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MANUFACTURING

Manufacturing and Biomanufacturing: Materials 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: Materials 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 for FY 2010 a new societal challenge focusing on transformative process improvements to manufacturing. In addition, the critical national need area of Manufacturing has been expanded to include 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 2009 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 retain competitiveness in the global marketplace, the United States must make investments in innovation, funding state-of-the-art technologies for manufacturing. Innovative research in key areas, including applications of novel materials and transformational changes in process engineering, is clearly required in order for U.S. manufacturers to retain global economic leadership.

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, there is a growing awareness of a critical need to support manufacturing. 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 materials advances*
2) *Predictive modeling for materials 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 materials 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: Materials 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.

In addition to the two societal challenges addressed in the TIP FY 2009 competition *Accelerating the Incorporation of Materials Advances into Manufacturing Processes,* the present paper also clarifies the need to address a third societal challenge for critical process advances in manufacturing and biomanufacturing.

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 health care related applications (e.g. imaging and therapeutics). Ceramics have new uses in improving electronic and photonic devices,[3] and glasses have many next-generation applications such as wireless communication, displays, optical telecommunication, integrated circuits, and ion exchange membranes for fuel cells.[4]

Overcoming scale-up issues of moving novel materials advances from the laboratory into manufacturing through “faster, better, cheaper” methods is just one way to help 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 retaining 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 fifth-largest economy in the world --- larger than China’s economy as a whole.[5] In 2008, the manufacturing sector represented 11.7 percent of the total GDP ($1,637 billion out of $14,264 billion total)[6] and supported 13.4 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.[7] 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.[8] 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.[9]

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 materials 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 room 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, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24]
  - 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 measurements 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**[25, 26, 27, 28, 29, 30, 31, 32]
  - Aerospace industry's emphasis on fuel efficiency favors use of polymer-matrix composites instead of 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)[33, 34, 35]
  - 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**[36, 37, 38, 39]
  - 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**[40, 41, 42, 43]
  - 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 "*materials advances*" as:

> *Materials that have been developed to the point that unique functionalities have been identified and these materials now need to 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:

> *A process that has a significant impact on capacity, output, quality, variability, efficiencies, performance, flexibility, etc., as well as a manufacturer's competitiveness and success.*

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 last year's 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: [44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59]

- 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 and 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 materials advances as national priorities. The current Administration has called for investments in *compelling advanced manufacturing strategies*[60] and for support of small- and medium-size manufacturers to *produce innovative new technologies*.[61]

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."[62]

In *Rising above the Gathering Storm,*[63] 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,*[64] 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. [65]

Numerous other organizations have also developed technology roadmaps for material advances and their processing. Groups as diverse as the National Science and Technology Council (NSTC),[66, 67] the Department of Energy's Industrial Technologies Program,[68, 69] and the aluminum[70] and steel[71, 72] 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 materials 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 materials advances and development of critical processes.

In NIST's three-year programmatic plan, the discussion of an R&D Investment Framework cites materials 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,[73] and new materials.

NIST's *Assessment of the U.S. Measurement System*[74] 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 biopharmaceuticals during manufacturing process)
- Self assembly of soft nanomaterials for bone and tissue replacement (e.g. development of nanocomposites, one of the advanced materials categories, for bio related applications)

NIST's involvement in the materials and process areas shows the importance of accelerating utilization of materials 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 biopharmaceutical production
- 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: Materials 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[75] or intelligent[76] manufacturing, sustainable manufacturing processes, specific manufacturing processes,[77, 78] 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 materials advances*; 2) *Predictive modeling for materials advances and materials processing; and 3) Critical process advances*.

1. **Process scale-up, integration, and design for materials advances.**
   New materials typically are developed in a laboratory setting, and then samples are given to end-users for alpha and beta testing. During this testing phase, it can take considerable time and experimentation to understand how the materials can be incorporated into a new product in a way that maintains and utilizes its unique functionality. Scaling-up from laboratory quantities to larger volumes, validating properties, and then incorporating the materials into product manufacturing lines is often non-linear and does not follow straightforward scaling laws, due to the unique functionality that has been obtained from the materials advances.

2. **Predictive modeling for materials advances and materials processing.**
   Predictive modeling capabilities are key to developing new processes, scaling-up these processes, and understanding how to utilize a materials advance’s unique functionality. Modeling capabilities are needed principally to:

   a. Analyze and understand why a newly discovered material does what 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 materials advances into new and more advanced products as well as 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 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 biopharmaceutical manufacturing 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 materials advances***, new processes will need to be developed. These processes will increase to 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 materials 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.

The first two proposed challenges for *Manufacturing and Biomanufacturing: Materials Advances and Critical Processes* require research in new technologies. The table below can be used to illustrate possible relationships between key challenges. TIP would expect solutions to the first two challenges to map into one or more cells in Table 1 below. It is possible that the areas below could also impact or involve health care applications and/or biomanufacturing approaches.

TABLE 1:

Technological Needs		**Nanomaterials**	**Superalloys, Alloys & Smart Materials**	**Composites**	**Ceramics**	**Glasses**
Processing of Materials	**Scale-up from Laboratory Quantities / Controls**					
	Incorporate into New Uses / Maintain Functionality					
Predictive Modeling	**Rules / Understand Why It Does What It Does**					
	Process Modeling / Design Tools					

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.

A table for guidance on categorizing applicable processes and pathways to critical processes advances is given below. TIP would expect solutions to the third societal challenge to map into one or more of the cells in Table 2 below.

TABLE 2:

State-Of-The-Art Approaches to Critical Manufacturing Process Advances for:	**Process**		
	Batch	**Discrete**	**Continuous**
Improving quality			
Increasing throughput			
Reducing costs			
Enhancing sustainability			
Enabling new capabilities			
Improving agility			
Other improvements			

A key characteristic to address for all three societal challenges above is how the outcomes of the research will enable manufacturers to produce materials advances and products faster, better, more cost-effectively, and sustainably, as well as leverage new uses for the materials advances or the intended products. The third societal challenge is not limited to materials processes or classes associated with Table 1 above.

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:

- 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 do what 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 biopharmaceutical production

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: Materials 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 materials advances; 2) predictive modeling for materials advances and materials processing; and 3) critical process advances. The results of these efforts are expected to inspire revolutionary uses of materials 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.

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