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**REPORT TO THE U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
CUMULATIVE PROGRESS REPORT FOR AWARD NUMBER W81XWH—10-1-0140
FORUM ON MICROBIAL THREATS
MARCH 2011 TO MARCH 2012**

Introduction

The Forum was established to provide a structured opportunity for stakeholder discussion and scrutiny of critical—and possibly contentious—scientific and policy issues of shared concern related to research on and the prevention, detection, and management of infectious diseases and dangerous pathogens. Because of the unofficial nature of its deliberations coupled with the neutrality of the Institute of Medicine, the Forum remains uniquely positioned to stimulate original thinking about new as well as long-standing problems in these areas. Indeed, it is expected that the Forum will continue to:

- promote a regular and ongoing exchange of information and ideas about critical issues among policymakers, public and private sector leaders, individuals, and groups who shape and influence public policy and opinion;
- clarify policy and research issues and identify options that require additional emphasis and research, and encourage leading scientists, public health professionals, medical care providers, private industry, and others to further explore these areas;
- inform public and private sector decision- and policymakers about the scientific basis and public health needs and understanding related to infectious diseases in the United States and worldwide, and;
- ◆ formulate priority and collaborative initiatives that require in-depth exploration, review, and/or analysis of existing data and research, particularly in instances where new strategies are necessary to advance progress on the emergence, detection, and response to infectious diseases.

Framework of the Forum

The Forum's work continually evolves to address the ever-changing challenges at the intersection of infectious diseases and human health, development, and security. Through public debate and private deliberation, the activities of the Forum seek to facilitate open discussion and inquiry into the most pressing and cross-cutting set of issues in light of recent or groundbreaking advances that may lead to further innovation or resolution. In recent years, the result of such cross-sector dialogue has fostered action toward addressing priority issues in infectious disease research and public health policy; the use of new scientific and policy tools, and; opportunities for more effective collaboration between the private and public sectors represented on the Forum. The activities of the Forum have highlighted and brought to the fore some of the most important infectious disease issues of the last decade that have included cutting-edge research findings and deliberations that provide not only the most up-to-date information, but also models that are useful in predicting what is not yet fully understood.

Building on the findings and recommendations of the 2003 IOM report, *Microbial Threats to Health: Emergence, Detection, and Response*, the Forum will continue to be a regularly convening mechanism of representatives from the upper policy levels of all the major stakeholders who represent a wide range of organizational interests and a breadth of scientific and policy expertise. Forum members serve anywhere from an 18-month to a three-year term. The strength of the Forum activity rests in the diversity of its expert membership and the commitment of its individual members to attend these activities on a regular and continuing basis. Individuals and representatives from organizations with relevant expertise are invited to

Forum meetings on an *ad hoc* basis to provide additional testimony and perspectives in particular areas of interest or concern, and in some cases, in the form of written documentation and review papers. In all of its activities, the Forum seeks to strengthen and forge global links among the public health, medical care, agricultural, veterinary, academic research, policymaking, and pharmaceutical and biotechnology industry, and national security communities that are involved in the research, surveillance, detection and response to domestic and global infectious disease challenges.

The Forum members continue to organize around activities designed to solve problems and identify critical issues in the field. Topical, issue-oriented, public workshops are followed by published summary reports. The Forum also will continue to meet in closed-session working groups to discuss topics of particular sensitivity, urgency, and interest to U.S. government agencies, public health specialists, public and private sector interest groups, and U.S.-based funders and implementers of research and control activities related to infectious diseases and dangerous pathogens. These closed-session meetings will seek to foster active and innovative collaboration among multiple sectors focused on the timely resolution of critical problems.

The Forum will convene three (3) public workshops and two (2) closed-session working group each year. The subject area and scope of the working group session and workshops will continue to be determined by the Forum members. It is important to note here that the active engagement and participation of the members of the Forum has been and must continue to be both substantial and consistent in shaping the direction and format of Forum activities.

Based on the outcomes of workshop and working group discussions, Forum members are able to recommend the formation of IOM study committees on issues where remaining questions and priorities clearly warrant further study. Such a committee would function independently of the Forum (though it may include some Forum members) and would offer conclusions and recommendations on the identified topic. The recommendations for IOM *Ad Hoc* Committee studies would be presented to the parent Board on Global Health (BGH) and developed through consultation with its members and other relevant Boards of the National Academies.

Issues and Activities

Against the backdrop of changing infrastructures, technology, and the continuing challenges posed by infectious diseases and dangerous pathogens in the United States and globally, the Forum focuses on five broad areas of inquiry: surveillance and detection; emerging tools and technology for diagnosis and treatment; research directions and priorities; education, training, and public communication; and, opportunities to strengthen public-private sector partnerships. It is anticipated that these overarching themes will continue to guide the activities of the Forum.

With this multi-faceted framework for examining a range of microbial threats, the Forum will examine both naturally occurring and intentionally-introduced pathogens and diseases. In 2004, the Forum has established parallel tracks of activities that will continue to address the threats to human health, the economy, and development posed by the worst that Mother Nature can muster. Additionally, through its public and closed-session activities, the Forum will consider topics defined as biosecurity threats. This track of activities will seek to engage a broader set of international and national security researchers and policymakers and will look to develop complementary and synergistic activities within the overall portfolio of the Forum's efforts. In this context, important areas for exploration might include: what investments are currently being made to identify and respond to a naturally-occurring disease outbreak or intentionally engineered pathogen; how to best utilize these resource investments in an integrated fashion within and across government agencies; and how to educate and advise the public, public health, and first responder communities on how to make wise use of these tools and technologies for local and regional emergencies.

Recently Completed Workshop Activities:

- ***March 6 – 7, 2012: The Social Biology of Microbial Communities***

All ecosystems on Earth – including extreme environments such as the human gut, deep sea hydrothermal vents, and the windswept terrain of Antarctica – teem with microbial life that interact and form associations with other microorganisms, and with plant, animal, and human hosts. The vast majority of these interactions with the microbial flora and fauna around us are either benign or beneficial to the host and microbes. Despite the ubiquity and importance of microbial communities, very little is known about the 'rules' that govern their formation, community stability and functional attributes.

The Institute of Medicine's Forum on Microbial Threats hosted a public workshop on March 6th and 7th, 2012, in Washington, D.C. to explore the emerging science of the social biology of microbial communities. Through invited presentations and discussions among participants, the workshop will explore, from a variety of perspectives, the ecological, evolutionary, and genetic factors contributing to the formation, stability, and function of microbial communities; how microbial communities adapt and respond to environmental stimuli; and potential applications for improving human, animal, plant, and ecosystem health.

- **December 13-14, 2011: “Improving Food Safety Through a One Health Approach”**

Recent outbreaks of *Listeria* in cantaloupe, *Salmonella spp.* in eggs and ground turkey, and *E. coli* in bean sprouts underscores the public health and economic impacts associated with our increasingly globalized food supply. In the United States, foodborne agents affect 1 out of 6 individuals, causing approximately 48 million illnesses, 128,000 hospitalizations, and 3,000 deaths each year. This figure likely represents just the tip of the iceberg, since it does not account for the broad spectrum of foodborne illnesses or for their wide-ranging repercussions for consumers, government, and the food industry domestically and internationally. The potential impact on human health of deliberate adulteration of food can be estimated by extrapolation from the many documented examples of unintentional outbreaks of foodborne disease, some of which have killed hundreds and sickened hundreds of thousands of people.

The Institute of Medicine's Forum on Microbial Threats hosted a public workshop on 13 – 14 December 2011, in Washington, D.C. that examined issues critical to the protection of the nation's food supply. Through invited presentations and discussions among participants, the workshop explored existing knowledge and unanswered questions on the nature and extent of foodborne threats to health. Participants discussed the globalization of the U.S. food supply and the burden of illness associated with foodborne threats to health; considered the spectrum of foodborne threats as well as illustrative case studies; reviewed existing research, policies, and practices to prevent and mitigate foodborne threats; and, identified opportunities to reduce future threats to the nation's food supply through the use of a “One Health” approach to food safety. The summary report for this workshop is being drafted and is expected to enter review in Spring 2012.

- **March 14 – 15, 2011: “Synthetic and Systems Biology”**

Progress in biology has been marked by successive shifts to new technologies with independent scientific and economic impacts. Indeed, the rapid growth of bio- and other relevant technologies over the last thirty years has been driven by two processes working together: a quantitative increase in performance and decrease in cost of existing technologies and instruments, and, qualitative changes resulting from unplanned new inventions, unexpected discoveries, and unforeseen historical events. Until the past decade, the work was often painstakingly slow, and able to address only relatively straightforward challenges such as using one gene to produce one protein.

In 2001, scientists finished the initial draft of the human genome sequence, representing a fundamental shift in the way biology is studied and opening a portal to vast post-genomic possibilities - from RNAi (RNA interference) therapeutics to synthetic biology. New strategies combining engineering and biological techniques have enhanced researchers' abilities to work with genetic, cellular or even tissue-level biology. These new synthetic techniques allow for genes and long chains of DNA to be designed and manufactured from scratch using a computer and relevant chemical compounds, rather than manipulating pieces of existing genes from living cells.

On March 14 – 15, 2011, the IOM's Forum on Microbial Threats convened a public workshop to explore the scientific and policy dimensions of recent developments in genetic engineering and their applications to emerging infectious diseases. Through invited presentations and discussions, this workshop will explore how the use of these advanced technologies will yield insights and greater understanding of infectious microbes, the mechanisms by which they cause disease; the applications of these tools and approaches for disease detection and diagnostic platforms; and the development of new therapeutics, vaccines and other infectious disease intervention technologies. The summary report of this workshop was released in November 2011.

Recently Completed Discussion Meetings

With representation from the three major sectors involved with issues surrounding emerging, resurgent, and endemic infectious diseases and the threat of dangerous pathogens, a primary objective of the Forum is to facilitate frank debate and robust discussion among the members. Closed-session working group discussions of Forum members provide an opportunity to explore complex, cross-cutting, and highly charged issues in a neutral setting—allowing provocative, off-the-record exchange about contentious and problematic issues as well as opportunities for innovation.

- June 28, 2011: Morning Session – “Microbial Forensics and Detection Technology”. The discussion leaders included Bernie Goldstein from the University of Pittsburgh; Tim Stearns from Stanford University; and Paul Keim, from Northern Arizona University.

Forum members were briefed on the findings and conclusions of the IOM/NRC report: *BioWatch and Public Health Surveillance: Evaluating Systems for the Early Detection of Biological Threats* by the Chair of this consensus committee Dr. Bernard Goldstein. The BioWatch program began in 2003 to detect certain biological agents released in aerosolized form. While BioWatch has the potential to provide a more timely alert than the public health and health care systems — under a narrow set of circumstances — the promise “remains theoretical”. The program’s current emphasis on detection technology over the information needs of users and the program’s lack of integration with the public health system limit this system’s contribution to national biosurveillance. Dr. Tim Stearns discussed the findings of a 2008 JASONs study on Microbial Forensics. Microbial forensics is an increasingly useful tool for natural and intentional outbreaks of infectious disease, but findings need to be supported by other evidence (e.g. derived from field work or intelligence work). In the short term, efforts to standardize methods and tools are needed (e.g., sample collection, reference library, bioinformatics tools) and longer-term goals should include development of novel methods to investigate microbial characteristics (e.g., transcriptome analysis, epigenetic modifications). Dr. Paul Keim of Northern Arizona University discussed whole genome sequencing, how this technology is revolutionizing the field and presented several examples of how detailed genomic information can be used to understand the ecological and evolutionary forces that shaped the phylogeography of recently emerged diseases, such as the geographic origins of several historical plague (*Y. pestis*) epidemics and the recent cholera epidemic in Haiti.

- June 28th – Afternoon Session – “The Microbiome and Microbial Ecology”

The Forum hosted a half-day discussion on June 28, 2011 to explore research on the Microbiome and Microbial Ecology. Participants included: David Relman, Stanford University; Sarkis Mazmanian, California Institute of Technology; Jeremy Nicholson, Imperial College London; Forest Rohwer, San Diego State University; Jonathan Eisen, University of California, Davis; and Cameron Currie, University of Wisconsin at Madison.

Microbial ecology characterizes microbial diversity, and the complex relationships between microbes and with their environment. Recent studies on the human microbiome have begun to reveal the complexity of these interactions within the human body and the effects of the environment on community composition – over space and time. Potential benefits from these interactions include: food digestion, nutrition (vitamins, energy), xenobiotic processing, metabolic regulation, development, the “education” or

regulation of the human immune system, epithelial “homeostasis”, barrier integrity, and colonization resistance to pathogens. Research on these interactions will help to characterize microbial contributions to “health” and “disease”. Studies on leafcutter ants have revealed a complex web of symbiotic interactions, among ants, bacteria, and fungi that are associated with fungal “gardens” cultivated by ants for food and transmitted from colony to colony. These associations are ancient and underscore the role microbes have played in driving adaptation and evolution of organisms. To date, most microbiome or microbial ecology studies have focused on bacteria, but viruses also play an important role in the dynamics of complex biological systems. The phylogenetic diversity of microbes is poorly sampled and a more systematic approach to sampling and analysis would greatly benefit the field. Improving the quantity, quality, and diversity of microbial sequence data is essential for understanding microbial biogeography, phylogeny, function, and community composition.

▪ June 29, 2011:

The Forum held a private half-day planning meeting on June 29, 2011 to discuss future workshop topics and to identify potential speakers to invite to future meetings.

Future Workshops:

Planning for the next 18 months has begun and the following topics have been proposed for exploration through workshop/symposia activities:

- ***“One Health” and Food Safety*** -- A public workshop on this issue was hosted in mid-December 2011 with overwhelming public participation – well over 200 people registered for and attended this workshop.
- ***The Social Biology of Microbial Communities*** – a March 2012 public workshop was hosted on this topic
- ***The future of new diagnostic modalities for rapid disease detection in primary and emergency care settings;***
- ***Domestic and international “real time” surveillance for “unusual disease outbreaks” in human, plant and animal populations;***
- ***The potential to exploit environmental monitoring as a tool for the detection and identification of “novel” agents;***
- ***Surveillance, Prediction, and Public Health Response to Emerging Infectious Diseases***
- ***The Possible Role of the Microbiome and Microbial Community Composition in Health and Disease***
- ***Microbial Forensics*** – mid-June 2012 workshop on this topic is being planned

PUBLICATIONS AND DISSEMINATION

Workshop Summaries

Reports of Forum workshops have highlighted and brought to the fore some of the most important infectious disease threats of the last decade. Through dissemination to public leaders, private industry, and policymakers, the summary reports have served as a useful decision-making tool and record of these innovative proposals and ideas.

After each workshop, a report summarizing the proceedings of the workshop is prepared, reviewed according to National Research Council report review procedures, and published by the National Academy Press. The workshop summary presents lessons learned from described experiences, delineates a range of pivotal issues and their respective problems, and puts forth response and research agendas as described by the workshop discussants.

Reports of the Forum's workshops and meetings will continue to be distributed to Forum members, sponsors, meeting attendees, and other interested constituencies. These reports summarize the proceedings of the workshop or meeting, but do not contain consensus advice or recommendations regarding government policy. Workshop or meeting summaries include a disclaimer indicating that the individual views described therein are those of the speakers/presenters and not necessarily those of the National Academies or Forum members. The National Academy Press publishes the reports.

The following is a list of recently published workshop summary reports of the Forum on Microbial Threats.

- ***The Science and Applications of Synthetic and Systems Biology*** (2011)
- ***Fungal Diseases: An Emerging Challenge to Human, Animal and Plant Health*** (2011)
- ***The Causes and Impacts of Neglected Tropical and Zoonotic Diseases - Opportunities for Integrated Intervention Strategies*** (2011)
- ***Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies*** National Academies Press (2010). This was one of the featured reports for the WHO's World Health Day on "Antibiotic Resistance" on April 7, 2011.
- ***The Domestic and International Impacts of the 2009-H1N1 Influenza A Pandemic: Global Challenges, Global Solutions*** National Academies Press (2010). This report served as the basis for the World Health Organization's review of the performance of the International Health Regulations in response to the first influenza pandemic of the 21st century.
- ***Infectious Disease Movement in a Borderless World***, The National Academies Press, 2010. At the urging of one of the speakers at this workshop, copies of this report were sent to the editors of three journals for review. The journals included: *Emerging Infectious Diseases*; *Clinical Infectious Diseases*; and the *Journal of Travel Medicine*.
- ***Infectious Disease Movement in a Borderless World*** National Academies Press (2010)