Measurement Challenges to Innovation in the Biosciences: Critical Roles for NIST

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Contents

Unique Role of NIST in the Biosciences

It is congruent with NIST's mission to support U.S. industry and other stakeholders in overcoming measurement- and standards-related challenges in the biosciences by:

- **Leveraging** NIST's vast multidisciplinary expertise in the quantitative physical, chemical, and information sciences
- **Providing** the measurement infrastructure that produces confidence in the results from measurements of complex biological systems
- **Thus, enabling**—as well as facilitating optimal economic and societal benefits from—new innovations.

Measurement Challenges to Innovation in the Biosciences: Critical Roles for NIST

Advancing the measurement and computational sciences of biological systems will be a decisive factor in fulfilling the promise of the biosciences to greatly enhance our economic security and quality of life. Biological systems are the foundation of all life on earth. The science of understanding how these systems operate and interact with one another (the biosciences) is increasingly important. As our population grows, we will need more efficient and sustainable ways to grow food, keep people healthy, produce energy, and manufacture biological drugs, therapeutics, and chemicals. These advances can only be realized by gaining a deeper understanding of how biological systems operate.

Major achievements in the biosciences over the last decade have built expectations for further major advances. Increased investment and growth have expanded the scope and complexity of the biosciences enterprise as well as the potential benefits that may be achieved. Just a few of the many possible advances that may be realized are personalized medicine; sustainable energy from biological sources; higher quality products through better bioprocess measurements; increased yield, quality, and safety of the world's food and water supply; and a clean and stable environment.

Biosciences Applications

This strategy considers:

- Healthcare
- Biomanufacturing
- Bioenergy
- Environment
- Food/Agriculture
- Homeland Security/Forensics

Despite major breakthroughs and discoveries in recent years, understanding of biological systems still faces many challenges. Biology is an informational science that depends on accurate measurements and standards. Whether quantifying the amount of protein in a cancer cell or how well an organism converts sugar to alcohol, measurements are the foundation for improving our understanding of biological systems. Future progress depends on our ability to measure key features—including the complex interplay of thousands of biochemicals that control living systems.

A Strategic Approach for the Biosciences

NIST takes a strategic approach to understanding and effectively addressing the measurement and standards barriers that pose the highest risk to economic security and quality of life in the U.S. In the burgeoning area of the biosciences, NIST proactively gathered information via recent workshops and many other interactions. These efforts revealed that, despite current NIST activities in the area of bioscience and health, there is strong stakeholder concern that numerous measurement, standards, and technology barriers are not being addressed.

Throughout its history, NIST has worked closely with industry to support innovation by addressing the relevant measurement and science needs of new technologies. Examples include work in food safety and nutrition, laboratory medicine, DNA forensics, metrology for gene expression, standards for the "-omics" (genomics, proteomics, etc.), and medical imaging. These and other NIST efforts address some of the biological measurement challenges holding back further advances in the biosciences.

NIST's role in providing measurement science and standards for the biosciences has developed along with advances in this critical field. Growth in the scope of NIST's highly regarded programs in healthcare is well-documented in the NIST Three-Year Plan.[1] NIST also has expanded in recent years into other bioscience and technology areas, such as energy, homeland security/forensics, manufacturing, materials, and more. To date, this expansion has occurred as needs are identified, rather than through a coordinated approach. Development of a NIST biosciences strategy is an important step to providing guidance for strategic decision-making and funding allocations, as well as coordinating research and measurement services programs at NIST. To meet this pressing need, a top-level, NIST-wide effort was initiated in 2007 to gather input from external sources, resulting in this initial scope, strategy, and direction for NIST programs in the biosciences.

Vision

A coordinated state-of-the-art measurement science, technology, and standards infrastructure with the capability to anticipate and meet emerging needs in the biosciences and address the challenges to technological innovation.

Vision for NIST's Role in the Biosciences

The stakeholders' message is clear: as bioscience technology continues to be a major driver for our economic growth and improved quality of life, the need for NIST to provide effective measurement and standards support for this field becomes increasingly critical.

NIST has created a vision to meet this need for the biosciences. In support of this vision, NIST's role for the biosciences is to:

"ensure confidence in the results of the measurement of complex biological systems and support technological innovation in the biosciences across diverse economic sectors."

These statements reflect NIST's overall mission, which is to promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life.

Drivers for NIST Bioscience Programs

Economic Impact

Biotechnology is a major driver of future U.S. economic growth with significant impact in multiple economic sectors, including healthcare, energy, agriculture, security, and manufacturing. Built around the recombinant DNA technologies discovered in the 1970s, the biotechnology sector in the U.S. has exploded. Today there are over 1,400 biotechnology companies, of which more than 300 are publicly traded and have a combined market capitalization value of $410 billion dollars. In addition, all major pharmaceutical companies, who have traditionally developed small-molecule drugs, are increasingly focusing major resources on developing biotechnology-based large-protein therapeutics.

Societal Benefits

Advances in the biosciences have been critical to improving human health, safety, and quality of life. The new technologies and improvements made possible by advances in the biosciences are found in nearly every aspect of modern life. Based upon advances in recombinant DNA technology alone, the biotechnology and pharmaceutical sectors have developed hundreds of new therapies and medical diagnostic tests, as well as advanced food crops and less hazardous industrial processes. Exhibit 1 illustrates some of the future promise of the biosciences—if today's measurement challenges can be overcome.

Leadership in Science and Technology Innovation

Converging advances in biotechnology, biosciences, and biomolecule sensors (e.g., gene expression microarrays) have positioned biological measurement sciences as a critical driver of future innovation in multiple U.S. industry sectors. These advances have been fueled by sustained Federal investment in the biosciences as well as other technology areas, such as computing. Federal investment in the life sciences was about $28 billion in 2007.[2]

The intersection of technology and biology has transformed fundamental knowledge and our ability to manipulate the basic building blocks of life. Tremendous amounts of new information are being generated, such as the recent sequencing of multiple human, animal, and plant genomes. Advances in genomics and proteomics have created entirely new fields of study, such as systems biology and comparative genomics. Once fully realized, these will allow scientists to look at the interaction of thousands of biological molecules rather than a single molecule or pathway. Advances in imaging and data analysis software have given doctors powerful new tools in the fight against disease. These and other new fields of study have the potential to dramatically increase the positive impact of the biosciences on society today and in the future.

Government Role and Guidance

Calls to support further innovation in the biotechnology industry have come from multiple sources. The Administration, through its annual Office of Science and Technology Policy/ Office of Management and Budget (OSTP/OMB) Budget Priorities Memorandum,[3] has stated the need for research to increase understanding of complex biological systems, including a call for the development of improved measurement tools.

Exhibit 1. Some Potential Benefits from New Innovations in the Biosciences[4]

Healthcare • Personalized medicine with the ability to predict, diagnose, and monitor the onset of diseases (disease signatures) in time to prevent their most deleterious effects, and the ability to accurately treat patients with greater knowledge of which drugs will work the best and not cause dangerous side effects • More efficient development of safe and effective drugs based on computational tools for more accurate prediction of their molecular pathology on drug targets, and assays to better evaluate the effectiveness of drug candidates
Food and Agriculture • Better nutritional quality and more abundant food through improved crop yield, elimination of harmful allergens, better detection of germs and toxins, improved animal health, and increased use of green chemicals for maintaining agriculture and aquaculture systems
Energy • Sustainable energy from non-petroleum sources through engineering living systems to produce combustible fuels and intermediates and improve the efficiency of converting existing biofuel precursor sources into usable fuels
Environment • Microbe- and plant-based products to clean up hazardous waste • More extensive monitoring of our environment for the effects of pollutants and the emergence of naturally arising biological threats that are the products of overpopulation
Manufacturing • Enzyme replacements for hazardous chemicals and inefficient processes in such industrial sectors as chemicals, pulp and paper, textiles, food, energy, and metals and minerals • More efficient ways to manipulate living systems to manufacture products using approaches that improve or replace chemical synthesis with methods that are more environmentally friendly

The FDA's Critical Path Initiative[5] and subsequent Critical Path Opportunities List[6] specifically call out the need for enhanced evaluation tools to support the development of drugs, diagnostics, and other innovations in healthcare.

The NIST external advisory board, the Visiting Committee on Advanced Technology (VCAT), has also recognized the economic importance of biotechnology and the role that NIST could play.

Federal Guidance

OSTP/OMB Budget Priorities Memo

"Agencies should target research on a deeper understanding of complex biological systems through multi-disciplinary collaborations aimed at developing new and improved measurement and management tools to provide valid data that can be compared across laboratories and platforms."

NIST Visiting Committee on Advanced Technology

"Technology advances in this area could be dramatically improved by implementing focused standards and measurement science programs at NIST which will have immediate impact on the quality of life of U.S. citizenry."

As a result, NIST has made support of the biosciences a top strategic priority and, accordingly, has expanded its efforts to improve the measurement science infrastructure and standards.

Challenges to Innovation in the Biosciences

Currently, the limited availability of adequate biomolecular measurement technologies constitutes a roadblock to achieving the promises of bioscience innovation, such as personalized/preventative medicine, safer therapeutics, sustainable energy resources, and disease-free foods. Revolutionary biomolecular measurement technologies will be needed to understand the complex biological networks that are the key to our future survival.

Despite advances in bioscience, two important factors continue to inhibit progress. First, while the intersection of scientific disciplines is often associated with innovation, the coordination of research across a number of disparate fields and scientific disciplines is inherently difficult. Few institutions have the necessary breadth of expertise in the physical, life, and computer sciences to effectively address the critical challenges that impede a transformational application of the biosciences. Second, there is growing recognition that without concurrent advances in biological measurement technology and standards development, it will be impossible to fully capitalize on the nation's investment in the life sciences.

Current bioscience measurement capabilities are inadequate for dealing with complex biological systems. For example, although it is understood that dynamic changes in the expression and activity of proteins are at the root of most diseases, the capability to accurately measure and visualize the dynamic interactions of thousands of proteins involved in "disease signatures" is lacking. Even in areas where measurement science is more robust, such as medical imaging, the lack of a well-defined measurement and standards infrastructure dramatically limits our ability to achieve the maximum benefit of these technologies.

NIST is uniquely positioned to address these challenges. NIST will leverage its expertise in the physical, chemical and information sciences to maintain the U.S. national references (methods, materials, and data) and calibration capabilities for providing confidence in the results from measurements of complex biological systems. This will enable and facilitate realization of optimal economic and societal benefits from new innovations in the biosciences. As a trusted third party, NIST has the capability to work collaboratively with industry and with regulatory agencies such as the FDA.

Assessing Measurement and Standards Needs

NIST systematically performs outreach to the scientific community to ascertain measurement needs and barriers to meeting those needs, and to work together in developing solutions to overcome the barriers and meet the needs. Major components of this ongoing effort are:

- Outreach to individual stakeholder communities – NIST seeks out measurement problems through meetings with individual stakeholders from industry, academia, nonprofit research institutes, and other government agencies. These meetings involve formal visits between stakeholders and NIST management and scientists.
- The United States Measurement System (USMS) Initiative – NIST has teamed with other organizations to assess the capacity of the nation's scientific and technical measurement infrastructure—the U.S. Measurement System. The result is an inventory of measurement needs in key economic sectors.
- Stakeholder workshops – NIST hosts and participates in numerous stakeholder workshops to gain insights on measurement needs. These have included participants from industry, industry associations, government agencies, standards organizations, academia, national laboratories, and private institutes involved in the biosciences.

The most recent assessment of measurement needs and barriers in the biosciences culminated in the 2008 Conference on Accelerating Innovation in 21st Century Biosciences: Identifying the Measurement, Standards, and Technological Challenges.[4] This international conference, held at NIST, brought together biosciences experts from industry, academia, and government to ascertain mission-critical measurement barriers impeding innovation in five critical application areas dependent upon the biosciences and biotechnology: medicine, bioenergy, agriculture, biomanufacturing, and environment.

Current and Historic NIST Role in the Biosciences

Founded in 1901, the National Bureau of Standards was authorized by statute to undertake the "custody, maintenance, and development of the national standards of measurement and the provision of means and methods for making measurements consistent with these standards." In 1988, its name was changed to the National Institute of Standards and Technology (NIST) and the U.S. Congress assigned NIST the additional role of assisting "industry in the development of technology … needed to improve product quality, to modernize manufacturing processes, to ensure product reliability … and to facilitate rapid commercialization … of products based on new scientific discoveries."

Exhibit 2 illustrates the role of NIST over the last century in addressing the challenges important to society, highlighting a long history of support for dentistry, medical imaging, and laboratory medicine. Now and into the foreseeable future, bioscience-related innovations certainly will have an increasing impact in the fields of energy, national security, the environment, manufacturing, nanotechnology, food and nutrition, and healthcare—and perhaps other areas. The impact of these innovations cannot be fully realized unless cutting-edge measurement science and the ability to generate relevant standards keep pace with the field.

It is fully congruent with the NIST mission to support U.S. industry and other stakeholders in overcoming measurement and standards-related challenges in the biosciences. While NIST traditionally has focused on the physical science and engineering disciplines, a strategic decision has been made to place more emphasis on the biosciences.

Exhibit 2. NIST Role in Medicine

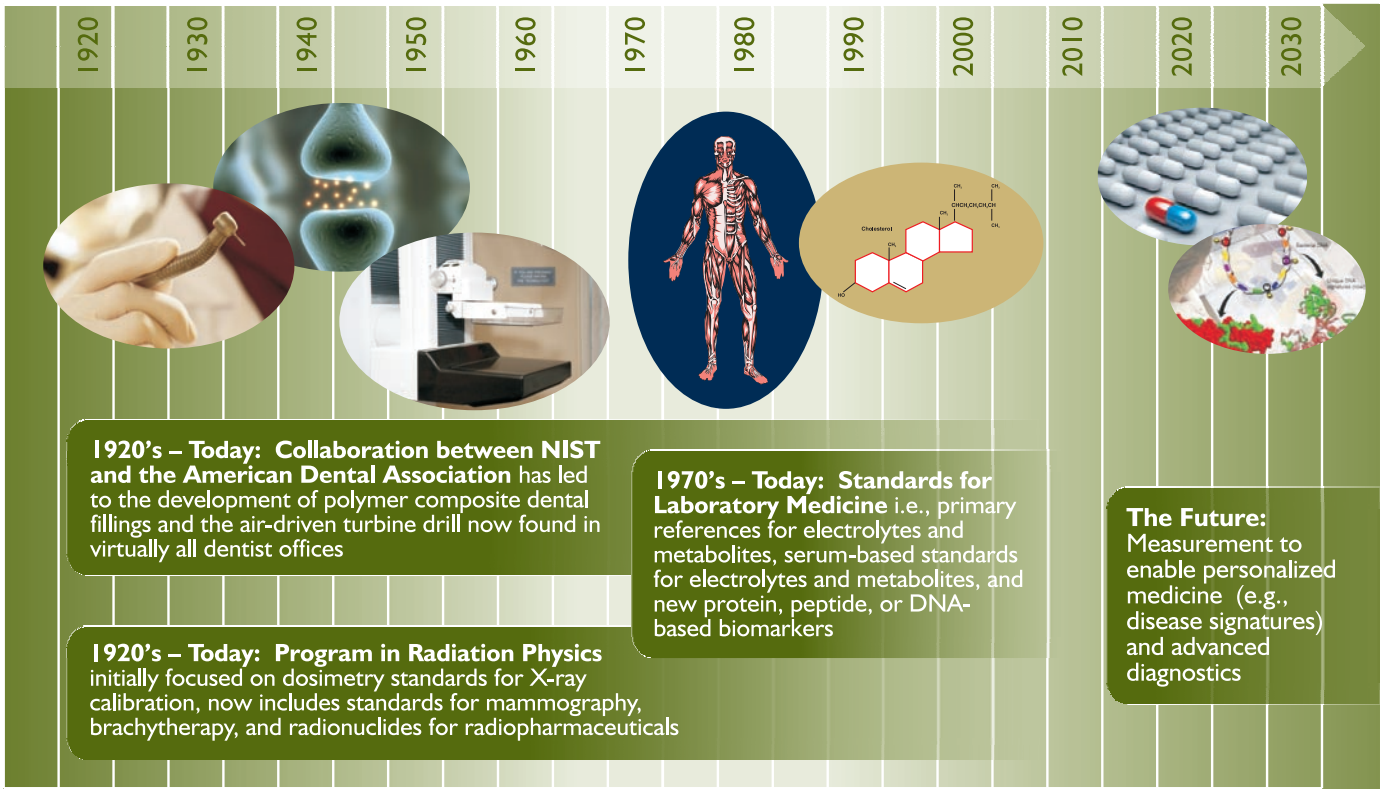

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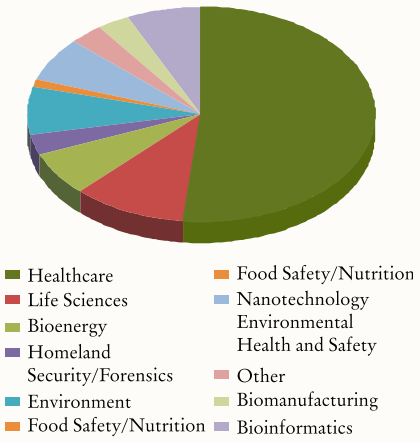
Exhibit 3. NIST Biosciences Appropriated Funds 2008

*Approximately $40 Million Dollars**



* Of this, less than $10 million was appropriated specifically for bio-related activities

NIST will leverage its vast multidisciplinary expertise in the quantitative physical, chemical, and informational sciences to:

- establish the measurement infrastructure needed to build confidence in the results from measurements of complex biological systems and
- enable increased innovation to improve the environment and health of our citizens and positively impact the U.S. economy.

Today, bioscience activities are carried out across the NIST laboratories with approximately $40 million of Congressionally appropriated funds, about $16 million from other government agencies, and an additional $2 million from other sources. When funds from all sources are combined, the total biosciences investment at NIST is about $58 million. Exhibit 3 illustrates the current approximate distribution of appropriated funds for this work throughout NIST laboratories and divisions. Less than $10 million of these funds were appropriated specifically for bioscience-related activities. The remaining allocations are the result of decisions made within individual NIST laboratories to reprogram resources from other areas to address growing challenges in the biosciences.

Healthcare, one of NIST's investment priorities, accounts for more than half of the appropriated funds. Diagnostics, long an area of NIST services, receives the majority of the funds in this area. Likewise, there are established programs in food safety and nutrition, life sciences, and environmental protection. Homeland security and bioenergy are categories that have been more recently funded in response to critical emerging needs. Other funds are spent for the provision of essential calibrations needed to ensure the accuracy of medical instruments or equipment.

Identification of Priority Measurement Needs for the Biosciences

NIST is taking a risk-based approach—identifying measurement needs from stakeholders in industry, government, and academia; looking for areas of potential overlap; and evaluating potential impact—in order to formulate plans for potential programs that would best address the challenges in industries and fields that are focused on biological processes or reliant upon biotechnology.

Overarching needs for bioscience-focused measurements identified from multiple stakeholder outreach efforts are highlighted in Exhibit 4.

Exhibit 4. Overarching Needs for Measurement in the Biosciences

- Better methodologies and practices for sample handling
- More robust protein measurements
- High-throughput multiplexed measurements
- Improved tools and standards for bioinformatics (e.g., data collection, analysis, modeling, archiving, etc.)
- Improved tools and methods to ensure confidence in data and enable comparability across multiple platforms (e.g., medical imaging, clinical assays, environmental sensors, etc.)

Critical Bioscience Sector Measurement Needs

NIST is evaluating needs in the sectors below to prioritize efforts to develop the necessary measurement infrastructure—measurement science, standards, and technology—to support innovation.

Healthcare – The rising cost of U.S. healthcare is a clear and present risk. NIST will support the industrial development and commercialization of tools to enable discovery and routine determination of disease signatures to enable a shift in the healthcare economy from a paradigm of diagnosis and treatment of later-stage diseases to one of prediction, prevention, and intervention of disease at its earliest stages. These capabilities would reduce hospitalizations (43% of healthcare spending) and usher in an age of interventional therapeutics.

Current targets are advanced multiplex measurement technologies and advanced biocomputing, two areas where the creation of new technologies, new measurement science techniques, and standards will benefit multiple fields. A priority is the ability to measure, in cells and blood, thousands of nucleic acids, proteins, and metabolites that comprise disease signatures, the sentinels of health and disease and a necessity for the advent of personalized medicine.

Bioenergy – Our continued reliance on foreign oil is a substantiated risk. NIST will support the development and commercialization of sustainable biofuel resources from multiple biological sources—including plants, algae, and microbes. Specific measurement needs include the ability to measure and predict the amount of energy produced by an artificial system genetically engineered to produce biofuels and the potential impacts on the environment. This would help move the U.S. toward energy independence and contribute to stabilization of energy costs—a major driver of the U.S. economy.

Environment – Technological advances in commerce, healthcare, agriculture, and energy production in the 21st century have the potential to adversely affect human well-being, including public health, economic sustainability, and the resilience of communities and cultures. "New" pollutants (e.g., prescription drugs and metabolites, new generation pesticides, and flame retardants) could impair natural processes and degrade environmental quality. NIST will support development of critical early warning systems to assess the status and trends of the environment and identify potential threats before irreparable harm ensues. NIST will also support technological advances to distinguish natural environmental changes from those that are caused by human activities, and will support the development and commercialization of systems to mitigate these risks.

Biomanufacturing – Low-cost and environmentally-friendly manufacturing systems are needed to enable the continued availability of all types of diverse and innovative goods and services to meet the needs of our expanding population and help grow our economy. Biological systems are a major resource that can be tapped to fill this need.

NIST will support the development of biological systems to enable clean, efficient, and less expensive manufacturing in all sectors. A major focus will be improved characterization and manufacturing of follow-on biologic drugs to support the establishment and growth of this new industrial sector that is vital to reducing the cost of healthcare.

Homeland Security – The availability of a safe food and water supply is critical to all people, as is protection against attacks of bioterrorism on American soil and around the world. Emerging infectious diseases and treatment-resistant bacteria (e.g., MRSA[7]) and viruses are major risks. NIST will support the industrial development and commercialization of tools to monitor the emergence and mitigate the risk of natural and man-made biological agents and work to establish metrics for evaluation of the overall risks to society.

Crosscutting Technology – NIST is also planning to expand efforts to develop the crosscutting computational and informatics tools relevant to the biosciences. Other crosscutting efforts include optimized sampling methods, biomarkers, and standards for biological systems.

The Path Forward

To move toward fulfilling its role in addressing the measurement challenges to innovation in the biosciences, NIST will, in the context of its overall strategic plan and associated investment priorities, undertake strategic actions to:

- Establish world-class biomeasurement capabilities:
  - — leverage current and establish new capabilities and facilities required to meet bioscience measurement challenges
- Optimize the impact of the biosciences portfolio:
  - — ensure that resources are focused on high-priority measurement needs and avoid duplication of effort

Exhibit 5. Address Measurement Challenges to Innovation in the Biosciences

- Establish strategic partnerships:
    - identify strategic partners for NIST to access resources, knowledge, and capabilities in order to leverage existing and future capabilities and help ensure that NIST remains focused on the most relevant bioscience issues
- Establish and maintain a process for evaluating the effectiveness and ongoing relevance of the NIST biosciences strategies and project portfolio:
    - consistently engage with external experts to establish and maintain a clear perspective on future bioscience trends and associated measurement challenges, so that NIST can be better positioned to address stakeholder needs with appropriate measurement infrastructure
    - meet with bioscience industry leaders and other Federal agency stakeholders for overarching discussions of the current NIST portfolio of activities and capabilities; the effectiveness of this portfolio in meeting needs; further identification, validation, and delineation of evolving measurement and standards issues that need to be addressed; and NIST's plan for biosciences program growth
- Establish an effective outreach program:
    - establish communication with measurement stakeholders in the biosciences, including both users and providers of measurement solutions (scientists, engineers, policy-makers, physicians, equipment vendors)

It is expected that NIST's bioscience strategies will need to continue to evolve over time as a reflection of changing measurement needs. This proposed path forward will enable NIST to periodically adjust its portfolio of activities and capabilities by identifying and understanding emerging measurement and standards issues that need to be addressed. This path will ensure that NIST is prepared to help the nation address the most important measurement barriers impeding new bioscience innovations and provide a high level of confidence in the measurements of complex biological systems.

Additional Resources

Additional information on the measurement challenges and priorities for select areas of the biosciences are provided in the biosciences conference report (endnote 4) and NIST's *Measurement, Standards and Technology Needs to Support Innovation in Healthcare*, May 2009.

Endnotes

1. *Three-Year Programmatic Plan for the National Institute of Standards and Technology*, U.S. Department of Commerce, Fiscal Years 2009-2011, http://www.nist.gov/director/reports/Final_NIST_3y.pdf
2. *National Science Board Science and Engineering Indicators 2008*, National Science Foundation, http://www.nsf.gov/statistics/seind08/
3. *Budget Priorities Memorandum FY 2009*. Office of Science and Technology (OSTP) and Office of Management and Budget (OMB). August 2007, http://www.ostp.gov/galleries/Budget09/FY2009FINALOMB-OSTPRDPriorityMemo.pdf
4. *Conference Report: Accelerating Innovation in 21st Century Biosciences: Identifying the Measurement, Standards and Technological Challenges*, March 2009
5. *Challenge and Opportunity on the Critical Path to New Medical Products*, 2004, Food and Drug Administration, http://www.fda.gov/oc/initiatives/criticalpath/whitepaper.pdf
6. *Critical Path Opportunities List*, 2006, Food and Drug Administration, http://www.fda.gov/oc/initiatives/criticalpath/reports/opp_list.pdf
7. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a very dangerous and life-threatening form of a common bacterium that has acquired the ability to resist killing with methicillin and other members of the penicillin antibiotic family.

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Front cover
Seedling – iStockPhoto
Blood cells, globe, plant, capsules – Microsoft Office Online

Exhibit 2
Dental drill, mammography machine, capsules – iStockPhotos
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Cholesterol molecule – National Institute of Standards and Technology
Leg bone scan, human form – Microsoft Office Online

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