2018 U.S.-EU: Bridging NanoEHS Research Efforts Workshop Synopsis

The U.S. National Nanotechnology Initiative (NNI) and the European Commission (EC) jointly hosted the annual meeting of the U.S.-EU Communities of Research (CORs)¹ on October 11–12, 2018, in Washington, DC. The CORs were established in 2012 to foster and develop a vibrant community equipped to explore and address critical issues related to research on the potential environmental, health, and safety implications of nanotechnology (nanoEHS). The goal of this workshop, the seventh meeting of the CORs, was to highlight progress toward COR goals and objectives, clarify and communicate plans, share best practices, and identify areas of crosscommunity collaboration. The 2018 U.S.-EU: Bridging NanoEHS Research Efforts² workshop was preceded on October 9–10 by the Second Quantifying Exposure to Engineered Nanomaterials in Manufactured Products (QEEN II) workshop,³ which facilitated a broad participation of the exposure science community in both meetings.

The nanoEHS research landscape has matured considerably since the U.S.-EU CORs were first proposed. The presentations at the 2018 workshop addressed several aspects related to nanoEHS knowledge gains. NanoEHS researchers have developed a better understanding of the key attributes that comprise the minimum information requirements for characterizing engineered nanomaterials (ENMs), based on a nanomaterial's intended use and relevant exposure routes and/or environmental compartments. The GRACIOUS project,⁴ funded under Horizon 2020, synthesized this information into a hypothesis-driven framework to support grouping of ENMs. This grouping could be used, for example, to facilitate targeted material testing or to inform safe innovation.⁵ In the United States, NNI agencies' research and engagement with industry have demonstrated that standard risk assessment methods are generally applicable to ENMs and engineering controls could be effective in managing exposures.

As in previous years, the workshop included an interactive exercise. The 2018 activity highlighted the importance of language and terminology in shaping the development of a shared understanding and in advancing (or sometimes impeding) collective progress. Each COR devoted a portion of its breakout session to considering a suite of words and phrases that workshop participants identified at the start of the workshop, based on the potential for varied and nuanced interpretations across scientific communities and between U.S. and European colleagues. The discussions covered words such as "exposure," "risk," "advanced materials,"

Any opinions, findings, conclusions, or recommendations expressed in this report are those of the meeting participants and do not necessarily reflect the views of the U.S. Government or the meeting participants' parent institutions. This report is not a consensus document but rather is intended to reflect the diverse views, expertise, and deliberations of the meeting participants.

¹ <u>us-eu.org/communities-of-research/</u>

² https://us-eu.org/2018-u-s-eu-workshop/

³ www.nano.gov/qeen2

⁴ www.h2020gracious.eu/

⁵ www.h2020gracious.eu/files/documents/2.%20AgnesOomen_RIVM.pdf

"governance," and "ecologically relevant," among others. In general, meanings and intent varied more by scientific discipline than by geographic area. However, there were clear differences between U.S. and European participants in their interpretation of the term "governance." U.S. participants initially identified "governance" more closely with the concept of "regulation" than did the European attendees. A broader vision of "governance" later emerged from the plenary discussions as referring to the establishment, monitoring, and application of polices, including tradeoff and cost-benefit analyses.

The success of the U.S.-EU nanoEHS COR model has led to the development of similar models for other disciplines. A nanomedicine COR was launched at the September 2018 meeting of the European Foundation for Clinical Nanomedicine (CLINAM) in Basel, Switzerland, and a nanomanufacturing COR is under consideration.

COR Breakout Session Summaries

The annual COR workshop provides an opportunity for the communities to review ongoing and completed activities, share important findings and developments, and frame plans for the upcoming year.

Characterization COR

Characterization assays and documentary standards have been a major area of U.S.-EU cooperation, with members contributing to standards developing organizations such as the International Organization for Standardization (ISO), the American Society for Testing and Materials International (ASTM), and the International Electrotechnical Commission (IEC). COR participants discussed the challenges in characterizing nanoplastics, and the implications for characterizing and identifying the sources of those materials. Methods such as thermal gravimetric analyses (TGA) may offer benefits in this area. Attendees also discussed advances in the informatics community, highlighting how improvements in the standardization, reporting, and availability of metadata could continue to support reproducibility.

Databases and Computational Modeling for NanoEHS COR

The final version of the EU-U.S. Nanoinformatics 2030 Roadmap was expected to be published shortly after the workshop.⁶ The roadmap had 40 coauthors from Europe, the United States, China, and Australia. A major activity, which started in late 2018 and would be ongoing in 2019, was a survey and assessment of the metadata for dissolution as part of a broader exploration of the types of metadata, the current state of the art, and an examination of how community consensus on metadata could enhance innovation and progress. Dissolution was selected as a topic based on recommendations in the roadmap, its importance to nanoEHS and nanomedicine, and the potential for community participation (including academia, industry, and government). Other potential case studies that were cited include images as metadata, integrating metadata in study design for electronic notebooks, and x-ray diffraction best practices. The following topics were identified as potentially forming the basis for a future of metadata discussion: machine learning, cross-community exchanges, and identification of data-driven funding priorities.

Ecotoxicity COR

The Ecotoxicity COR prepared, and planned to submit for publication, a paper on considerations and best practices for generating robust and reproducible engineered bioaccumulation measurements for a broad range

⁶ EU-U.S. Nanoinformatics Roadmap: https://www.nanosafetycluster.eu/outputs/eu-us-roadmap-nanoinformatics-2030/

of ecological receptors.⁷ This COR had previously published a perspective paper on aquatic toxicity testing of ENMs and related challenges and research opportunities.⁸ Breakout session attendees also discussed optimizing test methods and systems for more environmental realism. Important considerations included how to define worst case, environmental realism, and reproducibility/ease of testing. The Ecotoxicity COR's 2018 session included a presentation on the NanoFASE⁹ project's examination of nanosilver in the environment. The results of this research suggested the need to integrate information from more simple testing environments with the findings from more expensive, complex mesocosm experiments. Attendees also discussed the possibility of integrating the application of and potential risks associated with the use of nanotechnology in agriculture in future COR meetings.

Human Toxicity COR

Between September 2017 and January 2018, the Human Toxicity COR co-chairs conducted a survey of the nanoEHS community to look at areas of research and priority considerations. At the 2018 meeting, the COR discussed several issues: the survey's results, the framework of the "10 Essential Services for Public Health" to analyze workers exposure to ENMs, the existing worker registry at the U.S. Department of Energy (DOE Order 456.1A) and its implementation, and future topics for COR activity. Going forward, the COR activities could include exploring minimum standards for human toxicity data, further defining the "10 Essential Services" for worker exposure, repeating in the 2017 survey, and exploring the role of epidemiologic surveillance in understanding the potential effects of occupational exposure to nanomaterials and nanotechnology-enabled products.

Exposure through Product Life COR

Attendees at the Exposure through Product Life COR session discussed the importance of increasing awareness about the COR structure and exploring matching/collaborative funding possibilities. Participants discussed exposure assessments of indoor environments as a future area of interest for the Exposure COR. An objective identified for 2018/2019 was to prepare a paper examining the feasibility of using indoor air purifiers to efficiently collect nanomaterials. This research would assess the plausibility of using citizen scientists to carry out low-cost sampling and monitoring of home environments, and to compare this with workplace exposure sampling and control measures.

Risk Assessment COR

Attendees at the Risk Assessment COR session shared recent contributions to the field on the topics of risk assessment tools, quantifying adverse outcome pathways (AOPs), and multiscale modeling. For the upcoming year, the participants agreed to hold a series of teleconferences to further discuss topics of interest to the risk assessment community. Suggested topic areas for these teleconferences included AOP approaches and minimum metadata that support the intersection of toxicology and risk assessment.

⁷ Published as: <u>Petersen et al. (2019)</u>. Strategies for robust and accurate experimental approaches to quantify nanomaterial bioaccumulation across a broad range of organisms.

⁸ <u>Selck et al. (2016)</u>. Nanomaterials in the aquatic environment: A European Union–United States perspective on the status of ecotoxicity testing, research priorities, and challenges ahead. *Env. Tox. and Chem.* 35:1055-1067.

⁹ http://www.nanofase.eu/