Report on the
Joint Seminar on NanoSafety: ProSafe, NanoREG, SIINN, OECD, NanoDefine
at the
Euronano forum 2015, Riga, Latvija

Which research fields regarding safety of nanomaterials are carried out presently? Which aspects of toxicology, ecotoxicology, exposure assessment, mechanisms of interaction, risk assessment and standardisation are addressed in these research fields and what are the results? The Joint Seminar on NanoSafety gave a condensed and rather complete picture on the NanoSafety projects and research clusters (for the agenda and presentations see: http://www.nanoreg.eu/index.php/news-events/all-events/nanoreg-events/206-euronano-forum-2015-participation-of-nanoreg-siinn-prosafe-nanodefine-and-nanovalid.html).

In this report we give an overview on the projects presented and their results.

This report was funded by Velux Foundations as part the project “Ensuring proper risk assessment of nanomaterials to establish a precaution-based regulatory framework for their production and use”

1.1 Overview on the topics of the Seminar

- Introduction by the NanoSafety Cluster and Review Results (www.nanosafetycluster.eu);
- ERA-NET SIINN - Safe Implementation of Innovative Nanoscience and Nanotechnology, final results (www.siinn.eu/en);
- NANoREG - Current status and trends in precautionary measures, Safe-by-Design and regulation;
- Outlook ProSafe with first Call of common projects;
- Brokerage for the first ProSafe call;
- Overview of funded SIINN Projects:
  - FENOMENO;
  - NanoGeCo,
  - Nanoheter,
  - nanoIndEx,
  - NanOxiMet and
  - NANO_SAFE_LEATHER;
- Efficient characterisation and classification of materials according to the EC nano-definition: The EU FP7 NanoDefine project;
- Development of reference methods for risk and life cycle assessment of engineered nanomaterials;
- The EU FP7 NanoValid project (presentation was cancelled).

1.2 Overview on the NanoSafety Cluster

Iseult Lynch from the University of Birmingham (i.lynch@bham.ac.uk) presented the review process of **NanoSafety** in FP 7 (50 projects with altogether 180 Million Euro funding). The EU NanoSafety Cluster (www.nanosafetycluster.eu) is initiated by Directorate-General for Research & Innovation and has the purpose to maximise the synergies between projects under the Sixth (FP 6) and Seventh Framework Programme (FP 7) addressing aspects of nanosafety, like toxicology, ecotoxicology, exposure assessment, mechanisms of interaction, risk assessment and standardisation. The following projects belong to the NanosSafety Cluster:

- **Sinn ERA-NET SINN** (status: final conference),
- **NANoREG** (status: Midterm results),
- **ProSafe** (status: Preannouncement) and
- **NanoDefine,**
- **NanoValid.**

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Ms Lynch summarized the present results of the cluster on hazard issues as following:

- A deeper understanding of the role of the corona for toxicological tests was reached ensuring that test protocols are more suitable than five years ago;
- Considerable progress has been made in understanding that exposure in toxicological test systems (in vitro and in vivo) need to be characterized and cannot rely on the physical-chemical data provided by the supplier;
- No unexpected mechanisms of acute toxicity have been identified compared to what is already known for larger non-nanosized particles;
- Modes of actions of particles that were established in air pollution toxicology are still valid.

She stressed that in the NanoSafety Cluster ecotoxicity did not have as much emphasis as human toxicity and is still a gap. As areas for further investment regarding hazard mechanisms, biokinetics and vulnerable populations she identified:

- To move towards predictive toxicology the relationship of nanomaterials characteristics with harmful effects on living organisms at molecular, cellular, organ and organism levels needs to be established;
- The definition of dose metrics (characteristics) is an open issue;
- Thresholds in terms of nanomaterials physico-chemical properties needs investigation for all properties linked with toxicity;
- Still needs to be resolved how long-term low-level exposure effects can be measured with alternatives to animal testing.

Her key political messages are that with research investment the focus should move to:

- Understanding biological and environmental transformations of nanomaterials including at more realistic environmental concentrations;
- Understanding how transformation correlates with mechanisms of impact as basis for modelling, grouping, classification, read-across and risk categorization;
- Focus on scale-up of activities, and integration of emerging approaches within regulatory frameworks;
- Exposure determination at all products incorporation nanomaterials at all life stages.

1.3 ERA-NET SIINN

Katja Schumacher from Forschungszentrum Jülich presented the SIINN-Project. She explained that the rugged landscape of nanosafety research formed the starting point to launch SIINN ERA-NET. The main purpose of the ERA-NET is to set-up joint calls (3 joint calls were set-up), but moreover the project led to rapid transfer from science to industry and a glossary on nanosafety (comprehensive review of methods) was consolidated. After the

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end of SIINN the work will continue in the **ProSafe** project. The research Roadmap for EHS can be downloaded on SIINN-webpage (see: www.siinn.eu/en).

1.4 NANoREG - Safe-by-design

Karl Hoehener from TEMAS AG (Switzerland) focused in his presentation on the safe-by-design (SbD) approach within NANoREG. The NanoReg-Concept of SbD is a modular concept integrated in the current industrial innovation process. With SbD risks cannot be excluded but reduced to a level acceptable; they can be "outengineered". Within ProSafe the SbD concept will be combined with a Regulatory Preparedness (RP) concept and both concepts will be embedded into a Safe Innovation (SI) approach.

The Safe Innovation Approach aims at:

- Reduced uncertainty and managed risks of innovative materials, products and processes at the time of market introduction. This should be accomplished with the help of the SbD concept.
- Earlier, increased and improved interaction between innovators and regulatory authorities in trusted environments (so-called SAFE HOUSES): from sharing expertise and knowledge with innovators to identify uncertainties and potential risks towards guidance for registration or market approval. This should be accomplished with the help of the RP concept.

Both concepts and thus the approach will especially consider the characteristics and peculiarities of manufactured nanomaterials or products containing manufactured nanomaterials and related processes.

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1.5 Outlook "ProSafe" with first Call of common projects

Tom van Teunenbroek from the Dutch Ministry of infrastructure and the Environment gave an introduction into ProSafe. ProSafe is a coordination and Support action under the Horizon 2020 programme (see: http://www.h2020-prosafe.eu/prosafe/). The project has started in 1st February 2015 with 11 partners plus a "Strategic Policy Development Group" with the main aim to coordinate and strengthen existing and new initiatives on the field of nanosafety in a regulatory context of the still running 7th EU research and innovation funding programme (FP 7) & and the latest research programme "Horizon 2020" (H2020), with respect to international efforts of the EU at OECD-level and in the cooperation between EU and the US.

An important outcome of ProSafe will be a broadly accepted "White Paper" that will present a feasible philosophy and accompanying set of instruments for regulators and industry to address EHS aspects of manufactured nanomaterials (see project fact sheet at: http://www.h2020-prosafe.eu/prosafe/?p=175). Based on information from NANoREG, ProSafe and OECD the white paper will include evaluated methods for testing and assessing risks of nanomaterials including Safe by Design (SbD). Before the white paper will be published in spring 2017 a draft version will be reviewed by means of a scientific conference, a workshop for accessors and policy makers on safety policy and one on innovation policy.

1.6 Brokerage for the first ProSafe call

The presentation of Dina Carrilho (dina.carrilho@fct.pt) from Fundação para a Ciência e a Tecnologia (FCT) focused on the procedure of the call ProSafe (see homepage: http://www.h2020-prosafe.eu/?p=237). Invited to the call were countries from Europe, e.g. France, Germany, Austria, Belgium, Switzerland and outside Europe like Argentina, Brazil, India, Israel, Taiwan and USA. By September 2015 information which countries participate on the call is available. Regarding funding conditions one should contact funding organizations in the participant´s country. For questions on procedural issues one should contact Dina Carrilho of the ProSafe secretariat (prosafe@fct.pt).

1.7 Overview and Networking of funded SIINN Projects

The primary aim of the SIINN ERA-NET is to promote the rapid transfer of the results of nanoscience and nanotechnology (N&N) research into industrial application by helping to create reliable conditions. In order to strengthen the European Research Area and to coordinate N&N-related R&D work, the project has the aim of bringing together a broad

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network of ministries, funding agencies, academic and industrial institutions to create a sustainable transnational programme of joint R&D in N&N.

Within the framework of SIINN the following research projects have been launched in joint transnational calls from 2012 and 2013[1]:

1.7.1 FENOMENO

Holger Schönherr (University of Siegen, Germany, schoenherr@chemie.uni-siegen.de) presented the FENOMENO project (http://www.siinn.eu/en/joint-calls/2013-second-siinn-call/call-2-funded-projects/fenomeno/,168). FENOMENO stands for „fate and effect of wastewater-borne manufactured nanomaterials in aquatic ecosystems“. It is the aim of the project to analyse how manufactured nanomaterials (titanium dioxide and silver nanoparticles) alter on their way through water bodies (waste water treatment, lake without water purification, take-up by species). Manufactured nanomaterials are mostly removed during wastewater treatment (WWT), but the remaining levels of manufactured nanomaterials in the effluents are significant and may show an increased toxicity for aquatic organisms due to their modification during the WWT. With innovative analytical approaches the project will study the fate and effects of wastewater-borne nanomaterials in an aquatic ecosystem, develop the basis for robust evaluation systems, and design analytical sensor systems for quantitative nanoparticle detection using biochemical markers and Daphnia and fish as sensors.

No results were presented as the project has just started on 1.4.2015 and lasts 36 months.

1.7.2 NanoGeCo

Omar Lozano Garcia from the University of UNamur gave an introduction on the NanoGeCo project (for the project homepage see: http://www.siinn.eu/en/joint-calls/2013-second-siinn-call/call-2-funded-projects/nanogeco/,171). The acronym stands for “Nanoparticle generation by atomization processes in spray coating”. The project analyses the exposure of an “unprepared” worker in the case of overspray (here Nano titanium dioxide is used). In the research project, detailed investigations on the generation of nanoparticles by atomization processes in spray coating will be carried out. Different paint materials both with and without manufactured nanomaterials, such as organic and inorganic pigments as well as spray guns

[1] Another SIINN-project, which has not started and was not presented on the Seminar is ”PLATOX- In vitro and in vivo investigations to generate validated toxicity data of graphene nanoplatelets vs. a carbon black reference”, for more information see: http://www.siinn.eu/en/joint-calls/2013-second-siinn-call/call-2-funded-projects/platox/,172.

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and industrial spray cans will be used. By carefully sampling the non-volatile fraction of paint aerosols, experimental studies using different aerosol measuring techniques, and analyses of the chemical substances in the paint aerosol will be performed. Toxicological studies using a whole body exposure model will be carried out to evaluate the potential risk of human exposure.

1.7.3 Nanoheter

Jérôme Labille (labille@cerege.fr) from CEREGE at Aix-Marseille University introduced the Nanoheter-project (for the project homepage see: http://nanoheter.cerege.fr). As part of the risk assessment of nanotechnology, this project deals with the exposure aspect of engineered nanoparticles, focusing on their fate in surface water. Based on the trace concentrations expected to be present, the approach claims that the dispersion stability of engineered nanoparticles in the water column is not a driving characteristic for their fate, but that their potential for interaction with the mineral and organic suspended matter occurring in surface water will be the governing factor. The aim of this project is to identify among these materials the potential carriers for engineered nanoparticles. Mechanistic, holistic and model approaches will be conducted together. The interaction of engineered nanoparticles with surrounding materials will be investigated, and the potentially induced heteroaggregation and/or sedimentation mechanisms will be studied. The goal is to deliver a probability ranking of these potential scenarios that can be used to model the fate of engineered nanoparticles in natural aqueous systems at the river scale.

1.7.4 NanoIndEx

Project coordinator **Christof Asbach** (asbach@iuta.de) from Institute of Energy and Environmental Technology – IUTA explained the goal of NanoIndEx (for the project homepage see: http://www.nanoindex.eu). Nano-specific personal samplers and monitors were tested for their comparability, accuracy and field-practicability. This is done against the background that inhalation is seen as the most critical uptake route of nanomaterials for humans and especially for workers in the workplaces where nanomaterials are produced, handled or used. An important outcome of the project is the development of Standard operation procedures (SOPs) and guidance documents on the proper use of samplers and monitors and for the data evaluation. It is planned to introduce the project outcome into a CEN-Standard.

Event note: Final results of the NanoIndEx-project will be presented at a workshop on the 30/31st of May 2016 in Berlin.

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1.7.5 NanOxiMet

Bryan Hellack (hellack@iuta.de) from IUTA gave an insight into the project NanOxiMet which stands for “Assessment of the use of particle reactivity metrics as an indicator for pathogenic properties and predictor of potential toxicological hazard” (for the project homepage see: www.nanoximet.eu). Hellack explains that the prediction of pathogenic properties of nanomaterials is not per se possible and that significant knowledge on the nanomaterial itself is necessary. The study aims to standardize the use of the surface area and the oxidant generation potency in order to improve hazard and risk assessment. Therefore a grouping of manufactured nanomaterials is envisaged in order to bridge characterization and toxicity evaluation of nanomaterial by simplifying their classification.

1.7.6 NANO_SAFE_LEATHER

The project which started 1st January 2015 is coordinated by **Carmen Gaidau** (carmen.gaidau@icpi.roicpi@icpi.ro) from the National Institute for textile and Leather (for the project homepage see: http://www.siinn.eu/en/joint-calls/2013-second-siinn-call/call-2-funded-projects/nano-safe-leather/,170). Background of the project is the use of silver and titanium dioxide nanomaterials for advanced functions for leather surface finishing. The properties of silver and titanium dioxide nanomaterials on leather surface are due to their antimicrobial, self-cleaning and flame retardant characteristics. The cytotoxicity study of the silver and titanium dioxide nanomaterials efficiency for leather functionalization related to the dose response on human health is very important for their large scale application in footwear industry. In vitro assessment of the impact of silver and titanium dioxide nanomaterials use in leather surface finishing on different human cell lines will enrich knowledge regarding manufacture nanomaterials effects on human health at cellular level.

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1.7.7 Efficient characterisation and classification of materials according to the EC nano-definition: The EU FP7 NanoDefine project

Stefan Weigel (stefan.weigel@wur.nl) from Wageningen University & Research centre presented the challenges and expected results of the "NanoDefine project (for the project homepage see: www.nanodefine.eu). NanoDefine running from November 2013 to October 2017 aims to test whether the EU recommendation for a definition of nanomaterial is working in reality and to provide the affected industries and authorities with tools that support cost-efficient implementation of the EU-Definition in all regulatory contexts.

The concept is a tiered approach which takes into consideration the issues of the availability of suitable measuring techniques, reference material, validated methods, acceptable for all stakeholders (authorities, policies, industries). Based on examples of inorganic nanomaterials (for example calcium carbonate, barium sulfate, titanium dioxide, kaolin, zeolite), organic nanoamterials (pigments and polymers) and products containing nanomaterials (e.g. sun screen) the concept will be developed. The project has to cope with the following challenges:

- Number/Size distribution (particle counting techniques preferable; conversion to numbers (from intensities, volume, mass) prone to errors);
- Measuring range down to 1 nm (only few techniques available for under 30 nm);
- Agglomerates and aggregates (deagglomeration; find primary particles in aggregates).

Mr. Weigel closed his presentation with the following expected project results:

- A intelligent decision flow scheme e-tool - called "**NanoDefiner**" – which is a standardised automated procedure for method selection and classification on nanomaterials;
- A "**NanoDefine Method Manual**" that gives technical guidance on the use of available methodologies;
- Standard operation procedures (SOPs) for analysis of materials and products.

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