods. In this approach Life Cycle Assessment (LCA) is combined with Risk Assessment (RA) focusing on human risks, including the occupational risks. The nanoSCAN and in-depth assessment

was performed for 4 case studies: 2 on nanosilver, 1 on multiwalled carbon nanotubes and 1 on nanotitanium dioxide.

SWITZERLAND

National regulatory developments on human health and environmental safety

Depending on their use, nanomaterials are covered by existing regulations set forth in chemicals, environmental, foodstuffs and therapeutic products legislation. Existing threshold values and provisions on health protection at the workplace, on the prevention of major accidents and on waste management are also applicable.

Since 2012, nanospecific information (phys-chem properties) is requested for the registration of nanomaterials as new substances and for the notification of hazardous existing substances in nanoform, according to the Chemical Ordinance (ChemV, SR 813.11). The Swiss definition of nanomaterials is similar to the recommended definition of the European Commission with the difference that there is no number threshold and that the nanomaterial must be made on purpose for the delivery of a nanospecific effect. In addition to the nanospecific amendment to the ChemV, similar amendments were made to the Ordinance for plant protection products (PSMV, SR 916.161) and the Ordinance for biocidal products (SR 813.12). Moreover, nanomaterials must be declared in applications for admission of pharmaceuticals. As soon as more scientific and methodological knowledge for a refined risk assessment becomes available, the requested data from industry will be adapted. All adaptations to current regulation will be done with careful evaluation of regulatory activities abroad, in particular from the EU. OECD test guidelines will be further important building blocks of the Swiss test strategy for nanomaterials. Switzerland will also continue to promote and use voluntary tools for strengthening industrial responsibility for the risk management of nanomaterials. This is particular important as long as the regulatory framework for nanomaterials is still evolving. Such tools, developed and implemented in Switzerland, are the guidance documents for (i) “responsible care”, (ii) disposal of nanowaste, (iii) safety data sheet, and for (iv) the hazardous incidences. Moreover, the “Precautionary matrix for synthetic nanomaterials”, which was presented at the categorization workshop in D.C. (September 2014), has been proven a very valuable tool for small, medium and larger companies who are dealing with nanomaterials. Switzerland aims to include synthetic nanomaterials in the existing registration procedure for new chemicals. An easy one-step notification procedure is foreseen for industries which produce or process nanomaterials. The goal of this action is a better overview of application areas for nanomaterials.

Action Plan for synthetic nanomaterials

The “Action plan for synthetic nanomaterials” illustrates the work required in Switzerland for the safe handling of nanomaterials. It was adopted by the Federal Council in April 2008. The just mentioned tools were developed under this action plan. On 17 December 2014 the Federal Council decided to continue the action plan until 2019.

The action plan was developed by the Federal Office of Public Health (FOPH), the Federal Office for the Environment (FOEN) and the State Secretariat for Economic Affairs (SECO) in cooperation with an **inter-departmental task force** and the involvement of a **panel of scientific and economic experts**.

The **objectives** of the action plan include:

1. development of regulatory framework conditions for the responsible handling of synthetic nanomaterials;
2. creation of scientific and methodical conditions aimed at identifying and preventing potential harmful effects of synthetic nanomaterials on health and the environment;
3. promotion of the public dialogue about opportunities and risks of nanotechnology;
4. better utilisation of existing tools for the development and rollout of sustainable nanotechnology applications.

These objectives will be followed also in the next round of the action plan. A more detailed operational plan is currently being developed.

Developments related to Integrated Testing Strategies and/or Alternative test methods

Federal Office of Public Health is a consortium member in the EU project "NanoReg", with the Federal Office for the Environment and the State Secretariat for Economic Affairs SECO being co-sponsors. Swiss researchers (at EPFL Lausanne, Empa St.Gallen, IST Lausanne) are contracted. They are contributing to three work packages, focusing on development of harmonized characterization protocols, modelling nanoparticle workplace exposure based on real workplace measurements, and for organizing round robins with the goal of establishing SOPs for (high throughput) in vitro test methods with potential future regulatory relevance.

Link: www.nanoreg.eu

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

The National Research Programme "Opportunities and Risks of Nanomaterials" (NRP 64) aims to identify opportunities arising from the use of nanomaterials for consumers, environment and natural resources. At the same time it intends to bridge the gaps in our current knowledge on the potential risks of nanomaterials. The research projects (10 million Euro in total) have started in December 2010 and will come to an end this year. A report on the outcome of the multimillion research program is in preparation. The research carried out under this program should provide a scientific basis for recommendations and appropriate measures with regard to the production, use and disposal of engineered nanoparticles. It covers the five main areas biomedical applications, environment, food, energy, and construction materials. The insights gained from the study of engineered nanoparticles and their applications will benefit society at large and help to protect the consumer and the environment.

Link: www.NRP64.ch

Information on public/ stakeholder consultation

Expo Nano

Expo Nano is a mobile exhibition platform on nanotechnology. Focus of the exhibition are opportunities and risks of nanomaterials along their life cycle. Since summer 2013, Expo Nano stopped in French- and German-speaking regions in Switzerland and attracted more than 60,000 people. Expo Nano is multimedia-based, interactive, and open for free to everybody. Target audience is the broad public. Focus events for specific target groups (e.g. schools, small companies) are regularly organized. Visitors can experience

different experiments where "nano-effects" are shown. Posters provide the theoretical explanation to the multimedia-experiments.

Link: http://exponano.ch

Website InfoNano

Since April 2012, the main information platform for nanotechnology "InfoNano" is online. InfoNano provides information in German, French, Italian and English about the opportunities and risks associated with nanotechnology and synthetic nanomaterials. It is aimed at promoting the dialogue among stakeholders from industry, academia, society and administration. It presents all relevant governmental activities on nanotechnology and provide a structured entry into the world of nanotechnology. Among other topics, one can find international research highlights, safety of consumer products, regulatory activities of the ministries, and much more additional information.

Link: www.infonano.ch

Research programmes or strategies which focus on life cycle aspects of nanomaterials

Switzerland has several research groups which investigate life cycle aspects of nanomaterials (e.g. http://www.ifu.ethz.ch/ESD or http://www.empa.ch/plugin/template/empa/124/*/---/l=2). Moreover, the Federal Office of Public Health (FOPH) together with EMPA organized and hosted the OECD WPMN workshop in Zurich in January 2015. The aim was to discuss and finalize the draft of the guidance manual on the combined use of LCA and RA for the assessment of benefits and risks of nanoenabled products. More information will be made available at the 14th WPMN meeting.

UNITED STATES

Highlight of developments

On July 8, 2014, the U.S Environmental Protection Agency (EPA) issued final Toxic Substances Control Act (TSCA) significant new use rules (SNURs) for 2 carbon nanotubes, and on September 2, 2014, EPA issued TSCA SNURs on 15 carbon nanotubes or nanofibers. EPA's determination in a SNUR that a use of a chemical substance is a significant new use is made after consideration of all relevant factors, including production volume; changes to the type or form of exposure; increases in the magnitude and duration of exposure; and the manner and methods of manufacturing, processing, distribution in commerce, and disposal. A manufacturer or processor wishing to engage in a designated significant new use must submit a Significant New Use Notice (SNUN) to EPA at least 90 days before engaging in the new use. The SNUN provides USEPA with the opportunity to evaluate the intended use and, if necessary, to prohibit or limit that activity before it occurs.

The United States and Canada continued their cooperation on nanomaterials under the Regulatory Cooperation Council (RCC), and are preparing for public release the reports from the RCC Nanotechnology Final Results Workshop held January 14, 2014 in Washington, DC, formally concluding the Nanotechnology Work Plan. Under the RCC process, technical teams developed, disseminated and discussed with stakeholders products in the following areas: Classification/Priority Setting, Risk Assessment/Risk Management, and Commercial Information. Pragmatic changes stakeholders can expect from the two countries include (a) a consistent policy approach for nanomaterials based on the shared

policy principles; (b) consistent use of a classification scheme to identify data needs (short-term) and how information from one substance can be used for another substance (medium to long-term); (c) consistent use of data submitted to support risk assessments based on the framework for human health information and common assumptions for ecological fate and effects; and (d) using commercial use information to better qualify exposures in risk assessments and focus information requests in control measures. Moving forward, both governments will be looking at the best approaches to communicate the results of the RCC Nanotechnology Initiative.

EPA hosted two OECD workshops in Washington DC.

The first was the OECD WPMN Meeting on Nanomaterials Physical-Chemical Parameters: Measurements and Methods, which took place June 18 and 19, 2014. The objectives of the meeting were to identify the appropriate test methods for physical-chemical parameters for manufactured nanomaterials, building on the experience from the OECD sponsorship programme and the expertise of the experimenters and other physical-chemical and metrology experts, and if possible, to determine which test methods are appropriate for both a particular parameter and particular types of nanomaterials. This meeting took into consideration the results of the OECD Expert Meeting on the Physical-Chemical Properties of Manufactured Nanomaterials (Mexico, 28 February – 1 March 2013). The OECD Expert Meeting on the Physical-Chemical Properties of Manufactured Nanomaterials was organized in collaboration with the International Organization for Standardization Technical Committee on Nanotechnologies (ISO/TC 229). The results of the June P-Chem meeting will be: 1) meeting report; 2) recommendations for appropriate methods for each parameter (and where appropriate methods for each parameter by type of nanomaterial), recommendations for OECD test guidelines (including modification of existing OECD test guidelines); and identification of ways to address data gaps. The experts were encouraged to develop a matrix of parameters and associated appropriate methods and any inappropriate methods. The workshop will help improve how EPA does its chemical assessments under TSCA.

The second EPA-hosted workshop - the OECD Expert Meeting on Categorization of Manufactured Nanomaterials – was held September 17-19, 2014. The goal of the Category meeting was to provide recommendations on how manufactured nanomaterials should be categorized for purposes of testing, read-across/SAR, risk assessment and risk management. Discussion and conclusions from the workshop will be used to develop fit-for-purpose decision frameworks for categorization that can be utilized under different regulatory systems (e.g., TSCA New Chemicals Program) for manufactured nanomaterials. To support this, the workshop recommended 1) the identification and development, where needed, of methods for characterization of relevant physical-chemical properties for toxicokinetics, fate, hazard and exposure assessments (methods used should enable comparability, are reliable, and use the OECD Guidance on Sample Preparation and Dosimetry), and 2) agreeing on or developing experimental models (e.g., in-vitro and in-vivo assays) which are predictive of human health and environment effects and support categorization. Presentations and other information are now available at

http://www.epa.gov/oppt/nano/presentations.html.

National regulatory developments on human health and environmental safety

Regulatory Actions. Since January 2005, EPA has received and reviewed more than 160 new chemical notices for nanoscale materials under the Toxic Substance Control Act (TSCA) including fullerenes 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.

On July 8, 2014, EPA issued final significant new use rules (SNURs) for 2 carbon nanotubes and on September 2, 2014 SNURs for 15 carbon nanotubes or nanofibers. See http://www.gpo.gov/fdsys/pkg/FR-2014-07-08/pdf/2014-15874.pdf and http://www.gpo.gov/fdsys/pkg/FR-2014-09-02/pdf/2014-20783.pdf , respectively.

EPA is developing a section 8(a) rule under TSCA for nanoscale materials. The rule would propose that persons who manufacture these nanoscale materials notify EPA of certain information described in the rule which includes use, production volume, certain physical properties and chemical/structural characteristics, methods of manufacture and processing, exposure and release information, and available health and safety data.

UC CEIN. **University of California's Center for Environmental Implications of Nanotechnology (CEIN) is f**unded by a cooperative agreement from the National Science Foundation and EPA's Office of Research and Development, and is housed within the California NanoSystems Institute (CNSI) at **University of California**, Los Angeles (UCLA). Currently, there is an effort to select carbon nanotubes for an *in vitro*/HTS/HCS – in vivo verification inter-laboratory testing project. Further, CEIN held a workshop on methods for in vitro/HTS /HCS screening of MNs in the Spring; proceedings of this meeting should be available in early 2015.

The Carbonaceous Working Group (CWG) was created to ensure that CEIN research addresses those aspects of carbonaceous nanomaterials that are important to EPA's regulation of nanomaterials. To that end, regular teleconferences with EPA and members of the working group have been held to gain common understanding of EPA's needs for carbon nanomaterials and of the CWG's initial consideration of research directions. Discussion has focused on past or ongoing testing by EPA or CEIN of various carbon nanomaterials, potential synergies between the CWG and EPA's range of work on carbonaceous materials, and identifying key areas for collaboration moving forward.

RCC Nanotechnology Joint Work Plan. Following Prime Minister Harper and President Obama's announcement of the Canada-United States Regulatory Cooperation Council (RCC) in February 2011, Canada and the United States have been working to better align their regulatory approaches in a number of areas, including nanotechnology. The RCC Nanotechnology Final Results Workshop was held January 14, 2014 at US EPA Headquarters in Washington, DC. At this final workshop, key findings were presented and next steps discussed. Collaboration and discussion continues, between governments and with technical teams comprised of outside stakeholders. Moving forward, both governments will be looking at the best approaches to communicate the results of the RCC Nanotechnology Initiative.

Developments related to voluntary or stewardship schemes

Recommended Exposure Limit for Nanoscale Silver. The US National Institute for Occupational Safety and Health (NIOSH) is developing a publication which will contain Recommended Exposure Limit for nanoscale silver along with recommendations for exposure measurements and risk mitigation in the workplace. It is expected to go out for public review in the first half of 2015.

Participation in ISO TC229. National Institute of Standards and Technology (NIST) representatives as part of the committees of the US Technical Advisory Group to ISO TC229 (Nanotechnologies) have

facilitated cooperation and coordination between OECD WPMN and ISO TC229. The WPMN has a formal liaison with the ISO TC229 and the two organizations share work results prior to public release, and share work plans. ISO TC229 is assisting the WPMN in determining the physical-chemical parameters such as particle size, the relevant measurands and measurement methods for each parameter.

Developments related to good practice documents

Development of Protocols. NIST has developed a number of protocols related to physico-chemical characterization, toxicological measurements and the release of engineered nanomaterials from nanotechnology-enabled products; these protocols will be made available at http://www.nist.gov/mml/np-measurement-protocols.cfm. NIST will then work with its partners to bring these documents into the international standards process.

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

EPA Office of Research and Development. The EPA Office of Research and Development (ORD) Program on Chemical Safety and Sustainability maintains a coordinated research program on the public health and environmental implications of emerging chemicals including engineered nanomaterials. The program includes funding through grants and cooperative agreements and research in EPA National Laboratories and Centers. In 2014, the ORD integrated research for Chemical Safety for Sustainability, including research on emerging materials focused on engineered nanomaterials (ENM). A key scientific issue is the complexity of relating nanomaterial features directly to risks. An important avenue of investigation focuses on identifying critical intermediate properties of ENM that are predictive of potential risks. Another key issue is understanding interactions between ENM and biological or other complex media. Methods are required to characterize nanomaterials in simple and complex media; to evaluate the release of nanomaterials from consumer products; and alternative testing approaches are needed to evaluate adverse outcome pathways of nanomaterials. Predicting impacts of ENM use in real-world conditions will depend on properties of both the ENM and the matrix. Research will evaluate nanomaterials across a life cycle of product use ranging from manufacture, use and end-of-life disposal and consider the release, fate, transport and transformations of nanomaterials as they age.

EPA and the National Science Foundation (NSF) continue to support two previously awarded interdisciplinary Centers for the Environmental Implications of Nanotechnology. In 2013-14, EPA also funded the creation of The EPA STAR Center for Organotypic Culture Models: Predictive Toxicology Center for Organic Culture Models and Assessment of AOPs for Engineered Nanomaterials at the University of Washington. The overall goal of this Center is to develop innovative organotypic culture systems to better evaluate the potential for cellular and organ toxicity following exposure to ENMs within an adverse outcomes pathway (AOP) model. The work under this center will continue in 2015 and is planned for continued support in 2016.

NIOSH Nanotechnology Program. NIOSH maintains an active nanotechnology program, which aims to address five strategic goals:

- Increase understanding of new hazards and related health risks to nanomaterial workers.
- Expand understanding of the initial hazard findings of engineered nanomaterials.
- Support the creation of guidance materials to inform nanomaterial workers, employers, health professionals, regulatory agencies, and decision-makers about hazards, risks, and risk management approaches.

- Support epidemiologic studies for nanomaterial workers, including medical, cross-sectional, prospective cohort, and exposure studies.
- Assess and promote national and international adherence with risk management guidance.

More information about NIOSH nanotechnology program can be found at http://www.cdc.gov/niosh/topics/nanotech/

Information on public/ stakeholder consultation.

An expert meeting for the OECD "Guidance Document on Aquatic (and Sediment) Toxicology Testing of Nanomaterials" was held 1-2 July 2014 in Washington, D.C., USA at the Environmental Protection Agency. The need for this guidance document (GD) was identified at the OECD Expert workshop meeting held in Berlin (January 2013). The goals of the GD are to produce a testing framework to generate uniform and consistent nanomaterials ecotoxicology data to inform future risk decisions while adapting current water and sediment ecotoxicology guidelines, where appropriate. A summary of the meeting is being developed and will be circulated for WPMN review.

The National Nanotechnology Initiative (NNI) sponsored a webinar for the general public on July 31, 2014 that featured a Progress Review on the Coordinated Implementation of the NNI 2011 Environmental, Health, and Safety Research Strategy. The webinar included a brief overview presentation followed by a Q/A session with questions directed to representatives of several US federal agencies. Over 400 individuals logged in to participate in the webinar, demonstrating substantial public interest in the topics covered. An archived webcast is available at http://www.nano.gov/node/1166.

Information on research programmes or strategies which focus on life cycle aspects of nanomaterials

EPA and NSF co-funded a grant entitled: Network for Characterizing Chemical Life Cycle: Life Cycle of Nanomaterials, with Arizona State University. This project will evaluate the trade-offs between using nanomaterials to improve the functionality of consumer products and the potential risk to humans and the environment. In addition, the EPA Office of Research and Development is developing plans for a Life Cycle / Human Exposure Model project that should include a case study focused on engineered nanomaterials.

Development related to exposure measurement and exposure mitigation

The EPA Office of Research and Development research program on Emerging Materials contains a substantial focus on measurement and modeling of exposure to engineered nanomaterials and their environmental transformation products. The EPA and the U.S. Consumer Product Safety Commission (CPSC) are nearing completion of a collaborative research project evaluating potential release of copper from copper-treated commercial wood products. The composition, particle size distribution, leaching, bio-availability and exposure to micronized copper were evaluated. Initial reports are available and additional reports and manuscripts are currently being prepared. In addition, two manuscripts were recently published modeling exposures to nano cerium from use as a diesel fuel additive in England, and forecasting potential exposure to cerium and other air pollution products if cerium were to be used in the US as a fuel additive for on-road diesel vehicles.

Report on U.S. Industry Practices. NIOSH researchers publish a report characterizing current U.S. industry practices with respect to minimizing exposure to engineered nanomaterials (Mary K. Schubauer-

Berigan PhD, Matthew M. Dahm MPH, Paul A. Schulte PhD, Laura Hodson MSPH & Charles L. Geraci PhD (2014): Title: Characterizing adoption of precautionary risk management guidance for nanomaterials, an emerging occupational hazard, Journal of Occupational and Environmental Hygiene, DOI: 10.1080/15459624.2014.946515)

UNITED KINGDOM

Information on risk assessment decisions

Using modelling and comparisons with published ecotoxicological data, risk assessments of metal/metal oxide (Ag, Zn & Ce) MNs have been undertaken under the EU NanoFATE (www.nanofate.eu) project. Predicted river water concentrations would not exceed levels know or suggested to effect aquatic wildlife. Compared with nano Ag, nano ZnO was closer to effect levels of concern. Little risk appears to be associated with nano CeO_2 discharge when used as a fuel additive. Also, observed Ag levels in sewage effluent (particle size range 2-450 nm) and in sludge were not considered critically high. Higher Ag levels were found in urban river bed sediments.

Developments related to good practice documents

As part of the EC mandate M/46 and CEN TC352, the UK is project leading (1) Guidance on measures for characterizing nano-objects and materials that contain them and (2) Guidelines for aspects of Life Cycle Assessment specific to nanomaterials. The UK is also leading the development of an ISO standard on terminology for graphene and other 2D materials, plus has hosted ISO TC229/WG3 (Nanotechnologies – health, safety and environment; April 2014). UK Government's Health and Safety Executive agency has published information relating to: (1) *Managing human exposure to MNs (Using Nanomaterials at Work)* and (2) *The use of Nanomaterials in UK Universities: an overview of occupational health and safety*.

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

The EU NanoRem (www.nanorem.eu) project includes UK partners and focusses on facilitating practical, safe, economic and exploitable nanotechnology for *in situ* land and water resource remediation. It aims to develop a comprehensive understanding of the environmental risk-benefit for the use of MNs, market demand, overall sustainability, and stakeholder perceptions. Work to-date has assessed the relative risks and benefits of nZVI usage in *in situ* remediation. It is intended to help stakeholders by providing a basis for evidence-based decisions. A recent ecotoxicology study has focused on the potential effects of Zn and Ce oxide MNs to sentinel, freshwater species.

On-going, UK-funded genetic toxicology and ecotoxicology research (Elucidating the potential interaction of manufactured nanoparticles with polycyclic aromatic hydrocarbons, using an integrated toxicogenomics approach; http://gtr.rcuk.ac.uk/project/4BA1ED50-907D-427B-8878-0EB2EE1FAF41) aims to: (1) elucidate the main pathways through which carbon MNs [C_{60}-fullerenes and carbon nanotubes] could induce biological responses alone or in combination with ubiquitous polycyclic aromatic hydrocarbons and; (2) determine how the exposures could influence the health of an ecologically and economically important model marine invertebrate (mussels). Overall, the information obtained will be important for hazard and risk assessment for these chemicals in a complex environment.

Information on public/stakeholder consultations

UK government funded project (*Public dialogue to understand public perceptions of specific nanotechnologies*) commenced October 2014. The work aims to (1) discuss with members of the public specific nano products/applications to ensure governance mechanisms are appropriate, balanced and take account of public views; (2) provide opportunities to understand public aspirations and expectations and what they see as key priorities, including for the development and application of new products; (3) ensure that transparency measures and potential communications are relevant and targeted, to reassure the public about safety in the industries of interest; and (4) promote mature and nuanced discussions between public and MN industry representatives. A full report will be available July 2015.

Research or strategies on life cycle aspects of nanomaterials

Recent research at one UK university has focussed on investigating the impact of MNs on living organisms and ecosystems. Studies have determined the toxicity of capped and uncapped silver nanoparticles (cAgNP and uAgNP), titanium dioxide and multi-walled carbon nanotube to bacterial pure cultures and aquatic microbial communities, with focus on two key processes (i.e. hydrocarbon-degradation and ammonia oxidation). Whilst the TiO2NP and MWCNT were non-toxic up to 50 mg L^{-1}, both the cAgNP and uAgNP demonstrated bacterial toxicity. Aquatic microbial community compositions were in general, sensitive to uAgNP and cAgNP between 0.5 to 50 mg L^{-1}. A recent study has shown chlorophyll fluorescence has a great potential to be used as an analytical tool for monitoring the interaction of plants and MNs as well as investigating the effects of MNs on plants. It has also been established that AgMNs induce complex physiological modifications, ranging from inhibition of plant growth and photosynthesis to induction of stress signalling reactions in the model plant *Arabidopsis thaliana*.

Development related to exposure measurement and exposure mitigation

One UK university is engaged in sampling the MN fraction from outdoor and indoor air. This is characterised in terms of the size distribution of specific chemical components (trace metals and major ions), and by electron microscopy of individual particles to capture the morphology and major element content.

CURRENT ACTIVITIES IN OTHER ORGANISATIONS RELATED TO NANOTECHNOLOGIES/ NANOMATERIALS

THE EUROPEAN COMMISSION (EC)

(In case of no information under a heading below, please put "None" or delete the heading itself)

Regulatory developments on human health and environmental safety

a. Nanomaterial definition

The European Commission (the EC) intended to review the EC nanomaterial definition in 2014 '… in the light of experience and of scientific and technological developments' (Recommendation 2011/696/EU). In 2013 the policy services asked the in-house science service of the European Commission, the Joint Research Centre (JRC), for scientific advice on the question. The JRC accepted and agreed to develop a set of scientific–technical recommendations in the course of 2014. In August 2014, the JRC released the second report in a series of three, providing its scientific-technical assessment of information on relevant experience with the nanomaterial definition.

The new report is entitled 'Towards a Review of the EC recommendation for a definition of the term "nanomaterial" – Part 2: Assessment of collected information concerning the experience with the definition' (EUR 26744, https://ec.europa.eu/jrc/sites/default/files/jrc_nm-def_report2_eur26744.pdf).

The new report builds on the first report, which was published earlier this year: Part I: Compilation of information concerning the experience with the definition (EUR 26567). Report 2 analyses the information collected in Report 1 and provides JRC's assessment of the suggestions made by stakeholders.

The findings of Report 1 and 2 indicate that there is room for improvement to facilitate implementation and clarify communication. Based on these scientific-technical findings a third, upcoming report will describe options on how these improvements can be achieved. These will then be considered by the European Commission taking into account the current and future applications of the nanomaterial definition in legislation.

b. Test guidelines

JRC, on behalf of the EC, submitted a SPSF for developing Guidance on the micronucleus test for nano genotoxicity (TG 487) to the WNT for review and eventual inclusion in the TGP work plan. This submission addressed the recommendations made at WMNT-13 and followed a experts' workshop to prepare the final version of the SPSF organised by OECD in October.

c. Impact assessment on transparency measures for nanomaterials

The Commission is proceeding with the impact assessment on transparency measures for nanomaterials on the market. Policy options under assessment include a nanomaterial observatory (collecting & presenting data from existing databases and/or new market studies), an EU nanomaterial registry, a recommendation for the harmonisation of national registries or no new actions. The impact assessment report is expected to be finalised by Q2 2015.

As a result of a consultancy study in support of the impact assessment, two study reports have been published: an evaluation of existing nanomaterial registries, in particular the French notification system (the 'Evaluation Report'); and an overview of relevant data concerning hazards & risks of nanomaterials, as well as competitiveness and innovation related to nanomaterials (the 'Building Blocks Report'). The related public consultation has been concluded on 5 August 2014. 202 stakeholders have responded. The responses showed significant differences between groups of respondents regarding the need for and the impact of transparency measures. The consultation results will feed into the upcoming options assessment report and will be taken into account in the final impact assessment report.

Both the consultancy reports and the consultation results are available online:

http://ec.europa.eu/enterprise/sectors/chemicals/reach/nanomaterials/index_en.htm#h2-3

d. JRC Repository analysis

JRC published several comprehensive reports on the physical-chemical characterisation of the Representative Nanomaterials held in the JRC Repository and used in the OECD Testing Programme. These reports complete the series already initiated in previous years and compile in a systematic way information generated by JRC and several other European partners in several projects, including aspects of sample preparation. This information can complement the OECD dossiers in preparation (I included two old ones just for completeness, but you can decide to mention only the 2014 ones):

- NM-Series of Representative Manufactured Nanomaterials - Zinc Oxide NM-110, NM-111, NM-112, NM-113 Characterisation and Test Item Preparation. C. Singh et al.. ISBN: 978-92-79-22215-3; ISSN: 1831-9424; DOI: 10.2787/55008. (2011).

- Synthetic amorphous silicon dioxide (NM-200, NM-201, NM-202, NM-203, NM-204) : characterisation and physico-chemical properties - JRC repository: NM-series of representative manufactured nanomaterials. Kirsten Rasmussen et al. ISBN: 978-92-79-32323-2; ISSN: 1831-9424; DOI: 10.2788/57989. (2013).

- Titanium dioxide, NM-100, NM-101, NM-102, NM-103, NM-104, NM-105 Characterisation and physico-chemical properties properties - JRC repository: NM-series of representative manufactured nanomaterials. Kirsten Rasmussen et al. ISBN: 978-92-79-38188-1; ISSN: 1831-9424 ; DOI: 10.2788/79554 (2014)

- Cerium Dioxide, NM-211, NM-212, NM-213. Characterisation and test item preparation. Charanjeet Singh et al. ISBN 978-92-79-38308-3; ISSN 1831-9424; DOI:10.2788/80203. (2014).

- Multi-walled carbon nanotubes, NM-400, NM-401, NM-402, NM-403, characterisation and physico-chemical properties - JRC repository : NM-series of representative manufactured nanomaterials. Kirsten Rasmussen, et al. ISBN: 978-92-79-39648-9; ISSN: 1831-9424; DOI: 10.2788/10753 (2014).

e. ECHA Topical Scientific Workshop - Regulatory Challenges in Risk Assessment of Nanomaterials

The Topical Scientific Workshop on Nanomaterials was held on 23-24 October 2014 at ECHA. The workshop brought together close to 200 experts in the field of risk assessment of nanomaterials representing academia, policy makers, industry and NGOs.

The workshop provided a unique platform for academia and regulators to discuss how to address current challenges from the regulatory perspective which can be reflected and employed in the ongoing and future research topics on nanomaterials. The discussions were reinforced by information of the recent developments and of risk assessment methodologies applied in chemicals management both within and outside the European Union.

The workshop illustrated well the strategic objectives of ECHA, to serve as a hub for building scientific and regulatory capacity in the area of regulatory challenges. The anticipated outcome of workshop was early emergence of new and/or improved approaches in the context of risk assessment of nanomaterials. The outcome of the workshop clearly matched the expectations and its output will form a cornerstone in the guidance developments for the implementation of the REACH, CLP and Biocidal Products Regulations.

The proceedings of the workshop are foreseen to be published in the first quarter of 2015 but already now all presentations and background materials are available on ECHA's website;

http://echa.europa.eu/news-and-events/events/event-details/-/journal_content/56_INSTANCE_DR2i/title/topical-scientific-workshop-regulatory-challenges-in-risk-assessment-of-nanomaterials

Activities initiated to implement the OECD Council Recommendation.

Two Nano guidance documents (one for workers & one for employers and health and safety practitioners) have been prepared under contract to the European Commission. They have been scrutinised by the Advisory Committee on Safety and Health at Work of the European Commission who adopted a positive opinion on them.

Both Guidance documents are accessible either via the European Commission DG Employment, Social Affairs and Inclusion website http://ec.europa.eu/social/main.jsp?catId=716&langId=en under 'Related documents' in the right hand column of the page, and the website of the European Agency on Safety and Health at Work https://osha.europa.eu/en/news/eu-safe-use-of-nanomaterials-2013-commission-publishes-guidance-for-employers-and-workers.

In addition, the activities described above under title 1 (see in particular indents a); b) and e)) should be seen as implementing activities translating the thrust of the OECD Council Recommendation into a regulatory context.

Developments related to good practice documents

As such, no new activities to report even if ECHA's workshop, see indent 1 d) above could be seen as a contribution to a broad understanding of good practice in the field of use of data for the purpose of read across.

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

e. New projects selected under the Horizon 2020 Research Framework Programme (H2020) have started or will start in the coming month, by topic:

i) NMP-27-2014: Coordination of EU and international efforts in safety of nanotechnology

PROSAFE: "Promoting the Implementation of Safe by Design"

ii) The results of the following calls will be announced early March at the latest:

- NMP 26 – 2014: A joint EU&MS activity on the next phase of research in support of regulation – NANOREG II.

- NMP 28 – 2014: Assessment of environmental fate of nanomaterials.

f. Horizon 2020 calls for research proposals (submission deadline 26/03/2015)

- NMP 29 – 2015: Increasing the capacity to perform nanosafety assessment.

- NMP 30 – 2015: Next generation tools for risk governance of nanomaterials

The European Commission (JRC) is partner of the new H2020 Project PROSAFE that officially starts on 1st February 2015. This is a coordination action that will facilitate the assembling of the activities and results of on-going and new EU projects regarding nanomaterials safety.

More on: http://ec.europa.eu/research/participants/portal/desktop/en/opportunities/index.html

g. Other:

- DG RTD NMP initiative EU Nanosafety cluster also continues their activities. More details at:

www.nanosafetycluster.eu. The 2014 edition of the "Compendium of Projects in the European NanoSafety Cluster" is available: http://www.nanosafetycluster.eu/home/european-nanosafety-cluster-compendium.html

- The nanosafety cluster has published a "nano-EHS research strategy for 2015-2020":

http://www.nanosafetycluster.eu/news/83/66/Nanosafety-in-Europe-2015---2025.html

- The US-NNCO and European Commission DG RTD-Directorate G are fostering research cooperation on EHS issues of nanomaterials through joint workshops and the establishment of

Communities of Research. More on http://us-eu.org. The fourth workshop will be held in Venice (IT) on 12-13 March 2015 next to the SUSNANO conference held on 9-11 March 2015.

2. Information on public/ stakeholder consultations;

Please see above (Section 1) for the results of the public consultation on transparency measures for nanomaterials on the market.

BUREAU INTERNATIONAL DES POIDS ET MESURES (BIPM)

Introduction

The mission of the BIPM is to ensure and promote the global comparability of measurements, including providing a coherent international system of units for:

- Scientific discovery and innovation,
- Industrial manufacturing and international trade,
- Sustaining the quality of life and the global environment.

The unique role of the BIPM enables it to achieve its mission by developing the technical and organizational infrastructure of the International System of Units (SI) as the basis for the world-wide traceability of measurement results. This is achieved both through technical activities in its laboratories and through international coordination

The BIPM headquarters coordinates and provides the executive secretariat for a series of Consultative Committees, whose members are the National Metrology Institutes (NMIs) of the Member States of the BIPM. These expert scientific committees are structured to cover all of the principal areas of metrology: the SI (CCU), Acoustics, Ultrasound and Vibration (CCAUV), Electricity and Magnetism (CCEM), Length (CCL), Mass and Related Quantities (CCM), Photometry and Radiometry (CCPR), Chemistry (CCQM), Ionizing Radiation (CCRI), Thermometry and Humidity (CCT), and Time and Frequency (CCTF).

National Metrology Institutes have been developing measurement and calibration capabilities for nanotechnologies for several years now. This laboratory work already led to international comparisons, including in particular the EURAMET project 1282 on “Comparison of condensation particle counters”, performed within the framework of the European regional metrology organization EURAMET. This comparison is going to be repeated in the framework of the Gas analysis Working Group (GAWG) of the international committee for chemistry and biology (CCQM). As accurate measurements of aerosols are of interest to a large community, a workshop organised by the CCQM took place on 15 April 2015 at the BIPM headquarters (Paris). It will aim to clarify the requirements for aerosol measurements from the various stakeholders, to outline the present and future role of NMIs in supporting the accuracy of such measurements, and to define priorities and activities for the next few years. The next section focuses on activities linked to aerosols number concentration and size measurements. There are other activities on metrology for nanotechnologies within National Metrology Institutes, in particular on size measurements of nanoparticles, which are not covered here. More information can be found on the website of the Working Group on Dimensional Nanometrology of the consultative Committee for Length.

International comparisons to underpin aerosols number concentration and size measurement capabilities

Due to the increasing recognition that a metrology infrastructure is needed to support the measurement of nanoparticles EURAMET started in 2006 the project 893. The project established the requirements for coordination of national activities.

The first comparison of particle number concentration and size measurements was organised in 2008 at the Federal Institute of Metrology METAS in Switzerland. The project 1027 showed good comparability of particle number measurements with condensation particle counters, whereas particle number and size measurements of scanning mobility particle sizer showed larger deviations and the dependence on confidential data handling routines of instrument manufacturer.

As the newly issued ISO 27891 standard allows traceability for condensation particle counters either via a certified Faraday Cup Aerosol Electrometers or a certified Condensation Particle Counter two distinct subsequent comparisons were conducted in 2013:

The first comparison EURAMET project 1244 to demonstrate comparability of charge concentration measurements by Faraday Cup Aerosol Electrometers took place at the Tampere University of Technology. It made use of the university's unique facility to produce singly charged particles over a wide size range. In order to have a worldwide impact, participants from the US and Japan were invited to the comparison. For singly charged particles in the size range 20 nm to 100 nm and number concentrations above 5000 cm^{-3} participants agreed within 3 %. Larger deviations were observed at lower particle sizes and concentrations. In Figure 1 below the results for a soot aerosol (acetylene burner) with a particle size of 30 nm are depicted. Due to impaction in the internal sampling line of their instruments the JRC result is not concordant with the reference value (weighted mean of all participants except JRC).

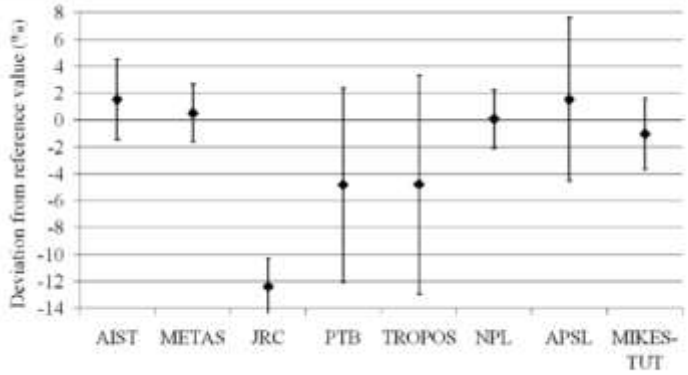

Figure 1: Comparison results for 30 nm soot particles and a charge concentration of 10 fC cm-3. The charge concentration corresponds to a particle number concentration of 3800 singly charged particles per cm3. The reference value is the weighted mean of participants except JRC.

The second comparison EURAMET project 1282 to demonstrate comparability of the number concentration measurements by Condensations Particle Counters was conducted in Leipzig. Again APSL from US and AIST from Japan participated in the comparison. Aerosol sources were silver, sintered silver and soot. The size range was between 6 nm and 100 nm and number concentrations varied between 100 cm^{-3} to 25'000 cm^{-3}. The results show discrepancies between instruments with a relatively high (23 nm) 50% cut-off size of the CPC, even at aerosol particle sizes well above the cut-off size. Apart from this, the

results showed that for the full concentration range, and sizes between 23 and 100 nm, agreement to ±10% between reference laboratories is currently achieved. In Figure 2 the results for soot at 41 nm are depicted.

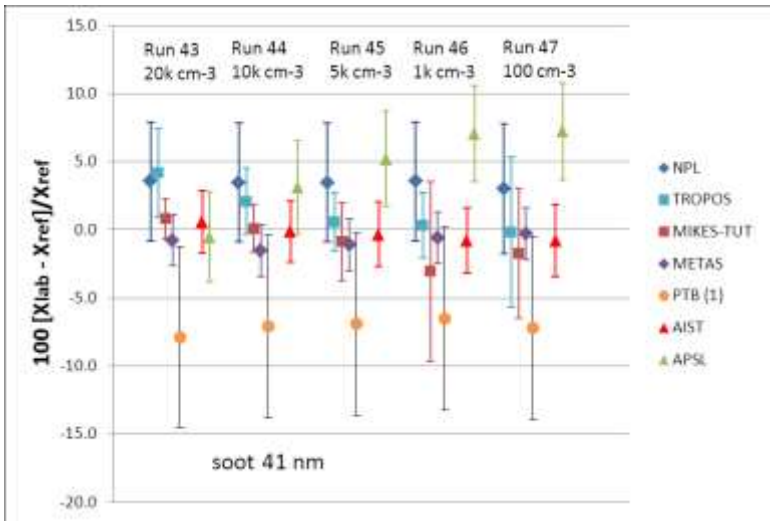

Figure 2: Comparison results for 41 nm soot particles in the particle number concentration range 100 cm-3 to 2×103 cm-3 are shown. The reference value is the weighted mean of all participants.

INTERNATIONAL COUNCIL ON ANIMAL PROTECTION IN OECD PROGRAMMES (ICAPO)

The PETA International Science Consortium is organizing a 2015 workshop that will review the state-of-the-science and determine the technical needs to develop an *in vitro* system to reduce or replace the use of animals in studies to assess the inhalation toxicity of engineered nanomaterials. To accomplish this goal, a steering committee has been convened comprising experts from industry, government, academia and non-profit organizations to define the project plan and focus. The project design will take into consideration the tools set forth by the OECD such as the 'Guidance on Sample Preparation and Dosimetry for the Safety Testing of Manufactured Nanomaterials' [ENV/JM/MONO (2012)40]. Proceedings from the workshop will be published.

Developments related to Integrated Testing Strategies and/or Alternative test methods

The Society for Risk Analysis Emerging Nanoscale Materials Specialty Group (ENM SG) convened a workshop in September 2014 to examine the use of Alternative Testing Strategies (ATS) for nanomaterials from a risk analysis perspective. The goal of the SRA Nano Risk II workshop was to explore ways to increase confidence in the use of ATS for testing nanomaterials and how to incorporate ATS into the risk assessment process in a multiple models approach designed to increase the weight of evidence. Three white papers were invited on the topics of a multiple models approach in human health risk assessment, ecological risk assessment, and exposure assessment, as well as a case study and a State of the Science report. ICAPO's scientist is the lead author on the white paper developed for exposure assessment and a contributing author on the final workshop report that will be shared with the OECD and will also published in the international journal *Risk Analysis* in early 2015.

INTERNATIONAL ORGANISATION FOR STANDARDIZATION TECHNICAL COMMITTEE (ISO)

The International Organisation for Standardization Technical Committee (ISO/TC) 229 - Nanotechnologies - was established in June 2005 with a UK secretariat and chair. It has held seventeen meetings to date, with the most recent being in New Delhi, India, in November 2014. The next meeting will be in September 2015 in Edmonton, Canada. The committee currently has 48 members - 34 "P" or, "Participating" members and 14 "O" or, "Observer" members. Forty two documents have been published to date –see http://www.iso.org/iso/standards_development/technical_committees/list_of_iso_technical_committees/iso_technical_committee.htm?commid=381983. Two publications most relevant to the WPMN since its last meeting, in June 2014, are ISO/TR 16197:2014 - Nanotechnologies - Compilation and description of toxicological screening methods for manufactured nanomaterials and ISO/TS 16550:2014 – Nanotechnologies - Determination of silver nanoparticles potency by release of muramic acid from *Staphylococcus aureus*. The current list of ISO deliverables under development is in Part II below.

ISO/TC 229 believes that close cooperation with the OECD WPMN will lead to valuable synergies and avoid duplication of effort by the two organisations. The relationship between TC/ 229 and the WPMN is governed by the terms of the "ISO/TC 229 – OECD WPMN coordination paper – version 2, February 2009'. As an example of the benefits of collaboration, since the last WPMN meeting two OECD workshops with a large amount of participation from relevant ISO/TC 229 experts have been held: the June 2014 p-chem workshop and the September 2014 categories workshop. In addition, OECD experts received updates on the activities of ISO/TC 229 and how these two organisations may collaborate with one another to develop documents of benefit to both communities.

ISO standards can be utilized to support regulation and legislation by, for example, providing validated and verifiable measurement methods for demonstrating compliance with regulatory requirements.

Further details about ISO TC 229 can be found at http://www.iso.org/iso/standards_development/technical_committees/list_of_iso_technical_committees/iso_technical_committee.htm?commid=381983, and about ISO at http://www.iso.org

II. List of projects under development

Working Group	Designation	Title
JWG 1/PG 1 Rev	ISO/TS 80004-2 (formerly ISO/TS 27687)	Nanotechnologies – Vocabulary – Part 2: Nano-objects – Nanoparticle, nanofibre, nanoplate
JWG 1/PG 5 Amd	ISO/TS 80001-4 Amd. 1	ISO/TS 80004-1:2010/AMD 1'Nanotechnologies — Vocabulary — Part 1: Core terms' –Amendment 1
JWG 1/PG 12	ISO/DTR 17302	Framework for identifying vocabulary development for nanotechnology applications in human healthcare
JWG 1 /PG 13	ISO/DTS 18110	Nanotechnologies - Vocabularies for Science, Technology and Innovation Indicators
JWG 1/PG 14	ISO/DTR 18401	Nanotechnologies - Plain Language Guide for Terminology
JWG 1/PG 17	ISO/DTS 80004-11	Nanotechnologies - Vocabulary - Part 11: Nanolayer, nanocoating, nanofilm and related terms

JWG 1/PG 18	ISO/DTS 80004-12	Nanotechnologies – Vocabulary – Part 12: Quantum phenomena
JWG 1/PG 19	ISO/DTS 80004-13	Nanotechnologies – Vocabulary – Part 13: Graphene and other 2d materials
JWG 2/PG 14	ISO/DTS 17466	Use of UV-Vis Absorption Spectroscopy in the Characterization of Cadmium Chalcogenide Semiconductor
JWG 2/PG 15	ISO/DTR 18196	Measurement technique matrix for nano-objects
JWG 2/PG 16	ISO/DTS 19590	Nanoparticles: Detection and characterization using single-particle ICP-MS
JWG 2/PG 17	ISO/DTR 19716	Nanotechnologies -- Characterization of cellulose nanocrystals -- Particle morphology, purity and surface properties
JWG 2/PG 18	ISO/DTR 19733	Matrix of characterization and measurement methods for Graphene
JWG 2	ISO/PWI	Determination of size and size distribution of nano-objects by scanning electron microscopy
WG 3/PG 1 Rev	ISO/TR 12885	Health and safety practices in occupational settings relevant to nanotechnologies
WG 3/PG 12	ISO/DTR 16196	Compilation and description for sample preparation and dosing methods for engineered and manufactured nanomaterials
WG 3/PG 15	ISO/DTR 18637	General framework for the development of occupational exposure limits for nano-objects and their aggregates and agglomerates
WG 3/PG 16	ISO/DTS 18827	ESR as a method for measuring ROS generated by metal oxide nanomaterials
WG 3/PG 17	ISO/AWI 19007	*In vitro* MTS Assay for measuring the cytotoxic effect of nanoparticles
WG 3/PG 18	ISO/DTS 19006	Dichloro-dihydro-fluorescein diacetate (DCFH-DA) Assay for evaluating nanoparticle-induced intracellular ROS production in Raw 264.7 macrophage cell line
WG 3/PG 19	ISO/DTR 19057	Nanotechnologies − the use and application of acellular in Vitro Tests and Methodologies to assess Nanomaterial Biodurability
WG 3/PG 20	ISO/DTS 19337	Characteristics of working suspensions of nano-objects for *in vitro* assays to evaluate inherent nano-object toxicity
WG 3/PG 21	ISO/DTR 19601	Aerosol generation for NOAA air exposure studies
WG 4	ISO/PWI	Specification for carbon nanotube dispersions

Acronym Key:
AWI – Approved Work Item
CD – Committee Draft (ballot at TC)
DIS – Draft International Standard
DTR – Draft Technical Report
DTS – Draft Technical Specification
FDIS – Final Draft International Standard
PWI – Preliminary Work Item
WD – Working Draft (being developed by WG)
TR – Technical Report
TS – Technical Specification

WORLD HEALTH ORGANIZATION (WHO)

WHO Chemical Risk Assessment Network
Project Description

Development of a WHO/IPCS Environmental Health Criteria Document on Principles and Methods to assess the risk of immunotoxicity associated with exposure to nanomaterials

Project Lead:

WHO will convene the expert group and manage the process, because it will result in a WHO publication. The WHO Collaborating Centre for Immunotoxicology and Allergic Hypersensitivity, National Institute of Public Health and the Environment (RIVM), Bilthoven, the Netherlands will provide the technical lead.

Project Title:

Principles and methods for Assessing the Risk of Immunotoxicity associated with exposure to nanomaterials

Project Objective:

Nanoparticles interact with components of the immune system, more than with any other organ system in the body. Some of these interactions may lead to perturbations of the immune system. Such perturbations may potentially have various consequences. One such consequence may be immune suppression leading to reduced resistance to infections and neoplasms. Another consequence that has been suggested to occur, through the induction of inflammatory responses, is represented by inflammatory diseases such as lung fibrosis, colitis, stimulation of respiratory allergy and allergic asthma, and facilitation of tumor formation. Knowledge concerning cellular responses to nanoparticles, and in particular, the relative contribution of mass, number of particles, size, surface area and charge, to toxicity is evolving.

Potential effects of nanomaterials as indicated above are not often tested for risk assessment purposes within regulatory frameworks; there is no mandatory system in place to do this. In addition, whereas many methods are available for assessing immunotoxicity of chemicals, the most appropriate approach for testing the toxicity brought about by exposure to nanomaterials remains yet to be assessed.

The objective of this project is to present the current state of the art of testing for toxicity to the immune system of nanomaterials, and to design strategies for assessing the risk for immune mediated health effects.

Summary of Proposed Work:

The project will be implemented in line with WHO policies and procedures for WHO expert meetings. It will start with convening a WHO scoping meeting of a core group of scientists. They will identify issues that need to be tackled in the document, produce a table of contents, and help to identify scientists who will contribute in producing texts covering issues indicated in the outline. As needed, meetings of the contributors will be convened and a final draft will be submitted for public and peer review.

Deliverables:

WHO/IPCS Environmental Health Criteria Document on Principals and Methods for Assessing the Risk of Immunotoxicity Associated with Exposure to Nanomaterials.

Draft outline of the EHC:

- Intro nanoparticles: definition, types, sources, routes of exposure, life cycle modification of particles, health concerns
- Intro immune system; testing systems, strategies and regulatory requirements for immunotoxicity (suppression, allergy, autoimmunity)
- Specific chapters on different types of nanoparticles, their effects, with special emphasis to the immune system
- Specific chapters on the mechanisms of toxicity of nanoparticles with special reference to the immune system
- Knowledge gaps with special reference to immunotoxicity testing of nanomaterials
- Dose metrics of nanoparticles with special reference to immune effects
- Approach to assess immunotoxicity of nanoparticles for risk assessment purposes