Workshop Summary

EU-U.S.: Bridging NanoEHS Research Efforts
Joint Workshop
25-26 October 2012
Helsinki, Finland

Contents

Introduction and Background

The 2012 *EU-U.S. Bridging NanoEHS Research Efforts* workshop was held October 25-26, 2012, in Helsinki, Finland. The workshop was organized by the Finnish Institute of Occupational Health (FIOH) on behalf of the European Commission and the U.S. National Nanotechnology Initiative (NNI). It was attended by approximately 90 scientists, policy makers, regulators, administrators, and authorities from the European Union and the United States.[1]

The purpose of this second joint workshop was to further deepen and promote EU-U.S. collaboration on nanotechnology-related environment, health, and safety (nanoEHS) research. Additionally, the goal was to develop the Communities of Research (CORs), which provide a platform for scientists to develop a shared repertoire of protocols and methods to overcome research barriers.

The CORs were proposed at the first U.S.-EU: Bridging NanoEHS Research Efforts workshop in Washington, DC, on March 10-11, 2011. The first three CORs were launched at the Society of Toxicology Annual Meeting in San Francisco in March 2012: *Predictive Modelling for Human Health*, *Ecotoxicity Testing and Predictive Models*, and *Exposure through the Life Cycle*. Three additional CORs were announced at the NanoSafety Cluster meeting in Grenoble, France, in May 2012: *Databases and Ontologies*, *Risk Assessment*, and *Risk Management and Control*. The October 2012 workshop provided the venue for all of these Communities to meet in person for the first time and to define their scope and goals.

[1] A full list of workshop participants and presentations slides are available at www.us-eu.org/previous-u-s-eu-nanoehs-workshops/eu-us-bridging-nanoehs-research-efforts-a-joint-workshop-2012/.

2. Welcoming Remarks

Words of Welcome

Harri Vainio, Finnish Institute of Occupational Health, Finland

Harri Vainio welcomed the workshop participants and noted the immense expectations of nanotechnologies in near future. Worldwide markets for products utilizing nanotechnologies are estimated to reach ~€2.3 trillion in 2020.[2] Technological innovations that rely on the unique properties of engineered nanomaterials (ENMs) are increasingly making their way into consumer and industrial applications with potentially profound impacts on the economy and on society. However, research on the effects of ENMs on human health and the environment is still developing. Uncertainties related to ENM safety and regulatory policy are a significant impediment to innovation and successful commercialization of nanotechnologies.

Prof. Vainio pointed out several important environmental, health, and safety research priorities. A deeper understanding is needed of the bioidentity of ENMs, i.e., the association between a material's properties and its effects on living systems. Also, novel monitoring concepts are required for ENM exposure assessment to enable the distinction of ENMs from background materials. This new information would be relevant to the creation of a biological foundation for safety classification of ENMs, facilitating novel hazard assessment paradigms. The ultimate goal is knowledge-based risk assessments for ENM safety management and governance.

Finally, Prof. Vainio mentioned the "safety by design" approach and its expected impacts. A safety-by-design culture allows for less regulation of nanotechnologies while alleviating safety concerns. For the general public, reliable information on the safety of ENMs increases trust and acceptance of nanotechnologies. Safety by design also promotes economic growth by enabling positive industrial innovations and by encouraging commercial investment in nanotechnologies through a more stable regulatory environment.

Welcome on Behalf of the United States

Danny Hall, U.S. Embassy in Helsinki, United States

Danny Hall welcomed the workshop participants on behalf of the United States. He highlighted the well-functioning collaboration between the United States and Europe and emphasized the importance of regulatory cooperation and dialogue.

[2] Roco, M.C., Mirkin, C.A., Hersam, M.C., *Nanotechnology Research Directions for Societal Needs in 2020*, Springer, Boston and Berlin, 2011.

Purpose and Goals of the 2012 Workshop

Christos Tokamanis, European Commission

Christos Tokamanis pointed out the importance of safety and implementation. He emphasized the need for scientists, regulators, and administrators to consider all aspects of nanoEHS and to not limit themselves to their particular areas of specialization. Nanotechnology and trade are of global interest; thus, harmonized guidelines, regulations, and standards are needed.

To assure the safety of nanotechnologies, more research on their implications to human health and the environment is necessary. The mechanisms of interactions of nanomaterials with living organisms and the environment are key issues to be studied more thoroughly. Furthermore, knowledge of metrics and dose-response as well as fate and behaviour of ENMs through their life cycles is essential. In the future, reliable exposure models; detection tools; and robust, cost-effective, and quickly validated methodologies to assess the exposure and possible risk of ENMs are needed. The goal of the workshop is to bring an interdisciplinary group of nanoEHS scientists together to identify and begin addressing the barriers to accomplishing these research goals.

Research could lead to a system in which ENMs are categorized according to their predicted toxicity. Implementation of nanoEHS knowledge has already started in terms of the EU's **R**egistration, **E**valuation, **A**uthorization and Restriction of **Ch**emicals (REACH) and **C**lassification, **L**abeling and **P**ackaging (CLP) legislation and downstream regulations (*e.g.,* cosmetics, biocides, novel foods, worker protection, environmental law, etc.). However, there is still an urgent need for common test methods, guidance, and standards.

3. Plenary Presentations

Emerging Issues of Nanosciences

Kenneth Dawson, University College Dublin, Ireland

Kenneth Dawson opened his talk by explaining that nanomaterials act differently than individual molecules. To illustrate this point, he showed a video of cells taking up nanoparticles that reach lysosomes. Thus, according to Prof. Dawson, nanoscience is new science. The size range of nanomaterials makes interactions with biological systems possible. When nanoparticles interact with biological systems, biomolecules cover the particles and they are biologically recognized, engaging in active cellular processes. In most realistic cases, ENMs are recognized in biological systems according to what is on the surface of the particles.

It is currently possible to identify which proteins bind to the surface of nanomaterials from surrounding media. Furthermore, it is possible to characterize the surface composition of nanoparticles when they are exposed to biological media through *in situ* protein array analysis. When scientists know exactly what proteins bind to an ENM surface, the corresponding targets on cells can be identified and the biological response potentially elucidated.

Another important question is the fate of nanoparticles; the bio-accumulation of these particles is of particular interest. Additionally, some of these materials are not biodegradable or they degrade slowly.

Currently, many new and innovative nanomaterials are being developed and produced. However, there is insufficient information on what these new materials (e.g., nanoparticles with complex shapes and compositions) do and how they act. There is a need to start dealing with this wide range of materials and to shift research focus from those twelve ENMs selected for the Organisation for Economic Co-operation and Development (OECD) Sponsorship Programme toward a new generation of nanomaterials.

Taking into account the growing number of new materials, Prof. Dawson raised a question of whether the current regulatory system is adequate or if there is a more practical method for performing safety assessments and regulating nanomaterials.

At the end of his presentation, Prof. Dawson highlighted several topics that were suitable for further discussion in the COR breakout sessions:

- Characterization of modifications from environment and formulation – *Exposure through the Life Cycle COR*;
- Predictors of biodistribution and fate – *Predictive Modelling for Human Health COR* and *Ecotoxicity Testing and Predictive Models COR*;
- Parameters of biodistribution, useful classification and organization of data, and safety by design – *Databases and Ontologies COR*; and
- Enabling and regulating the future – *Risk Management and Control COR*.

Research Priorities on Safe Nanotechnologies

Mark Wiesner, Duke University, United States

In his introductory remarks, Mark Wiesner explained his preference for the phrase "safer nanotechnologies" instead of "safe nanotechnologies." He highlighted general priorities for producing the safest nanotechnologies possible by using environmentally benign procedures. Furthermore, he stated that nanotechnology development should be supported by information on risks and benefits that allows for timely and informed decision making.

Prof. Wiesner next gave an overview of a conceptual framework developed by a committee at the National Research Council.[3] The framework focuses on emerging nanomaterials that may pose unexpected risks, on the properties of these materials, and on their potential hazards and exposure scenarios. The committee's report highlights critical research gaps and the tools needed to address them. Four priority areas were: 1) identification, characterization, and quantification of the origins of nanomaterial releases; 2) processes that affect both potential hazards and exposure; 3) nanomaterial interactions in complex systems ranging from subcellular systems to ecosystems; and 4) adaptive research and knowledge infrastructure. These research priorities recognize the need to continue exploring the following topics: "first generation" issues; transformation and measurement of nanomaterials in real and complex systems; bio-uptake; differences between natural, incidental, and ENMs; next-generation nanotechnologies; how nanomaterials are used (value chain considerations); life cycle assessment; and likely options for risk management.

Prof. Wiesner emphasized that defining what constitutes a nanomaterial still remains a challenge. For example, the new definition released by the European Commission only considers particle size; novel properties are not taken into account.

Scientists could try to predict the fate of ENMs based upon their initial intrinsic properties. However, nanomaterials are altered in different environments (e.g., changes in aggregation state, redox potential, solubility, and adsorption of biomolecules), and as a result, the materials' properties are also transformed. Therefore, nanomaterials should be evaluated separately at each stage of production, use, and disposal. Prof. Wiesner discussed the possibility of assessing nanomaterial risk by collecting data under a particular set of environmental conditions (e.g., sea water, blood, soil) to determine the influences of transformed properties on exposure and risk.

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[3] National Research Council. *A Research Strategy for Environmental, Health, and Safety Aspects of Engineered Nanomaterials*. Washington, DC: The National Academies Press, 2012. www.nap.edu/catalog.php?record_id=13347#toc

European Research Strategies on Nanotechnologies

Kai Savolainen, Finnish Institute of Occupational Health, Finland

Kai Savolainen began with a short introduction to the key points of Horizon 2020, the new EU Framework Programme that will run from 2014 to 2020. Horizon 2020 is the financial instrument implementing the Innovation Union[4] program, a Europe 2020[5] flagship initiative designed to promote and secure Europe's global competitiveness. The programme will have a strong focus on developing European industrial capabilities in Key Enabling Technologies (KETs); nanotechnology is included in the Competitive Industries section of Horizon 2020 as one of six Key Enabling Technologies.

Horizon 2020 emphasizes the safety of nanotechnology and its applications with a focus on the assessment of the impacts of ENMs on human health and the environment. Horizon 2020 also aims to promote science-based governance of nanotechnologies and to provide scientific tools and forums for hazard, exposure, and risk assessment and management of ENMs, taking into account life cycle considerations.

Prof. Savolainen also presented the main objectives and activities of the NanoSafety Cluster, which is a forum for scientists involved in EU-funded nanosafety projects. The NanoSafety Cluster was established to maximise the synergies between the projects and to improve the coherence of nanosafety research. The Cluster is also a nexus for dialogue on R&D activities in Europe, and it aims to promote a consensus on nanosafety. One of the activities of the Cluster at the time of the workshop was to produce the Strategic Research Agenda for Nanosafety.[6] The document was written by the members of the Nanosafety Cluster to inform the development of Horizon 2020. The Strategic Research Agenda is designed as a working document which will be updated every 4-5 years as nanoEHS knowledge evolves. It serves as an implementation plan and enables scientists and policy makers to monitor the recent developments in the field. Above all, it aims to focus and facilitate research on specific areas that are prerequisites for reliable and transparent risk management.

Finally, Prof. Savolainen briefly described the four research priorities identified in the Strategic Research Agenda: 1) Material identity; 2) Exposure, transformation, and the life cycle of ENMs; 3) Hazard mechanisms; and 4) Risk prediction tools.

[4] www.ec.europa.eu/research/innovation-union/index_en.cfm

[5] www.ec.europa.eu/europe2020/index_en.htm

[6] Savolainen, K., et al. *Nanosafety in Europe 2015-2025: Towards Safe and Sustainable Nanomaterials and Nanotechnology Innovations*. Finish Institute of Occupational Health, Helsinki. Released June 2013 at www.ttl.fi/en/publications/Electronic_publications/Nanosafety_in_europe_2015-2025/Documents/nanosafety_2015-2025.pdf

U.S. Research Strategies on Nanotechnologies

Sally Tinkle, National Nanotechnology Coordination Office, United States

Sally Tinkle presented an overview of the U.S. National Nanotechnology Initiative (NNI) and the relevant nanoEHS activities under this program. The NNI was established in 2000 as the U.S. Federal Government's multiagency, multidisciplinary research and development (R&D) program to promote nanotechnology innovation. The initiative supports collaborative R&D that will advance understanding and control of matter at nanoscale for national economic benefit, national security, and improved quality of life.

The NNI Strategic Plan[7] and the NNI Environmental, Health, and Safety Research Strategy[8] are high-level guidance documents that serve to focus NNI activities. The Strategic Plan describes four key goals: 1) Advance a world-class nanotechnology research and development program; 2) Foster the transfer of new technologies into products for commercial and public benefit; 3) Develop and sustain educational resources, a skilled workforce, and the supporting infrastructure and tools to advance nanotechnology; and 4) Support responsible development of nanotechnology. The EHS Research Strategy provides a framework to protect public health and the environment through science-based risk analysis and risk management.

The NNI is targeting and accelerating nanoEHS research. Efforts are underway to prioritize nanomaterials for research; to establish standard measurements, terminology, nomenclature, and assays; to develop informatics and predictive modelling tools; and to stratify knowledge for risk assessment. NNI member agencies recognize the need to partner nationally and globally to achieve their nanoEHS research goals. Dr. Tinkle concluded with a summary of potential areas for collaboration between the EU and the United States: 1) understanding physical and chemical properties at various length and time scales; 2) producing data and databases of mutual interest; 3) identifying procedural and technical issues in developing open innovation communities; and 4) sharing protocols and best practices.

[7] www.nano.gov/sites/default/files/pub_resource/2011_strategic_plan.pdf
[8] www.nano.gov/sites/default/files/pub_resource/nni_2011_ehs_research_strategy.pdf

Requirements for Reliable Exposure Assessment of ENMs in Air

Gerhard Kasper, Karlsruhe Institute of Technology, Germany

Gerhard Kasper outlined the current capabilities for measuring aerosol particles. It is relatively easy to measure particle size and concentration in terms of conventional metrics (e.g., number, surface area, or mass), either as a size distribution or as global concentration within a size range. However, existing techniques cannot distinguish background aerosol particles from the ENM particles of interest. Typically, differential analysis is used to address the issue of ambient particles, but variations in background levels, emissions from other industrial activities, and complex data analyses complicate the process. Properties such as material composition, which allows for discrimination from background, are typically measured offline. This process is time-consuming and introduces issues of how the morphology and other characteristics might change between sampling and measurement. On-line techniques for composition analysis or particle structure are sophisticated, expensive, and, broadly speaking, not applicable to the field. The NANODEVICE[9] project aims to address several of these issues by producing tools that are cheaper, more practical, and evaluate sample activity.

Dr. Kasper repeatedly emphasized that conventional metrics do not capture important changes in particle functionality caused by structural changes and/or rapid attachment of airborne nanoparticles to other much larger particles. As an example he cited supported noble metal catalysts used, for example, in automotive technology—an important class of ENMs—where subtle changes in structure can have a huge effect on activity (and probably also toxicity) but leave the primary particle mass or surface concentration unchanged.

Instead, Dr. Kasper proposed the use of "functionality" concentration as a more suitable metric. Toward the goal of producing analytical tools that can measure activity concentrations of airborne ENMs, the NANODEVICE project has developed the Catalytic Activity Aerosol Monitor (CAAM). It measures the catalytic activity per cubic meter of airborne materials in quasi-real time. Additional experiments are needed to correlate the measured catalytic activity with biological activity, but the direct measurement of particle activity avoids a hypothetical connection with conventional concentration measures. It also represents a useful strategy to discriminate ENMs from background aerosols. Dr. Kasper further pushed for new techniques to measure the bio-functionality of nano-aerosols that are more broadly available, practical, and cost-effective. He closed his presentation by emphasizing the need for stronger ties between the fields of aerosol science and toxicology. Scientists should work to build a bridge between nanoparticle properties and mechanistic pathways of bio-functionality.

In the ensuing discussion, several benefits of (bio-)activity-specific experiments were identified. For example, when using activity concentration as a measure of exposure, one does not need to track particle size or morphology and conventional detection problems are not an issue. If no activity is observed, then the concentration of noxious substance is implicitly low.

Several participants questioned the relationship of the catalytic activity measured by the CAAM to biological/toxic effects. Gerhard Kasper conceded that experiments remain to be devised that link the catalytic activity to bio-functionalities that are more closely related to toxicity endpoints. Nevertheless, there are indications already from recent activity experiments conducted with particles containing small amounts of palladium, platinum, or nickel that the generation of reactive oxygen species, a common mode of toxicity, was proportional to the CAAM signal. Functionality-based concentration measurements thus have the potential to become a universal approach to exposure assessment.

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[9] www.nano-device.eu/

Risk Assessment and Management of ENM

Christina Powers, Environmental Protection Agency, United States

Christina Powers began with a broad overview of the U.S. Environmental Protection Agency's (EPA) Comprehensive Environmental Assessment (CEA) approach, which is designed to strategically link research planning, assessment, and risk management efforts. With CEA, a framework is established to compile key information (e.g., product life cycle, transport, exposure, dose). Then, using the collective judgment of a diverse group of stakeholders, information gaps and risks are assessed and prioritized. This information may be used to direct new research and to manage identified risks.

Dr. Powers illustrated how the CEA approach is applied by discussing preliminary results from the EPA case study on multi-walled carbon nanotubes (MWCNTs) in flame-retardant coatings for textiles. Known information on MWCNTs for this application was collected in the CEA framework and compared with a conventional flame retardant, decabromodiphenyl ether (decaBDE). Two rounds of prioritization were carried out over the web with participants ranking topics according to two factors: importance to risk assessment and confidence that current data can support risk management decisions. These priorities will be reviewed at an upcoming a face-to-face workshop with discussions structured to engage all participants equally and to avoid "group think." The outcomes from the structured discussion will serve as the foundation for the third and final round of prioritization at the workshop.[10] Dr. Powers concluded her presentation by demonstrating how the CEA approach could be useful in examining the trade-offs between two chemicals (i.e., decaBDE versus MWCNTs).

In the ensuing discussion, audience members who were also participants in the CEA case study complemented Dr. Powers on the utility of the web interface. The question was raised if the objective was to have a single list of priorities, and Dr. Powers replied that each agency/entity should work with its stakeholders to develop a plan according to its individual mission. As to balancing sociological aspects versus technical aspects in setting priorities, Dr. Powers stated that the EPA is looking to be more inclusive by opening up voting to a wider array of stakeholders. One participant questioned if there was an overemphasis on preparing the work agenda rather than actually doing the work with this approach, to which Dr. Powers replied that CEA would help to focus the significant amount of work already underway.

[10] Additional information on the workshop and the final case study document is available at cfpub.epa.gov/ncea/nano/recordisplay.cfm?deid=253010.

4. COR Breakout Sessions

The U.S.-EU Communities of Research function as a platform for scientists to develop a shared repertoire of protocols and methods to overcome research gaps and barriers and to enhance their professional relationships. The COR concept was proposed at the first U.S.-EU workshop on *Bridging nanoEHS Research Efforts*, which was held in Washington, DC, in March 2011.

Three CORs were announced at the Society of Toxicology Annual Meeting in San Francisco in March 2012: *Predictive Modelling for Human Health*, *Ecotoxicity Testing and Predictive Models*, and *Exposure through the Life Cycle*. The U.S. National Nanotechnology Coordination Office provides administrative support for these CORs.

An additional three Communities were announced at the NanoSafety Cluster meeting in Grenoble, France, in May 2012: *Databases and Ontologies*, *Risk Assessment*, and *Risk Management and Control*. The European Union provides administrative support for these communities.

Breakout sessions for the six CORs were designed to promote collaboration and progress toward COR goals.[11] In particular, the participants discussed the following issues in each breakout session:

1) Scope (science-based approaches for risk management, completeness, validation, approval, etc.)

2) Membership (adequacy, further development)

3) Work modalities

4) Key activities and schedule

[11] The presentation slides from the breakout sessions are available at www.us-eu.org/previous-u-s-eu-nanoehs-workshops/eu-us-bridging-nanoehs-research-efforts-a-joint-workshop-2012/presentations/.

Exposure through the Life Cycle, with Material Characterization

Chairs: Richard Canady, ILSI Research Foundation, United States
Thomas Kuhlbusch, Institut für Energie- und Umwelttechnik e.V., Germany
Rapporteurs: Jérôme Rose, Centre de Recherche et d'Enseignement de Géosciences de l'Environnement, France
Stacey Standridge, National Nanotechnology Coordination Office, United States

Overview

The session started with a summary by Richard Canady that detailed the objectives of the COR and the two proposed projects: 1) gathering/providing measurement methods to detect and quantify ENMs in complex media and 2) focusing on fate assessment of ENM. Presentations from Gabrielle Windgasse (Effort 1) and Geert Cornelis (Effort 2) summarized the state of the art and the scientific gaps in each field. The ensuing discussion was fruitful and revealed first that the term "life cycle" creates confusion between "exposure through the life cycle" and "life cycle assessment," which are distinct concepts. Therefore, the proposal was made to use the term "product life" instead of "life cycle."

COR members discussed the need to increase the understanding of the fate and behaviour of ENMs at every stage of the product life. This includes 1) release processes from production, use, and end of life; 2) ENM characterization and exposure at every product life stage; 3) transformation, partitioning, and bioaccumulation; 4) accumulation in environmental sinks; 5) synergism with other potential toxicants; and 6) databases and models for exposure evaluation and clustering materials. With such a large domain to investigate, the suggestion was made to clearly define the end points of exposure, fate, and transport. One of the high-priority targets can be defining objectives to implement models toward risk assessment needs.

Recommendations and next steps

One of the first efforts of the Community can be the development of a "Relational Database for Analytical Concepts and Methods for ENMs in Environmental Media." The requirements for such a database would be 1) queries for analytical procedures in various media and for various ENMs; 2) queries for instrumentation; 3) easy data entry (crowd-sourced/wiki model); 4) building of new analytical concepts; and 5) connections with other nano-databases. A list of researchers and their projects can be collected, but the database must go beyond a catalogue of skills and projects, including the detection limits of tools and a flow chart to determine the most appropriate method (e.g., how to detect ENMs in sediment). A graphical interface was also proposed to simplify the use of the database.

One of the short-term objectives of the Exposure through the Life Cycle COR could be the formation of four sub-groups based on priorities: 1) cataloguing references environments (soils, sediments, waters, etc.); 2) cataloguing key transformations (biotransformation, etc.); 3) cataloguing fate and transport parameters; and 4) cataloguing standard exposure scenarios. The issue of how to manage efforts was also discussed. While the database can be a central tool, face-to-face meetings and workshops will be essential to make meaningful progress. Finally, the need to closely coordinate and communicate with the other Communities was repeatedly emphasized.

Ecotoxicity Testing and Predictive Models, with Material Characterization

Chair: Henriette Selck, Roskilde University, Denmark
Rapporteur: Jacques-Aurélien Sergent, L'Oréal, France

Overview

The breakout session was composed of four talks and a discussion to refine the scope of the COR, evaluate the possible collaborations with other Communities, and identify middle-term development milestones.

Henriette Selck gave an introduction to define a shared COR vision. She outlined several pressing challenges, including the requirements for research innovation, standardization of protocols, and data sharing. The interaction with biota is still poorly understood and requires fundamental research on topics such as bioavailability and bioaccumulation, uptake, and distribution monitoring. Addressing this issue necessitates the development of characterization methods for every stage of exposure, including complex environments, that are affordable, reliable, and relatively easy to implement in a standard laboratory. Further, these methods would help understand the exact bioavailable dose and how this dose correlates to the quantified response. The establishment of predictive models needs databases with validated information. The main scope of the COR is, therefore, to engage the community in environmental research, to connect similar efforts, and to encourage evolution of predictive models and hazards assessment. The second talk given by Prof. Selck (on behalf of Steve Klaine) presented an example of collaboration between the United Kingdom and the United States: the Manufactured Nanoparticle Bioavailability and Environmental Exposure (nanoBEE) project.[12] The goal of the project is to develop modified biodynamic models for nanomaterials bioavailability.

Annemette Palmqvist introduced the concept of mechanistic effects models during her talk. Presenting a case study, she identified the major endpoints required to share data among experimentalists and modellers, noting that occasionally more data are required to be able to implement a whole set of data. Keeping in mind the necessity to share and model data when designing protocols will help the community to federate. Defining an annotated file format, like the FASTA format for sequence analysis, that is relevant to experimentalists and modellers appears to be a priority. The talk by Alexander Orlov was about designing nano-enabled products with minimal toxicity, citing the example of buildings coated with self-cleaning materials. In addition, the positive environmental impact of <1 nm particles assembled via an atom by atom assembly approach was discussed, particularly in terms of their application to the conversion of CO_2 into hydrocarbons.

Recommendations and next steps

The group will set up an online, 10-question survey to collect information on research priorities and knowledge gaps. This information will be used to refine the COR's scope and to plan focused, relevant events for the Community. The need to collaborate with other CORs was noted and a possible student exchange within the Community suggested. Finally, the recommendation was made to hold a workshop for the COR within one year in concert with a relevant meeting.

[12] gtr.rcuk.ac.uk/project/FC6D34C2-763B-4358-A02C-68CA546E12A5

Predictive Modelling for Human Health, with Material Characterization

Chairs: Yoram Cohen, University of California Los Angeles, United States
Bengt Fadeel, Karolinska Institutet, Sweden
Rapporteur: Lang Tran, Institute of Occupational Medicine, United Kingdom

Overview

The session was focused on approaches, including quantitative structure-activity relationships (QSARs), to predict biological responses induced by nanomaterials. Bengt Fadeel presented the opening remarks and provided an overview of the COR's scope. The COR had a preparatory call several months before the workshop, and three critical themes were emphasized: *correlation* (between *in vivo* and *in vitro* studies, between high-throughput results on cell lines and organisms, between physico-chemical properties and human hazard, etc.); *modelling* (e.g., with physiologically based pharmacokinetic and QSAR models); and *new approaches* (e.g., bioinformatics and/or systems biology processing and implementation of new model organisms).

The presentations from Yoram Cohen and Enrico Burello highlighted the several concepts that are essential for accurate modelling. At the most basic level, modellers must keep in mind that risk is a combination of exposure and hazard. Appropriate dose metrics must be selected, and the entire product life cycle should be taken into account. Scientists should also keep in mind the difference between QSAR, which is quantitative, and SAR, which is categorical and for classification. Finally, it was noted that QSAR is useful for determining dose metrics because it uses high-throughput test results. QSAR requires a considerable amount of structured data, and the use of databases is extremely important. It is also important to keep in mind that not all data is quantitative.

During the discussion, clear documentation, appropriate selection of nanomaterials and environmental descriptors, and quantification of uncertainty were identified as critical modelling requirements. The identification of meaningful toxicity metrics and the inclusion of SAR in experiments were also addressed. The group discussed potentially creating an inventory of nano-specific QSAR and SAR models and developing a database of physico-chemical characteristics of standard reference materials, in collaboration with other CORs. Finally, the scope of the Community should include clear guidelines for model validation and publicly accessible datasets.

Recommendations and next steps

Continued U.S.-EU dialogue on areas of interest for modelling is needed. Additionally, datasets for model validation should be identified, and existing models in both the United States. and the European Union should be subjected to further validation.

Participants recommended the following four steps to advance the goals of the Community: 1) encourage additional scientists to sign up for the COR; 2) implement regular webinars on topics of interest; 3) share documents through us-eu.org; and 4) link, where appropriate, to relevant international collaborations and events, such as COST Action MODENA TD1204[13] and NANOTOXICOLOGY 2014.[14]

[13] www.cost.eu/domains_actions/mpns/Actions/TD1204
[14] www.nanosustain.eu/future-events/118-nanotox-2014

Risk Assessment

Chairs: Derk Brouwer, TNO, the Netherlands,
Mark Wiesner, Duke University, United States
Rapporteur: Andrea Haase, German Federal Institute for Risk Assessment (BfR), Germany

Overview

The breakout session opened with an overview of the COR's draft scope and objectives from Derk Brouwer. Mark Wiesner gave a presentation on a risk forecasting framework for nanomaterials that touched on issues of uncertainty and nanomaterial value chains. Aleksandar Jovanovic presented a talk on the industrial perspective on the risks and safety of nanotechnologies based on nanotechnology projects under the Seventh Framework Programme of the European Commission.

The initial conversation during this session addressed the draft scope and objectives and was centred on the possibility of including the concept of benefit analysis into the group's title and/or scope. After a long discussion, the participants agreed that benefit analysis should be included as one focus group within the COR, but not in the Community's title. Another major topic of the discussion was the concept of life cycle. Several participants voiced the opinion that the phrase "life cycle assessment" might create confusion as it implies something different than intended by the Community. The use of alternative terms such as "product cycle," "value chain," or "fate analysis" was proposed.

The group also discussed the fact that most current research is focused on hazard assessment and on pristine, simple nanomaterials. Little work is done on exposure scenarios or on second- or third-generation nanomaterials in complex matrices.

The connection of this COR to the other Communities seems to be a very central point. The group is strongly dependent on input from the other CORs, particularly on terminology and resources from the Databases and Ontologies COR. It is also important to exchange data with the CORs on exposure, ecotoxicity, and predictive modelling. Finally, this Community should support the COR on Risk Management and Control.

Recommendations and next steps

The Community wants to establish focus groups within the next months to provide a basis for collaborations and projects. The co-chairs will circulate a questionnaire to all COR members to identify which focus groups should be established and who wants to participate in each. During the discussion, several potential focus groups were identified, including benefit analysis, product cycle/ fate analysis/ value chain, exposure pathways/ scenarios, data needs, data harmonization, inventory tools, and human risk assessment as well as environmental risk assessment.

Additionally, the group will recruit new participants and connect to the other CORs. The Community will also build on events that members plan to attend to organize small satellite workshops. Finally, the Community plans to identify projects in Europe and the United States that can feed content into the COR.

Databases and Ontologies

Chairs: Nathan A. Baker, Pacific Northwest National Laboratory, United States
Hubert Rauscher, European Commission
Rapporteur: Martin Fritts, U.S. National Institute of Standards and Technology

Overview

This session included three short presentations and significant discussion. The first presentation was provided by Hubert Rauscher, who gave an overview of the previously established goals and scope of this COR. The second presentation was given by Nathan Baker, who provided an overview of relevant U.S. nanotechnology information resources. The final presentation was provided by Iseult Lynch, who surveyed European resources.

The group discussion focused on the key issues in nanotechnology informatics research: barriers to information sharing and the driving scientific problems that motivate the need for more facile and effective collaboration and sharing. In particular, much of the conversation involved ways to incentivize data sharing, including establishing publication equivalency for data sharing, curation, and annotation; making data sharing a prerequisite for publication as well as fulfilling funding agency requirements for data management; and providing access to analytic capabilities as a result of data sharing.

Recommendations and next steps

The group identified a set of short-term and mid-term objectives. The short-term objectives are geared toward the six to 12 months following the workshop and include communicating with other CORs to determine their data infrastructure needs, creating an inventory of existing nanotechnology informatics infrastructure, and growing the group's membership. The Community recognizes that the other CORs provide essential information about the scientific applications (use cases) that require mechanisms and infrastructure for information sharing and improved databases and ontologies. In addition to describing the driving scientific applications from each COR, the cross-Community discussions will also identify the sources and quality of the data for each application and the computational tools necessary to analyse or model the data.

The development of an inventory of existing resources will allow the COR to better understand the current scope of available data and ontology in nanotechnology as well as the available user applications for accessing, evaluating, and using both experimental and modelling data. The Community will also become more able to identify gaps in critical domain areas and to aid in prioritizing research efforts. To provide incentives for participation in the nanotechnology informatics resource inventory and to provide broader awareness of these resources, this effort will be focused initially on the development of invited articles for a special issue of *Computational Science and Discovery*.

The mid-term objectives for this Community fall into two broad categories: mechanisms for increased data sharing and projects based on specific use cases collected from other CORs. In terms of increasing data sharing, four possible approaches were outlined: 1) identify incentives for data sharing; 2) mandate data sharing through publisher and funding agency policies; 3) develop data-sharing and minimal information requirements for publication; and 4) provide incentives for collaborative development, validation, and continual improvement of experimental methods and models, including means of sharing intellectual property for both data and models.

Risk Management and Control

Chairs: Lawrence Gibbs, Stanford University, United States
Tom van Teunenbroek, Ministry of Infrastructure and Environment, the Netherlands
Rapporteur: Garry Burdett, United Kingdom

Overview

Three presentations set the stage for the discussion during the session: Larry Gibbs presented the COR's vision statement; Tom van Teunenbroek reviewed regulatory frameworks for nanomaterials in the European Union; and Charles Geraci outlined key research areas for nanoEHS success.

During the subsequent discussion, the meeting participants agreed that the draft objectives of the COR were relevant, and they identified three main knowledge gaps. A lack of information on environmental impacts is clearly a major gap, but this cannot be easily or quickly remedied. An equally important, but easier to address, gap is determining reasonable practice in the occupational environment. There are three basic workplace nano-environments: research, scale-up or pilot, and production. The recent publication of advice by various sources (e.g., the U.S. National Institute for Occupational Safety and Health, UK universities, and Swiss universities) suggests that the university research environment is improving and larger companies are likely to have a well-developed safety system. It is more difficult, however, to put proper safety systems into pilot plants because substantial amounts of product are brought in or synthesized in a batch or trial basis, and these processes are prone to unexpected problems, blockages, faults, etc. Also, these plants often lack engineering control systems, or the systems are not sufficiently tested for effectiveness. Finally, it was felt that a better understanding of abilities and limitations of hazard and control banding would be beneficial and would yield a useful, reliable tool to apply to these pilot-scale operations.

As expertise and ideas evolve, it is important that this information is captured by the COR. Safer by design and practice (e.g., the production and supply/use of materials in liquid state rather than as powders) was viewed by several participants as an important avenue to pursue. There was recognition that improved systems of data collection and management will both aid and improve data management and collection for risk management and regulatory purposes. This will be even more important as scientists are able to better identify and define realistic exposure scenarios (e.g., based on the form/type of the material).

Recommendations and next steps

The recommendation was made to continue U.S.-EU dialogue to identify and share best practices in occupational settings, specifically to encompass both intelligent test strategies and intelligent risk management. It was also concluded that the COR should first develop and provide mechanisms to share information on high-risk occupational situations. This was seen as being readily achieved before expanding into other more difficult areas.

The COR could look for opportunities to further expand stakeholder participation and interdisciplinary expertise by soliciting new members. A membership roster that includes names and expertise could aid in the development of working groups. Finally, the Community will convene two follow-up conference calls prior to March 2013 to focus on one of the three top identified priorities: containment and control, an expert basis for decision analysis, and a mapping of exposure and release scenarios where there are problems with applicability and effectiveness.

5. Summary of Breakout Session Reports

During the discussions following the summaries of each breakout session, several cross-cutting issues emerged. Namely, each Community is working to quickly give substance to their activities. Many of the CORs are undertaking initial projects with intentionally narrow scopes to quickly produce tangible outcomes and form a basis for future progress. Several CORs also mentioned the need to expand their membership and include key experts in their respective fields.

Following the presentation from the Databases and Ontologies COR, there was a lively discussion on how to create incentives for scientists to deposit their data in databases. The database models for the genomics community (scientists must deposit data before they can retrieve data) and the crystallography community (deposition of data is the primary form of publication/certification) were cited as potential models for the nanoEHS community.

6. Conclusions and Closing

Conclusions, and the Next Steps and Ways Forward

Georgios Katalagarianakis, European Commission
Sally Tinkle, National Nanotechnology Coordination Office, United States

Georgios Katalagarianakis described how this workshop builds on the first U.S.-EU: Bridging NanoEHS Research Efforts joint workshop, which was held in Washington, DC, in 2011. These face-to-face meetings enhance collaboration and information exchange among scientists. Dr. Katalagarianakis noted that science is evolving with a stronger focus on teams and informatics, and it benefits the community to evolve as well.

Sally Tinkle detailed the goals behind bringing the European and U.S. nanoEHS scientific communities together: to address issues in nanoEHS research across the innovation pipeline; to identify gaps; and to solve critical issues. This collaborative effort is part of an experiment to advance science in spite of tight budgets, and meaningful progress was made during the workshop. Dr. Tinkle announced the 3rd U.S.-EU nanoEHS workshop, which will be held in Washington, DC, in early 2014. This event will further focus on the CORs and continue to evolve the EU-U.S. collaboration.

Closing the Meeting

Chris Cannizzaro, Department of State, United States

Chris Cannizzaro noted that the agenda for this workshop was completely focused on the Communities of Research. As such, the enthusiastic participation of the meeting attendees was crucial to the success of the event. Dr. Cannizzaro recounted how the U.S.-EU joint effort was first proposed at a Joint Consultative Group in 2010 and the first joint workshop was held in early 2011. The next U.S.-EU Joint Consultative Group will be held in December of 2012, and the U.S.-EU nanoEHS planning team will continue to work with the European Commission and the Emerging Technologies Interagency Policy Committee in the United States to ensure broad stakeholder participation in the collaboration.

Appendix A. Workshop Agenda

Thursday, 25 October 2012	
8.30	Registration
Room:	Main Lecture Room
Chairs:	Kai Savolainen, Finland Chris Cannizzaro, United States
Plenary Rapporteurs:	Lea Pylkkänen, Finland Marit Ilves, Finland
Technical Coordinator for the Proceedings:	Elina Juntunen, Finland

PLENARY:	**WELCOME REMARKS**
9.00	**Words of Welcome** *Harri Vainio, Director General, Finnish Institute of Occupational Health, Finland*
9.10	**Welcome on Behalf of the U.S.** *Danny Hall, Deputy Chief of Mission, U.S. Embassy, United States*
9.20	**Purpose and Goals of the 2012 Workshop** *Christos Tokamanis, Head of Unit, European Commission*

PLENARY (I):	**BACKGROUND FOR 1ST DAY CORS**
9.30	**Emerging Issues of Nanosciences** *Kenneth Dawson, CBNI/UCD, Ireland*
10.00	**Research Priorities on Safe Nanotechnologies** *Mark Wiesner, Duke University, United States*
10.30	Break

PLENARY (II):	**EU AND U.S. RESEARCH STRATEGIES AND IMPACT OF RESEARCH**
11.00	**European Research Strategies on Nanotechnologies** *Kai Savolainen, Finnish Institute of Occupational Health, Finland*
11.15	**U.S. Research Strategies on Nanotechnologies** *Sally Tinkle, National Nanotechnology Coordination Office, United States*
11.30	Discussion
12.00	Lunch

GROUPS:	**BREAKOUT SESSIONS**		
13.00	**Risk Assessment COR**	**Ecotoxicity Testing and Predictive Models, with Material Characterization COR**	**Predictive Modelling for Health, with Material Characterization COR**
Room:	Main Lecture Room	Topelius	Haartman
Chairs:	Derk Brouwer, the Netherlands Mark Wiesner, United States	Henriette Selck, Denmark	Bengt Fadeel, Sweden Yoram Cohen, United States
Rapporteurs:	Andrea Haase, Germany	Jacques-Aurélien Sergent, France	Lang Tran, Scotland
13.00	COR Vision Statement *Derk Brouwer, the Netherlands*	COR Vision Statement *Henriette Selck, Denmark*	COR Vision Statement *Bengt Fadeel, Sweden*
13.10	A Risk Forecasting Framework for Nanomaterials *Mark Wiesner, United States*	The Challenges of Collaborating and Communicating across the Pond *Henriette Selck, Denmark (on behalf of Steve Klaine, United States)* Do Mechanistic Effect Models Have a Place in era of Engineered Nanoparticles? *Annemette Palmqvist, Denmark*	Predictive Modelling for Health *Yoram Cohen, United States*
13.25	Industrial Perspectives on Emerging Risks and Safety of Nanotechnologies *Aleksandar Jovanovic, Germany*	Designing Superior Nanomaterial-Containing Consumer Products with Minimal Toxicity *Alexander Orlov, United States*	QSARs for Nanomaterials *Enrico Burello, the Netherlands*
13.40	Discussion	Discussion	Discussion
14.40	Summary and Conclusions	Summary and Conclusions	Summary and Conclusions
15.00	Break		
15.30	Finalizing Workshop Reports: chairs, rapporteurs and the breakout groups		

PLENARY (III):	**REPORTS**
16.00	Workshop Report Risk Assessment COR
16.30	Workshop Report Ecotoxicity Testing COR
17.00	Workshop Report Predictive Modelling for Human Health COR
17.30	End of 1st Workshop Day

Friday, 26 October 2012

8.30	Registration
Room:	Main Lecture Room
Chairs:	Kenneth Dawson, Ireland Sally Tinkle, United States
Plenary Rapporteurs:	Chris Cannizzaro, United States Stacey Standridge, United States

PLENARY (IV): **BACKGROUND FOR THE 2ND DAY CORS**

9.00	**Requirements for Reliable Exposure Assessment of ENMs in Air** *Gerhard Kasper, KIT, Germany*
9.30	**Risk Assessment and Management of ENMs** *Christina Powers, EPA*, *United States*
10.00	Break

GROUPS: **BREAKOUT SESSIONS**

10:30	**Exposure through the Life Cycle, with Material Characterization COR**	**Databases and Ontologies COR**	**Risk Management and Control COR**
Room:	Main Lecture Room	Haartman	Topelius
Chairs:	Thomas Kuhlbusch, Germany Richard Canady, United States	Hubert Rauscher, European Commission Nathan Baker, United States	Tom Von Teunenbroek, the Netherlands Larry Gibbs, United States
Rapporteurs:	Jerome Rose, France	Martin Fritts, United States	Garry Burdett, United Kingdom
10.30	COR Vision Statement Richard Canady, United States	COR Vision Statement Hubert Rauscher, European Commission	COR Vision Statement Larry Gibbs, United States
10.40	Environmental Risk Assessment of ENP *Geert Cornelis, Sweden*	U.S. Resources *Nathan Baker, United States*	Regulatory Review of Nanomaterials in the EU *Tom van Teunenbroek, the Netherlands*
10.55	Developing a Resource Tool for Concepts and Methods to Analyze Engineered Nano Materials in Environmental Media throughout Their Life Cycle *Gabriele Windgasse, United States*	Nanosafety Databases: Harmonisation Efforts in Europe *Iseult Lynch, Ireland*	Key Research Areas for NanoEHS Success *Charles Geraci, United States*

11.10	Discussion	Discussion	Discussion
12.10	Summary and Conclusions	Summary and Conclusions	Summary and Conclusions

12.30 Lunch

13.30 Finalizing Workshop Reports: chairs, rapporteurs and the breakout groups

PLENARY (V): **REPORTS**

14.00 Workshop Report Exposure through the Life Cycle COR

14.30 Workshop Report Databases and Ontologies COR

15.00 Workshop Report Risk Management and Control COR

PLENARY (VI): **CONCLUSIONS AND CLOSING**

15.30 **Conclusions, Next Steps, and Ways Forward**
Sally Tinkle, United States
Georgios Katalagarianakis, European Commission

16.00 **Closing the Meeting**
Chris Cannizzaro, *United States*

16.10 End of the Workshop

Appendix B. Participant List

Affiliations current as of October 2012.

Christoffer Aberg, University College Dublin, Ireland

Jukka Ahtiainen, Finnish Safety and Chemicals Agency - Tekes, Finland

Melanie Auffan, CEREGE CNRS, France

Nathan Baker, Pacific Northwest National Laboratory, United States

Markus Berges, DGUV-IFA, Germany

Daniel Bernard, ARKEMA, France

Derk Brouwer, TNO, the Netherlands

Garry Burdett, Health and Safety Laboratory, United Kingdom

Enrico Burello, Netherlands Organization for Applied Scientific Research (TNO), the Netherlands

Marcello G. Cacace, National Research Council - Italy, Italy

Richard Canady, Center for Risk Science Innovation and Application - ILSI Research Foundation, United States

Christopher Cannizzaro, U.S. Department of State, United States

Carlos Fito, ITENE, Spain

Riccardo Concu, ITENE, Spain

Geert Cornelis, University of Gothenburg - Dept. Chemistry & Molecular Biology, Sweden

Kenneth Dawson, University College Dublin, Ireland

Diana de la Iglesia, Universidad Politecnica de Madrid, Spain

Francesco Dondero, Università del Piemonte Orientale, Italy

Albert Duschl, University of Salzburg, Austria

John Elliott, NIST Biosystems and Biomaterials Division, United States

Julia Fabrega, ECHA, Finland

Bengt Fadeel, Karolinska Institutet, Sweden

Ghita Falck, ECHA, Finland

Martin Fritts, NIST, United States

Charles Geraci, NIOSH, United States

Lawrence Gibbs, Stanford University, United States

Francesc Giralt, Universitat Rovira i Virgili, Spain

Roland Grafström, Medical Biotechnology VTT, Finland

Andrea Haase, German Federal Institute for Risk Assessment (BfR), Germany

Rainer Hagenbeck, Forschungszentrum Jülich GmbH, Germany

Sabina Halappanavar, Health Canada, Canada

Daniel Hall, U.S. Embassy Helsinki, Finland

Anton Ilin, Emerging Technologies Ventures LCC, United Kingdom

Marit Ilves, Finnish Institute of Occupational Health, Finland

Angela Ivask, National Institute of Chemical Physics and Biophysics, Estonia

Elzbieta Jankowska, Central Institute for Labour Protection - National Research Institute, Poland

Aleksandar Jovanovic, EU-VRi European Virtual Institute for Integrated Risk Management, Germany

Elina Juntunen, FIOH, Finland

Rune Karlsson, Nordmiljö AB, Sweden

Gerhard Kasper, Karlsruhe Institute of Technology, Germany

Georgios Katalagarianakis, European Commission, Belgium

Frederick Klaessig, Pennsylvania Bio Nano Systems LLC, United States

Zuzana Klöslova, ECHA, Finland

Thomas Kuhlbusch, IUTA - Air Quality & Sustainable Nanotechnology Unit, Germany

Ha-Young Lee, National Nanotechnology Policy Center - KISTI, Republic of Korea

Duarte Lisboa, ECHA, Finland

Cecilia Lopez, Catalan Institute of Nanotechnology, Spain

Iseult Lynch, Centre for BioNano Interactions, University College Dublin, Ireland

Maxine McCall, CSIRO, Australia

Axel Mustad, Nordic Quantum Computing Group AS, Norway

Hannu Norppa, Finnish Institute of Occupational Health, Finland

Alexander Orlov, SUNY Stony Brook, United States,

Annemette Palmqvist, Roskilde University, Denmark

Hyun-Mee Park, Korea Institute of Science & Technology, Republic of Korea

Mercedes Peleteiro Olmedo, University of Vigo, Spain

Alexander Pogány, BMVIT, Austria

Christy Powers, EPA, United States

Stefano Pozzi Mucelli, Veneto Nanotech SCpA, Italy

Víctor Puntes, Catalan Institute of Nanotechnology, Spain

Lea Pylkkänen, FIOH, Finland

Ilmari Pyykkö, University of Tampere, Finland

Robert Rallo, Universitat Rovira i Virgili, Spain

Hubert Rauscher, European Commission Joint Research Centre, Italy

Jerome Rose, CNRS-CEREGE, France

Kai Savolainen, Finnish Institute of Occupational Health, Finland

Henriette Selck, Roskilde University, Denmark

Jacques-Aurelien Sergent, L'Oréal, France

Kwang Min Shin, National Nanotechnology Policy Center - KISTI, Republic of Korea

Rosana Simón-Vázquez, University of Vigo, Spain

Hermann Stamm, European Commission Joint Research Centre - Institute for Health and Consumer Protection, Italy

Stacey Standridge, National Nanotechnology Coordination Office, United States

Claus Svendsen, Centre for Ecology and Hydrology, United Kingdom

Jose Tarazona, ECHA, Finland

Sandrine Testaz, French Embassy / Institut Français, Finland

Sally Tinkle, National Nanotechnology Coordination Office, United States

Christos Tokamanis, European Commission, Belgium

Lang Tran, IOM, United Kingdom

Timo Tuomi, Finnish Institute of Occupational Health, Finland

Harri Vainio, Finnish Institute of Occupational Health, Finland

Tom van Teunenbroek, Ministry of Infrastructure & Environment, Netherlands

Christopher Weis, NIEHS, United States

Peter Wick, Empa - Swiss Federal Laboratories for Materials Science and Technology, Switzerland

Eeva Viinikka, Culminatum Innovation Oy Ltd, Finland

Gabriele Windgasse, California Dept. of Public Health, United States

Ulla Vogel, National Research Centre for the Working Environment, Denmark

Frank Wolf, Federal Ministry of Education and Research, Germany

Henrik Wolff, FIOH, Finland

Robert Yokel, University of Kentucky Academic Medical Center, United States