U.S. Department of Health and Human Services | Assistant Secretary for Preparedness and Response
Biomedical Advanced Research and Development Authority

BARDA Strategic Plan 2011-2016

Inside front cover
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BARDA Strategic Plan 2011-2016

CONTENTS

BARDA STRATEGIC PLAN 2011-2016

Message from the BARDA Director

Dear Colleagues,

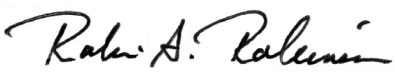
The nation has endeavored over the past ten years to become better prepared for the medical consequences of catastrophic events such as bioterrorist events and pandemic influenza. During that time period Project BioShield, The National Strategy for Pandemic Influenza, and the Biomedical Advanced Research and Development Authority have emerged to support the development and acquisition of medical countermeasures (MCMs) and the domestic manufacturing capacity to prepare for and respond to an emergency. Where very limited medical countermeasures were available in 2001, there are now vaccines, therapeutic drugs, and diagnostic devices for anthrax, smallpox, botulism, and pandemic influenza and a robust pipeline of products in development for these and other threats. While only one manufacturing site existed in the U.S. during the influenza vaccine shortage of 2004, now there are three with more on the way. Yet there is much more work to be done, and a clear path is needed to guide the way.

Thus I am pleased to provide an update of the BARDA Strategic Plan for 2011-2016. The Plan describes our strategic goals and vision to accomplish BARDA's mission over the next five years and beyond to develop and provide medical countermeasures for Chemical, Biological, Radiological, and Nuclear threats, pandemic influenza, and emerging infectious diseases. The implementation measures to achieve these strategic goals include support of product advanced development, stockpile acquisition, manufacturing surge capacity infrastructure building, and product innovation. These medical countermeasures include vaccines, biological and small molecule therapeutics, antiviral drugs and antibiotics, diagnostics, respiratory devices, and other medical supplies.

As BARDA completes its fifth year of existence, the results of our advanced development support are becoming evident with a robust product development pipeline for nearly all threats. Many of these products in the development pipeline will become mature enough for acquisition and regulatory review over the next five years. Initiatives recommended by the 2010 Public Health Emergency Medical Countermeasure Enterprise Review are expected to enable more of the MCM products to become available as FDA-licensed approved or cleared products. BARDA will lead several of these initiatives including the establishment of Centers for Innovation in Advanced Development and Manufacturing and the Medical Countermeasures Strategic Investor. Greater emphasis on multi-purpose MCMs and more flexible and innovative manufacturing technologies will make improved and greater quantities of MCMs available sooner. MCMs and manufacturing capabilities that afford the nation the ability to respond immediately to known and unknown threats will be high priorities.

The BARDA Strategic Plan is a dynamic process with the steadfast aim to enhance national MCM preparedness and the flexibility to adopt better technologies, meet unforeseen challenges, and avoid unnecessary risks. MCM preparedness and response and this Plan are the results of the dedicated professionals at BARDA, ASPR, and across federal, State, local, and industry sectors. I wish to thank them for their tireless efforts to ensure that ours is "a nation prepared."

Respectfully,



Robin A. Robinson, Ph.D., Director

Introduction

WITHIN THE LAST TEN YEARS, THE UNITED STATES HAS experienced an intentional attack with a biological agent in the form of the anthrax letters as well as naturally emerging outbreaks of high-consequence infectious diseases, including pandemic influenza and SARS. These events represented national security threats and public health emergencies. The past decade has also witnessed the dramatic spread of antimicrobial resistance and community outbreaks of multidrug-resistant bacteria that had previously been confined to hospitals. Concerns persist about the potential use of chemical, biological, radiological and nuclear agents by terrorists. Effective medical countermeasures such as vaccines, antimicrobials, therapeutics, and diagnostics have the potential to reduce the impact of such threats and are a bulwark of our national defense and public health emergency preparedness.

The mission of the Biomedical Advanced Research and Development Authority (BARDA) is *to develop and procure medical countermeasures that address the public health and medical consequences of chemical, biological, radiological, and nuclear (CBRN) accidents, incidents and attacks, pandemic influenza, and emerging infectious diseases.*

Specifically, BARDA supports the advanced development and procurement of drugs, vaccines and other products that are considered priorities for national health security. BARDA funding bridges the "valley of death" characterizing the late stages of product development. BARDA's support ensures continuity of funding at a critical point for medical countermeasures developed by industry or emerging from the basic research and preclinical development activities sponsored by the National Institutes of Health (NIH). In procuring medical countermeasures for the Strategic National Stockpile, BARDA enhances the capabilities of the Centers for Disease Control and Prevention (CDC) to organize an effective response.

BARDA is a core component of the Office of the Assistant Secretary for Preparedness and Response (ASPR) and as such contributes to the broader ASPR mission to "Lead the country in preparing for, responding to, and recovering from the adverse health effects of emergencies and disasters by supporting our communities' ability to withstand adversity, strengthening our health and response systems, and enhancing national health security."[1]

The first *BARDA Strategic Plan for Medical Countermeasure Research, Development, and Procurement (Draft)* was published in July 2007. The specific goals of the 2007 Plan included aligning and coordinating BARDA goals and programs with key pandemic influenza and CBRN strategy documents; developing an HHS Public Health Emergency Medical Countermeasure Enterprise CBRN implementation plan; and establishing programs that promote innovation in MCM development.

The 2011 BARDA Strategic Plan builds on BARDA's successes in achieving those goals, defines BARDA's vision, and lays out a series of capability goals over the next five years (2011-2016). This Plan reflects the dynamic evolution of BARDA's mission and responsibilities, since its establishment in early 2007 and is informed by the *National Health Security Strategy* (NHSS; December 2009)[2], *The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs* (PHEMCE Review; August 2010)[3], and the many lessons learned from the 2009 H1N1 pandemic influenza response.

[1] HHS Assistant Secretary for Preparedness and Response Strategic Plan 2011-2015. http://www.phe.gov/about/aspr/strategic-plan/Pages/default.aspx

[2] National Health Security Strategy of the United States of America. U.S. Department of Health and Human Services. 2009. http://www.phe.gov/Preparedness/planning/authority/nhss/strategy/Documents/nhss-final.pdf

[3] *The Public Health Emergency Medical Countermeasures Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs*. U.S. Department of Health and Human Services. 2010. https://www.medicalcountermeasures.gov/documents/MCMReviewFinalcover-508.pdf

WHO WE ARE AND WHAT WE DO

The Biomedical Advanced Research and Development Authority is the component of the Public Health Emergency Medical Countermeasures Enterprise that focuses on the advanced development, manufacturing and acquisition of medical countermeasures against chemical, biological, radiological and nuclear (CBRN) threats, pandemic influenza, and emerging infectious diseases. BARDA's staff includes experts in the fields of physical, chemical and biological sciences, engineering, clinical medicine, public health, product development, regulatory affairs, and program management. The Pandemic and All-Hazards Preparedness Act (PAHPA) established BARDA in December 2006. BARDA oversees the Project BioShield program and Special Reserve Fund and is charged by statute with (1) promoting collaboration and communication between the U.S. Government and interested parties in the advanced development and licensure of needed medical countermeasures; (2) directing and coordinating the countermeasure and product advanced research and development activities of the U.S. Department of Health and Human Services (HHS); (3) facilitating medical countermeasure development by providing advice or directing interested parties to the relevant Centers of the U.S. Food and Drug Administration (FDA); and (4) supporting innovation through strategic initiatives and investment in technologies and research tools that facilitate countermeasure development.

PAHPA established a dual mandate for BARDA. BARDA is charged with coordinating the development of, and bridging the "valley of death" for, MCMs determined to be critical to the Nation's health security. It is important to note that many such MCMs lack meaningful commercial markets and without U.S. Government support would be unlikely candidates for development. In supporting their development, BARDA fills the gap between NIH, which supports basic and preclinical research, and CDC, which develops utilization plans and deploys MCMs during public health emergencies. BARDA fulfills its mission by supporting advanced research and development of needed medical countermeasures; working in collaboration with manufacturers, the NIH, the CDC, the FDA, and the Departments of Defense (DoD) and Homeland Security (DHS); supporting technology innovation through strategic initiatives; and overseeing Project BioShield acquisitions.

BARDA is comprised currently of the Office of the Director and seven functional divisions that oversee BARDA's programmatic activities. These divisions include

- Division of Chemical, Biological, Radiological and Nuclear (CBRN) Countermeasures
- Division of Influenza
- Division of Strategic Science and Technology
- Division of Manufacturing, Facilities and Engineering
- Division of Regulatory and Quality Affairs
- Division of Clinical Studies
- Division of Modeling

Additionally, to address issues relating to countermeasure development that cut across divisional boundaries, BARDA operates collaboratively in "matrix teams" in the areas of vaccines, biological therapeutics, small molecule therapeutics, and diagnostics. These matrix teams help knit the BARDA organization together and facilitate sharing of information and best practices.

BARDA'S FUTURE

BARDA is committed to improving its workforce, increasing the expertise and skills of BARDA personnel, and helping to prepare the pharmaceutical industry to meet the challenges of the 21st Century. The investment BARDA makes now in developing needed infrastructure, capabilities, processes, and human resources will pay off in the long run by enhancing national preparedness to meet the public health threats of the future.

Continually looking forward, scanning the horizon for new technologies, and striving to develop a fast, flexible and efficient armamentarium of medical countermeasure capabilities and products will be key contributing factors to BARDA's success in addressing medical countermeasure requirements for the nation. BARDA

will address these current and evolving requirements, aggressively seek out and support promising technology and platforms, and facilitate collaboration across HHS and other Federal Departments and agencies participating in medical countermeasure research and development while striving continually for greater overall transparency.

CONTEXT OF THE BARDA STRATEGIC PLAN

The BARDA strategic plan is guided by the priorities of the Administration and of ASPR and BARDA leadership, and by other guidance including the U.S. Department of Health and Human Services Strategic Plan, governing legislation, Presidential Policy Directives, the 2009 NHSS, the 2010 PHEMCE Review, and the 2011 *HHS Assistant Secretary for Preparedness and Response Strategic Plan 2011-2015* (ASPR Strategic Plan). The NHSS establishes a framework for national efforts, to promote health security and encompasses BARDA's mission. National health security is a state in which the nation and its people are prepared for, protected from and resilient in the face of health threats or incidents with potentially negative health consequences. All elements of this strategic plan align with and support the BARDA role in contributing to national health security under the NHSS and, as specified in PAHPA, the BARDA Strategic Plan is considered to be incorporated as part of the NHSS.

ORGANIZATION OF THIS PLAN

This strategic plan sets the direction for BARDA over the next five years. Five strategic goals define the highest level aims of BARDA, each one is supported by strategies for accomplishing that goal. These goals are interrelated and derive from the mission outlined in the PHEMCE Review that "Our nation must have the nimble, flexible capacity to produce medical countermeasures rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease."

A number of themes cut across one or more of the strategic goals. Cultivating public-private partnerships, for example, is a critical element in almost every aspect of BARDA's work. Developing tools and processes to facilitate systematic portfolio management and program and project evaluation is an important priority for BARDA, given BARDA's broad mandate and foreseeable budgetary constraints. In pursuing its mandate to develop medical countermeasures to protect civilian populations, BARDA must also address the needs of vulnerable populations such as children, pregnant women, persons with compromised immune systems, and the elderly. These and other cross-cutting issues have been considered as each one of the five strategic goals was developed and are reflected in the guiding principles.

IMPLEMENTATION

BARDA will implement this strategic plan with full involvement of its leadership and a firm commitment to turning strategy into action, tracking progress, and correcting course when needed. The strategic plan maps out a broad five-year strategic direction. More detailed actions for accomplishing the goals and strategies as well performance measures and milestones will be developed and annually reviewed by BARDA staff and leadership. All BARDA employees are critical to the organization's success, and should see themselves and their work directly in one or more of the goals and strategies. BARDA divisions and program teams may develop even more granular action plans, and budgets will be formulated and executed in line with strategic priorities.

Like the HHS and ASPR strategic plans, the BARDA strategic plan will be published online and updated periodically to reflect evolving activities and progress toward goals. BARDA's partners and the public will be able to see the latest information on priorities and accomplishments, reinforcing the plan's purpose as an evolving, living tool for guiding decision making and action.

BARDA'S Vision, Mission, and Values

BARDA'S OVERARCHING VISION IS OF A NATION WITH the capability to respond quickly and effectively to deliberate, natural, and emerging threats so as to minimize their impact and recover promptly. A critical enabling factor for the realization of this vision is the existence of a robust domestic pharmaceutical and biotechnology sector that actively collaborates with the U.S. Government to address unmet medical countermeasure and public health requirements.

BARDA's vision for the next five years is to enhance the capability of the U.S. Government to respond quickly to both known and emerging threats by supporting the development of a comprehensive portfolio of medical countermeasures, needed manufacturing infrastructure, and countermeasure production platforms while establishing an affordable and sustainable foundation for the maintenance and future operations of the PHEMCE.

BARDA's mission is to develop and procure needed medical countermeasures, including vaccines, therapeutics, diagnostics, and non-pharmaceutical countermeasures, against a broad array of public health threats, whether natural or intentional in origin. BARDA was created to address gaps in the U.S. Government medical countermeasure development and procurement process and to bridge the "valley of death" that separates candidates identified in early research from potential FDA licensure/approval by providing funding, technical support and services necessary to advance candidate products through the developmental pipeline.

BARDA supports the ASPR Values Statement and endeavors to embody these values in its efforts to fulfill its mission and realize its vision.

ASPR VALUES

Diversity

We are dedicated to creating and maintaining an open, inclusive environment that nurtures differing world views.

Excellence

We demonstrate quality in what we do, set high expectations for ourselves and others, and innovate and improve through the introduction of new concepts and methods.

Integrity

We are honest and reliable, we hold ourselves accountable, and our actions and decisions are guided by fairness and transparency.

Leadership

We motivate and inspire our colleagues to achieve success through shared vision and unity of effort.

Public Service

We commit to serve our country, our community, and our fellow citizens, and are accountable to the public for our actions

Respect

We treat people with dignity and consideration and listen openly to what others have to say, to benefit from varied perspectives and create environments that foster trust.

Teamwork

We support and motivate each other, achieving more together than we can alone.

BARDA Guiding Principles

BARDA WILL PURSUE ITS STRATEGIC GOALS THROUGH an approach comprised of the following core principles.

COLLABORATING IN PUBLIC-PRIVATE PARTNERSHIPS

The PHEMCE Review highlighted the critical role of public-private partnerships in addressing the challenges that arise throughout the product development process and in rapidly adapting to new technologies and changing needs. BARDA's commitment to public-private partnerships is deep-rooted and extends across its entire portfolio.

Where vaccine and biological therapeutics manufacturing capacity is concerned, BARDA will continue to enter into public-private partnerships with manufacturers to build and/or retrofit medical countermeasure production facilities within the U.S., increasing domestic access to medical countermeasures. Internationally, BARDA will maintain its financial and technical support of the WHO Global Action Plan, working in concert with the Developing Countries Vaccine Manufacturers Network and other partners to expand influenza vaccine manufacturing capacity in developing countries.

BARDA will establish its Centers of Innovation for Advanced Development and Manufacturing as partnerships in which the U.S. Government and private sector partners share facility construction costs, collaboratively facilitate medical countermeasure product development, and jointly ensure domestic vaccine manufacturing surge capacity. These Centers will provide advanced development and manufacturing capabilities for medical countermeasures to address both national security and public health needs on a cost-effective, reliable, and sustainable basis. In order to minimize delays in the availability of critical medical countermeasures during public health emergencies, BARDA will establish a network of providers to formulate, fill, and finish bulk vaccine product provided by primary manufacturers in the event that the primary manufacturers lack sufficient surge capacity of their own.

PROMOTING PLATFORM TECHNOLOGIES

BARDA is supporting the development of novel platform technologies that provide flexible systems for the production of medical countermeasures against a variety of threats. BARDA will also leverage established programs to maximize the value of current investments in technological innovations. Strategic support for platform technologies will greatly enhance the value provided by BARDA investments and position the U.S. Government to respond more effectively to the unknown threats of the future.

As an illustration, adjuvants, which can be used to increase the supply of pandemic influenza vaccine, may have the potential to enhance the efficacy of vaccines against biological threats or emerging diseases and may be essential components of next-generation recombinant protein influenza vaccines. By supporting the development and use of adjuvant "platforms" to enhance the efficacy of currently licensed vaccines, BARDA is also supporting the establishment of a regulatory pathway for other vaccines that exploit adjuvant technology – a critical step in speeding the availability of new vaccines against a broad array of threats.

PRIORITIZING MULTIPURPOSE PRODUCTS

BARDA is committed, where feasible, to developing products that demonstrate efficacy against a wide range of specified threats and will seek out products

with such potential through its Strategic Science and Technology program. Investing in multi-use products such as broad-spectrum therapeutics and diagnostic platforms that can find durable and well-defined commercial markets and leverage market forces will greatly facilitate the development of medical countermeasures for use in public health emergencies and enhance long-term sustainability for the PHEMCE.

BARDA's Broad Spectrum Antimicrobial Program was established in January 2010 and is focused on developing novel antibacterial and antiviral drugs for the treatment or prevention of disease caused by currently defined and future biological threats. Recognizing the immediate value of new antimicrobials in addressing the increasingly prevalent public health threat of antibiotic resistance, as well as the likelihood that antimicrobial resistance will complicate primary treatment of a wide array of threats, BARDA is supporting the development of public-private partnerships for the development of novel antimicrobials. Through these partnerships, BARDA will support the development of candidate antimicrobials for their commercial, clinically prevalent infectious disease indications, as long as our private sector partners concomitantly support the development of these products for biodefense threat agent indications. By adopting this approach, BARDA will support the development of new classes of antimicrobials, increase the number of antimicrobial drugs in the developmental pipeline, address the important and immediate threat of antimicrobial resistance, and prepare the nation for the predictable threat of biological terrorism and the unpredictable threat of emerging infectious diseases.

Many other BARDA projects demonstrate the variety of ways in which "dual utility" and multi-use value can be achieved. For example, next-generation, low-cost, easy-to-use ventilators and improved respiratory protective devices all have applications against a wide array of threats. BARDA will continue to seek out multipurpose products and support their development in order to enhance our Nation's ability to respond effectively to the broad array of threats we face.

USING CASE MANAGEMENT AND A MATRIXED ORGANIZATIONAL STRUCTURE

The PHEMCE Review requested by the Secretary of HHS included recommendations to adopt a new, more intensive approach ("case management") to program and project management. Under case management, BARDA leads the effort to ensure that intra- and inter-agency stakeholders are kept abreast of product development progress and issues in the identified programs. BARDA is adopting a rigorous approach to project, program, and portfolio management that will establish cost and schedule metrics for each phase of product development, and allow the identification of best practices and earlier interventions in troubled programs. In Process Review of program contracts occur on a regular basis by a team of experts from HHS and PHEMCE partners who provide critical input on key decisions in program development and guidance on issues that may arise during product development.

When challenges with product development arise, BARDA employs a case management approach of intensive support and guidance to private sector partners, which also entails appropriate input and expertise from relevant federal agencies (BARDA, CDC, DoD, FDA, and NIH). Case management of BARDA programs is essential to the proper stewardship of the funding provided for these endeavors and will ensure that all U.S. Government stakeholders are aware of products being developed and the long-term budgetary impact those products may have on other agencies through the course of their life cycle.

BARDA has adopted a matrix-like organizational structure that makes the specialized capabilities of its different components available to project managers throughout the organization. This matrix-like organizational structure will maximize efficiency and collaboration across BARDA, promote a culture of continual process improvement, and facilitate the ultimate application of case management to all supported programs.

ENSURING AN INTEGRATED PORTFOLIO WITH DOD

In addition to the management of specific programs under the effort highlighted above, BARDA, in collaboration with its HHS and DoD partners, has adopted an integrated approach to co-managing the nation's aggregate portfolio of medical countermeasure development programs for CBRN threats. The overall goal is to optimize the use of resources to address the broad range of common threats and requirements with greater efficiency and effectiveness. Although DoD and HHS each have certain unique requirements due to their different missions and focus, there are many areas of convergent requirements for products or capabilities where resources and information will be appropriately shared to optimize investments and preclude unnecessary redundancies. This integrated approach will ensure balance and completeness across all agencies funding the research, development, and procurement of medical countermeasures for CBRN threats.

Goals and Strategies

GOAL 1

An advanced development pipeline replete with medical countermeasures and platforms to address unmet public health needs, emphasizing innovation, flexibility, multi-purpose and broad spectrum application, and long-term sustainability

Since its inception, BARDA has prioritized the development and procurement of medical countermeasures for the highest risk threats, including pandemic influenza and terrorist use of chemical, biological, radiological, or nuclear materials. The Pandemic and All-Hazards Preparedness Act additionally called for the public health and medical needs of at-risk individuals to be taken into account in developing a national stockpile of medical countermeasures. Consistent with statutory requirements, BARDA supports the advanced development of medical countermeasures for all populations, with the goal of making them available for use as needed during public health emergencies.

BARDA's CBRN programs have focused on developing medical countermeasures to meet the requirements determined to be necessary to address the 13 Material Threats identified by the DHS in accordance with Project BioShield. BARDA's influenza program has contributed to pandemic preparedness by supporting the development of improved and/or next-generation influenza vaccines, antiviral medications, ventilators, and other non-pharmaceutical countermeasures; stockpiles of pre-pandemic vaccines and antiviral medications; and increased domestic influenza vaccine manufacturing capacity. More recently, BARDA has begun to address the threat of antimicrobial resistance, emerging infectious diseases, and other novel threats by initiating programs supporting the development of broad-spectrum antimicrobials and technologies and platforms with multi-use potential. BARDA will maintain this three-pronged focus on CBRN threats, pandemic influenza, and emerging infectious diseases, modifying its current portfolio as needed to (1) ensure that the medical countermeasure needs of all populations are addressed and (2) enhance long-term sustainability of our preparedness posture.

GOAL 1 STRATEGIES

- Promote development and acquisition of needed medical countermeasures by
  - Maintaining and where appropriate expanding the portfolio of medical countermeasures against CBRN threats and pandemic influenza
  - Establishing a program to support the development of platforms and countermeasures to address the threats of emerging infectious diseases and antimicrobial resistance
  - Supporting the development of medical countermeasures suitable for use in special populations such as children, pregnant women, the elderly, and persons with compromised immune systems, prioritizing and supporting projects that provide benefits to all populations where possible and exploring focused development projects or studies where necessary.
  - Improving processes governing the solicitation, review, and award of medical countermeasure contracts
- Promote the development of flexible, multiproduct platforms and countermeasures with broad-spectrum activity and application by
  - Expanding BARDA's Broad Spectrum Antimicrobials and Innovations programs to develop a robust portfolio of countermeasures to address an array of known and unknown threats

- Investing in the development of host-directed therapeutics, such as small molecule immune modulators, anti-inflammatory agents, and regulators of innate immunity

- Invest more strategically by
  - Supporting the development of robust diagnostic capabilities in order to improve surveillance, facilitate earlier treatment, and minimize medical countermeasure wastage
  - Engaging in more proactive outreach, identifying candidate technologies and innovations that promise greater sustainability or that BARDA wishes to see advance because of portfolio requirements
  - Establishing a medical countermeasures Strategic Investor that will pursue the strategic objectives of the PHEMCE while acting as, and providing all the services and benefits of, a venture capital firm

GOAL 2

A capability base to provide enabling core services to medical countermeasure innovators

Considerable expertise and capabilities are required to overcome the technical, regulatory, manufacturing, commercialization, and business challenges inherent in the development of innovative medical countermeasure candidates. Over the past ten years, innovative companies developing CBRN medical countermeasures have encountered many challenges moving products along the process development, manufacturing, and regulatory pathways. BARDA already provides an array of services to manufacturers and innovators of medical countermeasures but has observed that many of these companies would benefit from additional support in moving from laboratory to commercial scale production and clinical evaluation through the regulatory approval process.

GOAL 2 STRATEGIES

- Provide core product development services by
  - Establishing the Centers for Innovation in Advanced Development and Manufacturing (CIADM), which will have the capability to support analytical testing, scale-up manufacturing, manufacturing process optimization; provide regulatory and quality expertise and analytical and process validation support; and produce clinical investigational lots, engineering lots, process validation lots, and commercial-scale lots for stockpiling
  - Developing and qualifying animal models through the new Animal Models Development Program
  - Performing GLP efficacy evaluation and testing of CBRN countermeasures in qualified animal models

- Provide biotechnology firms working on medical countermeasures access to financial and business services by establishing a medical countermeasures Strategic Investor that will serve as a non-profit venture capital firm

- Reduce regulatory barriers and clarify regulatory pathways by
  - Assisting private sector partners in the development of regulatory strategies and design and execution of clinical studies for needed medical countermeasures
  - Involving FDA experts in providing technical assistance on projects supported by CIADM
  - Contributing to the development and implementation of a PHEMCE regulatory science agenda

- Promote the development of a highly trained biopharmaceutical workforce by:
  - Incorporating training in biopharmaceutical science and other workforce development opportunities into the day-to-day functions of the CIADM

GOAL 3

Agile, robust and sustainable U.S. manufacturing infrastructure capable of rapidly producing vaccines and other biologics against pandemic influenza and other emerging threats

The 2005 *National Strategy for Pandemic Influenza* established a commitment to making vaccine available for all Americans within six months of the emergence of a virus with pandemic potential. BARDA has made significant progress towards increasing and securing domestic manufacturing capacity for pandemic influenza vaccine development. However, the recent response to 2009 H1N1 shows that we are still hampered by the limits of current technology. The first domestic cases of 2009 H1N1 influenza were identified in April and the pandemic peaked about six months later, in late October. Despite an intensive effort to develop a pandemic vaccine, the 2009 H1N1 vaccine arrived too late to have a significant effect on the dynamics of the fall disease wave. Influenza vaccines licensed in the U.S. use egg-based technology that is more than 50 years old and a substantial portion of the manufacturing capacity is based overseas.

Consistent with recommendations from the President's Council of Advisors on Science and Technology in its August 2010 *Report to the President on Reengineering the Influenza Vaccine Production Enterprise to Meet the Challenges of Pandemic Influenza* BARDA is working with several partners to develop more modern platforms for manufacturing influenza vaccines and this investment is beginning to pay off. In 2011, two manufacturers plan to file Biologic License Applications (BLAs) for cell-based influenza vaccines, with new vaccines based on recombinant technologies to come in following years. Products based on these newer, faster, more scalable technologies will move the field forward and significantly increase the flexibility, surge capacity, and reliability of influenza vaccine production increasing and securing domestic manufacturing capacity for pandemic influenza vaccine development.

GOAL 3 STRATEGIES

- Speed the delivery of pandemic influenza vaccines following the emergence of an influenza virus with pandemic potential by
  - Developing improved vaccine seed strains, sterility tests, and potency reagents and testing
  - Expanding the number of FDA-licensed influenza vaccines, to include cell-based products
  - Supporting the development of faster, more scalable next-generation recombinant influenza vaccines
  - Completing the development and evaluation of adjuvanted pandemic influenza vaccines
  - Optimizing the BARDA emergency manufacturing response
- Increase domestic manufacturing surge capacity for pandemic influenza by
  - Supporting the construction or retrofitting of influenza vaccine manufacturing facilities
  - Supporting the development of next-generation manufacturing processes
  - Securing the availability of essential vaccine supplies and services by enhancing domestic fill finish networks and ensuring a year-round supply of eggs for pandemic vaccine surge production
  - Requiring CIADM awardees to maintain a capability to manufacture pandemic influenza vaccine
- As in GOAL 2, promote the development of a highly trained biopharmaceutical workforce to ensure commercial-scale manufacturing capacity by
  - Incorporating training in biopharmaceutical science and other workforce development opportunities into the day-to-day functions of the CIADM
  - Sponsoring academic training programs in bio-manufacturing techniques as part of a broader initiative to build influenza vaccine manufacturing capacity in developing countries

GOAL 4

Responsive and nimble programs and capabilities to address novel and emerging threats

The Pandemic and All-Hazards Preparedness Act charges BARDA with the advanced development of medical countermeasures for emerging infectious disease threats, which come in many forms. New and lethal infectious diseases, such as MRSA, Dengue, Ebola, SARS, and Nipah virus, continue to emerge in nature. The extensive use of antiviral and antibacterial agents has resulted in the propagation of drug resistant strains of bacteria and viruses and promoted the evolution of extensively drug-resistant strains of many common pathogens. As has been the case with past influenza pandemics where secondary infections with resistant organisms accounted for a significant proportion of deaths, drug-resistant strains are likely to complicate the treatment of CBRN-caused illnesses. Where deliberate threats are concerned, advances in genetic engineering and synthetic biology may provide a means for bioterrorists to generate more dangerous pathogens through the insertion of virulence factors or drug-resistance genes.

Preparing for the threat of previously unknown emerging diseases, whatever the source, requires a different approach than preparing for known threats or pathogens. To address these evolving threats to public health, acquisition of broad spectrum antibiotic and antiviral medications and new classes of antimicrobials, including host-directed therapeutics and small molecule immune modulators, will be a major focus of BARDA's efforts in coming years.

Over the next five years, building on the experiences of the CBRN, Influenza, and Strategic Science and Technology Divisions, BARDA will enhance its efforts to provide solutions to the growing problem of emerging pathogens and antimicrobial resistance. In the near term, BARDA is developing programs to address the threat posed by multidrug-resistant pathogens and future unknown biological threats. A key element of this effort is identifying and supporting the development of broad spectrum antimicrobials. In addition, BARDA's next-generation influenza antiviral drug advanced development program is pursuing new classes of drugs and innovative candidate antiviral therapies that will be less susceptible to viral resistance.

GOAL 4 STRATEGIES

- Develop a formal methodology to identify medical countermeasure projects that are appropriate for inclusion in the BARDA Emerging Infectious Diseases portfolio
- Implement a long-term strategy to address previously undefined threats by
  - Expanding BARDA's Broad Spectrum Antimicrobials and Innovations programs
  - Emphasizing the development of multipurpose and/or broad-spectrum products
  - Investing in capabilities (platforms and facilities) for the rapid development and production of countermeasures
  - Investing in the development of host- directed therapeutics, such as small molecule immune modulators, anti-inflammatory agents, and regulators of innate immunity
  - As in GOAL 1, establishing a medical countermeasures Strategic Investor that will pursue the strategic objectives of the PHEMCE while acting as, and providing all the services and benefits of, a venture capital firm
- Combat the growing problem of antimicrobial resistance through development of new antimicrobials and innovative therapeutics by pursuing new classes of drugs and innovative antimicrobial therapies that will be less susceptible to drug resistance

GOAL 5

A ready capability to develop, manufacture and facilitate distribution of medical countermeasures during public health emergencies

Ensuring the availability of safe and effective medical countermeasures during public health emergencies is BARDA's core mission. Supporting the scientific development of vaccines, therapeutics, and diagnostics is only one aspect of BARDA's role in promoting pandemic influenza and public health preparedness. The 2009 H1N1 pandemic underscored the critical importance of advanced development, manufacturing, and distribution planning. During the pandemic, BARDA worked in coordination with the NIH, FDA and CDC to procure, test, license and deliver the vaccines and antiviral drugs deployed as part of the U.S. Government response.

Ultimately, 138 million doses of licensed 2009 H1N1 vaccine were produced and distributed for use by the U.S. civilian population, 2.7 million doses for DoD, and 16.9 million doses for international assistance. As part of a contingency-based public health response, BARDA also purchased supplies of adjuvants to be used, if necessary, as part of a pandemic vaccine and additional supplies of antiviral medications to replenish treatment courses that were distributed from the Strategic National Stockpile, focusing on pediatric formulations to address critical needs for this population. BARDA's collaborations with domestic vaccine manufacturers and coordination with the response activities of CDC and industry partners to ensure effective and timely distribution of pandemic countermeasures within regional, state, and tribal jurisdictions were critical enablers of the overall response to the pandemic.

GOAL 5 STRATEGIES

- Refine BARDA planning and readiness capabilities by drawing on the many lessons learned during the pandemic
- In concert with the ASPR Office of Preparedness and Emergency Operations and in close coordination with CDC, FDA, and other U.S. Government departments and agencies, develop comprehensive plans that will facilitate the response to future pandemics, CBRN events, and emerging epidemics by
  - Establishing mechanisms for interfacing with medical countermeasure manufacturers and distributors during a public health emergency
  - Establishing mechanisms for positioning BARDA medical countermeasure production subject matter experts in manufacturing plants as needed
  - Providing a framework for developing and validating emergency funding requests
  - Facilitating the prompt evaluation of investigational products for emergency use authorization as warranted.
- Exercise these readiness capabilities plans to ensure that they are fully consistent with existing ASPR and HHS response plans as well as the overarching National Response Framework

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