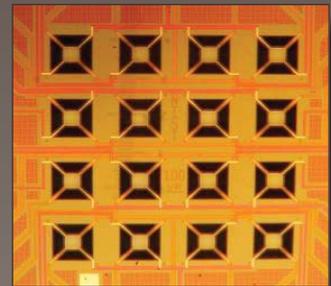
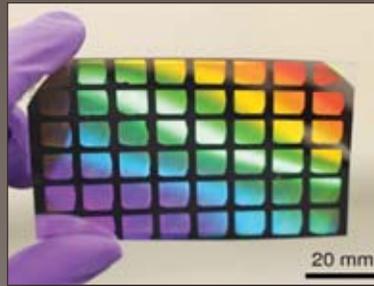
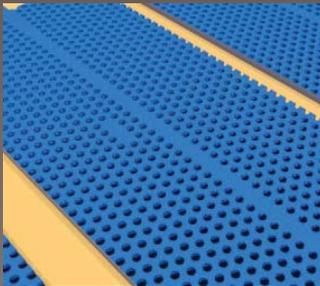


NNI Sensor Fabrication, Integration, and Commercialization Workshop

Proceedings
September 11–12, 2014



About the National Nanotechnology Initiative

The National Nanotechnology Initiative (NNI) is a U.S. Government research and development (R&D) initiative involving 20 Federal departments, independent agencies, and independent commissions working together toward the shared and challenging vision of a future in which the ability to understand and control matter at the nanoscale leads to a revolution in technology and industry that benefits society. The combined, coordinated efforts of these agencies have accelerated discovery, development, and deployment of nanotechnology to benefit agency missions in service of the broader national interest.

About the Nanoscale Science, Engineering, and Technology Subcommittee

The Nanoscale Science, Engineering, and Technology (NSET) Subcommittee is the interagency body responsible for coordinating, planning, implementing, and reviewing the NNI. NSET is a subcommittee of the Committee on Technology (CoT) of the National Science and Technology Council (NSTC), which is one of the principal means by which the President coordinates science and technology policies across the Federal Government. The National Nanotechnology Coordination Office (NNCO) provides technical and administrative support to the NSET Subcommittee and supports the Subcommittee in the preparation of multiagency planning, budget, and assessment documents, including this report. More information about the NSET Subcommittee, the NNI, and the NNCO can be found at www.nano.gov.

About the Nanotechnology Signature Initiatives

The Federal agencies participating in the National Nanotechnology Initiative have identified focused areas of national importance that may be more rapidly advanced through enhanced coordination and collaboration of agency research and development efforts. These Nanotechnology Signature Initiatives (NSIs) provide a spotlight on critical areas and define the shared vision of the participating agencies for accelerating the advancement of nanoscale science and technology to address needs and exploit opportunities from research through commercialization. They are intended to be dynamic, with topical areas rotating and evolving over time. More information about the NSIs can be found at www.nano.gov/signatureinitiatives.

About this Document

This document is the report of the Sensor Fabrication, Integration, and Commercialization Workshop, held September 11–12, 2014, in Arlington, VA. The workshop was sponsored by the NNI and focused on identifying challenges faced by the sensor development community. Both of the NSI *Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment* thrust areas, sensors enabled by nanotechnology and sensors to detect nanoscale materials, were represented. Any opinions, findings, conclusions, or recommendations expressed in this report are those of the authors and workshop participants and do not necessarily reflect the views of the United States Government or the authors' or other workshop participants' parent institutions. This report is not a consensus document but rather is intended to reflect the diverse views, expertise, and deliberations of the workshop participants.

About the Report Cover and Book Design

Book layout was designed by NNCO staff. Report cover design is by Kristin Roy of the NNCO. The three images on the front cover illustrate the fabrication, integration, and commercialization themes from the workshop. From left to right: (1) schematic of a silicon nanophotonic device post-fabrication, (2) image of a fully integrated, chemiresistive microhotplate array gas nanosensor, and (3) image of a flexible photonic, nanodome biosensor system. Image credits from left to right: (1) Omega Optics, and (2) and (3) National Institute of Standards and Technology.

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Workshop Proceedings

Sensor Fabrication, Integration, and Commercialization Workshop

September 11-12, 2014

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Workshop Planning

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We are grateful to all of the participants (listed in Appendix C) for interesting and lively discussions during the workshop, and to the notetakers who helped capture the workshop output.

Preface

This report is the result of a National Nanotechnology Initiative (NNI) Sensor Fabrication, Integration, and Commercialization Workshop, convened September 11–12, 2014, in Arlington, VA. This report was made possible with the help of the Nanoscale Science, Engineering, and Technology (NSET) Subcommittee of the National Science and Technology Council and with staff support from the National Nanotechnology Coordination Office (NNCO). The workshop and resulting report build on efforts by Federal agencies participating in the Nanotechnology Signature Initiative *Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment* (Sensors NSI). The Sensors NSI exists to address the opportunity of using nanotechnology to advance sensor development as well as the challenges of developing sensors to keep pace with the increasingly widespread use of engineered nanomaterials. The Sensors NSI has built upon existing NNI member agency efforts to support research on nanomaterial properties as well as the development of device and supporting technologies that enable next-generation sensing of biological and chemical materials, including those on the nanometer scale.

In his landmark speech at the California Institute of Technology on January 21, 2000, in which he announced the establishment of a new national initiative in nanotechnology, President Clinton imagined the possibility of “detecting cancerous tumors that are only a few cells in size.” Federal agencies participating in the NNI also recognize the considerable potential for nanotechnology to enhance the development of inexpensive, portable devices that can rapidly detect, identify, and quantify a vast array of biological and chemical entities for multiple applications. However, the sensor development community is currently facing key challenges related to standards, technology development and validation, and manufacturing that inhibit progress. Therefore, the NNI workshop brought together some of the Nation’s leading experts in sensor technologies from industry, academia, and Government to identify and discuss challenges that are faced by the sensor development community during the fabrication, integration, and commercialization of sensors. Meeting participants further identified a range of actions that could help mitigate these challenges and facilitate the commercialization of nanosensors. Workshop discussions also informed the development of the Sensors NSI web portal, which can now be accessed at www.nano.gov/SensorsNSIPortal. This web resource was created to share information on the sensors development landscape, including Federal program and funding opportunities, federally supported facilities, regulatory guidance, and published standards.

On behalf of the NSET Subcommittee, we thank Dorothy Farrell, Mark Hoover, Lisa Friedersdorf, Hongda Chen, Paul Shapiro, and Kim Sapsford for taking the lead in organizing this workshop. We also thank the speakers, discussion leaders, and other participants for their valuable contributions as well as the NNCO staff for logistical support and assistance in planning and executing this meeting. We trust that you will find this report to be a valuable resource for the NNI, the nanomaterials and sensor communities, and all other stakeholders as we work together to promote the NNI’s vision of creating “a future in which the ability to understand and control matter at the nanoscale leads to a revolution in technology and industry that benefits society.”

Lori Henderson
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Executive Summary

This report is a summary of the technical presentations and discussions that occurred at the National Nanotechnology Initiative (NNI) Sensor Fabrication, Integration, and Commercialization Workshop, held at the National Science Foundation (NSF) on September 11–12, 2014. The goal of the workshop was to identify and discuss challenges that are faced by the sensor development community during the fabrication, integration, and commercialization of sensors, particularly those employing or addressing issues of nanoscale materials and technologies.

Discussions at the workshop highlighted key challenges for the sensor development community, specifically related to standards, technology development and validation, manufacturing, and commercialization. These challenges include:

- Timely development of nanosensor-specific consensus standards.
- Access to rapid and precise characterization tools as well as testbeds designed for specific sensor applications.
- Scarcity of cost-effective semiconductor device foundries in the United States for low-to-medium-volume prototype production.
- Understanding and navigating the regulatory process that applies to specific sensor products and determining relevant points of contacts in Federal agencies.
- The ability to anticipate unintended consumer use of sensor products, which could possibly place consumers at risk.
- Decreasing financial support from the venture capital community.

Sensor developers and Federal agencies participating in the workshop identified a range of actions that could help address these challenges and facilitate the commercialization of nanosensors, which include:

- Enhancing communication among researchers, developers, manufacturers, customers, and the Federal Government agencies that support and regulate sensor development.
- Leveraging resources by building testbeds that are easily accessible to sensor developers and improving access of university and private researchers to federally supported pilot-scale foundries.
- Encouraging sensor developers to consider and prepare for market and regulatory requirements early in the development process.

In response to these actions and discussions at the workshop, the Nanotechnology Signature Initiative *Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment* resources web portal [1] was created to share information on the sensors development landscape, including funding agencies and opportunities, federally supported facilities, regulatory guidance, and published standards. Ongoing dialogue and collaboration among various stakeholder groups will be critical to effectively transitioning nanosensors to market and to meeting the U.S. need for a reliable and robust sensor infrastructure.

1. A Life Cycle Approach to Sensors Development

A sensor is a device that responds to a physical, chemical, and/or biological stimulus and converts its response into an output [2]. Sensors are increasingly being used in settings ranging from health diagnostics and chemical-biological threat detection to agricultural applications such as building crop yield maps. The Nanotechnology Signature Initiative *Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment* (hereafter, “Sensors NSI”) is the fifth Nanotechnology Signature Initiative launched by the agencies of the U.S. National Nanotechnology Initiative (NNI). NNI agencies recognize the considerable potential for nanotechnology to enhance the development of inexpensive, portable devices that can rapidly detect, identify, and quantify biological and chemical substances. Agencies participating in the Sensors NSI coordinate efforts (see Appendix A) and stimulate existing and emerging projects to explore the use of nanotechnology in two thrust areas [3]:

- Using nanotechnology and nanoscale materials to build more sensitive, specific, and adaptable sensors in order to overcome the technical shortcomings of conventional sensors (*Thrust 1*).
- Developing new sensors to detect engineered nanomaterials across their life cycles, in order to assess the potential impact on health, safety, and the environment (*Thrust 2*).

The Life Cycle Approach to Sensors Development

The sensors development life cycle defines steps that will enable successful and safe use of a nanosensor device throughout its lifetime [4, 5]. Widespread adoption of *Thrust 1* or *Thrust 2* nanosensors requires support at each step of the development life cycle, from conception to retirement, as shown in Figure 1 below.

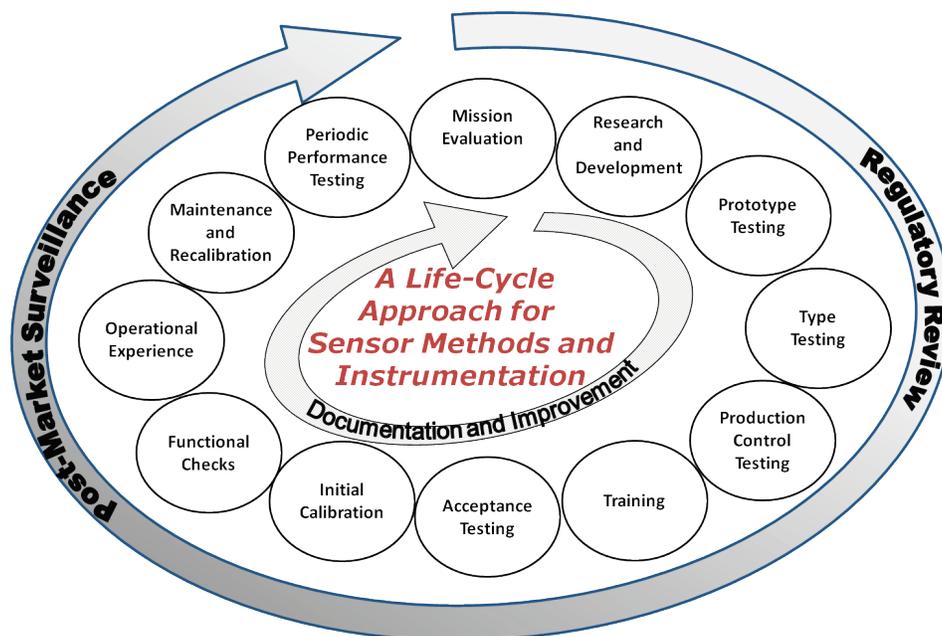


Figure 1. Diagram summarizing life cycle stages for development and application of sensors [3].

The life cycle steps highlighted in Figure 1 have been defined previously [4, 5]. Through an ongoing process of documentation and improvement, the interrelated life cycle activities enable an instrument to progress logically from the development phase involving regulatory review through the user-application phase of what can be viewed as post-market surveillance. In brief:

- The *mission evaluation* step serves the role of “problem formulation” and defines the objective of the measurement and identifies constraints on when, where, or by whom the instrument is to be used. Most importantly, it also identifies the value proposition, other candidate technologies, and clarifies the need for the instrument and optimal design endpoints.
- The *research and development* step first determines the circumstances in which the specific instrument design would meet the intended specifications. Understanding such requirements would allow manufacturers to produce a sensor that is likely to meet the engineering requirements set in the mission evaluation step.
- *Prototype testing* and *type testing* define and document the performance and limitations of the new sensor. The major difference between these two steps is that *type testing* is a formal process to meet specific requirements set by national and international standard organizations.
- *Production control testing* ensures that manufactured sensors meet critical user requirements for reliability and performance in accordance with documented procedures for quality management and assurance.
- Although positioned between the sensor development and application steps, *training* is a crucial cross-cutting step that is conducted at each phase of the life cycle. Training requirements apply to a wide range of individuals, from the technicians in the manufacturing line to the ultimate users.
- *Acceptance testing*, done by the organization that will deploy the sensor, ensures that each instrument has arrived undamaged and meets the specifications for its intended use.
- Although *initial calibration* can be performed as part of *production control testing*, it is generally performed after *acceptance testing* and before initial use of the instrument.
- *Functional checks* determine that an instrument is operational and capable of performing its intended function. Software development can play a critical role in enabling automatic diagnostics and self-checking features.
- *Operational experience* involves the evaluation of actual data collection to ensure proper sensor operation and interpretation. Careful tracking of operational experience can provide early evidence of sensor performance inconsistencies.
- *Maintenance and recalibration* ensures that sensor components, including replacement parts or alterations, have been successfully integrated into the supply chain and are equivalent to those specified by the manufacturer. Modified sensors, in particular, would require additional performance tests and documentation prior to issuance for field use, unless the modifications are shown not to affect the instrument performance or intended use for regulatory purposes.
- *Periodic performance testing* is essential to ensuring that the sensor continues to provide adequate performance under the intended and actual conditions of use.

The Sensors NSI Request for Information: Relating Stakeholder Inputs to the Sensors Development Life Cycle

NNI agencies participating in the Sensors NSI released a Request for Information (RFI) on October 1, 2013, to gather input from the public on specific needs for the accelerated development and commercialization of nanosensors [6]. The request focused on the following themes: standards, testing, manufacturing, commercialization, and regulation. The fifteen thematic questions included in the RFI could be summarized by the following general questions:

- What are the existing resources, facilities, and capabilities for sensor development?
- What are current testing and manufacturing practices in sensor development?
- How well do the existing resources, facilities, and capabilities meet sensor development needs?
- What new resources, facilities, capabilities are needed?
- How can we prioritize among needs?
- What are the new tools, processes, and applications for sensors that will have the largest immediate impact?

Responses collected from this RFI included diverse perspectives from trade groups, academia, technical experts, social scientists, and industry [7]. Common themes were identified based on these inputs. For example, the need to improve communication and collaboration among stakeholders was a common response. There was agreement that, as sensors become the backbone of the “Internet of Things” and software development continues to play a crucial role in sensor performance, data security is necessary for the acceptance of ubiquitous sensing. Responses indicated that access to test conditions beyond standard laboratory environments and closer to field use is critical for sensor development, and that transition of prototype sensors from research to commercial use depends on the availability of realistic testbeds. Other needs highlighted in the responses to the Sensors NSI RFI included:

- Additional standards to guide performance and operability of sensors; for example, standards to guide measures and reporting of sensitivity and accuracy by sensing.
- Standards for interoperability and data security.
- Access to restricted facilities such as biohazard laboratories and to advanced equipment for testing sensors in physiologically or environmentally relevant conditions.
- Guidance on how to better engage with appropriate contacts within regulatory agencies.

Examples of promising *Thrust 1*-type sensor applications mentioned in the RFI responses include physiological or metabolic nanosensing, medical diagnostics, gas-phase nanosensing, and “agrifood”-based applications. Responses also highlighted the promise of distributed nanosensor network applications, not only for a specific measurement field, but across several stages of a product life cycle. Furthermore, adapting sensors to detect nanomaterials for environmental, health, and safety applications (i.e., *Thrust 2*) could represent a critical component of safety and quality control for the manufacturing of nanosensors, as well as for tracking the fate and transport of nanoscale components of sensors and other products throughout their life cycles. To achieve this goal, it will be necessary to recognize those nanoscale properties that distinguish nanomaterials from chemical species or that distinguish engineered nanomaterials from incidental (or naturally occurring) nanomaterials in a matrix.

2. Sensors Development and Commercialization

The Sensor Fabrication, Integration, and Commercialization Workshop gathered experts from a wide range of application areas, stages of product development, and manufacturing of sensors. This section of the report summarizes keynotes and panel presentations that comprised the first day of the workshop.

Navigating from Lab to Market

Sydney Ulvick

In-Q-Tel

Launched in 1999 as an independent, not-for-profit organization, In-Q-Tel (IQT) was created to meet the technology needs of the U.S. Intelligence Community by identifying and investing in venture-backed technology startups [8]. IQT investments aim to accelerate product development and add mission-critical capabilities for the delivery of cutting-edge technologies to the intelligence community. Dr. Ulvick discussed essential strategies for successful nanosensor commercialization based on IQT's experience with sensors and related technologies. In general, targeting a specific market segment and business position are both critically important for successful commercialization of sensors. A high priority should be placed on building value in order to sustain a profitable market position. This requires an enterprise to recruit staff and board members with appropriate expertise in marketing and business management, rather than embracing a singular focus on research and technology development. Also crucial to the success of a startup company are thoughtful investors capable of accurately assessing the technology's value. Government funding can facilitate this value-building step by extending non-dilutive grant support during the initial stages of the sensor development life cycle.

Small Business Panel Presentations

Abhishek Motayed

N5 Sensors

Ray Chen

Omega Optics

Steve Gibbons

Brewer Science

Omowunmi Sadik

Binghamton University, State University of New York (SUNY)

Four members of the small business community and academia participated in a panel to present perspectives on sensor development issues ranging from prototype development to market launch. The panelists listed above, were from the following enterprises:

- *N5 Sensors*, a University of Maryland spin-off founded in early 2012. It commercializes low-power, chip-scale microsensor arrays that can detect various toxic and hazardous gases present in air [9].

- *Omega Optics*, founded in 2001, is currently based in Austin, Texas. The company develops and commercializes lightwave components using planar integrated polymer and silicon waveguide technology [10].
- *Brewer Science*, founded in 1981, is currently headquartered in Rolla, Missouri. The company focuses on the development and manufacturing of innovative materials, processes, and equipment for the reliable fabrication of cutting-edge microdevices [11].
- *Professor Sadik's group* at the Department of Chemistry at SUNY Binghamton has developed a portable, fully autonomous, and remotely operated sensing device, the "Ultra-Sensitive Portable Capillary Sensor" (U-PAC™), with funding from the Department of Defense. U-PAC has been tested for a range of biological and environmental applications, including the detection of biological threat agents (e.g., anthrax, *Bacillus globigii*, toxins, and live cells), diagnosis of diseases such as cancer, and detection of food poisoning [12].

Several persistent challenges faced by the small business community were discussed by the panel (see Manufacturing and Commercialization sections of Chapter 4 for additional details). One major challenge is the limited availability of test facilities to validate sensor reliability and performance in preparation for field testing. Additional standards are needed to guide performance metrics for sensitivity and accuracy by sensing applications. Panel members also felt constrained by manufacturing services provided by semiconductor device fabrication facilities in the United States that have not been cost-effective for small-capacity orders. Finally, additional clarity on the regulatory implications of the use of nanomaterials in sensors would greatly benefit the small business community, including relevant regulation of factory operation and product disposal by the U.S. Environmental Protection Agency (EPA) and the Occupational Safety and Health Administration (OSHA), as well as regulation of the safety and performance of finished products by the Food and Drug Administration (FDA) and the Consumer Product Safety Commission (CPSC).

Case Study on Commercialization Success

Ernest Streicher

John Deere

John Deere is an American company that manufactures agricultural, construction, and forestry machinery, parts, and equipment [13]. The company portfolio covers multiple aspects of the agricultural technology production system, from basic mechanization, scale, and productivity, to intelligent equipment and integrated solutions [14]. Sensing applications at John Deere include measuring various parameters of equipment functionality, including machine control (pressure, position, and speed), crop output (yield, weight, and moisture), and sample collection (soil characteristics, grain quality, moisture, and oil condition). The scale of potential sensing needs in the agricultural sector can be overwhelming, with millions of sensors needed for farms, billions for agronomic zones, and trillions for individual plants. Integration of data in large-scale measurement systems is crucial, as is the reliability of sensors in the field, which can involve challenging environments with large variations in temperature, vibration, dust, and chemical exposure. Representative sampling is a challenge in agricultural applications, as delicate crops can shift position with wind and rain and must be measured by non-contact sampling methods. Variations in ground conditions (e.g., soil composition, water content, and topology) across a field further complicate sampling. A case study on the commercialization of a fluid property sensor highlighted the importance of building value before entering a market and being able to quickly adapt to

shifts in market behavior. For example, consumer needs for a sensor product might change by the time the product is developed and released to the market. Dr. Streicher saw unique opportunities for nanotechnology to meet the needs for remote sensing and increased measurement points for higher-resolution yield maps in industrial agriculture, and to enhance the range of parametric data that is captured by current sensing platforms.

Navigating the Regulatory Process

Kevin Lorick

Food and Drug Administration¹

The framework for FDA's regulation of devices is based on several statutes [15]: the Federal Food, Drug, and Cosmetic Act (the FD&C Act) and the Public Health Service Act. These laws have been amended over the years [16], for example by the Medical Device Amendments of 1976, the FDA Modernization Act of 1997, the Medical Device User Fee and Modernization Act of 2002, the FDA Amendments Act of 2007, and the FDA Safety and Innovation Act of 2012. *In vitro* diagnostic (IVD) products are a subset of devices that are "reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body. These products are devices as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act, and may also be biological products subject to section 351 of the Public Health Service Act" [17]. Detailed information on how to market a device may be found on FDA's website [18].

The classification of an IVD is risk-based and is determined, in part, by the intended use of the device [19]; here, calculation of risk is largely based on the consequence of a false result. Intended use of an IVD encompasses a device's indications for use, which is defined as a general description of the disease or condition that the device will diagnose, treat, prevent, cure, or mitigate, including a description of the patient population for which the device is intended. For IVDs, the specific type of specimen to be tested may also affect the intended use.

The Center for Devices and Radiological Health (CDRH) is responsible for the regulation of most devices within FDA. FDA categorizes devices into one of three classes [20]: Class I, which are generally for low- to moderate-risk devices; Class II, generally for moderate- to high-risk devices; and Class III, generally for the most high-risk devices and for many devices with novel intended uses. General controls are applicable to all devices regardless of class [21]. General controls include an obligation for registration of manufacturing establishments and listing of the devices produced. Many devices must be manufactured in a controlled manner following Good Manufacturing Practices (GMP) as per Title 21 Code of Federal Regulations (CFR) Part 820 [22]. Manufacturers generally must submit reports of certain adverse events and of corrections and removals, follow general device labeling provisions, and maintain FDA-required records reports. IVDs are also subject to additional, complementary labeling requirements [23].

Devices that fall into Class II are subject to general and special controls. These typically require a Premarket Notification, according to section 510(k) of the FD&C Act. Special controls are additional requirements for devices when general controls alone are insufficient to provide a reasonable assurance

¹ CDRH currently has no published device-specific policy concerning nanotechnology. For FDA guidance on use of nanotechnology in FDA-regulated products generally, see Reference 25. All opinions expressed here are Dr. Lorick's and do not reflect official FDA policy on nanotechnology.

of the safety and effectiveness of a device [21]. Generally, Class III devices also require submission of a Premarket Approval application (PMA) and are subject to certain other requirements, which may include premarket inspection of manufacturing and clinical sites, annual reporting, and prior approval of most significant changes to the device design or manufacturing processes [21].

FDA has been working to address the challenges that nanotechnology presents [24, 25] and has provided guidance for the use of nanotechnology in FDA-regulated products, including medical devices. As described in FDA guidance, FDA will regulate nanotechnology products under existing statutory authorities, in accordance with the specific legal standards applicable to each type of product under its jurisdiction. FDA considers the current framework for safety assessment sufficiently robust and flexible to be appropriate for a variety of materials, including nanomaterials. Issues such as the safety, effectiveness, public health impact, or the regulatory status of nanotechnology products are currently addressed on a case-by-case basis using FDA's existing review processes [25].

Simply using nanotechnology in the manufacture of a device does not necessarily cause it to fall into a different classification than similarly marketed Class I or II devices. Such nanotechnology-enabled devices may still be determined to be substantially equivalent to legally marketed devices. If the nanotechnology enables a device to function through different principles than the predicate, it likely will not be considered substantially equivalent to the predicate, but the risk associated with the new device still may not be considered high. As with non-nanotechnology products, in such cases where a nanotechnology product is determined to be a unique device, the *de novo* classification process may allow a pathway to Class I or Class II for which general controls or general and special controls provide a reasonable assurance of safety and effectiveness, but for which there is no legally marketed predicate device. If classified as Class I or II through the *de novo* process, similar devices could come to market as 510(k)-exempt devices or by use of the 510(k) pathway rather than via PMA [26].

In addition, the investigational device exemption (IDE) regulations allow an investigational device to be used in a clinical study in order to collect safety and effectiveness data [27]. Clinical studies are most often conducted to support PMAs (a few 510(k) submissions require clinical data). While each device and study is different, most IVD investigations are exempt from IDE requirements if the IVD test meets certain requirements, including being noninvasive, not requiring an invasive sampling procedure that presents significant risk, not by design or intention introducing energy into a subject, and not being used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure [28].

An important review question when assessing the safety and effectiveness of a nanosensor is whether the use of nanotechnology makes the device "better." There is a wide range of engineered nanomaterials with unique physical and chemical properties that lend themselves to many potential biomedical applications. This variety in properties extends to diverse shapes, structures, and even textures. As such, physico-chemical characterization of an enabling material is necessary to establish control of nanoparticle synthesis and application, and to determine the effect of associated properties on device performance. Importantly, the characterization technique should match the intended use of the device. The use of nanotechnology for IVD applications will rarely represent a biocompatibility risk to the patient beyond a similar device that does not involve nanotechnology. However, manufacturing processes involving nanotechnology may affect device effectiveness, quality, or performance [22, 25]. CDRH may consider these and other factors when evaluating a device.

Navigating the Regulatory Process

Ronald Williams

Environmental Protection Agency²

The EPA has identified six “criteria pollutants” as air pollutants of particular concern because of their impact on public health and the environment [29]. These criteria pollutants are ozone (O₃) [30], particulate matter [31], carbon monoxide (CO) [32], nitrogen dioxide (NO₂) [33], sulfur dioxide (SO₂) [34], and lead (Pb) [35]. Under the Clean Air Act, the EPA has established primary and secondary National Ambient Air Quality Standards (NAAQS) for these six pollutants. Primary standards are designed to protect public health, particularly sensitive populations, while secondary standards are designed to protect the public welfare, which includes the environment. If a geographical area does not meet one or more of the NAAQS, it is designated as a non-attainment area and a plan must be designed and implemented to meet the standard [36].

The current monitoring network for criteria pollutants is comprised of monitors that meet Federal Reference Method (FRM) or Federal Equivalent Method (FEM) requirements. Monitors are operated by State, local, and tribal air pollution regulatory agencies across the United States to assess pollutant concentrations relative to the NAAQS. A variety of instruments and techniques are needed to measure specific pollutants. Regulatory monitoring generally requires very sophisticated and well-established instrumentation to meet measurement accuracy requirements and an extensive set of procedures (e.g., calibration, maintenance, audits, and data validation) [37] to ensure the collection of high-quality data (refer to 40 CFR, Parts 50, 53, and 58, and the EPA Quality Assurance Handbook for Air Pollution Measurement Systems, Volume II, for activities/criteria for monitoring network data). The overall quality and credibility of measurements are determined by both the type of measurement instrument and how it is operated.

Under the Clean Air Act, EPA regulates a list of 187 hazardous air pollutants, commonly referred to as “air toxics.” National Air Toxics Trends Stations (NATTS) were set up across the United States to monitor air toxics [38]. These stations ensure that quality data is collected in a consistent manner. Starting in 2003, EPA has worked with State and local partners to develop the NATTS program to monitor several air toxics. The principal objective of the NATTS network is to provide long-term monitoring data across representative areas of the country for priority pollutants, including benzene, formaldehyde, 1,3-butadiene, hexavalent chromium, and polycyclic aromatic hydrocarbons such as naphthalene, in order to establish overall trends. Additionally, some regulated industrial sources are required to submit air toxics emissions information to the EPA. The quality and completeness of emissions data varies significantly by region and source.

² All opinions expressed here are those of Dr. Williams and do not reflect official EPA policy on nanotechnology.

3. Federal Programs and Resources to Support Sensor Development

Member agencies of the Sensors NSI participate in all stages of the life cycle noted in Chapter 1. This includes supporting basic research and development, providing state-of-the-art fabrication facilities, developing standards, serving as regulatory authorities, and in many cases, serving as the end users for nanosensors. As a result, these NNI member agencies have put in place multiple mechanisms to support nanosensor development and nanomaterials characterization. Detailed information on various resources for sensor development is included in the Sensors NSI portal [1]. Through the NSI, Federal agencies foster communication, coordinate efforts in regulation, and promote deployment of sensors developed with agency support to meet sensing needs across participating agencies [3].

Federal agencies recognize the considerable potential for nanotechnology to enhance the development of inexpensive, portable devices that can rapidly detect, identify, and quantify biological and chemical substances. Several resources have been established to support the sensor community, including funding opportunities and user facilities at government laboratories and facilities. Examples of relevant Federal programs include the EPA National Center for Environmental Research [39], the FDA Office of *In Vitro* Diagnostics and Radiological Health [40] (formerly called the Office of *In Vitro* Diagnostic Device Evaluation and Safety), the National Cancer Institute (NCI) Alliance for Nanotechnology in Cancer [41], the NCI Innovative Molecular Analysis Technologies Program [42], and the recently established Center for Direct Reading and Sensor Technologies of the National Institute for Occupational Safety and Health (NIOSH) [43], among many others.

Government laboratories and facilities continue to be an invaluable resource for the development of emerging technologies, including sensor nanotechnologies. Examples of government facilities and resources available for the development of nanosensors include the National Institute of Standards and Technology Center for Nanoscale Science and Technology [44], EPA's Air Sensor Toolbox for Citizen Scientists [45], the NCI Nanotechnology Characterization Lab [46] and Antibody Portal [47], the NIOSH Field Studies Team [48], and the Department of Energy Nanoscale Science Research Centers [49]. This sensing infrastructure is augmented by various Federal centers and networks to support multidisciplinary research, advance knowledge, and enhance the transition of basic research results to the development of devices and other applications.

Federal agencies continue to determine regulatory approaches that encourage the continued development of innovative, safe, and effective products that use nanoscale materials, including nanosensors. NNI agencies identify and recommend ways to address any knowledge or policy gaps that exist so as to evaluate possible adverse health effects from products that use nanoscale materials. Examples of Federal regulatory resources for the responsible development of nanosensors include the CPSC Small Business Ombudsman [50] and the FDA final guidance documents on the use of nanotechnology in consumer products [24].

4. Key Challenges in the Development of Sensor Technologies

A fundamental goal of the Sensors NSI is the development of technologies that enable next-generation sensing of biological and chemical materials, including those on the nanometer scale [3]. As described in Chapter 1, agencies participating in the Sensors NSI address this goal through two primary thrusts in sensing R&D: *Thrust 1* for developing nanotechnology-enabled biological and chemical sensors, and *Thrust 2* for detecting and identifying engineered nanomaterials across their life cycles. As researchers and businesses develop nanosensor technologies in these two topics areas, they face several key challenges related to standards, development and validation, manufacturing, and commercialization. A summary of the workshop discussions regarding these challenges is provided below.

Standards

The term “standards” can include physical standards, reference materials, measurement protocols, documentary standards, technical specifications, guidance documents, and best practices [51]. These materials and documents, when appropriately developed and disseminated, can provide a valuable resource for sensors research and commercialization. Yet, given the complex nature of standards development, small startup companies may not be fully aware of existing standards or understand the value of using reference materials or complying with published documentary standards.

Further, if standards are released prematurely, they may not be based on sound scientific evidence or represent consensus among the relevant communities. Alternatively, if standards are released too late, they may no longer be applicable, or companies may have to manage uncertainty while the standards are under development. This tension is reflected by the fact that there is a perception that there are too many standards in some areas and too few standards in others, such as safety and performance metrics.

Development and Testing

There are many potential performance specifications that sensor developers can pursue, such as sensitivity, specificity, speed, and reliability. However, the exact requirements for each sensor ultimately depend on the application. Some sensors, such as those that will be used in harsh environments, may be designed with more emphasis on robustness than on sensitivity. Ease of use also should be kept in mind, and the need for complex sample preparation procedures should be minimized. Networks of sensors could provide powerful information on systems such as the human body, the environment, and climate, among many others. Yet, a systems-level approach to sensors development puts tremendous burden on the developers because it requires developing strategies—for example, for information management and network performance evaluation—that may be outside of their core areas of expertise.

As researchers develop and test new sensor technologies, a primary challenge is access to rapid and precise characterization tools. In particular, more high-throughput, quantitative tools are needed to aid the development of sensors for nanomaterials. There is also strong demand for new computational tools that provide materials and risk models.

Ideally, new sensor technologies will undergo extensive calibration and validation, including long-term tests, to ensure performance and reliability. The validation process should include tests under actual

working conditions, which could involve variations in temperature and humidity, vibration, or dusty operating conditions. Validation must also include tests for false positives. Small business cannot afford to set up individual testing and validation facilities, and workshop participants indicated that more testbed user facilities are greatly needed. However, testbed requirements strongly depend on the sensor's application and potential regulatory considerations (e.g., health, food, pharmaceutical, environmental, or defense). Thus, testbeds designed for the sensors' intended uses would be much more valuable than general-purpose facilities. Testing facilities must also protect businesses' intellectual property and ensure reliability in measurements to maintain credibility. Finally, testbeds should be developed in tandem with appropriate standards to ensure maximum applicability and relevance of both the testbeds and the standards.

Manufacturing

The most pressing manufacturing challenge identified by workshop participants is the scarcity of nanofabrication facilities that can produce small batches of devices on a scale necessary for field testing at a reasonable price and with short turnaround time. In the absence of access to such cost-effective foundries in the United States, companies may need to consider whether to manufacture their products abroad. However, assembling sensors overseas can be slow and can raise questions about the security of intellectual property. Also, if the final product will be acquired by the Department of Defense, it may be subject to export controls and may need to be manufactured domestically [52].

In this context, it can be difficult for small businesses to identify manufacturing facilities for the production of an entire device. For example, some sensors need complicated sample-acquisition components, while others need optical components that cannot be outsourced. The systems-level approach presents a unique challenge in light of mass-production requirements, export restrictions, and intellectual property concerns, as well as cost and time constraints. Once a suitable manufacturing facility is found, the manufacturing process needs to be simple and cost effective. Quality control procedures are still needed to ensure repeatability and reproducibility in high-throughput settings. In-line sampling would be ideal but may be prohibitively expensive. Collaboration among the manufacturers, government, and research laboratories is needed to develop appropriate quality control tools for the sensors industry.

Finally, workforce education, training, and safety must be considered for all aspects of the development cycle. During the R&D phase, highly skilled industrial and software engineers are needed to design and fabricate prototypes and the software that operates the sensors. In the manufacturing phase, more mid-level technical training and standard operating procedures are needed. Finally, the safety and health of the entire workforce needs to be a central goal when designing and implementing manufacturing systems, and workers should be trained in the safe handling of engineered nanomaterials.

Commercialization

Environmental, health, and safety considerations, including life cycle analysis and regulatory approval, are crucial components of successful commercialization of all sensors. Yet, many businesses are unsure of which regulatory agencies have purview and which statutes apply to their products. This uncertainty can slow down the development and commercialization of new sensor technologies. Medical device companies can use FDA's pre-submission program [53] to get feedback on what data will be requested during regulatory review. However, this resource is underutilized, and some commercial organizations still report difficulty in identifying which specific aspects of nanotechnology-enabled sensor technologies

need to be considered before commercial use. Businesses have also called for regulations tailored to the scale of production. For example, the quantity of carbon nanotubes used in composites such as cement is many orders of magnitude larger than that used in individual sensors [11]. Finally, life cycle analysis of nanotechnology-enabled sensors is more complex than that of conventional sensors because nanomaterials may undergo transformations, such as the formation of surface films or particle aggregates, throughout their manufacture, use, and disposal. Example of research on the nature and implications of these transformations can be found in the *Progress Review on the Coordinated Implementation of the 2011 NNI Environmental, Health, and Safety Research Strategy* [54].

In addition to standard product liability considerations, companies must anticipate how consumers will interact with and operate their sensors. Consumers may use products in ways the producers did not intend, which could open up new markets or result in new risks to the consumer and pose liability concerns for the company. One specific example is the impact of the sensor–user interface on intended product use. Although software development might not fall within the initial phases of sensor design, it is an integral component of the sensor system that regulators will consider during product review [55]. Further, as portable sensors make home testing kits more common, companies should design their sensors to minimize the chances that consumers will misinterpret the sensor readings.

Venture capitalists generally can be reluctant to invest in projects that have relatively long development timelines and inconsistent returns. For example, venture capital accounts for less than 5% of nanotechnology funding [56]. Workshop participants suggested that the scarcity of venture funds also extends to the development of nanosensors. Yet, there is still a need for financial support throughout the sensor development cycle. As such, small businesses may need to consider alternative finance strategies, such as matchmaking services, crowdfunding, and strategic partners.

5. Identifying Next Steps for Accelerating Nanosensor Development in the United States

Sensor developers and the Federal Government can take a range of actions to address the standards, validation, manufacturing, and commercialization challenges that were identified at the workshop and summarized in Chapter 4. The sections below describe specific approaches discussed at the workshop for each type of challenge, as well as several cross-cutting themes and best practices that can be applied across the development cycle: leveraging resources, proactive planning, and timely and ongoing communication.

Standards

The Federal Government plays an important role in the development and use of standards. At times this role includes direct contributions to standards development, while in some specific instances it is appropriate for the Government to convene relevant groups and facilitate key conversations. In the United States, standards and specification setting is led by industry, is responsive to market needs, and drives technology development and innovation. For example, if industry stakeholders agree to use a similar methodology, groups could share equipment and tool time during early, low-volume production runs. Industry participation in standards setting is especially important to ensure that the resulting standards are balanced and enable trade and competitiveness.

An overarching organizational framework for standards would be valuable to many stakeholders, particularly those who are not directly involved in the standards development process but who are impacted by the final published documents [57]. Ideally, such a framework would include broad overview standards based on intended use and more detailed specific subparts. The International Organization for Standardization's 10993 document for biological evaluation of medical devices [58] is an example of such a broad framework. To further clarify the standards landscape, relevant standards information has been added to the Sensors NSI portal based on discussions at this workshop [59, 60].

Testing

As outlined in Chapter 4, limited access to testbeds is a key challenge for sensor developers. Given the scarcity of test facilities, the National Nanotechnology Coordination Office (NNCO) has added a list of available user facilities to the Sensors NSI portal, under testing and commercialization support for sensor development [61]. The updated web portal also includes information on standard reference materials that could be used in performance tests. Public and private resources should be leveraged, shared when appropriate, and expanded to increase availability of and access to critical test facilities.

The development and distribution of reference test kits may present a cost-effective, complementary alternative to the construction of new testing facilities. Ideally, these kits could be used to economically and reliably test sensors at users' home institutions or in the field to replicate the sensors' intended operating conditions. In addition, reference test kits could provide a method for sensor developers to compare the performance of their new sensor candidates to current sensors under similar test conditions.

Manufacturing

Several potential approaches identified at the workshop could be applied to increase the availability of and access to fabrication facilities, which is one of the most pressing sensor manufacturing challenges, as described in Chapter 4. To increase the number of available foundries, small companies could help guide the needs for shared fabrication facilities, including manufacturing batch volumes and duration cycles. To improve awareness of the facilities that are currently available, the NNCO, in collaboration with member agencies of the Sensors NSI, has included a list of federally supported foundries for nanomaterials and devices on the Sensors NSI portal facilities page [62]. Further, Federal agencies can promote innovations in manufacturing technologies through the use of precompetitive prizes and challenges. Sensor developers also should plan proactively for the manufacture of their products. This planning should occur as early as possible in the development phase.

Commercialization

Participants suggested events to promote matchmaking between potential partners or between businesses and potential customers. This matchmaking could be accomplished by encouraging relevant associations and societies to hold partnering sessions at existing conferences or by the Sensors NSI agencies organizing matchmaking events, which is in line with recommendations from the President's Council of Advisors on Science and Technology in 2014 [63]. The NNCO and agencies participating in the Sensors NSI could also curate and share a collection of best practices in commercialization. This collection could include case studies and lessons learned from companies that have successfully traversed the "valley of death" (between development and successful commercialization) to bring their products to market. Further, the portfolio of best practices could include successful approaches used by university technology transfer offices.

One particularly effective practice that businesses can employ is proactive planning for commercialization and regulatory approval. Early market analysis can guide the development process because the sensors can be designed, for example, for specific working conditions or performance parameters. Additionally, sensor developers should determine why their products would be attractive to potential customers as early as possible—ideally during the mission evaluation stage. An innovative technical design is not sufficient for successful commercialization; the final product must create tangible value for the customer.

Early communication between regulators and businesses could facilitate better awareness of the regulatory approval process. In this case, sensor developers would get timely access to information on requirements they will have to meet, such as required tolerances or acceptable deviations. Businesses should approach regulators early in the development process, and regulatory agencies should also improve their outreach, engagement, and education strategies to clarify regulatory approval requirements and processes. For example, as described in Chapter 4, some companies are seeking clarity on which agencies have jurisdiction over their products. In response to feedback at the workshop, information has been added to the Sensor NSI portal to summarize regulatory resources for sensing nanomaterials [64, 65].

Cross-Cutting Approaches

Three cross-cutting best practices emerged from the workshop discussions: leveraging resources, proactive planning, and enhanced communication. In resource-constrained environments, it is critical for businesses and the Federal Government to leverage resources and build critical facilities, such as

testbeds and pilot-scale foundries, that multiple users can access. Proactive planning includes considerations of manufacturing and regulatory requirements, as well as market potential, early in the development process. Enhanced communication includes improved engagement among researchers, developers, manufacturers, customers, and the Federal Government. In response to discussions at the workshop, the Sensors NSI portal [1] was created to share information on the sensors development landscape, including funding opportunities, available facilities, regulatory guidance documents, and published standards. Future collaborative efforts, such as this workshop, will be the key to meeting agencies' sensing needs and more efficiently ushering nanosensing products to market.

Appendix A. Collaborating Agencies Participating in the Sensors NSI³

Collaborating Agency

Description

Consumer Product Safety Commission (CPSC)



CPSC staff support the responsible research and development of nanotechnology for implementation in innovative rapid sensing and monitoring devices to improve safety for consumers. The development of novel sensitive, discriminative, and low-cost nanosensors for use in consumer products to detect pre-hazardous conditions and to provide warning or enable preventive action can reduce the likelihood of deaths and injuries. CPSC staff will provide support to the NSET Subcommittee on currently available tools, standards, and approaches to assess the safety, efficacy, quality, and performance of products under CPSC's jurisdiction.

Defense Threat Reduction Agency (DTRA)



DTRA supports the discovery and development of analytical methods and enabling nanomaterials for rapid and sensitive detection and identification of chemical and biological threats and of new materials to enhance protection against such threats. DTRA also supports the discovery of diagnostic methods for identifying biomarkers indicative of exposure or infection by biological agents, and new approaches in sensor data analysis and algorithms for threat detection.

Environmental Protection Agency (EPA)



The National Center for Environmental Research (NCER) at the EPA has supported research in the development of innovative and rapid sensing and monitoring devices. These devices enable accurate assessment of the environment as well as identification and quantification of environmental contaminants. The research was accomplished through the Science to Achieve Results (STAR) grants program. Additionally, the EPA used the Small Business Innovation Research program as the means by which promising technologies, such as sensors, were solicited and funded.

Food and Drug Administration (FDA)



FDA supports the responsible development of nanotechnology, including products relevant to nanosensors. FDA will provide guidance on currently available tools, standards, and approaches, as appropriate, to assess the safety, efficacy, quality, and performance of FDA-regulated products that may incorporate nanomaterials or otherwise involve the application of nanotechnology.

National Aeronautics and Space Administration (NASA)



NASA currently develops nanosensors that are highly sensitive and miniaturized, and that have low power consumption, for detection of chemical and biological species. Applications for these sensors include incorporation into lab-on-a-chip technologies for crew health monitoring, water quality monitoring in the International Space Station, and detection of biomarkers in planetary exploration. NASA also develops nanotechnology-based chemical sensors for a variety of gases and vapors encountered in planetary exploration, Earth monitoring, and aircraft and spacecraft vehicle safety. NASA is also working on the development of nanosensors to measure mechanical strain and detect the early onset of damage in structural materials for use in structural health monitoring for aircraft and spacecraft. The technology and test bed platforms are generic to leverage for biomedical and security applications.

³ Please note that "collaborating agencies" is meant in the broadest sense and does not necessarily imply that agencies provide additional funds or incur obligation to do so. Agencies are listed in alphabetical order.

National Institutes of Health (NIH)



National Institutes of Health

NIH supports nanosensor R&D programs in biomarker discovery and validation, platform development for multiplexed biomarker detection (including microfluidics platforms, proteomic devices, and surface-enhanced Raman spectroscopy instrumentation), multi-analyte arrays for exposure monitoring (both point-of-contact and biomonitoring), molecular probes, DNA sequencing and bioinformatics, and characterization of nanoparticles *in vivo*.

National Institute for Occupational Safety and Health (NIOSH)



The NIOSH Nanotechnology Research Center (NTRC) has designated applications of nanotechnology for occupational safety and health as one of the 10 critical areas in its organized program of research to identify, investigate, and develop science-based solutions to workplace health and safety knowledge gaps. Through activities such as its Manual of Analytical Methods, NIOSH supports development of guidelines and voluntary consensus standards for identification of sensor needs and objectives; methods development, testing, and certification; user training, documentation, and improvement; sensor acceptance, calibration, and reliability checks; evaluation of operational experience; and periodic performance testing, including realistic applications in complex workplace situations. NIOSH also partners and conducts sensor-related work through the NIOSH Center for Direct Reading and Sensor Technologies.

National Institute of Standards and Technology (NIST)



The NIST laboratories are developing a variety of measurement methods to characterize nanosensors and nanomaterials and are creating nanosensors and nanomaterials for measurement applications and standards. Nanoscale reference materials developed at NIST support the validation of new sensing platforms. The NIST Center for Nanoscale Science and Technology user facility provides access to the tools and processes needed to accelerate the commercialization of nanosensor systems. Research addressing information quality, integrity, and usability will contribute to the reliability and security of sensor networks and data analysis. NIST's complementary nanoEHS programs and projects support the safe manufacture, use, and disposal of engineered nanomaterials and nanotechnology-enabled products.

National Science Foundation (NSF)



Through its Biosensing, Biophotonics, and other programs, NSF supports development of novel sensitive, discriminative, low-cost, and easy-to-operate biosensing systems; innovative ideas in the development of novel biorecognition strategies; multifunctional nanomaterials and interfaces with predefined physical, chemical, or biological characteristics for biosensing applications; and fundamental study of biomacromolecules confinement and orientation at the micro- and nanoscale interfaces for biosensing applications. NSF also supports the development of sensors to detect engineered nanoparticles in a variety of environmental matrices.

National Institute for Food and Agriculture (NIFA, part of the United States Department of Agriculture)



NIFA's activities in nanotechnology for biosensors support its mission, strategic goals, and high priorities and apply broadly to plant and animal production systems, food quality and safety, nutrition and health, the environment, and nano-biomaterials. The primary thrusts are in the following areas: (1) develop novel technologies for characterizing fundamental nanoscale bioprocesses; (2) construct and characterize self-assembled nanostructures; (3) develop nanoscale devices and systems incorporating micro-fabrication and nanotechnology; (4) develop a framework for economic, environmental, and health risk assessment for nanotechnologies applied to food, agriculture, and biological systems; and (5) produce education and outreach materials on nanofabrication, sensing, systems integration, and application risk assessment.

Appendix B. Meeting Materials

Meeting Agenda⁴

Day 1

- 8:46 ***September 11th: Moment of Silence Observed***
- 9:00 [Welcome Remarks](#)
[Lloyd Whitman](#) –NNCO
- 9:15 [Overview of the Sensors NSI, Purpose of Workshop](#)
[Lisa Friedersdorf](#) –NNCO
- 9:30 [Keynote presentation –Case Study on Commercialization Success](#)
[Ernest Streicher](#) –John Deere
- 10:45 Keynote presentation –Navigating from Lab to Market
[Sydney Ulvick](#) –In-Q-Tel
- 11:30 [Keynote presentation –Navigating the Regulatory Process](#)
[Kevin Lorick](#) –FDA/CDRH
- 13:30 Keynote presentation –Navigating the Regulatory Process
[Ronald Williams](#) –EPA
- 14:00 Small Business Panel: Nanotechnology for Sensors and Sensors for Nanotechnology:
Challenges Faced in the Commercialization of Sensors
[Abhishek Motayed](#) –N5Sensors ([Presentation](#))
[Ray Chen](#) –Omega Optics ([Presentation](#))
[Steve Gibbons](#) –Brewer Science, Corp. ([Presentation](#))
[Omowunmi Sadik](#) –Binghamton University ([Presentation](#))
- 16:00 [Summary of Request for Information](#)
[Dorothy Farrell](#) –NIH/NCI
- 16:30 Recap and Preview of Day 2
Lisa Friedersdorf –NNCO
- 16:45 Poster Session and Networking

⁴ NOTE: The original full agenda, including times for coffee and lunch breaks, as well as links to presentation slides, biographies, and abstracts, may be found at the NNI workshop webpage, www.nano.gov/2014SensorsWorkshop. This agenda version notes substantive activities only. The links are to speaker biographies and to presentations.

Day 2

- 8:30 Opening Remarks –Charge to Participants
Dorothy Farrell –NIH/NCI
- 8:45 Federal Panel –Programs and Resources to Support Sensor Research and Development:
[Eddie Chang](#) –NSF ([Presentation](#))
[Hongda Chen](#) –NIFA ([Presentation](#))
[Dorothy Farrell](#) –NCI
[Mark Hoover](#) –NIOSH ([Presentation](#))
[Kim Sapsford](#) –FDA
[Steve Semancik](#) –NIST ([Presentation](#))
[Paul Shapiro](#) –EPA
[Trey Thomas](#) –CPSC ([Presentation](#))
- 10:30 Breakout Session I: Standards and Testing
- 13:00 Breakout Session II: Manufacturing and Commercialization
- 14:30 Breakout Session Reports
Mark Hoover –NIOSH
- 15:45 Identification of Key Challenges –Next Steps
Dorothy Farrell –NIH/NCI
Lisa Friedersdorf –NNCO
- 17:15 Summary and Closing Comments
Trey Thomas –CPSC

Breakout Session Topics and Discussion Points

Breakout I: Standards

- What existing standards have helped in measuring sensor performance in meeting desired specifications?
- What standards need to be developed (for performance or manufacturing) to meet industry/consumer expectations for emerging sensor technologies?
- What have you done so far to overcome challenges related to the absence of standards for certain stages of sensors development?

Breakout I: Testing

- What facilities for testbeds have you used to develop nanosensors?
- What additional testing facilities would aid the sensor development community in improving sensor performance or manufacturability?
- What sample types have you utilized to develop convincing demonstrations of sensor performance, and how were these samples obtained?

- What have you done so far to overcome challenges related to unavailability of testbed facilities or test samples?

Breakout II: Manufacturing

- Are there unique challenges in manufacturing nanosensors, and if so, how can they be successfully addressed?
- What are the main technical issues in scaling-up the manufacture of sensors, and how can they be addressed?
- Are there any unique workforce issues, and if so, how can they be addressed?
- What new integration, engineering, and manufacturing tools are needed to facilitate the engineering and manufacture of sensors? Do these tools already exist, and are they properly deployed in nanosensor engineering and manufacturing?
- What lessons have been learned that would be useful to pass on to those who contemplate manufacturing nanosensors?

Breakout II: Commercialization

- What are the primary challenges faced for nanosensor commercialization when trying to traverse the “valley of death,” and how can they best be addressed?
- How best can various public and private sector funding sources be identified and used at the various stages of sensor development and commercialization? Are there sources that are currently underutilized?
- How can market potential (e.g., size of market, competition) best be assessed at early stages in the development and commercialization process?
- What, if any, regulatory challenges exist to nanosensor development? How can regulatory challenges for commercializing sensors be addressed?
- What lessons have been learned that would be useful to pass on to those who contemplate developing and commercializing sensors?
- What are the greatest needs and opportunities for developing nanosensors now and in the future?

Appendix C. Workshop Participants⁵

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Appendix D. List of Acronyms

| | |
|-------------|--|
| CDRH | Center for Devices and Radiological Health (FDA) |
| CFR | Code of Federal Regulations |
| CPSC | Consumer Product Safety Commission |
| EPA | U.S. Environmental Protection Agency |
| FDA | Food and Drug Administration |
| IDE | investigational device exemption |
| IQT | In-Q-Tel (not-for-profit intelligence-related technology investment organization) |
| IVD | <i>in vitro</i> diagnostic device |
| NAAQS | National Ambient Air Quality Standards |
| NATTS | National Air Toxics Trends Stations |
| NCI | National Cancer Institute (NIH) |
| NCL | Nanotechnology Characterization Lab (NIH) |
| NIFA | National Institute for Food and Agriculture (USDA) |
| NIOSH | National Institute for Occupational Safety and Health (U.S. Centers for Disease Control and Prevention) |
| NNCO | National Nanotechnology Coordinating Office of the NNI |
| NNI | National Nanotechnology Initiative |
| NSET | Nanoscale Science, Engineering, and Technology Subcommittee of the National Science and Technology Council's Committee on Technology |
| NSF | National Science Foundation |
| NSI | Nanotechnology Signature Initiative of the National Nanotechnology Initiative |
| PMA | Premarket Approval |
| RFI | request for information |
| Sensors NSI | Nanotechnology Signature Initiative <i>Nanotechnology for Sensors and Sensors for Nanotechnology: Improving and Protecting Health, Safety, and the Environment</i> |
| SUNY | State University of New York |
| U-PAC™ | Ultrasensitive portable capillary sensor (Binghamton University, SUNY) |
| USDA | U.S. Department of Agriculture |

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