MANUFACTURING:
Manufacturing and Biomanufacturing: Material Advances and Critical Processes

Technology Innovation Program
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The Technology Innovation Program (TIP) at the National Institute of Standards and Technology (NIST) was established for the purpose of assisting United States businesses and institutions of higher education or other organizations, such as national laboratories and non-profit research institutions, to support, promote, and accelerate innovation in the U.S. through high-risk, high-reward research in areas of critical national need.

TIP seeks to support accelerating high-risk, transformative research targeted to address key societal challenges. Funding selections will be merit-based and may be provided to industry (small- and medium-sized businesses), universities, and consortia. The primary mechanism for this support is cost-shared cooperative agreements awarded on the basis of merit competitions.

AN AREA OF CRITICAL NATIONAL NEED

The proposed topics within "*Manufacturing and Biomanufacturing: Material Advances and Critical Processes"* are part of the critical national need area of Manufacturing. These topics were selected from a larger set of challenges in manufacturing where transformative research could be expected to have large societal impact and include a societal challenge focusing on transformative process improvements to manufacturing. In addition, the critical national need area of Manufacturing includes aspects of biomanufacturing. Input regarding potential challenges in manufacturing was obtained from government agencies and advisory bodies (such as the National Research Council, the National Academy of Sciences, and the National Academy of Engineering), the Science and Technology Policy Institute (STPI), industry organizations, leading researchers from academic institutions, and others, as well as feedback from the public on the FY 2010 white papers prepared by TIP and additional input from external white papers submitted to TIP by the public.

The competitiveness of U.S. manufacturing is being challenged by other industrialized nations such as Japan, Germany, and Korea, as well as emerging economies such as China.[1] To remain competitive in the global marketplace, the United States must invest in innovation by funding research that will lead to new manufacturing technologies. These technologies include applications of novel materials and transformational changes in process engineering.

High-risk, high-reward research is necessary to achieve these innovations. However, company fiduciary responsibilities often limit the levels of risk in research that companies can undertake on their own, with acceptable risk levels varying by different manufacturing sectors. As a result, a critical need to support manufacturing is increasingly evident. TIP can be helpful by partnering with the small- and medium-sized businesses, institutions of higher learning, and others, providing cost-shared funding to make important investments that increase America's competitiveness through investments that the private sector does not reasonably have available to meet the need in a timely way.

The mission of TIP is to help facilitate high-risk, high-reward research that addresses the nation's areas of critical national need. In the manufacturing sector, there are three areas of research where support is vitally needed but is currently not reasonably available:

1) *Process scale-up, integration, and design for material advances*
2) *Predictive modeling for material advances and materials processing*
3) *Critical process advances related to the manufacturability of materials and the manufacture of both new and existing products*

Manufacturing innovations resulting from high-risk, high-reward research and development have the potential to:

Create significant improvements in new and existing products and in their manufacture by accelerating the utilization of material advances and overcoming critical manufacturing process bottlenecks to improve the competitiveness of U.S. manufacturers in the global marketplace.

This white paper, *Manufacturing and Biomanufacturing: Material Advances and Critical Processes,* examines selected challenges within the critical national need area of Manufacturing. These topics were selected from a larger set of challenges in manufacturing in which high-risk, high-reward research could be expected to have large societal impacts and benefits to the nation.

Materials performance is often a critical consideration and controlling factor in the innovation process.[2] High strength alloys are used to build stronger, lighter and safer vehicles; superalloys are used to make higher efficiency gas turbines; composites make larger, more efficient wind turbine blades and provide improved performance in aerospace applications; and nanomaterials are finding their way into better performing batteries, energy storage devices, electronic inks, high voltage transmission lines, and applications related to health care (e.g. imaging and therapeutics). Ceramics and glasses are expected to have a large number of next-generation applications in the next 10 to 15 years,[3,4,5] including adaptronic and mechatronic components for active noise and vibration suppression, video display and optoelectronic devices, environmentally friendly lead-free large-area sensors and actuators for micro-electromechanical systems (MEMS), highly integrated modules for power electronics and microwave technology, insulating packages for integrated circuits, energy conversion and fuel cell devices, optical and wireless communications, high-density information storage media, advanced thermal barrier coatings for high-temperature gas turbines, in the manufacture of filters for clean drinking water, and wear-resistant mechanical parts used in pipes, valves, cutting tools, pumps and compressors. In addition, more cost-efficient and environmentally benign manufacturing methods are increasingly needed to produce these materials: low-temperature sol-gel and hydrothermal processes, free-form fabrication, near-net-shape fabrication, and novel joint and coating processes. Overcoming scale-up barriers associated with these processes will facilitate "faster, better, more cost effective" methods that will help U.S. manufacturers be more successful and competitive.

Critical processes are generally manufacturing processes that have the greatest impact on one or more of the following characteristics: product quality, product yields from raw materials, scrap rates, efficiency of raw material consumption, and/or other measures of efficiency. Many critical manufacturing processes are not flexible enough to easily incorporate novel material advances into new products and many critical processes limit the nation's capacity to supply existing strategically-important products. Finding technical solutions to these challenges in manufacturing can give the comparative advantages necessary for strengthening manufacturing in the United States.

MAGNITUDE OF THE PROBLEM

Manufacturing has a rich history and has long been a significant part of the American economy. The United States is the world's leading producer of manufactured goods. Standing alone, the manufacturing sector in 2002 represented the seventh-largest economy in the world.[6] In 2008, the manufacturing sector represented 11 percent of the total GDP ($1,569 billion out of $14,256 billion total)[7] and supported 13.3 million jobs, or about 9.8 percent of total U.S. employment. Manufacturing provides and depends on innovation, accounting for more than 90 percent of all U.S. patents registered annually.[8] Transformative research often achieves broad national impact only through incorporation into manufactured products. The manufacturing sector must continue to implement technology advances to assure preservation and future competitiveness of this element of our economy.

Manufacturing's leverage on the rest of the economy tops all other sectors, generating an additional $1.43 in economic activity in the rest of the economy for each $1 in merchandise sales.[9] The manufacturing sector is the primary source of U.S. trade revenues, accounting for almost two-thirds of the Nation's exports. It is widely acknowledged that R&D is the fundamental basis of innovation, but the fact that the manufacturing sector drives the majority of U.S. R&D efforts is often overlooked. The manufacturing sector accounts for more than 70 percent of U.S. industrial R&D, with more and more of the research effort and production coming from the high-technology portion of the manufacturing sector, which has tripled its output over the past 25 years.[1]

The ability of companies to introduce rapid product innovations is foundational for U.S. manufacturing to maintain or increase market share, competitiveness, and to create and retain highly skilled, well-paying jobs. Companies also need a greater degree of manufacturing agility to take advantage of the unprecedented long-term manufacturing opportunities being created by new approaches to energy, the environment, health care, and transportation. Domestic manufacturers' overall productivity and agility are essential to national defense and homeland security, ensuring the availability of high-performance and high-quality products and systems in a timely and cost-effective manner.

One technological need of manufacturing that cuts across many of the proposed solutions to today's challenges involves material advances and how to more effectively get these materials into new products. For example, there are applications using nanomaterials to make high voltage transmission wires that behave like high temperature superconductors; new composites to produce larger, more efficient wind turbine blades; and new alloys to reduce vehicle weight. The increasing need for these ultra-high performance materials in production quantities at competitive costs spans many industries: aerospace, automotive, energy, mining and construction, electronics, defense, and even consumer goods. These materials challenges have been identified in various industrial road maps as well as white papers submitted to TIP. A non-exhaustive list of challenges and opportunities for material advances by broad material type includes the following:

- **Nanomaterials**[10, 11]
  - Cost of manufacturing carbon nanotubes is a barrier to widespread use in products
  - Control and measurement of feature size could lead to enhanced materials properties and device functions not currently foreseen (or even considered feasible)
  - Robust and reliable production methods with correct control and measurement at the atomic scale are needed for consistent features
  - Development of new instrumentation and measurement techniques for real-time process control and measurement are needed
  - Byproducts, wastes, and impurities associated with manufacturing hinder acceptance and adoption in commercial applications
  - Scalable, cost-effective manufacturing of newly-discovered materials is needed
- **Composite materials**[12]
  - Aerospace industry's emphasis on fuel efficiency favors use of polymer-matrix composites as an alternative to aluminum
  - Automotive industry recognizes advantages of weight reduction, parts consolidation, and increased cost-effective design options for polymer-matrix composites
  - Energy sector's growing use of wind energy has led to increased demand for polymer-matrix composite turbine blades
  - Better processes and tools needed to recognize special properties such as the anisotropic nature of these materials (strength and stiffness greatest in direction parallel to axis of the embedded reinforcements)
  - Need to overcome cost barriers to use such as expensive starting materials, time-consuming fabrication processes, autoclaves, and expensive tooling
  - Multiple industries require accommodation of production of large, structurally complex parts
  - Use of multiple composites fused in a single component, required by emerging applications
  - Increased application of recyclable composites and use of bio-based materials for improved sustainability and carbon footprint reduction

- **Alloys** (Super, specialty, aluminum, magnesium, titanium, smart materials)[13]
  - Performance advantages from novel metallic alloys could displace other materials in a variety of structural applications (i.e., defense, transportation, energy, electronics and process industries)
  - Major barriers to widespread use of smart (alloy) materials include the need for low-cost, robust and reliable production processes, and improved design tools to enable non-experts to use the materials with confidence
  - Smart (alloy) materials hold promise of combining sensor capabilities in coatings for a wide variety of applications

- **Glasses**[3, 14, 15]
  - Controlling heat, light and glare via structural and processing enhancements for architectural, automotive, aerospace, and marine applications
  - Environmentally-benign processing for high-performance glass substrates
  - Tailoring of glass composition and processing techniques for improved energy efficiency and greenhouse gas emission reductions, development of bioactive glass scaffold for improving bone generation

- **Ceramics**[3, 4, 16, 17, 18]
  - Removal of barriers to widespread use of sodium zirconium phosphate (NZP) ceramics for an array of applications, including environmental and biomedical applications
  - Improved bone engineering with zirconia-based macroporous ceramics as 3-D scaffolds and biodegradable ceramics such as tricalcium phosphate and hydroxyapatite
  - Use of ceramics and glass-ceramics as machine components
  - Pushing optical and electromagnetic metamaterials towards shorter wavelengths for broader and more advanced applications
  - Increasing output power and efficiency of piezoelectric ceramic devices for energy scavenging

For the remainder of this paper, we will define "*material advances*" as:

Materials that have been developed to the point that unique functionalities have been identified and these materials must now be made available in quantities large enough for innovators and manufacturers to test and validate in order to develop new products.

The unique functionality that these materials represent will require new levels of understanding in the sciences of materials processing and process control. Nanomaterials, for example, will require manipulation and measurement at the atomic level. In alloys, the measurements and control would be at the microscale (and eventually at the nanoscale) with an emphasis on anisotropic features of the micro (nano) structure. With composites, ceramics, and glasses, measurements and control would be at the mesoscale and would take advantage of the anisotropic layering of the process. Control of one material or phase within another will also be an important consideration.

For the remainder of this paper we will define a "*critical process*" as:

An existing or new manufacturing operation that has significant control over, or influence on, one or more key manufacturing performance metrics.

For the remainder of this paper, we will define "biomanufacturing " as:

"Use of living genetically modified organisms or living genetically modified cells to manufacture a product." A genetically modified organism is defined as "an organism whose genetic characteristics have been altered by the insertion of a modified gene or a gene from another organism or by modification/disabling/deletion of a gene, using the techniques of genetic engineering." A variety of living genetically modified organisms, such as bacteria, fungi, algae, plants and animals could be used for biomanufacturing.

This broad definition of biomanufacturing includes in scope projects that address critical processes in the manufacture of biopharmaceuticals (health related) as well as non-biopharmaceutical (non-health related) products. A non-exhaustive list of examples of biomanufacturing processes includes those that could be used to manufacture products such as biopharmaceuticals (e.g. recombinant proteins when used as vaccines, therapeutics, or as molecular probes for diagnostics; or cell or tissue-based biopharmaceuticals such as engineered cells and engineered tissues as therapies – engineered tissues are complex structures involving cells, scaffolds and/or signaling molecules); small molecule pharmaceuticals (e.g. antibiotics); vitamins; and biopolymers.
Process improvements made through high-risk, high-reward research and development, rather than simple engineering improvements or redesign, could lead to significant and quantifiable

improvements in process output measures. As an example from 2009 news headlines, consider the vaccine production response to the H1N1 flu outbreak. Experts were able to decode the virus to prepare a vaccine in record time, but encountered problems supplying the large volumes of vaccine needed in a timely fashion. Vaccines are grown in chicken eggs in a process that dates back to World War II. Each egg is in effect its own factory with product variability and purity issues. Development of new processes for production of recombinant vaccines as well as processes for real time monitoring and analysis could address these problems and would not only help to respond rapidly to new virus outbreaks, but could also reduce the cost of clinical trials through better scale-up methodologies. Addressing these challenges and needs could also impact other industries such as chemicals, biofuels, etc.

Biomanufacturers are not the only ones with critical process issues that affect the quality of their products. TIP has received white papers and reviewed process challenges identified in various industrial road maps and published reports from a broad range of manufacturing sectors. A non-exclusive list of examples would include: [19, 20, 21]

- The ability to deploy or repair energy systems is being controlled in part by overseas companies because the U.S. has limited capabilities to make large parts such as wind turbine bearings, turbine blades, and megawatt stator windings, or to forge large gas turbine hubs
- The challenge of making the “first part right” for limited production runs or rapid prototyping impacts competitiveness and profitability --- new approaches to additive or subtractive/cutting processes are needed
- Greater control over process variability, consistency and contamination levels impacts product quality in many industries; in the case of biomanufacturing for example, process improvements for continuous aseptic manufacturing of protein biopharmaceuticals would enhance the safety, consistency, quality, and availability for their use as therapeutics or *in vivo* diagnostics
- Greater process control could also be achieved through improved and/or new approaches to rapid on-line real-time monitoring and analytical techniques for biopharmaceuticals, engineered tissues, and other products
- Novel ideas for process optimization, scale-up, and product analysis based on approaches using technologies such as microchannels, microreactors, and microbioreactors

MAPPING TO NATIONAL OBJECTIVES

There is a long history of recognizing the need for government investment in manufacturing and material advances as national priorities. The current Administration has called for investments in *compelling advanced manufacturing strategies* and for support of small- and medium-size manufacturers to *produce innovative new technologies*.[22]

There are several components to these investments enumerated in the *Framework for Revitalizing American Manufacturing*. One of these components is to “invest in the creation of new technologies and business practices. Our efforts in this area should focus on advanced research without immediate commercial application, where private actors are likely to under-invest.” To accomplish this, the Administration proposes to “spur innovation in manufacturing by increasing the Technology Innovation Program (TIP)… awards in [the manufacturing] area [which] have the potential to spur new and much-needed capabilities in the manufacturing sector – whether in production techniques, material sciences or cutting edge design options.”[22]

In *Rising above the Gathering Storm,*[23] the National Academies identified developments in metal alloys and composite materials for aerospace applications; and high performance materials such as super alloys, steel and aluminum alloys, titanium, superconductors, and others as being of critical importance to the economic future of the nation.

The critical need for improved or novel processes for biopharmaceutical manufacturing was highlighted by the Food and Drug Administration (FDA) in its 2004 document *Challenges and Opportunities on the Critical Path to New Medical Products,*[24] which provided the FDA's analysis of the pipeline problem relating to the recent slowdown in innovative safe and effective medical therapies reaching patients. This analysis indicated that a better biomanufacturing tool kit is needed to provide the infrastructure necessary for translating laboratory prototypes into commercial products. Specifically, novel process analytical technologies are needed for cost-effective scale-ups of biopharmaceuticals. Moreover the 2004 FDA guidance document on Process Analytical Technology recommended designing a process measurement system to allow real-time or near time (e.g. in-line or on-line) monitoring of all critical attributes for a real time product release based on acceptable quality of the in process or final product based on in process data.[25]

Biopharmaceuticals is not the only product class where process improvements and new analytical technologies are needed. Cost-effective sustainable biomanufacturing systems are also needed to enable the continued availability of other products at low cost such as antibiotics, biopolymers, and vitamins.

Numerous other organizations have also developed technology roadmaps for material advances and their processing. Groups as diverse as the International Society for Optics and Photonics (SPIE)[26], the National Science and Technology Council (NSTC)[27], the Department of Energy's Industrial Technologies Program,[28, 29, 30] and the aluminum[31] and steel[32] associations have acknowledged these technical areas of need. These roadmaps, from a wide range of public and private sources, demonstrate the fundamental need for widely available, affordable new materials to meet a broad range of challenges. Other countries have developed similar roadmaps and corresponding research efforts in these areas, suggesting the U.S. leadership role in material advances and manufacturability may be at risk.

NIST Laboratory Activities

The mission of the Department of Commerce (DOC) is to advance economic growth and jobs and opportunities for the American people. It has cross-cutting responsibilities in the areas of trade, technology, entrepreneurship, economic development, environmental stewardship, and statistical research and analysis. NIST, an agency within DOC, is charged with promoting 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. In support of this mission, NIST research and development supports material advances and development of critical processes.

In NIST's three-year programmatic plan, the discussion of an R&D Investment Framework cites material advances as one research area for consideration because it is among the most strategic. The plan also emphasizes the development of measurements and standards to support characterization and manufacturing of products such as protein-based biological drugs,[33] and new materials.

NIST's *Assessment of the U.S. Measurement System*[34] includes some of the following relevant topics in the materials sector/technology area as well as manufacturing processes for chemicals and biochemicals:

- The absence of measurement instruments and methods capable of accurately characterizing the composition and the behavior of complex materials systems and structures
- The anticipated need to evaluate the performance and reliability of new materials successively at the production and market stages of their development. The timely delivery of measurement solutions in the materials sector/technology area is increasingly challenged by the growing complexity of materials systems and structures and their interfaces
- New sensor technologies for in-line, real time, and continuous monitoring of process variables in chemically aggressive environments are needed to overcome technical barriers to manufacturing process innovation
- Industries face common measurement problems that impede innovations related to processes needed to improve production efficiency, in terms of cost, time, and energy
- Advances in process-control capabilities are needed that include innovations in process simulation for both existing and new chemical processes and in-line sensing of process conditions and parameters
- Shifting raw material sources to biological sources (e.g. manufacturing of nanomaterials or nano composites using microbial production systems)
- Need for accurate in line and real time measurements of physical attributes of manufactured parts and assemblies, relevant to a spectrum of applications (e.g. real time monitoring and analysis of products during biomanufacturing process)
- Self assembly of soft nanomaterials for bone and tissue replacement (e.g. development of nanocomposites for bio related applications)

NIST's involvement in the materials and process areas shows the importance of accelerating utilization of material advances with novel properties as well as critical process improvements in manufacturing.

MEETING A TIMELY NEED NOT MET BY OTHERS

Many sectors of the manufacturing community have not fared well for some time under the current economic climate, and there are fewer resources available to develop new high-risk, high-reward technologies. The National Science Foundation (NSF) and other agencies generally fund basic scientific research. No single Federal agency has a lead responsibility to support research in manufacturing. An analysis of the funding gaps shows there is a need to fund research that examines issues such as:

- New processes for materials scale-up from small scale laboratory quantities ("bench top" efforts) while assuring composition and functionality
- New processes that rapidly incorporate the functionality of new material developments into new products that exhibit revolutionary performance
- Critical process developments to allow faster, less energy-intensive, less toxic processing of raw materials into finished products
- New measurement and analytical processes that enable rapid, on-line monitoring, analysis, and active feedback for real-time control of the production of biopharmaceuticals and other products.
- New predictive modeling capabilities to characterize the behavior of a new material's functionality and the effect of materials processing on material properties, and application of such knowledge in manufacturing processes and final product design
- Novel microreactor and microbioreactor arrays for process and bioprocess development and optimization.

TIP, in supporting the topic *Manufacturing and Biomanufacturing: Material Advances and Critical Processes,* addresses a timely need that is not currently being met by others within the critical national need area of manufacturing.

SOCIETAL CHALLENGES

Manufacturing has a variety of challenges that need to be addressed. There are challenges associated with agile or intelligent manufacturing, sustainable manufacturing processes, specific manufacturing processes, and a host of others. Analysis of current funding needs and consideration of an investment strategy that could benefit the broadest range of manufacturers suggests that there are three important challenges: 1) *Process scale-up, integration, and design for material advances*; 2) *Predictive modeling for material advances and materials processing; and 3) Critical process advances*.

1. Process scale-up, integration, and design for material advances.

New materials typically are developed in a laboratory setting, and then samples are given to end-users for alpha and beta testing. This testing phase can involve considerable effort to understand how the material can be incorporated into a new product in a way that takes best advantage of the material's unique functionality. Scaling up from laboratory quantities to larger volumes, validating properties, and then incorporating the material into product manufacturing lines is often nonlinear and does not follow straightforward scaling laws, due to the unique functionality that has been obtained from the material advances.

2. Predictive modeling for material advances and materials processing.

Predictive modeling capabilities are key to developing new processes, scaling up these processes, and understanding how to utilize a material advance's unique functionality. Modeling capabilities are needed principally to:

a. Analyze and understand why a newly discovered material has the properties it does and then extrapolate its behavior to new conditions
b. Incorporate this knowledge more efficiently into process design tools so new products can be made while maintaining the unique functionality of the materials as predicted

3. Critical process advances.

As the availability of new materials increases and the modeling of their behavior becomes more refined, there is a complementary need to improve processing or manufacturing methods. High-risk, high-reward approaches are needed to exploit the properties of the material advances into new and more advanced products as well as to support the processing of existing materials in new and different ways, resolving key bottlenecks or critical problems such as energy consumption, processing time, scrap rates, quality, and throughput. Current methods of manufacturing often are not rapidly adaptable to making new or different products, and are often not optimized towards making existing products faster, more cheaply, and more sustainably. Improving processes used in the manufacture of new and existing products is an imperative for the continued global competitiveness of U.S. manufacturers. Creation of agile, flexible, and increasingly interoperable systems are necessary enhancements to base manufacturing technologies in order to meet new productivity challenges.

Significant biomanufacturing process improvements are needed to enhance safety, quality, and consistency of biopharmaceuticals and other products while reducing the manufacturing cost. For example, current sensing technologies typically require manual sampling, are not rapid or robust to cleaning agents or processes, and are not sufficiently reliable for embedding in the manufacturing environment as automated technology. Critical process advances are needed, enabling rapid on-line sensing and analytical capabilities. New tools are needed for bioprocess optimization, control and improvement to enable a cost-effective batch or a continuous manufacturing process. Processes that involve integrated sensing and detection capabilities for measuring multiple parameters will be useful. Moreover, purification and separation process advances involving novel membranes and affinity reagents are needed for cost-effective downstream processing in biomanufacturing processes.

Environmental, Health and Safety (EHS) issues are an important consideration for all three challenges. In order to be competitive in a global economy, products and processes should be designed to support good EHS practices. While TIP is not considering a specific challenge in EHS at this time, one would expect a solution for any of the proposed challenges to include key EHS concepts.

RELATIONSHIP BETWEEN SOCIETAL CHALLENGES WITHIN MANUFACTURING

For the first challenge, ***process scale-up, integration, and design for material advances***, new processes will need to be developed. These processes will increase to pre-commercial scale the quantity and quality of available advanced materials; or help incorporate these advanced materials into new, revolutionary products based on a new material's properties. These scaled-up processes may be next generation or an entirely new process. For example, forging ever-larger parts cannot be solved by building ever-larger forges (which becomes prohibitively expensive), but instead by developing new techniques such as partial forging.

New instrumentation and measurement capabilities also will be needed to support these new processes. These instruments will need to measure real-time process parameters such as the properties that provide the unique capabilities of the advanced materials (e.g. composition). In addition, instruments for real-time inspection are needed to ensure and/or verify materials are being correctly incorporated into manufactured products that require the revolutionary functions of these new materials.

For the second challenge, ***predictive modeling for material advances and materials processing***, new tools are needed to enable researchers to use constitutive relations and rules (with validation) concerning the underlying behavior of materials (understanding structure versus function) and the changes to behavior due to manufacturing processes. For example, new tools will need to account for the scale-dependent behavior of advanced materials. This capability will enable a better and quicker understanding of materials' behavior. These efforts will also enable extrapolation of that knowledge beyond the laboratory conditions for which they were developed, and therefore will need new validation and verification capabilities.

Additionally, critical knowledge is needed as to why certain decisions or assumptions were made, in order to incorporate new modeling capabilities for laboratory results into process design and modeling. Again, new validation and verification methodologies will be essential.

With successful development of these tools, processes, and technologies, the manufacturing communities will have significantly improved capabilities to quickly incorporate advanced material breakthroughs into revolutionary products based on new material functionality, and thus establish new competitive advantages in a global economy.

The third challenge, ***critical process advances,*** requires modifications in manufacturing processes that augment and expand current limited capabilities. Applications could include those oriented towards the creation of novel methods to fabricate unique components from complex, difficult-to-machine materials (advanced engineering materials or smart materials), or the design and implementation of real-time, sensor-based, feedback-optimized systems for discrete, continuous or batch manufacturing processes. One discrete manufacturing example could be a process for making customized parts such as medical implants, using techniques such as additive manufacturing, near net-shape fabrication, or partial forging. Processes are needed for the manufacture of parts possessing complex geometries from existing and novel materials while preserving the properties of the material. A batch process example would be improved process monitoring and *in situ* analytical tools, enabling a reduction in batch-to-batch variability and an improvement in quality and quantity of biopharmaceuticals or other products produced in a reliable and cost-effective manner.

Proposers generally need to address improvements such as quality, throughput, costs, sustainability, new capabilities and agility, relative to the state-of-the-art for the process being proposed for improvement. However, a general discussion without appropriate metrics to illustrate the magnitude of the improvement outcomes is not sufficient.

A key characteristic to address for all three societal challenges above is how the outcomes of the research will enable manufacturers to produce material advances and products faster, better, more cost-effectively, and sustainably, as well as leverage new uses for the material advances or the intended products.

ANALYSIS OF COMMITMENT

Potential participants, including small- and medium-sized companies, universities, national laboratories and other organizations, have indicated interest in the challenge areas, and have the capabilities or relevant experience to conduct high-risk, high-reward research, for example:

- Develop laboratory-scale processes to make small quantities or test runs of materials
- Develop and validate predictive modeling tools that analyze and help to understand why new materials have the properties they do
- Develop and validate predictive modeling tools used in process design and development for new uses of advanced materials
- Develop new or modify existing manufacturing processes that incorporate advanced materials into new uses or produce significant benefit for existing uses
- Develop tools for transformational process development, optimization and improvements
- Develop or modify biomanufacturing processes that enable rapid on-line monitoring, feedback, and control of the production of biopharmaceuticals and other products such as biopolymers and vitamins.

As further evidence of commitment, TIP has received a number of white papers from the public directly related to the manufacturability of materials and various manufacturing processing operations, as well as numerous comments and feedback on the TIP-produced white papers on these topics.

SUMMARY

Manufacturers are being especially hard hit in the current economic climate. They are having greater difficulty than in the past finding the capital necessary to develop new technological capabilities to enhance their competitiveness. Several gaps in funding have been identified that are not currently being addressed, but if addressed, could provide manufacturers with new and needed abilities for "*Manufacturing and Biomanufacturing: Material Advances and Critical Processes".* Three societal challenges need to be addressed by high-risk, high-reward research: 1) process scale-up, integration, and design for material advances; 2) predictive modeling for material advances and materials processing; and 3) critical process advances. The results of these efforts are expected to inspire revolutionary uses of material advances based on new material functionality, resulting in new products, with advanced features and improved characteristics, entering the market faster. Advances in critical manufacturing processes will support new and existing industries with significant process improvements, allowing them to use less energy, produce less waste, reduce costs, and reduce time to market while improving or preserving product quality (better, faster, cheaper, leaner, and greener), substantially benefitting the manufacturing and biomanufacturing sectors, as well as U.S. security and competitiveness.

Those seeking further information should consult the Federal Funding Opportunity notice.

Appendix 1: List of Supporting Roadmaps for this Topic –

1. Nanotechnology Roadmaps

- *The National Nanotechnology Initiative: Strategic Plan February 2011*, National Science and Technology Council (NSTC)

  Establishes national goals for Federal science and technology investments in nanotechnology, defines Program Component Areas (PCAs) http://www.nano.gov/nnistrategicplan211.pdf

- Report to the President and Congress on the Third Assessment of the National Nanotechnology Initiative, President's Council of Advisors on Science and Technology, March 2010

  Assesses trends and developments in nanotechnology and the strategic direction of the NNI as it relates to maintaining U.S. leadership in nanotechnology research http://www.whitehouse.gov/sites/default/files/microsites/ostp/pcast-nano-report.pdf

- *Chemical Industry R&D Roadmap for Nanomaterials By Design: From Fundamentals to Function*, Chemical Industry Vision2020 Technology Partnership, December 2003

  Challenges to the chemical industry to develop new products based on nanomaterials, suggests timelines and risk levels for technology http://www.chemicalvision2020.org/nanomaterialsroadmap.html

- *Proceedings: Instrumentation, Metrology and Standards for Nanomanufacturing*, Final Report from the Workshop of the National Science and Technology Council (NSTC) Interagency Working Group on Manufacturing Research and Development, October 17-19, 2006,

  Describes, among various technical needs predictive modeling capabilities http://www.manufacturing.gov/pdf/NanomfgMetrology_WS_rpt.pdf

- *The International Technology Roadmap for Semiconductors*, 2010 Update

  Roadmaps the manufacturing needs of the semiconductor industry, including the identification of problems with no known solutions http://www.nist.gov/nist-exit-script.cfm?url=http://www.itrs.net/Links/2010ITRS/Home2010.htm

- *Nanomanufacturing for Energy Efficiency*, Workshop Report, DOE Industrial Technologies Programs, December 2007

  Prioritizes the greatest contributions by nanotechnology to energy reduction http://www.bcsmain.com/mlists/files/NanoWorkshop_report.pdf

- *Manufacturing the Future*, National Science and Technology Council (NSTC), Interagency Working Group on Manufacturing R&D, Committee on Technology, March 2008

  Nanomanufacturing is the number 2 of 3 priorities http://www.manufacturing.gov/pdf/NSTCIWGMFGRD_March2008_Report.pdf

- *Defense Nanotechnology Research and Development Program*, Department of Defense, Director, Defense Research and Engineering, April 26, 2007

  Describes DOD efforts in nanotechnology as well as their activities in support of the National Nanotechnology Initiative (NNI) http://www.fas.org/irp/agency/dod/nano2007.pdf

- *Productive Nanosystems: Launching the Technology Roadmap*, The Society of Manufacturing Engineers , October 2007

  Describes results from SME roadmap on atomically precise manufacturing processes http://www.sme.org/cgi-bin/get-event.pl?--001739-000007-020696--SME-

- *NanoRoadMap Project Sectoral Report: Energy*, VTT Technology Studies, October 2004

  Describes key nanotechnology developments needed for energy conversion, storage, and efficiency http://www.dynamo.tno.nl/efmn/download.asp?id=609

- *Nanotechnology for the Forest Products Industry: Vision and Technology Roadmap*, Agenda 2020 Technology Alliance, American Forest and Paper Association, March 2004 http://www.agenda2020.org/PDF/fp_nanotechnology.pdf

- *Cross-Industry Issues in Nanomanufacturing*, National Institute of Standards and Technology, May 20-22, 2008 http://www.nist.gov/mml/upload/nano_small_web-4.pdf

2. Alloys and Composites Roadmaps

- *FreedomCAR and Fuel Partnership: Materials Technology Roadmap,* DOE EERE, October 2006.

  Lightweight materials in some instances are less recyclable than other materials, therefore recycling technologies becoming more important as their use increases; discusses advanced high-strength steels (AHSS differ from conventional mild steels because they are manufactured using a combination of alloy compositions and processing methods to achieve high strength without significantly compromising formability; what remains is the difficult task of developing the manufacturing technologies to make the production and use of these new materials possible and economically attractive on a high volume scale), aluminum (developing new innovative tools and technologies to reduce manufacturing costs and raw material costs can further improve affordability), magnesium, (affordable creep resistant and corrosion resistant magnesium alloys, large magnesium cast structures, processing recycled material), metal matrix composites, titanium (processing and manufacturing cost reductions)

  Discusses carbon-fiber, polymer composites (cost reduction, high volume manufacturing, durability, recycling) http://www1.eere.energy.gov/vehiclesandfuels/pdfs/program/materials_team_technical_roadmap.pdf

- *Magnesium Casting Industry Technology Roadmap,* American Foundry Society, September 2005

Identifies grand challenges for magnesium that include: matching desired properties of components (microstructure) with quality levels, expanding the range of casting processes, versatile casting machines, affordable heat treatment cycles, and address cost issues
http://www.es.anl.gov/Energy_systems/docs/process_tech/industrial_metals/mag_roadmap.pdf

- *Magnesium Vision 2020*, U.S. Automotive Materials Partnership (USAMP)*,* November 1, 2006

  Improve understanding of microstructure, new computer modeling that uses new multi-scale modeling methodology that includes history effects, validate with experiments; produce powders by new processes; metal powder injection molding
  http://www.uscar.org/commands/files_download.php?files_id=99

- *Forging Industry Technology Roadmap: Update*, National Center for Manufacturing Sciences (NCMS) *,* October 14, 2003

  Increase global competitiveness by improvements in processes (die materials, die surface modification, lubrication) and simulation
  http://www.forging.org/pdf/Roadmapws.pdf

- *Aluminum Industry Technology Roadmap*, U.S. DOE, February 2003

  Develop manufacturing processes for scrap-tolerant alloys; develop new or improved non-contact sensors; develop integrated models that relate structural properties to manufacturing processes and the material employed; develop integrated numerical methods for analysis and robust design of products, processes, and materials; need new real time sensors for process control
  http://www1.eere.energy.gov/industry/aluminum/pdfs/al_roadmap.pdf

- *Steel Industry Technology Roadmap: Barriers and Pathways for Yield Improvements*, American Iron and Steel Institute*,* October 7, 2003

  Robust, low-cost sensors to measure key iron making and steel making parameters (chemistry, temperature, etc.); real-time off-gas analysis method and chemistry adjustment methods; improved control of heat treatment processes for precise control of properties; advanced combustion control systems for furnaces; improved microstructure control; reliable property data for advanced steels
  http://www.steel.org/~/media/Files/AISI/Public%20Policy/YieldReportlkOct7-03.ashx

- *Steel Industry Technology Roadmap*, DOE EERE ITP, December 2001, last updated on January 2009

  Advance alternate iron making processes and models to achieve commercial scale; continue development of process modeling and tools
  http://www1.eere.energy.gov/industry/steel/roadmap.html

- *The Steel Industry Technology Roadmap for Automotive,* American Iron and Steel Institute

  Applications in automotive industry, description of needed process improvements
  http://www.autosteel.org/en/sitecore/content/Autosteel_org/Document%20Types/Technical%20

Documents/2006%20and%20Before/The%20Steel%20Industry%20Technology%20Roadmap%20for%20Automotive.aspx

- *NADCA Research 2011 Strategic Plan and Roadmap*, North American Die Casting Association, 2011 http://www.diecasting.org/research/roadmap.htm

- *Materials Research to Meet 21st Century Defense Needs*, Committee on Materials Research for Defense, National Academies Press, 2003 http://www.nap.edu/catalog.php?record_id=10631
- *Roadmap for Process Equipment Materials Technology*, Materials Technology Institute, Inc., Communications, Fall 2003

  http://www.mti-global.org/mti/app/public_files/MTI%20October03.pdf

- *Aluminum Metal Matrix Composites Technology Roadmap*, Aluminum Metal Matrix Composites Consortium, May 2002 http://www.almmc.com/

Appendix 2: List of Supporting White Papers Submitted to TIP

- *A New Generation of Thermal Insulation by Affordable Manufacturing*, Industrial Science and Technology Network : Discusses the need for manufacturing processes capable of making nanopore material at prices and volumes that would make it available for home insulation.

- *A Solution for Manufacturing High Volume Precision Micro Scale Components*, Rockford Engineering Associates, LLC (REALLCo): Discusses the challenges in developing new machining processes for micro scale components.

- *A Solution for the Critical Technical and Manufacturing Challenges Facing the Wind Power Industry*, Rockford Engineering Associates, LLC (REALLCo): Discusses the problems the US is encountering in machine tools for the wind industry and the reliability issues relating to the failure rate of the large bearings in the generators. The paper advocates the industry switching from rotary table design to a fluid bearing design which will require far more precise machine tools such as vertical turning lathes.

- *A Systematic Platform for Unifying and Defining Nanoscience: An Enabling Framework for Defining Risk and Benefit Boundaries*, Central Michigan University: Discusses the development of a system for defining the characteristics of nanoscale particles.

- *Accelerating the Development and Scale Up of Energy Efficient, Clean Manufacturing Process Technologies*, Advanced Electron Beams: Discusses the need to maintain U.S. competitiveness in manufacturing while managing the impact on the environment, and how this need is currently hindered by a lack of adequate process technology, novel energy sources, and industrial chemistries.

- *Accelerating United States Automotive Manufacturing Innovation*, Coherix: Discusses the need for agility in automotive manufacturing through dynamic quantitative and comprehensive feedback of actual manufacturing process capability to product engineering function.

- *Advanced Composites for Flywheels*, Nanotech Plus, LLC: Discusses the need for new manufacturing processes for composites to address the problem of integrating multiple composites in large flywheel manufacture for energy storage applications.

- *Advanced Nanotechnology Research & Development into Nanomanufacturing for Commercialization*, AeonClad Coatings, LLC: Discusses the challenges of process control in nanomanufacturing and need for research in this area.

- *Advanced Processing Technology in Composite Material Manufacturing*, Rockford Area Ventures/EIGER Lab and Ingersoll Machine Tools: Discusses the need to "break the bottleneck in the cost and predictability of composite material manufacturing" (p.1); the paper also states that this could enable more widespread use of composite materials to reduce energy consumption.

- *Advancement of Versatile Waterjet Technology to Rebuild Competitiveness in Manufacturing Technology*, OMAX Corporation/FLOW International Corporation: Discusses the need for the next generation of waterjet technology for improved manufacturing processes.

- *Affordable Fabrication Methods Development for Lightweight Components Manufactured from Low Cost Titanium Powders*, Boeing: Discusses the availability of lower cost titanium powder but the lack of manufacturing processes to take advantage of those low cost powders and use them effectively for wide-spread adoption of this material.

- *Arrayed Microchannel Manufacturing: Enabling a New Efficiency Paradigm* in the Chemical and Energy Industries Green Columbus: Discusses the challenges in the development of microchannel process technology.

- *Chemical Imaging for Better Healthcare,* Infrasign, LLC: Discusses the FDA's Process Analytical Technology (PAT) initiative for cost effective pharmaceutical manufacturing, the state-of the art in pharmaceutical detection techniques and the technical challenges and need for innovative sensing imaging technologies.

- *Commercial Value of Used Nuclear Fuel Reprocessed with Elements Separated, Purified and Reduced to Metals*, Mr. Edwin D. Sayre, Independent Engineer: Discusses the challenges in developing new technologies to reprocess used nuclear fuel and recycle valuable metals.

- *Computational Analytical Micromechanics of Composites and Nanocomposites. New Background and Perspective*, Micromechanics & Composites LLC: Discusses the need for new tools for predictive modeling about material properties in a variety of scales.

- *Cooperative Research on the Metal Oxide Magnetic Nanoparticles*, University of New Hampshire: Discusses the need for new research on metal oxide magnetic nanoparticles including the processes to manufacture those particles.

- *Critical Nanotechnology Needs in the Forest Products Industry*, Agenda 2020 Technology Alliance / American Forest & Paper Association: Discusses the challenges and advantages of incorporating wood-based materials into nanocomposites.

- *Design and Fabrication of Optical Metamaterial Films with Large Physical Area for Biomedical Applications.* The University of Texas-Austin: Discusses the challenges of developing and manufacturing new classes of optical films for healthcare applications.

- *Developing Manufacturing Innovations Needed to Achieve Solar Photovoltaic Grid Parity*, 1366 Technologies, Inc.: Discusses the challenges of developing new manufacturing processes needed to manufacture photovoltaic wafers.

- *Distributed Storage-Generation Grid*, Richard E. Smalley Institute for Nanoscale Science and Technology at Rice University: Discusses development and application of the Distributed Storage-Generation Grid as a means to meet the demand for affordable energy.

- *Engineering Quantum Engineering: Manipulating atoms and molecules for practical applications,* Seize Particles Research Center, Inc.: Discusses the need for tools and techniques to manipulate atoms and molecules.

- *Energy harvesting technologies based on advanced materials*, University of Wisconsin-Madison: Discusses the need to control properties of advanced materials to improve the material's effectiveness in energy harvesting applications.

- *Green Engineered Materials (GEM) Objectives and Focus,* University of Delaware: Discusses the need for new processes in the manufacture of advanced bio-based materials.

- *High Efficiency and Low-Emissions Combustion Technology for Manufacturing Industries*, University of Michigan: Discusses energy efficient and low-emissions combustion technologies for manufacturing industries which could provide at least a 50% improvement in energy efficiency and reduce pollutant formation in high temperature industrial heating processes.

- *The High Impact of Green And Sustainable Construction Materials*, CCS Materials, Inc.: Discusses the need for "designer materials" (p.6) and "understanding… structure / property relationships that operate across broad classes of materials" (p.6); the goal would be next generation materials and manufacturing processes for the construction industry.

- *High Performance Rare Earth Permanent Magnets for Advanced Motors and Alternative Energy Applications*, Electron Energy Corporation: Discusses the potential for permanent magnets as an enabling material for use in motors, wind power generation, nuclear reactors, and other alternative energy sources.

- *High-performance Si-based Optoelectronic Materials for National Security and Economic Development,* EPIR Technologies, Inc.: Discusses the need for perfecting techniques to grow high-quality optoelectronic materials on pure silicon.

- *Improvement of Vital Measurement Capabilities for Manufacturers and Compliance*, X-Ray Optical Systems, Inc.: Discusses the need to develop a new generation of measurement systems to support the manufacturing process in identifying and reducing toxins in processes and products.

- *Innovative Decision-Making Technology for Sustainable Competitiveness of US Productive Enterprises*, GME International Corp.: Discusses the need for better simulation of machine tool condition to enhance process control.

- *Intelligent and Integrated Manufacturing Systems*, Integrated Manufacturing Technology Initiative, Inc.

- *Knowledge Discovery and Analysis in Manufacturing,* Marquette University: Discusses the need for new quality and reliability techniques in manufacturing.

- *Low-Cost Manufacturing Technology for Transforming Nanotechnology into Energy Applications*, University of California, Berkeley: Discusses the need for new manufacturing technology to transform basic research in nanotechnology into commercial products for energy applications especially the development of flexible, low-cost, scalable, printable manufacturing of nano material-based devices, such as roll to roll processing.

- *Maintaining A Viable Defense Industrial Base*, National Defense Industrial Association: Discusses the need to develop and implement new manufacturing process technology to enable new product development and promote greater productivity.

- *Manufacturing of Nanomaterials by CVD-FBR (Fluidized Bed Reactor) Process,* SRI International: Discusses the need for new manufacturing processes for nanomaterials for solid-state lighting applications.

- *Nanomanufacturing Processes Using Mechanosynthesis Applications*, NanoSource, Inc.: Discusses novel techniques for scalable manufacturing of carbon nanotubes.
- *Nanomanufacturing: The Missing Link Between Discovery and Products,* Liquidia Technologies: Discusses the need to address the challenges of manufacturing nanomaterials and of incorporating those materials into products especially organic nanomaterials.
- *Nanomaterials/Nanotechnology: Carbon Based Electronics Infrastructure*, Nantero, Inc.: Discusses the challenges in developing carbon based electronics manufacturing infrastructure.
- *Nanomaterials/Nanotechnology: Nanoelectronics to improve energy efficiency*, Everspin Technologies: Discusses the need for new processes in nanomaterials manufacturing for electronics applications.
- *National Nanomanufacturing Testbed Program: Integrated Hierarchical Nanomanufacturing,* University of Massachusetts at Amherst: Discusses the challenges of developing nanomanufacturing processes and the need for research on specific issues enabling nanomanufacturing.
- *New Approaches Toward Making Thin Film Solar Cells Cost Competitive*, AccuStrata, Inc.: Discusses the problem of process control for thin film deposition in solar cell manufacturing. The need for a very high degree of uniformity creates significant demands on the control of the process. Discusses the costs of lack of sufficient process controls and the need for improved, lower cost solar cells.
- *Next Generation Bioprocessing*: Univ. of Maryland/Baltimore County: Discusses biomanufacturing technologies state of the art and need for technologies.
- *Precision Additive Manufacturing of Medical Device*, The POM Group, Inc: Discusses the research challenges of applying precision engineering (e.g. direct metal deposition and laser ablation), custom design techniques, and tailoring coating properties to develop and manufacture patient specific medical implants.
- *Product-Use Prerequisites, Advanced Product Finishing*, Ms. Barbara E. Williams: Discusses the need for new finishing processes.
- *PVC Film Replacement*, Unileaf: Discusses the need for an advanced material to replace PVC film in a variety of industrial applications.
- *Reduce Energy Intensity and Demand, CO2 and GHG Emissions in Glassmaking Through Formula Changes*, Glass Manufacturing Industry Council: Discusses the potential to reduce energy usage and emissions in the glassmaking industry through changes in processing.
- *Reduction of CO2 emissions by more efficient cement production*, FEI Company: Discusses the challenges in the development of more efficient chemical processing for cement production.

- *Scalable Architecture for Nanotechnology*, Imiplex LLC: Discusses the need to develop the techniques and processes to ability to control the structural and functional properties of materials at the nanoscale level.

- *The Need in Industry for a Rapid and Effective Process Characterization Capability*, Atodyne Technologies LLC: Discusses the need for tools to characterize the operating range of processes to improve the conversion of raw materials into higher value materials; the paper discusses the fact that the lack of "optimized production processes …makes it very difficult to bring new relatively high volume materials to the marketplace".

- *The Need Research and Development in Manufacturing and Metrology,* University of North Carolina at Charlotte: Discusses the need to develop new manufacturing processes including tools and techniques to support those processes enabling higher precision in and integration of technologies across all scales – nano, micro, and meso.

- *A 21st Century approach to polymer production, and its impact on energy, environment, and jobs*, Tulane University: Discusses the need for developing manufacturing processes that use "online monitoring and control of polymerization reactions based on fundamental physical and chemical paradigms" (p.2).

- *Twenty First Century Practices: Processing and Repair of Composites, Adhesives, & Sealants,* AvPro, Inc.: Discusses the need for transformative processes in manufacturing of smart materials and composites.

- *Ultracapacitors Based on Novel Electrode Materials,* TRI/Princeton University: Discusses the need to develop new advanced materials to support the development of ultracapacitors for energy storage.

- *Ultrathin-Film Optical Characterization*, Brewer Science, Inc: Discusses the need to develop an optical modeling tool for material characterization and simulation for manufacturing processes.

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