MULTIDISCIPLINARY SCIENTIFIC RESEARCH

Research Coordination Network

SOUTHEAST ASIA STAKEHOLDERS WORKING GROUP MEETING

Final Report

Bangkok, Thailand
23 - 25 February 2016

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HANDLING INSTRUCTIONS

- The title of this document is The Melioidosis Research Coordination Network Southeast Asia Stakeholders Working Group Meeting Final Report
- Approved for public release; distribution is unlimited.
- For information, please consult one of the following point of contact (POC):

U.S. Government:
Martha Stokes, Ph.D.

Regional Science Manager
Cooperative Biological Engagement Program
(CBEP)
Defense Threat Reduction Agency (DTRA)
Department of Defense
Martha.m.stokes.civ@mail.mil

WORKING GROUP MEETING OVERVIEW

BACKGROUND AND OBJECTIVES

Research Coordination Networks (RCNs) were established in 2000 by the United States National Science Foundation (NSF) to advance fields of research and / or create new directions in research through communication and coordination in research, training, and education activities across geographic, organizational, disciplinary, and international boundaries. The Defense Threat Reduction Agency (DTRA) Cooperative Biological Engagement Program (CBEP) Science Managers for the Middle East / Northern Africa and Southeast Asia (SEA) regions aim to enhance collaborative research efforts through partnerships with in-country scientists for improved biosurveillance and general threat reduction. They leverage the RCN concept to build and accelerate transparency for scientific partnerships around the world. Leading scientists and researchers in SEA founded the RCN on melioidosis in collaboration with CBEP with the intent to foster broad, multidisciplinary dialogue to enhance and sustain regional health and security in SEA.

The working group meeting took place in Bangkok, Thailand over three days and incorporated plenary sessions from international subject matter experts in diagnostics, epidemiology, health economics, and public health. Time was granted to researchers to present on the status, focus, and goals of their current research. Researchers and health implementers attended from Australia, Cambodia, Laos People's Democratic Republic (Lao PDR) Malaysia, Thailand, Singapore, and Vietnam representing Ministries of Health, University Research Hospitals, and non-profit research organizations. The Workshop organizers also invited several representatives from U.S. agencies which included the Department of Homeland Security (DHS), the Food and Drug Administration (FDA), the Department of Defense (DoD) Armed Forces Health Surveillance Branch (AFHSB), the Centers for Disease Control and Prevention (CDC), DTRA CBEP, and DTRA Chemical Biological Technologies (J9) that fund *Burkholderia pseudomallei* research.

The specific objectives for the participants included:

- Define risk and prevalence of melioidosis in SEA
- Outline the health burden and economic impact of melioidosis at national and regional levels across SEA
- Outline coordinated solutions and associated activities for the RCN
- Identify and de-conflict available funding programs, which are currently operating from multiple institutions within and with interests in SEA
- Adopt an informal charter agreement for the establishment of the RCN on melioidosis

EXECUTIVE SUMMARY

SEA is a nexus for socioeconomic and environmental change, thus presents a significant global threat for emerging infectious disease. Regional networking to strengthen expertise in fighting against emerging diseases is critical for effective biological preparedness and resiliency. This can be accomplished through forums to promote transparency, outlining specific approaches to control disease, and building

professional networks across disciplines and between countries. Leveraging these mechanisms and relationships can dramatically minimize the threat of pandemics and the spread other emerging infectious diseases nationally, regionally, and globally.

On February 23-25 2016 researchers and health implementers gathered in Bangkok, Thailand for a three-day conference to discuss melioidosis, a disease of high, but relatively unknown prevalence and risk throughout the region. The group gathered to formalize a network for melioidosis research at an Inaugural SEA Stakeholders Working Group Meeting. While there are many informal and formal networks on melioidosis and its causative agent, *Burkholderia pseudomallei*, the RCN effort, sponsored by DTRA's CBEP and supported by DTRA Chemical and Biological Technologies Division (J9CB), intends to integrate multi-disciplinary research efforts and align those efforts with funding opportunities within DTRA and other relevant organizations.

The economic burden of melioidosis in highly endemic countries in SEA further highlights the need for aligned investments to identify and develop improved prevention, detection, and control strategies. The February meeting was the first step to connect and unite researchers and health implementers in understanding the epidemiology of melioidosis, and how to better diagnose and treat the disease, which is not only highly endemic and prevalent across the region, but widely under-reported and misdiagnosed.

This important whole-of-DTRA-sponsored and supported event provided an opportunity to (1) promote a common understanding of the risk and prevalence of melioidosis; (2) connect researchers to establish needs and gaps in melioidosis research across the biological resiliency spectrum (prevent, detect, respond, and recover) and (3) convene funders from agencies that can support areas in melioidosis researcher. This meeting served as an opportunity for scientists and researchers to broaden their networks and share perspective, experiences, and standards for protocols. Event organizers created eight sessions on the following themes:

- Session 1: Presentation of Individual Research
- Session 2: Regional Risk and Burden of melioidosis
- Session 3: Diagnostics and Environmental Detection
- Session 4: Disease Pathogenicity and Immune Response
- Session 5: Vaccines and Therapeutics
- Session 6: Breakout Group Discussions to Identify and Prioritize Research Needs and Gaps
- Session 7: Funding Cooperative Research
- Session 8: RCN Next Step

Event facilitators used breakout group sessions to address two focus areas: (1) needs for researching risk, burden, and diagnostics and surveillance methods and (2) needs for researching disease pathogenesis, immune response, vaccine development, and therapeutics. This effort demonstrated whole-of-DTRA coordination to assess research for melioidosis as a comprehensive portfolio of prevention, detection, and response, rather than a collection of unrelated projects that match individual department missions.

Overall the meeting was well-received, and with the exception of adopting an informal charter, participants and organizers felt they achieved all the intended objectives of the event. Participants were

treated to many opportunities to network, they were also granted time to discuss and present their research, this was a highly noted outcome of the event. More in-depth feedback from attendees and organizers may be found in ANNEX C within this report.

WORKING GROUP MEETING IN PERSPECTIVE

RESEARCH COORDINATION NETWORKS

RCNs were established in 2000 by the NSF to advance a field of research and/or create new directions in research through communication and coordination in research, training, and education activities across geographic, organizational, disciplinary, and international boundaries. An RCN allows for new collaborations, which can include international partnerships. The DTRA CBEP science managers for Middle East / North Africa and SEA adapted the RCN concept to enhance collaborative research efforts through partnerships with in-country scientists for improved biosurveillance and threat reduction.

Leading scientists and researchers in SEA founded this RCN on melioidosis in collaboration with CBEP, with the intent to foster a broad, multidisciplinary dialogue to enhance and sustain regional public health and security in SEA.

THE COOPERATIVE BIOLOGICAL ENGAGEMENT PROGRAM

CBEP is the biological engagement component of the Cooperative Threat Reduction Program (CTR). It strives to address the risks posed by natural or manmade disease outbreaks by promoting best practices in biological safety and security (BS&S) and improving partner countries' capacities to safely detect and report biological threats. CBEP directly supports CTR strategic objectives by working cooperatively with partner governments to 1) reverse biological weapons (BW) programs by dismantling and destroying stockpiles, equipment, and means of delivery; 2) account for, secure, and safeguard biological material, equipment, and expertise, which, if vulnerable to diversion, could result in WMD threats; and 3) prevent the acquisition, proliferation, and use of BW and expertise. CBEP enhances partner country/region's capability to rapidly survey, detect, diagnose, and report biological terrorism and outbreaks of pathogens in accordance with international reporting requirements[1]. Implementation activities of CBEP include strengthening and deploying biosurveillance and information systems to rapidly confirm deliberate biological attacks, including differentiating between endemic pathogens and those introduced by accident or nefarious intent. Furthermore, CBEP seeks to strengthen linkages between disease surveillance and reporting systems to national, regional, and global outbreak response systems. CBEP promotes multi-sectoral engagement to enhance discussion and exercise systems across health, foreign affairs, law enforcement, and other relevant communities[2].

DTRA CHEMICAL / BIOLOGICAL TECHNOLOGIES

DTRA Chemical/Biological Technologies works to protect American warfighters and their allies from threats posed by chemical and BW. They provide a wide spectrum of support to the military services, combatant commands and international partners, from innovating new technologies to detect chemical

[1] Department of Defense Strategic Policy Guidance for the Cooperative Biological Engagement Program, 21 Aug 2013.
[2] Strategic Implementation Guidance for the Cooperative Biological Engagement program, 21 Aug 2013.

and biological threats, to developing new capabilities to protect them through programs such as the Transformational Medical Technologies Initiative.

Not only do chemical and biological threats imperil our nation's warfighters and our allies; they are a danger to innocent civilians in the homeland and throughout the world. Defending the country against chemical and biological threats presents a wide variety of challenges. DTRA Chemical/Biological Technologies works to tackle these challenges by partnering with interagency organizations such as the Department of Health and Human Services (HHS), to prepare for biological and chemical events. In cooperation with DoD and HHS, DTRA is using state-of-the-art technology and executing our first agent-based, high performance computational analysis system, which has resulted in a revolutionary pandemic influenza modeling capability.

WORKING GROUP SESSION-BY-SESSION PRESENTATIONS AND DISCUSSIONS

OPENING COMMENTS

Dr. Elizabeth George (Director, J3 CT) and Colonel Timothy Greenhaw (Deputy Director, J9 CB) enthusiastically co-opened the meeting with statements about the significance of broadening research on melioidosis for their respective missions of capacity building and global health security and U.S. Mission Assurance, Force Health Protection and Readiness.

RESEARCH COORDINATION NETWORKS

DR. MARTHA STOKES

COOPERATIVE BIOLOGICAL ENGAGEMENT PROGRAM

Dr. Stokes opened her presentation with a brief history of RCNs, which were established by the NSF in 2000 to serve as a coordination mechanism for investigators to exchange information, data, samples and protocols. She explained how this mechanism aims to join people together to work on a common issue, and she described the evolution of adapting the concept for melioidosis research in SEA, honoring the many people gathered at the RCN for their contributions and participation in a community of thought exchange. She acknowledged that the RCN was an organic gathering of informal networks and relationships that will help enhance long term, programmatic goals for providing biosurveillance, BS&S capabilities with the ultimate intent of reducing the threat of infectious disease. Dr. Stokes also pointed out that the benefit, particularly from a funding perspective, is for the RCN to generate and have access to global support.

GOALS OBJECTIVES, AND A BRIEF HISTORY

DR. DIREK LIMMATHUROTSAKUL

MAHIDOL-OXFORD RESEARCH UNIT

Dr. Limmathurotsakul defined the goals for the seminar: (1) reduce burden of melioidosis worldwide and (2) establish a network of researchers/ funders/ policy makers. Objectives for goal (1) are to identify what research needs to be done, identify and discuss funding opportunities, to exchange information among fellow researchers, and to establish a support network. The objective for goal (2) is to develop a mechanism/system for a network of researchers/funders/policy makers to steer melioidosis research. Local network impact efforts include the Thailand-Lao Melioidosis Network Meeting with situation reanalysis efforts and establishing an enhanced surveillance system for melioidosis research. Additional local impact events include the National Conference on Melioidosis in Vietnam and the South Asian Melioidosis Congress. Global impact efforts consist of promoting communications, providing information to both researchers and the general public, as well as supporting global meetings (WMC/EMN) via the International Melioidosis Society (IMS).

SESSION 1: PRESENTATION OF INDIVIDUAL RESEARCH

During the RCN, select participants were granted time within the agenda to present their research. Event organizers collected their information on a single formatted power point slide, which was then provided with other event resources to attendees at the end of the meeting. The information presented during the meeting was collected and translated on a map of SEA, which can be found in ANNEX E of this report. This map provides an operating picture of current research activities within the region.

SESSION 2: REGIONAL RISK AND BURDEN OF MELIOIDOSIS

LTC Kurt Schaecher served as the session moderator for this portion of the working group meeting. Presentations focused on highlighting the SEA region and Australia as the most prevalent for melioidosis risk and burden.

MELIOIDOSIS: A DISEASE OF SURPRISE

DR. BART CURRIE

MENZIES SCHOOL OF HEALTH RESEARCH AND ROYAL DARWIN HOSPITAL, AUSTRALIA

Dr. Bart Currie discussed surprises and uncertainties of melioidosis. He highlighted recent modelling that predicted prevalence in SEA: Estimated 165 thousand cases of melioidosis and estimated 89 thousand deaths due to melioidosis for the year 2015. These estimates now need verification through enhanced surveillance and diagnosis. He outlined potential contributing factors for the global dissemination of *B. pseudomallei* from endemic regions: (1) the importation of animals, (2) importation of contaminated plants/soil, (3) importation of contaminated medical supplies, (4) human travel, (5) aerosolisation and severe weather events, (6) migratory birds and marine mammals. Further, Dr. Currie stressed the determinants of clinical severity: infectious dose, host factors, infection route (percutaneous, inhalation, ingestion). He noted an important contrast between the Thai vs. Australian seropositivity gap: in the Darwin region of Australia where melioidosis is particularly endemic, only 3% of health residents were seropositive by indirect hemoagglutination tests (IHA), despite high exposure to the *B. pseudomallei* organism; this rate is considerably lower than that seen in northeast Thailand, where melioidosis is similarly endemic at a high rate.

MELIOIDOSIS REGIONAL RISK ASSESSMENT AND PREVENTION MEASURES

DR. GLADYS TAN GEK YEN

DSO NATIONAL LABS, SINGAPORE

Dr. Gladys Tan Gek Yen highlighted three major regional risk challenges of melioidosis: (1) epidemiology, (2) outbreaks and case-clusters, and (3) environmental health investigations. Melioidosis has a wide spectrum, non-specific clinical manifestation, which presents as a unique challenge to early recognition/detection by clinicians. By increasing awareness among healthcare professionals in endemic areas, Dr. Yen stressed that this can lead to better prevention and or intensive care when cases occur.

She emphasized that the geographic distribution of SEA contributes a particular challenge due to high level of exposure to soil/surface water in endemic regions (e.g. Thailand, rice farmers), as well as climatic/seasonal attributes. Increased rainfall and severe flooding contributed as a major factor for disease transmission in 2004 post-tsunami outbreak of melioidosis. Dr. Yen identified three (3) important prevention measures: (1) disease control, including personal/individual, community, and environment; (2) occupational risk, including laboratory workers (both clinical and research), and (3) BS&S measures for diagnostic and research laboratories.

ECONOMIC BURDEN OF MELIOIDOSIS IN SOUTHEAST ASIA

DR. SAITHIP BHENGSRI

CDC GDD, THAILAND

Dr. Saithip Bhengsri discussed conservative estimates of the total economic impact of bacteremic melioidosis for 11 SEA countries, noting high endemic regions in Northeast Thailand, Singapore and Malaysia (incidence rate 4.0 – 21,3 per 100,000 persons and a case fatality rate (CFR) range of 16-60%). Data obtained from a review of published papers from 1910 – 2015 for confirmed melioidosis cases or the presence of *B. pseudomallei* in soil, estimated the predicted global burden of melioidosis in 2015 is set at 165,000 total cases (95% CI 68,000-412,000) and 89,000 total death cases (95% CI, 36,000-227,000). Dr. Bhengsri stressed that due to limited resources, it is important to identify economic aspects of public health, as this assists in maximizing health and minimizing costs, all while making the economic impact of disease persuasive to policy makers. She identified four types of economic evaluations: (1) cost minimization analysis (CMA), (2) cost effectiveness analysis (CEA), (3) cost utility analysis (CUA), and (4) cost benefit analysis (CBA); and presented an estimate for eastern Thailand Province from 2011, where the total cost/year of bacteremic melioidosis in Sa Kaeo was ~$152,159, with nearly 73%($111,552) of these costs attributed to indirect costs from premature mortality. She pointed out that majority of costs are attributable to productivity losses from premature death, with cost per fatal case being 3 times higher than Thailand GDP per capita ($4,600 in 2011) and the cost per non-fatal case being 15% to 33% of GDP per capita. This presentation highlighted the challenges of limited information on melioidosis burden in a region with few to no cost-effectiveness, cost-benefit, or cost-utility analyses to evaluate or compare treatment and prevention options; however, meropenem and vaccine treatments are likely to demonstrate cost-effective solutions to the economic burden of melioidosis.

SESSION 3: DIAGNOSTICS AND ENVIRONMENTAL DETECTION

The following presentations were moderated by Direk Limmathurotsakul of Mahidol University. Clinical detection and diagnosis challenges were noted in this segment of the workshop.

DETECTION (CLINICAL / ENVIRONMENTAL)

DR. DAVID DANCE

LAO-OXFORD MAHOSOT HOSPITAL – WELLCOME TRUST RESEARCH UNIT

Dr. David Dance noted that the most significant problem identified in clinical detection of melioidosis is the lack of access to diagnostics; the second most significant was the lack of awareness and familiarity, especially in areas not known to be endemic. He stated that culture identification is still the "gold standard" for clinically identifying *B. pseudomallei*; however, even though there are microbiological facilities with well-trained doctors and laboratory technicians, about 60% of cases may go undetected, in addition to the challenge of slow turnaround times. Dr. Dance asserted that matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) showed promise for identification of the organism, and immunofluorescence was as useful for rapid diagnosis, but still cumbersome to conduct. Lateral flow immunoassays (LFI) show significant promise as a faster alternative to culture as well, but still lack sensitivity compared with culture. Environmental detection methods and variations were outlined, however, it was noted that few comparative studies exist. Quantitative culture methods had questionable accuracy and reproducibility while being labor intensive. Molecular methods are most sensitive and appropriate for screening a large number of environmental samples, but still require culturing techniques in order to obtain isolates for further study. Comparative evaluations of methods are needed for future efforts in environmental sampling of *B. pseudomallei*.

RAPID DIAGNOSTIC TESTS FOR INFECTIOUS DISEASES

DR. DAVID AUCOIN

UNIVERSITY OF NEVADA, U.S.

Dr. David AuCoin presented on *In vivo* Microbial Antigen Discovery (InMAD) for identification of shed/secreted microbial antigens in patient samples. He also presented on a novel point-of-care antigen detection assay to detect *B. pseudomallei* capsular polysaccharide identified by InMAD. Proper diagnosis of melioidosis presents a challenge due to symptoms mimicking other common infectious diseases. Additionally, other diagnostic techniques such as real-time polymerase chain reaction (RT-PCR) may be difficult as well due to low levels (CFU/ml) of *B. pseudomallei* in the blood stream. Dr. AuCoin presented that an indirect hemagglutination assay (IHA) presents difficulty due to a high percentage of the population in endemic areas being seropositive for the organism. To address these challenges, InMAD was used to identify a *B. pseudomallei* biomarker leading to development of a rapid and inexpensive point-of-care diagnostic test. The *B. pseudomallei* capsular polysaccharide (CPS), in addition to other protein antigens, was identified as potential diagnostic biomarkers. Dr. AuCoin identified that new updates include the development of a diagnostic immunoassay based on the detection of CPS. With the production of a CPS-specific monoclonal antibody (mAb), this was used to produce a prototype Active Melioidosis Detect Lateral Flow Immunoassay (AMD LFI). He stated that an analytical reactivity of *B. pseudomallei* strains was reported at 98%, while an analytical specificity (neighboring strains of *B. humptydooensis*, *B. oklahomensis*, *B. thailandensis*) was reported at 97%. LFI may be used directly on patient samples, and works rather well on cultured samples and colonies. Additionally, LFI is available to any endemic site for analysis and a large, preclinical analysis is planned for the next two years in the Darwin Region and Thailand. Further efforts include a pre-submission inquiry to the FDA within a year, and an FDA clearance within the next 2-3 years.

SESSION 4: DISEASE PATHOGENICITY AND IMMUNE RESPONSE

Dr. Ayanna Flegler moderated a session that highlighted pathogenicity, immunological response, and antimicrobial resistance attributes.

INSIGHTS INTO PATHOGENICITY AND IMMUNE RESPONSE

DR. GANJANA LERTMEMONGKOLCHAI

KHON KAEN UNIVERSITY

Dr. Ganjana Lertmemongkolchai outlined several research efforts exploring pathogenicity and the immune response to melioidosis. She noted the biofilm formation mechanism of *B. pseudomallei*, which contributes to an advantageous, environmental persistence, which, in turn, may increase the risk of its transmissibility to humans. High throughput approaches such as proteomic microarrays, genome transcriptomics, large scale T cell epitopes, and metabolomics were described as techniques applied in 15 years of Northeast Thai studies of human immune response to *B. pseudomallei*. The Immune Epitope Database and Analysis Resource was identified as an important tool in conducting *B. pseudomallei* and melioidosis research. Dr. Lertmemongkolchai noted ongoing and future studies include the analysis of T cell epitopes of candidate peptides from *B. pseudomallei*, developing a cocktail of peptides for T cell assays, analysis of B-cell epitopes on selected *B. pseudomallei* proteins, and the identification of T & B cell epitopes by an immunodeficient animal model.

ANTIBIOTIC RESISTANCE

DR. NARISARA CHANTRATITA

MAHIDOL UNIVERSITY, THAILAND

Dr Narisara Chantratita outlined two types of recommended antimicrobial therapy for *B. pseudomallei*: (1) Initial intensive therapy and (2) oral-eradication therapy. Initial intensive therapy includes the antimicrobial drugs ceftazidine, meropenem, and imipenem. She noted that oral-eradication therapy consists of trimethoprim/sulfamethoxazole (TMP/SMX) dosages by body weight. Antimicrobial resistance was outlined in Thailand, Malaysia, and Australia. In Thailand, antimicrobial resistance rates were explored in a total of 4,021 patients. Of these patients, 24 exhibited resistance to ceftazidime only (N=8, 0.2%), amoxicillin-clavulanic acid only (N=4, 0.1%), and both drugs (N=12, 0.3%). For Malaysia, 170 clinical isolates were identified and all were sensitive to meropenem. Resistance to ceftazidime, imipenem, amoxicillin/clavulanic acid and doxycycline resistance was observed in 1 isolate (0.6%) for each of antibiotics. Dr. Chantratita stated that one isolate demonstrated resistance to all four (4) antibiotics used in treatment. For Australia, 234 clinical isolates were identified and all demonstrated susceptibility to meropenem and ceftazidime. Additionally, 226 isolates (96.6%) were susceptible to doxycycline and 232 (99.1%) were susceptible to Co-trimoxazole. TMP-SMX resistance was described in Thailand (0.33%), Laos (0.8%), Australia (0.9%), and Cambodia (0%), where all 10 TMP-SXT resistant isolates were susceptible to AMC and 91% were susceptible to doxycycline. *B. pseudomallei* was described as possessing intrinsic antimicrobial resistance; however, other factors that contribute to antimicrobial resistance include biofilm formation, intracellular life cycles, mode of growth, stress and salinity environments. Trends were identified in alternative drugs or combined treatment, including bactenecin, an

antimicrobial peptide able to inhibit the growth and biofilm formation of *B. pseudomallei.* Dr. Chantratita posited that challenges such as drug susceptibility, lack of targets for current drugs, and inhibitors of virulence factors were identified as major contributors of the intrinsic resistome of *B. pseudomallei*.

SESSION 5: VACCINES AND THERAPEUTICS

Dr. Julie Boylan facilitated a session that focused on new therapy tactics, treatment durations, and improved outcomes.

A NEW TREATMENT PARADIGM: THERAPY DURATION AND OUTCOMES

DR. BART CURRIE

MENZIES SCHOOL OF HEALTH RESEARCH AND ROYAL DARWIN HOSPITAL, AUSTRALIA

Dr. Bart Currie noted that *B. pseudomallei* is a dynamic pathogen with complex, intrinsic antimicrobial resistance properties, but also possesses minimal diversity in susceptibility patterns, rare acquired resistance, and no evidence of plasmid- or transposon-mediated acquired resistance. He stated that acquired antimicrobial resistance in other antimicrobials such as carbapenem was described as extremely rare and efflux pump over-expression may account for doxycycline resistance. Dr. Currie stated that previous international melioidosis treatment guidelines recommend a minimum 10 to 14 days of intravenous antibiotic therapy (intensive phase), succeeded by 3 to 6 months of oral therapy (eradication phase), which are associated with significant correlations of relapse. Intravenous Therapy Duration and Outcomes in Melioidosis: A New Treatment Paradigm explored a new antibiotic treatment regimen that was received by patients with melioidosis over a three year period. Relapsed melioidosis was rare in patients who received a minimum intensive phase duration specific by this new guideline and lowering the bar for prolonged IV “intensive” therapy most likely accounts for the decreased relapse rates in the Darwin Prospective Melioidosis Study. Further follow up research questions include, “Is IV intensive treatment with ceftazidime or meropenem required in localized disease (e.g. skin lesions)?” and “Is longer IV intensive treatment alone adequate for uncomplicated pneumonia?”

MELIOIDOSIS VACCINE: HOW FAR ARE WE?

DR. RICK TITBALL

EXETER UNIVERSITY, UK

Dr. Rick Titball discussed the topic of immune control of melioidosis being possible due to the fact that most individuals in endemic areas appear to have been exposed, but do not develop the disease itself. He identified the primary risk factors for developing melioidosis including diabetes mellitus (DM) and chronic renal failure, which impair immune responses. Additionally, antibody titers of *B. pseudomallei* correlate with severity of illness in melioidosis patients. Achieving sterilizing immunity is difficult and disease relapse occurs in 10-15% of patients; the reason why this is believed to be difficult to achieve is due to protective immune responses from antibodies and T cells. Dr. Titball also stated that the best vaccine candidate characteristics include live attenuated mutants, heat-killed whole cell, outer membrane

vesicle (OMV), sub-units, naked DNA, and epitope. However, with increasing complexity comes a decreased ease of licensing the vaccine. Research in how a pathogen evades the immune response needs to be further explored in order to fully understand when a vaccine candidate can be sufficiently protective to warrant investment in development.

ANIMAL MODELS

DR. GREGORY BANCROFT

LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE, UK

Dr. Gregory Bancroft noted that *B. pseudomallei* demonstrates high species cross-infectivity. Animal models are used in melioidosis research due to the inability of current *in vitro* human cell/tissue models to recapitulate the complexities of the host. Additionally, preclinical screening of multiple combinations of candidate vaccines cannot (ethically) be performed in human clinical trials for safety and efficacy. He stated that the shortcomings of animal models include not fully representing the "human situation"; also, with increasing the complexity of the animal model, its utility as a high throughput, pre-clinical screen is reduced. Non-human primate (NHPs) animal models used in melioidosis research include rhesus macaque (*M. mulatta*), common marmoset (*C. jacchus*), and African green monkey (genus *Chlorocebus*). Dr. Bancroft identified future areas of research in experimental animal models that include human tissue models (Hu-mice), better understanding of *in situ* immune responses, and improved use of non-invasive imaging. Transcriptomics, in conjunction with functional assays, may lead to correlation of protection from animal models to humans as well.

SESSION 6: BREAKOUT GROUP DISCUSSIONS TO IDENTIFY AND PRIORITIZE RESEARCH NEEDS AND GAPS

Meeting organizers and facilitators arranged for a breakout group session in the agenda, which was organized into smaller groups, by multiple countries and disciplines, to discuss multinational and multidisciplinary solutions to address melioidosis research needs and gaps. Groups were assigned, on-site prior to the second day of the meeting.

GROUP 1

KEY DISCUSSIONS AND DETERMINATIONS

Group 1 focused on identifying needs for researching risk, burden, and diagnostic and surveillance methods, such as:

- Coordinated surveillance strategies for potential endemic regions (clinical, environmental, and serological)
    - Identify needs for enhanced or strengthened microbiology facilities for referral hospitals
- Identifying emerging distribution of the disease through increased public awareness
    - Identify practical behavior modifications and mitigation methods for risk prone groups
    - Develop criteria for education modules to build melioidosis awareness amongst risk-prone groups

- Mapping regional human and animal cases to determine more accurate prevalence estimates and subsequent control measures
- Identifying emerging distribution through building awareness among physicians and improving diagnostic capabilities
- Establishing diagnostic standard (culture)
- Developing commercially available and reliable rapid diagnostic tests for melioidosis

GROUP 2

KEY DISCUSSIONS AND DETERMINATIONS

Group 2 focused on identifying needs for researching disease pathogenesis, immune response, vaccine development, and therapeutics, such as:

- Improving clinical outcome of infected persons, which depends on
  - Host's immune system
  - Virulence of the strain
  - Size and route of initial inoculum
- Improving clinical recognition of the disease
  - Physicians should consider melioidosis in the differential diagnosis of patients with acute febrile illnesses, risk factors for melioidosis, and compatible travel or exposure history
  - Melioidosis cases are classified using the standard case definition adopted by the Council of State and Territorial Epidemiologists in 2011
- Developing vaccines as a cost-effective intervention, particularly if used in high-risk populations, such as diabetics
  - Vaccines could represent one strand of a public health initiative to reduce the global incidence of melioidosis
  - Studies for vaccine development should include diabetic models, which are central to any evaluation of a melioidosis vaccine for natural infection, since diabetes is the most important risk factor

GROUPS BRIEFOUT

KEY DISCUSSIONS AND DETERMINATIONS

During the brief out, Group 1 identified according to gaps into three categories and assigned needs for each category:

1. **Awareness**
   a. Need to raise awareness of the disease at the policy-maker / ministerial level. Participants acknowledged that this would require outside assistance and would probably need to involve ASEAN (and other existing regional groups and international organizations) to establish a coordinated strategy for awareness building and set melioidosis as a regional priority.
   b. Need to increase physician and lab technician awareness, with special attention to targeting early career training and making training readily available in microbiological labs.
2. **Burden of melioidosis**

a. Need to establish regional and global open database of culture confirmed cases. This was acknowledged as a priority and goal for the RCN
b. Need to enhance country-by-country diagnostic lab capabilities
c. Need to include melioidosis in existing surveillance and reporting systems
d. Need to coordinate with other regional disease surveillance groups for observation of information sharing best practices, such as severe cases of sepsis / pneumonia
e. Need clear and agreed-upon definition of a probable confirmed case

3. **Environmental reservoirs**
    a. Need to assess environmental reservoirs (soil, rivers, weather)
    b. Need to conduct environmental studies. For example, it was highlighted as a research focus to study areas where there are no human cases, but a known persistence in the environment
    c. Need to involve specific experts, such as environmental microbiologists
4. **Laboratory capacity**
    a. Need to strengthen lab networks and establish SOPs for sample packaging and transport procedures for quicker confirmation of cases from rural areas; further a consistent and overarching system for BS&S
    b. Need for lab equipment for detection and confirmation of cases
    c. Establish sentinel sites to better define regional prevalence
    d. Need standards and protocols within reference labs in SEA to quickly identify *Bp.*
    e. Need to establish treatment guidelines
    f. Need for quality management / control for media development

Additionally, Group 1 presented a list of associated risks and challenges to the needs that they outlined, citing the following:

- Political sensitivities
- Limited government resources
- Private labs releasing information
- Collaboration of national authorities
- Public information awareness challenges (mitigating panic)
- Cross-border disease reporting
- High confidence in confirmed cases
- High costs of procuring equipment and sustaining supplies
- Incentivizing reporting
- Communication between lab and clinic
- Unsolved environmental issues (e.g., temperamental environmental samples)

During the brief out, Group 2 listed gaps by four categories, and assigned needs for each category:

- **Disease pathogenesis**
    - Need a central repository case, a database and reference lab.
    - Need Clinical Outcome from each isolate
    - Need to identify Genomic / transcriptomic / phenotypic virulence patterns
        - Surveillance of resistance patterns

  - Need to identify genetic diversity of all strains (environmental and clinical)
    - Philippines, Indonesia, Myanmar, Malaysia, Taiwan and possibly broader South America
- **Immune response**
  - Need immune correlates of protection across animal models/human
  - Need to develop functional assays (e.g. killing assays)
  - Need to identify risk factors of healthy individuals (e.g. alcohol, tobacco…)
  - Need to characterize occupational exposure
  - Need to identify high risk populations (e.g. diabetics)
- **Needs for vaccine development:**
  - Animal Models (primate studies)
  - Diabetic Challenges (public health use) versus healthy individuals (Mission Assurance)
- **Therapeutics**
  - Need for comprehensive education for Physician/Clinician to recognize clinical presentation
  - Need education on latest treatment protocols
  - Need to assess wider availability of ceftazidime
  - Need to understand therapeutic supply chain
  - Need to research alternative administration (e.g. mobile treatment- outside of hospital)

DEVELOPING PUBLIC AWARENESS AND INFLUENCING POLICY

DR. DIREK LIMMATHUROTSAKUL

MAHIDOL-OXFORD RESEARCH UNIT

Dr. Limmathurotsakul discussed an approach to building awareness for melioidosis, outlining his efforts to do so in Thailand. He stated that government policy makers can be influenced by building general public awareness. In Thailand the Ministry of Public Health did not have a full awareness of the morbidity and mortality of the disease. A study with MoPH was needed to fully understand scope of this issue. Dr. Limmathurotsakul determined, via retrospective cross-sectional study using an electronic database from hospitals nationwide, that there was country-wide underreporting of the disease. Dr. Limmathurotsakul discussed policy changes that need to take place at the top, which could improve the burden estimates of melioidosis. He discussed his public engagement campaign to build awareness and ways that the RCN could facilitate raising awareness to policy makers and the ministerial level.

SESSION 7: FUNDERS DISCUSSION

KEY OUTCOMES

FACILITATED BY MR. CHRISTOPHER RUSSELL

GLOBAL SYSTEMS ENGINEERING

Mr. Christopher Russell facilitated a group discussion between the melioidosis researchers and representatives from U.S. funding agencies for *Bp* research. The discussion included in-person representatives from AFHSB, HHS, FDA, CDC, Global Emerging Infections Surveillance (GEIS), DHS's Security National Biosurveillance Integration Center (NBIC), DTRA CBEP, and DTRA J9 CB who were invited to present on their respective solicitation mechanisms for research proposals. Each in-person representative in addition to a virtual representative from the National Institute of Health (NIH) National Institute of Allergy and Infectious Disease (NIAID) submitted a one-slide presentation of their processes and foci; for reference the results of this session can be found in ANNEX E.

Immediately following the representatives' presentations, they participated in a panel discussion in which the research audience was granted an opportunity to ask questions about all the various mechanisms for funding. According to the comments and feedback gathered from the participants, most felt this was a significant accomplishment of the RCN meeting, and provided something uniquely different from other conferences of its type. Many suggested that this be a recurring session and organizers intend to take that point for action.

Discussions focused on many topics. Most of the government representatives talked through the importance of a process, outlining the importance of each step of preparing a proposal. Dr. Julie Boylan (DTRA J9CB) acknowledged that USG mechanisms for funding may appear slow, but have intent. For example, she stated that the pre-coordination phase may include a BS&S inspection / walk-through in the lab to ensure that the research is being conducted safely and securely. She pointed various obstructions, such as not being able to send money to foreign sites, which is critical for melioidosis, and acknowledged the need for an easier mechanism. She discussed Small Business Technology Transfer (STTR) grants as a work-around, stating that one way for funders to support the manufacture and wide distribution is to use STTR. She acknowledged that it was slightly different than small business credits, but that the POC within an organization can help transfer to a larger grant.

Dr. Carl Newman (DTRA J3CT CBEP) built on Dr. Boylan's comments about BS&S, stating that a BS&S review of facilities would occur in the context of working with select agent or shipping the samples to the U.S. He emphasized that the intent would not be to impose USG standards on labs, rather to make sure that broadly the work is being done safely and the risk is minimized (standpoint of accidental exposure, and high risk materials are being handled safely).

Dr. Direk Limmathurotsakul (MORU) asked the panel if melioidosis was identified in a new area, could there be an emergency mechanism to facilitate quicker funding for research and response. Dr. Jay Gee (CDC) stated that if a major outbreak of melioidosis occurred then the responding country's MoH would work through the normal and appropriate World Health Organization (WHO) alert notifications, to access and request support from CDC. He stated that his branch could assist, but only by invitation and coordination through WHO. LTC Kurt Schaecher (USAMRIID) stated that this kind of assistance within the DoD falls under contingency crisis response / disaster relief and that there are mechanisms that fund this assistance (e.g., Operation United Assistance, Ebola Outbreak Response in West Africa 2014-2015). Rebecca Lipsitz (HHS FDA) stated that her organization can be reached similarly to the process for CDC: work through WHO by invitation to access people from FDA to provide technical advice on product development.

Dr. David Dance (LOMWRU) asked about mechanisms for funding smaller-scale pilot studies, proof of concept, and projects with shorter timelines. Dr. Boylan stated that the BAA fundamental research grant at DTRA is always open without timeline. She stated that they are one-year grants that take a bit of time, but that there are always option years built into the end that they could turn into something larger.

Dr. Newman emphasized the importance leveraging reference lab networks, since it builds on capacity building functions of the intended research. He further stated that the important part is for people to know what those networks are. Dr. Gee agreed, highlighting the importance of informal collaborations as well, stating that his connection with Dr. David AuCoin (University of Nevada) resulted in an introduction from a colleague and lead to collaboration. He emphasized that the RCN, which aims to integrate formal and informal networks and relationships, will go far to build awareness of what more people are working on, work to coordinate activities, and ultimately, avoid duplication of efforts.

RCN NEXT STEPS

SESSION 8: FUTURE OUTPUT AND ACTIVITIES

At the conclusion of the workshop, Dr. Direk Limmathurotsakul outlined the next steps for the RCN listing short and long-term approaches, output, and activities. He stated that the most immediate priority should be to improve the burden estimates of melioidosis from unpublished data. He identified several potential ways to get data:

- Determine total number of culture-confirmed melioidosis cases (2013 – 2015)
- Determine number of fatal cases
- Determine total number of other method diagnosed melioidosis cases (2013 – 2015)
- Determine references to “contact persons”
- Determine “agreed / detailed case definitions” on how to identify *Bp*
- Set up a database of locations, sites, hospitals, institutions, laboratories that can identify *Bp* and report total number of culture-confirmed melioidosis cases
- Setup a database with locations of reference centers that can support *Bp* confirmation for other sites in the country and worldwide with or without cost and with national guidelines

Dr. Limmathurotsakul stated that the RCN would next seek to improve awareness and knowledge of the disease amongst policy makers, clinicians / nurses, and laboratory employees and identified the following ways to accomplish this goal:

- Implement country-by-country meetings with policy makers and local clinicians / researchers with support from experts and international organizations such as WHO, CDC, CBEP (and others as appropriate)
- Establish a database of guidelines that could also include public awareness documents, teaching documents, meeting reports, in multiple languages and learning formats
- Support training and workshops on how to do bacterial identification, set up clinical cohort, Dx, Tx, save organisms (safely and securely), save clinical specimens, and improve communication
- Support each country with media outreach and response / share media response when the country lead / leading person for the work needs
- Set standard that all reference labs in SEA and worldwide should be able to identify *Bp* accurately (e.g., should not misidentify *Bp* as contaminants, *Pseudomonas spp*, or other bacteria
    - Then set a standard that all microbiology labs in SEA should be able to do the same protocols established by this effort

Dr. Limmathurotsakul emphasized that the RCN would aim to do more research and identified the following ways to potentially achieve this intent:

- Establish regular meetings between funders and researchers ; leverage this forum as a way to identify gaps and needs
- Connect research locations to the funders via a database to conduct more studies and collaborations (for cutting-the-edge/Dx/Tx/Environment – base on set up and potential availability)

- Present open data as to where in the world one can diagnose melioidosis and conduct research

Dr. Limmathurotsakul stated that the immediate goals (within the first year) of the RCN would be to seek support to set up a system to collect, curate, and set up databases and location data. He would next form a steering committee that represents all SEA countries, which are affected by the burden of melioidosis. He stated that as the steering committee head of the RCN, that he would likely look for support from CBEP SEA and that the main thrust of effort would come from SEA member countries (with invited experts for specific tasks). He emphasized that he felt the work is a global problem (not limited to SEA) and acknowledged that the funders are focused on worldwide collection of data / solutions. He stated that they would seek support from other agencies to use tools / personnel as applicable within the region. He solicited the funders to request for open data sharing as part of their agreements for the research that they fund. He stated that we cannot underestimate the burden and the need to increase awareness on this disease.

Dr. Limmathurotsakul outlined some longer-term goals for the RCN, including holding an annual meeting. He highlighted the discussions and networking that concluded as a wonderful example of the community and stated that he looks forward to opportunities to meet in the future.

ANNEX A – FINAL EVENT AGENDA

Day 1:	
0830 – 0930	**Opening and Introduction to Melioidosis RCN**
0830 – 0850	**Welcome Remarks** Dr. S. Elizabeth George (Director of Cooperative Threat Reduction (J3CT), Operations, Readiness, and Exercises (J3/7), US) Colonel Greenhaw (Deputy Director DTRA Chemical / Biological Technologies (J9CB)
0850 – 0910	**Around the Room Introductions** *Everyone will have the opportunity to briefly introduce themselves and their organization*
0910 – 0930	**Workshop Goals, Objectives, and Brief History of RCNs its Application in Southeast Asia** Dr. Marty Stokes (Cooperative Biological Engagement Program (CBEP) SEA Science Manager, US) and Dr. Direk Limmathurotsakul (Mahidol University, Thailand)
0930 – 1200	**Session 1: Presentation of Individual Research (5-10 min each)** *Session Moderators: Dr. Marty Stokes and Dr. Direk Limmathurotsakul*
0930 – 1030	**Overview of Current melioidosis Research in Southeast Asia** All participants *Participants will be invited to the stage to present their melioidosis research*
1030 – 1100	**Tea Break**
1100 – 1200	**Overview of Current melioidosis Research in Southeast Asia (continued)** All participants *Participants will be invited to the stage to present their melioidosis research*
1200 – 1300	**Lunch**
1300 – 1500	**Session 2: Regional Risk and Burden of melioidosis** *Session Moderator: LTC Kurt Schaecher*
1300 – 1330	**Melioidosis: A Disease of Surprise** Dr. Bart Currie (Menzies School of Health Research and Royal Darwin Hospital, Australia)
1330 – 1400	**Melioidosis Regional Risk Assessment and Prevention Measures** Dr. Gladys Tan Gek Yen (DSO National Labs, Singapore)
1400 – 1430	**Economic Burden of melioidosis in Southeast Asia** Dr. Saithip Bhengsri (CDC GDD, Thailand)
1430 – 1500	**Open discussion – Risk and Burden** All participants
1500 – 1530	**Tea Break**
1530 – 1700	**Session 3: Diagnostics and Environmental detection** *Session Moderator: Dr. Direk Limmathurotsakul*
1530 – 1600	**Detection (Clinical/Environmental)** Dr. David Dance (Lao-Oxford Mahosot Hospital – Wellcome Trust Research Unit)
1600 – 1630	**Rapid Diagnostic Tests for Infectious Diseases** Dr. David Aucoin (University of Nevada, US)
1630 - 1700	**Open discussion – Diagnosis and Environmental Detection** All participants
1700 -1730	**GROUP PHOTO** We will take a group photo in the main lobby under the elephant mural

Day 2	
0800 – 0815	**Review Day 1 and Brief Overview of Objectives for Day 2** *Dr. Marty Stokes*
0815 – 0945	**Session 4: Disease Pathogenicity and Immune Response** Session Moderator: Dr. Ayanna Flegler
0815 – 0845	**Insights into Pathogenicity and Immune Response** Dr. Ganjana Lertmemongkolchai (Khon Kaen University)
0845 – 0915	**Antibiotic Resistance** Dr. Narisara Chantratita (Mahidol University, Thailand)
0915 – 0945	**Open discussion – Disease Pathogenicity and Immune Response** All participants
0945 – 1015	**Tea Break**
1015 – 1215	**Session 5: Vaccines and Therapeutics** *Session Moderator: Dr. Julie Boylan*
1015 – 1045	**A New Treatment Paradigm: Therapy Duration and Outcomes** Dr. Bart Currie (Menzies School of Health Research and Royal Darwin Hospital, Australia)
1045 – 1115	**Melioidosis Vaccine: How Far Are We?** Dr. Rick Titball *(Exeter University, UK)*
1115 – 1145	**Animal Models** Dr. Gregory Bancroft (London School Hygiene and Tropical Medicine)
1145 – 1215	**Open discussion – Vaccine and Therapeutics** All participants
1215 – 1330	**Lunch**
1330 – 1630	**Session 6: Breakout Group Discussions to Identify and Prioritize Research Needs and Gaps**
1330 – 1500	**Breakout Group Discussions** Group 1 (Identifying Needs for Researching Risk, Burden, and Diagnostic and Surveillance Methods) Moderators: Dr. Carl Newman, Dr. Marty Stokes, and Dr. Direk Limmathurotsakul Group 2 (Identifying Needs for Researching Disease Pathogenesis, Immune Response, Vaccine Development, and Therapeutics) Moderators: Dr. Julie Boylan and LTC Kurt Schaecher
1500 - 1530	**Tea Break**
1530 – 1630	**Breakout Group Key Findings Report Out /Open Discussion** Moderated by Dr. Marty Stokes, Dr. Direk, Dr. Julie Boylan, and LTC Kurt Schaecher 15 min Group 1 Presentation; 15 min Group 2 Presentations; 15 min Open Discussion
1630 – 1700	**Path Forward: Developing Public Awareness and Influencing Policy** Dr. Direk Limmathurotsakul
1730 – 1900	**Social Event** All participants are invited to an evening social event by the pool

Day 3:	
1000 – 1015	Review Day 2 and Brief Overview of Objectives for Day 3 *Dr. Marty Stokes*
1000 – 1200	**Session 7: Funding Cooperative Research** *Session Facilitator: Chris Russell*
1000 – 1110	**Opportunities and Funding Mechanisms Across the U.S. Bioresiliency Mission Space: – Quad Charts**
1110 – 1200	**Opportunities and Funding Mechanisms Across the U.S. Bioresiliency Mission Space: Q&A** Panel Discussion on Processes for Response to Calls for Proposal and Review
1200 – 1300	**Lunch**
1300 – 1545	**Session 8: RCN Next Steps** *Session Moderator: Direk Limmathurotsakul*
1300 – 1400	**Group Discussion:** **Strategic Report Review and RCN Informal Agreement** **Potential RCN Activities as a Mechanism to Align Research** All participants
1400 – 1430	**Tea Break**
1430 – 1500	**Summary of the Meeting and Outlining Next Steps** Dr. Direk Limmathurotsakul
1500 – 1515	**Closing Remarks** Dr. Carl Newman (DTRA CBEP Science Lead) Col Timothy Greenhaw (DTRA CB Technologies)

ANNEX B – WORKING GROUP MEETING STEERING COMMITTEE

The following individuals were instrumental in the development, design, and scope of this working group meeting (*note: names are in alphabetical order, not by order of importance)*.

- Dr. Julie Boylan
  Science and Technology Manager for CB Transitional Medicine, Vaccines and Pre-treatments
  julie.boylan.civ@mail.mil

- Dr. David Dance
  Clinical Research Microbiologist, Lao Oxford Mahosot Hospital Wellcome Trust Research Unit and Center for Tropical Medicine, University of Oxford
  David.d@tropmedres.ac

- Dr. Ayanna Flegler
  Science Lead, SEA *CTR Advisory and Assistance Contractor, Cooperative Biological Engagement Program*
  ayanna.j.flegler.ctr@mail.mil

- Lieutenant Commander Matt Johns
  United States Public Health Service
  HHS Global Health Security Advisor- Asia Pacific
  Matthew.Johns@hhs.gov

- Dr. Direk Limmathurotsakul
  Assistant Professor, Head of the Microbiology Department at Mahidol-Oxford Tropical Medicine Research Unit
  direk@tropmedres.ac

- Lieutenant Colonel Kurt Schaecher
  Deputy Chief, USAMRIID, Medicine Division
  kurt.e.schaecher.mil@mail.mil

- Dr. Marty Stokes
  SEA *Regional Science Manager, Cooperative Biological Engagement Program*
  martha.m.stokes.civ@mail.mil

ANNEX C – PARTICIPANT FEEDBACK

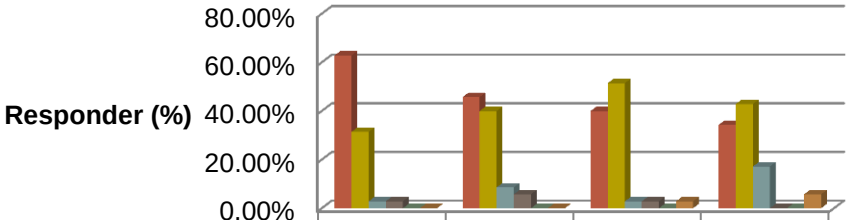
Participants were asked to fill out evaluation forms which were used to assess the effectiveness of the SEA Stakeholders Working Group Meeting.

Overall, the feedback demonstrates that the meeting was well-received and the participants valued the opportunity to network first and foremost. The participants understood and agreed that there is a need for increased geographical awareness of melioidosis in the region, as well as the need to identify and pursue funding opportunities for future research activities. Participant feedback described the speakers and scientific content as informative and interesting, as well as properly-paced and cohesive. It was additionally noted that future events will help close current gaps within melioidosis research.

The feedback forms also granted the participants an opportunity to suggest improvements for future meetings. These recommendations include more focus on developing specific activities to be set in-motion after the meeting; in addition to the inclusion of more public health experts and scientists from other areas of research associated with melioidosis (e.g., environmental science). Other suggestions consist of a participant list with contact information (name, email, phone number) to be available, as well as more time allotted for networking during the day.

Below are some key findings and the aggregated results from the evaluation forms.

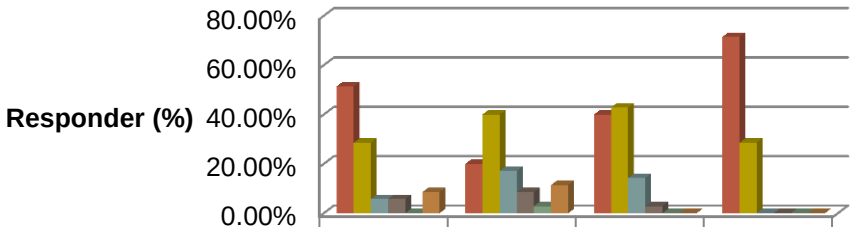
Meeting Objectives



	1	2	3	4
Strongly Agree	62.86%	45.71%	40.00%	34.29%
Agree	31.43%	40.00%	51.43%	42.86%
Neither Agree/Disagree	2.86%	8.57%	2.86%	17.14%
Disagree	2.86%	5.71%	2.86%	0.00%
Strongly Disagree	0%	0.00%	0.00%	0.00%
Not Applicable (n/a)	0%	0.00%	2.86%	5.71%

1. Define risk and prevalence of melioidosis in SEA
2. Outline the health burden and economic impact of melioidosis at national and regional levels across SEA
3. Outline coordinated solutions and associated activities for the RCN
4. Identify and de-conflict available funding programs, which are currently operating from multiple institutions within and with interests in SEA

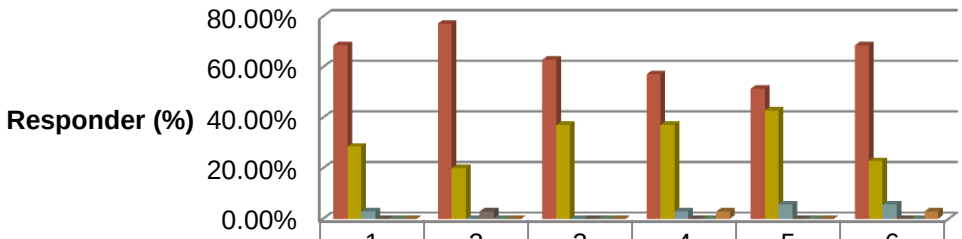
This meeting provided a forum to effectively:



	1	2	3	4
Strongly agree	51.43%	20.00%	40.00%	71.43%
Agree	28.57%	40.00%	42.86%	28.57%
Neither Agree/Disagree	5.71%	17.14%	14.29%	0.00%
Disagree	5.71%	8.57%	2.86%	0.00%
Strongly Disagree	0.00%	2.86%	0.00%	0.00%
Not Applicable (n/a)	8.57%	11.43%	0.00%	0.00%

1. Adopt an informal agreement for the establishment of an RCN on melioidosis
2. Discuss and draft an outline for the Strategic Report
3. Determine specific research targets for (1) risk and prevalence of disease, (2) environmental factors, and (3) development of diagnostics and countermeasures
4. Improve and strengthen coordination amongst existing research networks

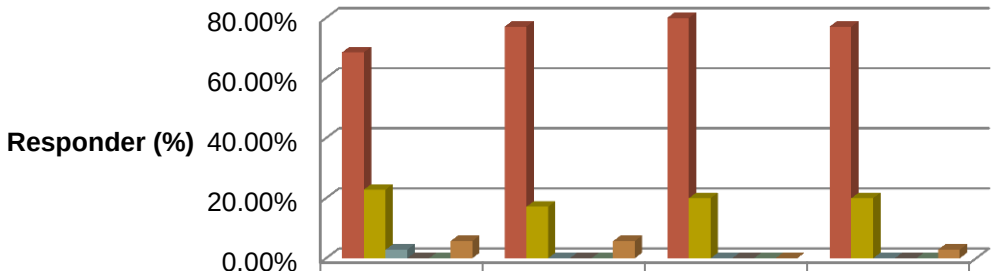
Process and Effectiveness



	1	2	3	4	5	6
Strongly Agree	68.57%	77.14%	62.86%	57.14%	51.43%	68.57%
Agree	28.57%	20.00%	37.14%	37.14%	42.86%	22.86%
Neither Agree/Disagree	2.86%	0.00%	0.00%	2.86%	5.71%	5.71%
Disagree	0.00%	2.86%	0.00%	0.00%	0.00%	0.00%
Strongly Disagree	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Not Applicable (n/a)	0.00%	0.00%	0.00%	2.86%	0.00%	2.86%

1. The overall working group meeting forum and format enabled participants to identify an address relevant issues
2. The presentations and facilitated discussions were interesting and relevant to the objectives of the working group meeting
3. The pace of the meeting was appropriate
4. The material covered was relevant to my personal work
5. The materials provided were helpful to me
6. This meeting allowed me to expand my network

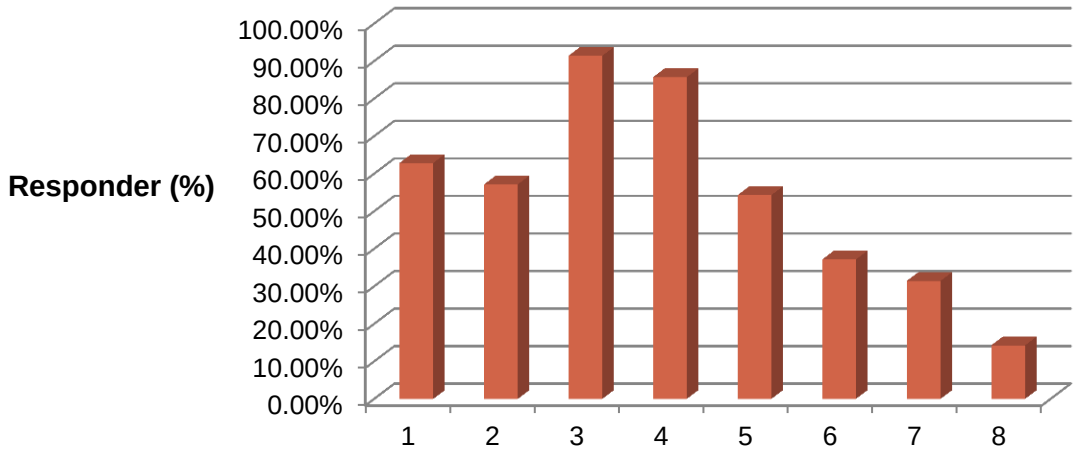
Experience with CBEP



	1	2	3	4
Strongly Agree	68.57%	77.14%	80.00%	77.14%
Agree	22.86%	17.14%	20.00%	20.00%
Neither Agree/Disagree	2.86%	0.00%	0.00%	0.00%
Disagree	0.00%	0.00%	0.00%	0.00%
Strongly Disagree	0.00%	0.00%	0.00%	0.00%
Not applicable (n/a)	5.71%	5.71%	0.00%	2.86%

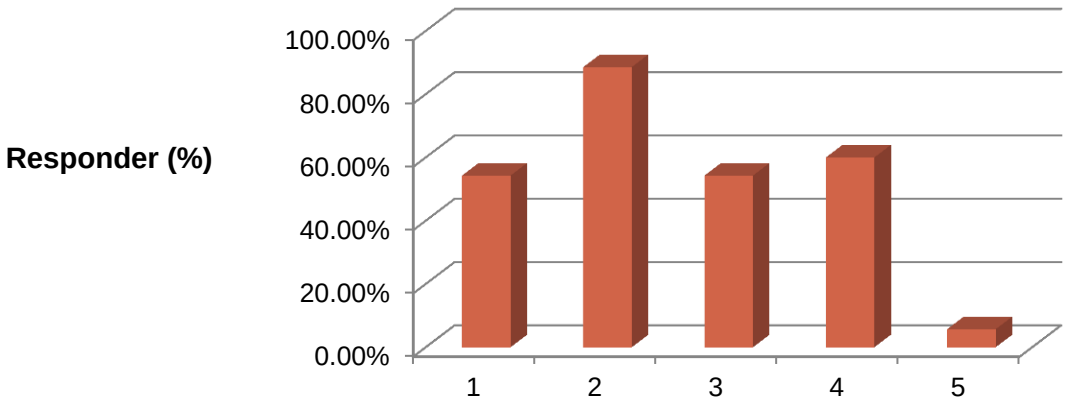
1. CBEP was responsive prior to the event
2. CBEP was responsive during the event
3. The event was well organized
4. The hotel was responsive to my needs

PLEASE DESCRIBE HOW YOU FORESEE THE APPLICATION OF NEW KNOWLEDGE AND NEW CONTACTS GAINED AT THE MEETING IN YOUR WORK AND AT YOUR INSTITUTION



1. Become a resource person
2. Deliver a lecture on the subject matter at my organization
3. Share new knowledge with colleagues
4. Collaborate with professionals I met at the meeting
5. Conduct a series of seminars / workshops
6. Publish
7. Draft a guideline or policy related document
8. Other

OF THE FOLLOWING, WHAT ADDITIONAL RESOURCES WOULD HELP YOU ACCOMPLISH THE GOALS LISTED IN THE QUESTION ABOVE?



1. Training materials (books, DVDs, posters, etc.)
2. Networking / contacts
3. Outreach Assistance
4. Phone / email / video-conferencing with international experts
5. Other

ANNEX D – FUNDERS SLIDES

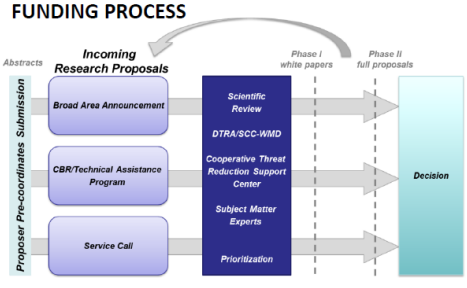
Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X				X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. Defense Threat Reduction Agency (DTRA), Cooperative Threat Reduction (CTR), Cooperative Biological Engagement Program (CBEP)
2. Mission: Reduce the threat posed by pathogens of security concern and related materials and expertise; other emerging infectious disease risks; terrorist acquisition and the use of biological weapons
3. Research foci: International research collaborations at nexus between threat reduction and public/animal health, conducted in safe and responsible manner, that inform and enhance disease surveillance and health security

FUNDING PROCESS

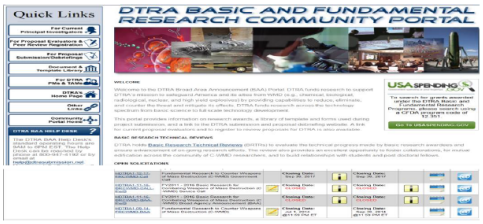


FUNDING ANNOUNCEMENT TYPES

1. BAA
   1. Academia, Industry, Non Governmental Organizations, Foreign Gov't Labs, etc....no USG
   2. Grants, typically 3-5year projects
2. Service Call
   1. US Government only (including National Labs)
   2. Interagency Agreements & Military Interdepartmental Purchase Requests, typically 3-5 year projects
3. www.dtrasubmission.net, www.grants.gov

POINTS OF CONTACT

1. Dr. Martha Stokes (CBEP Regional Science Manager, Southeast Asia)



DTRA/CTR Cooperative Biological Engagement Program (CBEP)
www.dtrasubmission.net

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X				X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. Defense Threat Reduction Agency (DTRA)
   - The Department of Defense's official combat support agency for countering weapons of mass destruction (WMD)
2. J9 (Research & Development) Directorate
   - Support DTRA' s mission by identifying, conducting, and delivering innovative science and technology via systematic, risk-balanced processes.
3. Chemical and Biological Technologies Dept.
   - Countering chemical and biological weapons
4. Research Portfolio
   1. Disease Surveillance, Threat Detection and Point of Need Diagnostics
   2. Threat Activity Sensing and Reporting
   3. Medical Countermeasures
      1. Vaccine Research
      2. Therapeutics
   4. Applied and Basic Science

FUNDING ANNOUNCEMENT TYPES

1. Small Business Innovation Research (SIBR) Grants – funds early stage small businesses that are seeking to commercialize innovative biomedical technologies
2. Small Business Technology Transfer (STTR) – requires small businesses to formally collaborate with a research institution in Phase I and Phase II
3. Broad Area Announcements (BAA) – solicitation mechanism for basic and applied research directed toward (1) advancing the state-of-the-art or increasing knowledge or understanding and (2) that part of development not related to developing a specific system for procuring hardware
4. Other Research Grants
5. Service Calls

POINTS OF CONTACT

Dr. Julie Boylan
Julie.boylan.civ@mail.mil

DTRA J9 (CB Technologies)
www.dtrasubmission.net

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X				X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

DHS S&T: The Department of Homeland Security (DHS) Science and Technology Directorate (S&T) monitors those threats and capitalizes on technological advancements at a rapid pace, developing solutions and bridging capability gaps at a pace that mirrors the speed of life. S&T's mission is to deliver effective and innovative insight, methods and solutions for the critical needs of the Homeland Security Enterprise. https://www.dhs.gov/science-and-technology

Program: The Apex Real-Time Biothreat Awareness program aims to provide timely information to multiple authorities, enabling a collaborative, confident, and effective response that ultimately minimizes the impacts of a biological incident. DHS envisions a biosurveillance system that integrates and analyzes data from multiple sources and provides real-time, actionable information. Through this program, S&T will help authorities better prepare for incidents in which biological material is released. Authorities will be able to quickly gain situational awareness about the potential biological threat, the exposed population and the likelihood of infection to provide responders and decision makers with the data needed to make informed, confident decisions that will saves lives and money and restore normal operations quickly.

FUNDING ANNOUNCEMENT TYPES

- Broad Area Announcements (BAA) – solicitation mechanism for basic and applied research directed toward (1) advancing the state-of-the-art or increasing knowledge or understanding and (2) that part of development not related to developing a specific system for procuring hardware- http://apfs.dhs.gov
- Grants: https://www.dhs.gov/how-do-i/find-and-apply-grants

FUNDING TIMELINES

1. Multiple- See: https://www.dhs.gov/science-and-technology/business-opportunities

POINTS OF CONTACT

Teresa Quitugua PhD.
Teresa.quitugua@hq.dhs.gov

DHS S&T
https://www.dhs.gov/science-and-technology

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X				X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. Organization: Armed Forces Health Science Center (AFHSC) Global Emerging Infections Surveillance (GEIS)
2. Mission: **Inform force health protection decision making and enhance global health security by preventing, detecting, and responding to infectious disease threats through strengthening: coordination, collaboration, surveillance, and outbreak response of the global DoD laboratory network**
3. Research foci: Surveillance in AMR (STI), Respiratory, Enterics, Febrile Vector Borne Infections (FVBI)

FUNDING ANNOUNCEMENT TYPES

1. RFP March (link to DoD PI)

FUNDING TIMELINES

1. Process
    1. Apr: Pre-proposal-> July Full proposal -> Oct Selections announced

POINTS OF CONTACT

1. Paige.e.waterman.mil@mail.mil (AMR/STI
2. Barbara.c.cloutier.mil@mail.mil (enterics)
3. Brett.m.forshey.ctr@mail.mil (FVBI)
4. Michael.j.cooper119.mil@mail.mil (resp)

Defense Health Agency – Armed Forces Health Science Center- Global Emerging Infections Surveillance
https://www.afhsc.mil/Home/Sections/GEIS

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X				X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. Organization: Bacterial Special Pathogens Branch, CDC
2. Mission: Serve as the subject matter experts on melioidosis, leptospirosis, glanders, brucellosis, anthrax
3. Research foci: Epidemiological methods, molecular genetics, rapid diagnostics

FUNDING ANNOUNCEMENT TYPES

1. Seeking collaborations with international partners
2. Can provide technical expertise and training
3. Higher level funding may be available through CDC Regional Offices

FUNDING TIMELINES

1. TBD based on announcement type

POINTS OF CONTACT

1. Jay Gee xzg4@cdc.gov
2. Henry Walke
3. Tony Mounts
4. Chris Gregory

CDC Bacterial Special Pathogens Branch
http://www.cdc.gov/ncezid/dhcpp/bacterial_special/

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X			X	X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. National Institute of Allergy and Infectious Diseases (NIAID) / National Institute of Health (NIH)
2. NIAID conducts and supports basic and applied research to better understand, treat, and ultimately prevent infectious, immunologic, and allergic diseases.
3. Research Portfolio
    1. Biodefense and Emerging Infectious Disease
        - Funding Inbios and Univeristy of Nevada in developing LFI
        - A major study on the correlation of deaths from acute melioidosis by Mahidol and 6 other sites (trying to include Cambodia)
        - Basic research grants (6) for understanding the pathogenies of the BP and BM
    2. Vaccine Research
    3. Immune System Research
    4. Infectious and Immunologic Diseases

FUNDING ANNOUNCEMENT TYPES

1. Small Business Innovation Research (SIBR) Grants – funds early stage small businesses that are seeking to commercialize innovative biomedical technologies
2. Small Business Technology Transfer (STTR) – requires small businesses to formally collaborate with a research institution in Phase I and Phase II
3. Broad Area Announcements (BAA) – solicitation mechanism for basic and applied research directed toward (1) advancing the state-of-the-art or increasing knowledge or understanding and (2) that part of development not related to developing a specific system for procuring hardware
4. Other Research Grants (R01. R21, U01 and PO1) and other targeted RFA's and RFP's.
5. Other Contracting Mechanisms (FedBizOpps)
6. (https://www.niaid.nih.gov/researchfunding/grant/pages/other.aspx)

FUNDING TIMELINES

1. Investigator Initiated: R01, R21- 8 months (https://www.niaid.nih.gov/researchfunding/grant/Pages/default.aspx)
2. Other Mechanisms: RFA/RFP (U –series On e year or more) (https://www.niaid.nih.gov/researchfunding/grant/pages/other.aspx)

POINTS OF CONTACT

1. Suman Mukhopadhyay

Program Officer, Zoonotic Disease
Bacteriology and Mycology Branch
Division of Microbiology and Infectious Diseases
HHS/NIH/National Institute of Allergy and Infectious Disease
5601 Fishers Lane, Room 7E39, MSC 9826
Rockville, MD 20852
Phone: (240) 627-3321

NIAID / NIH
https://www.niaid.nih.gov/Pages/default.aspx

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X			X	X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. Biomedical Advanced Research and Development Authority (BARDA)
2. Develop and procure medical countermeasures that address the public health and medical consequences of deliberate attacks, pandemic influenza, and emerging infectious diseases.
3. Supports the advanced development and procurement of drugs, vaccines and other products that are considered priorities for national health security

FUNDING ANNOUNCEMENT TYPES

1. Broad Area Announcements (BAA) – solicitation mechanism for basic and applied research directed toward (1) advancing the state-of-the-art or increasing knowledge or understanding and (2) that part of development not related to developing a specific system for procuring hardware
2. Other Research Grants (R01. R21, U01 and PO1) and other targeted RFA's and RFP's.
3. FedBizOpps- www.fbo.gov

POINTS OF CONTACT

1. Mark Albrecht Mark.Albrecht@hhs.gov
2. Clay Hughes Claiborne.Hughes@hhs.gov

US Department of Health and Human Services (HHS)- Biomedical Advanced Research and Development Authority
http://www.phe.gov/about/BARDA/Pages/default.aspx

Funding Assignments Based on Needs

	DTRA CBEP	DTRA CB	DHS S&T	AFHSB GEIS	CDC BSPB	NIAID / NIH	BARDA	HHS FDA
Awareness	X		X		X			
Burden	X	X	X	X	X	X		
Environmental Reservoirs	X	X	X	X	X			
Laboratory Capacity	X	X			X			
Pathogenesis	X	X			X	X	X	X
Immune Response		X				X	X	X
Therapeutics		X				X	X	X
Vaccine Development		X				X	X	X
Diagnostics Development		X				X	X	X

ORGANIZATION'S DESCRIPTION

1. US Food and Drug Administration, Office of Counterterrorism and Emerging Threats
2. FDA is responsible for ensuring that medical countermeasures (MCMs) —including drugs, therapeutic biologics, vaccines, and devices, such as diagnostic tests—for melioidosis and other threat agents are safe, effective, and secure
3. Regulatory science – the science of developing new tools, standards, and approaches, to assess the safety and efficacy, quality and performance of all FDA-regulated products.
   - **MCM-related Regulatory Science Areas:**
   - Develop, characterize, and qualify animal models for MCM development
   - Modernize tools to evaluate MCM product safety, efficacy, and quality
   - Identify and qualify biomarkers of diseases or conditions
   - Enhance emergency communication

FUNDING ANNOUNCEMENT TYPES

1. Broad Agency Announcement
   1. Extramural research component

BAA Areas

1. Modernize Toxicology to Enhance Product Safety
2. Stimulate Innovation in Clinical Evaluations and Personalized Medicine to Improve Product Development and Patient outcomes
3. Support New Approaches to Improve Product Manufacturing and Quality
4. Ensure FDA Readiness to Evaluate Innovate Emerging Technologies
5. Harness Diverse Data through Information Sciences to Improve Health Outcomes
6. Implement a New Prevention-Focused Food Safety Sytem to Protect Public Health
7. Facilitate Development of Medical Countermeasures (MCMs) to Protect Against Threats to the U.S. And Global Health Security
8. Strengthening Social and Behavioral Science at FDA by Enhancing Audience Understanding
9. Advancing Global Public Health

FUNDING TIMELINES

1. FDA Regulatory Science BAA Process

Step 1: Complete i)cover page, ii) Quad chart, iii) white paper (rolling submission).

Step 2: Offerors whose Quad chart and white paper receive a favorable evaluation may be invited to submit a Full Proposal (within 30 calendar days of invitation)

POINTS OF CONTACT

1. Rebecca Lipsitz, PhD, Senior Advisor for CBRN and Influenza
   Email: Rebecca.Lipsitz@fda.hhs.gov
2. Robert Fisher, PhD, Director, FDA's Medical Countermeasure initiative
   Email: Robert.Fisher@fda.hhs.gov

US Food and Drug Administration

Additional FDA Resources:

1. **Advancing Regulatory Science**:
   http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm?utm_campaign=Goo
2. **2015 FDA BAA Announcement**:
   http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm?utm_campaign=Goo
3. **Current MCM extramural funded research**:
   http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391617.htm
4. **FDA's Public Workshop on *Burkholderia*:** to present the most current information on melioidosis with the general purpose of identifying future areas of research needed to advance animal model development and to advance candidate medical countermeasures:
   http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMRegulatoryScience/ucm391617.htm
5. **FDA Counterterrorism and Emerging Threats**:
   http://www.fda.gov/EmergencyPreparedness/Counterterrorism/default.htm (Many references within)
6. **Product Development Under the Animal Rule, Guidance for Industry**:
   http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm399217.pdf
7. **Workshop on Treatment of and Postexposure Prophylaxis for *Burkholderia pseudomallei*and *B. mallei* Infection, 2010**: http://wwwnc.cdc.gov/eid/article/18/12/12-0638_article

US Food and Drug Administration

ANNEX E – SEA RESEARCH MAP (AMONG THOSE WHO PARTICIPATED)

Vientiane, LAOS

Dr. Koukeo Phmmasone, Dr. David Dance, and Dr. Paul Newton
Lao-Oxford-Mahosot Hospital Wellcome Trust Research Unit (LOMWRU)
(1) Characeterizing the clinical and epidemiological features of melioidosis in Lao PDR
(2) Working on case series from Mahosot Hospital (>900 culture-positive cases confirmed)
(3) Conducting data collection on standard template as cases arise in real time
(4) Planning WGS on approximately 720 patients.
(5) Conducting data cleaning and analysis; aim to complete and submit by end of 2016
(6) Determining impact to highlight melioidosis regions in Laos geographically
(7) Highlighting potential under diagnosis in developing countries with poor laboratory infrastructure

Dr. Kate Woods, Dr. David Dance, Dr. Latsaniphone Bouthasavon, Dr. Paul Newton
LOMWRU
(1) Aiming to evaluate recently described RDT (lateral flow – David AuCoin/InBios) on clinical samples in routine diagnostic lab. The approach consists of collecting clinical samples and compare with culture and IF 2 years of data collection and testing completed; preliminary results presented at EMC 2015; further data analysis underway. The main impact to clarify role of RDT as a diagnostic tool.

Dr. Rosalie Zimmermann, Dr. Oliver Ribolzi, Dr. Alain Pierret, Dr. Jakob Zopfi, Dr. Ivo Steinmetz, Dr. David Dance
LOMWRU
(1) Researching detection of *B. pseudomallei* in major rivers in Lao PDR on macro and meso scale in relation to biotic and abiotic factors within context of the surrounding catchment area. The main impact is to Approximate geographical distribution of Bp in Lao PDR and increase knowledge of physic-chemical factors influencing Bp presence and quantity in aquatic environments (including streambed sediments)

Hanoi, VIETNAM

Dr. Trinh Thanh Trung
Institute of Microbiology and Biotechnology, Vietnam National University
(1)Organizing workshops and training courses at different provincial hospitals ; give lectures on melioidosis and to introduce a simple culture protocol for detection of *B. pseudomallei* from clinical specimens in different regions of Vietnam
(2) Assisting with bacterial identification by molecular methods
(3) Implementing environmental surveillance of *B. pseudomallei* in different agriculture regions using culture and molecular techniques
(4) Using 595 soil samples at 119 sites in Southern Vietnam to create risk map for population acquiring the disease

Prof. Dang Duc Anh and Dr. Hoang Thi Thu Ha
National Institute of Hygiene and Epidemiology
(1) Isolating *B. pseudomallei* strains from patients and environment source by different diagnostic tools; determination of virulent factors and antimicrobials of *B. pseudomallei* strain isolates
(2) Genetic characterization of *B. pseudomallei* in Vietnam, in order to establish etiology of *B. pseudomallei*, and an epidemiological picture of melioidosis in

Nakhon Ratchasima, THAILAND

Dr. Supaporn Wacharapluesadee, Ms. Teerada Ponpinit, and Professor Thirabat Hemaachudha
Neuroscience Center for Research and Development & WHO-CC for Research and Training on Viral Zoonoses; King Chulalongkorn Memorial Hospital; Faculty of Medicine, Chulalongkorn University
(1) Conducting a study to monitor the prevalence of melioidosis, brucellosis, and Q fever in this Nakhon Ratchasima province, in both at-risk human and animal populations

Bangkok, THAILAND

Dr. Direk Limmathurotsakul
Mahidol-Oxford Tropical Medicine Research Unit (MORU)
(1) Rectifying surveillance database of MOH, Thailand
(2) Identifying problems with misdiagnosis
(3) Performing first spatial modeling work on published data
(4) Evaluating genreal public awareness and exploring associated problesm with poor awarenss / lack of prevention
(5) Conducting ongoing RCT prevention of melioidosis

Dr. Christopher Gregory
Division of Global Health Protection, CDC
(1) Improving recognition of burden of melioidosis
(2) Demonstrating incidence in "non-endemic" and endemic areas of Thailand
(3) Building culture capacity in referral hospitals in NW Thailand
(4) Evaluating POC tests using Bayesian Latent Class Analysis

Dr. Supaporn Wacharapluesadee, Ms. Teerada Ponpinit, and Professor Thirabat Hemaachudha
Neuroscience Center for Research and Development & WHO-CC for Research and Training on Viral Zoonoses; King Chulalongkorn Memorial Hospital; Faculty of Medicine, Chulalongkorn University
(1) Conducting a study to monitor the prevalence of melioidosis, brucellosis, and Q fever in this Nakhon Ratchasima province, in both at-risk human and animal populations

Pehang, MALAYSIA

Dr. Imad, M.A. Mustafa, Dr. How, S.H., and Dr. Jamaluddin, Janaki, Aniza
International Islamic University
(1) Utilizing Pahang melioidosis registry
(2) Utilizing early diagnostic tests (e.g., serology and PCR)
(3) Reducing melioidosis mortality in Pahang

SINGAPORE

Dr. Gladys Tan
DSO National Labs
(1) Evaluating efficacy of 3 candidate vaccines in conjunction with AGP as an adjuvant against lethal inhalational murine model of melioidosis
(2) Work on 2 vaccine candidates has commenced; preliminary data on 1 candidate demonstrated that *Bp*-specific adaptive immune responses were generated and corresponded to bacterial burden and survival outcome
(3) Best vaccine candidate in murine model amongst the three will be identified, and subjected to further testing in the NHP model (with DTRA)

Distributed locations, PHILIPPINES

Dr. Apichai Tuanyok, Dr. Herbert Schweizer, and Dr. Elizabeth Telan
University of Florida Emerging Pathogens Institute
(1) Investigating the burden of melioidosis in both humans and animals in different regions of the Philippines
(2) Studying the occurrence of *B. pseudomallei* in natural environment and risk of environmental exposures

Takeo Province, CAMBODIA

Kevin L. Schully, Danielle V. Clark, James V. Lawler
The Austere Environments Consortium for Enhanced Sepsis Outcomes, NMRC-Frederick
(1) research aimed at improving prevention, early recognition, diagnosis, and effective treatment of severe sepsis syndrome from all causes in austere environments
(2) Identifying of unique physiological and biochemical markers for sepsis, severe sepsis, and agent identification based on host-pathway responses
(3) Observational trial of sepsis in Takeo Province, Cambodia; 220 patients currently enrolled, 13 culture confirmed melioidosis patients

Ho Chi Minh City, VIETNAM

Dr. Diep The Tai
Pasteur Institute
(1) Working to isolate *Burkholderia* from environment and patient, characterization and distribution of *B. cepacia* complex, and to survey the antimicrobial resistance of *Burkholderia*. The main impact is the control of *Burkholderia* and additional information on treatment strategy.

Other on-going research, but not currently underway within the geographic bounds of SEA, included the following efforts presented:

Dr. Herbert Schweizer
University of Florida Emerging Pathogens Institute

1) Conducting studies to establish molecular mechanisms governing resistance.
2) Identification and archiving of resistant clinical isolates in endemic regions, and ensuring availability for laboratory studies.
3) Convey knowledge gained from basic science studies to guide therapeutic strategies (in conjunction with clinical experiences).
4) Surveys on-going; Surveys of clinical and environmental isolates from geographically diverse regions identified mechanisms of *B. pseudomallei* antibiotic resistance

Kevin L. Schully, Danielle V. Clark, James V. Lawler
The Austere Environments Consortium for Enhanced Sepsis Outcomes, NMRC-Frederick

1) ACESO is a consortium of investigators executing a coordinated program of research aimed at improving prevention, early recognition, diagnosis, and effective treatment of severe sepsis syndrome from all causes in austere environments.
2) Identification of unique physiological and biochemical markers for sepsis, severe sepsis, and agent identification based on host-pathway responses
3) Observational trial of sepsis in Takeo Province, Cambodia; 220 patients currently enrolled, 13 culture confirmed melioidosis patients

Dr. Bart Currie
Northern Territories, Australia

1) Darwin Prospective Melioidosis Study

Dr. Gregory Bancroft (LSHTM), Dr. Patrick Tan (GIS), Dr. Martino Bolognesi (U. Milan), Dr. Gan Lertmemongkolchai (KKU), Dr. Phil Felgner (UC Irvine)

1) Genome wide studies; including genomic diversity of pathogen, transcrptome and proteome changes on infection, and changes in methylome of infected cells
2) Mapping immune responses to infection
3) Alternative infection models

Dr. Gregory J. Bancroft with Dr. G. Lertmemongkolchai (KKU, Thailand) and Dr. R.W. Titball (Exeter, UK)

1) Using murine models to study mammalian immune response to *B. pseudomallei*
2) Validate models against infection with *B. pseudomallei* in humans
3) Develop new models which more closely resemble human disease (acute v. chronic)
4) Develop new tools for efficient screening of vaccine candidates under ABSL-3 conditions

Dr. Ivo Steinmetz in collaboration with Dr. T.T Trung (Hanoi), Dr. D. Limmathurotsakul (Bangkok) and Dr. A. Tuanyok (Gainesville, Florida, USA)

1) Identification of novel *B. pseudomallei* qPCR gene targets by comparative genomic assays
2) Validation of a multi-target based qPCR method for the direct detection and quantification of *B. pseudomallei* in soil samples from different Asian regions.
3) Demonstration of direct multi-target qPCR improves the *B. pseudomallei* detection rate in soil samples.

ANNEX F – AFTER ACTION / EVENT HOTWASH DISCUSSION

Planners and members of the RCN Steering committee met to discuss the event after its close on the final day. They talked through what went well and where improvements could be made for future RCN meetings. Most agreed that it was a very interactive meeting and complimented the planners on providing enough time in the schedule me to thoroughly discuss gaps and needs amongst the community. They also commented that the event's organization was carried out effectively with good objectives and nice balance within the breakout groups.

Many agreed that future events should include endemic countries, such as Myanmar, Indonesia and Brunei. It was discussed that both the U.S. DoD (Pacific Command) and World Health Organization could help bring incorporate expertise from additional countries in the region. The group also agreed that more concrete objectives for future meetings would help keep the group working towards common goals.

In addition to other endemic countries, the group also discussed bringing in additional expertise, which could include:

- Sub-regional disease networks in the region, such as the Mekong Basin Disease Surveillance group
- Country government representation from Ministries of Health and Veterinary Medicine to broaden awareness on the disease
- Other U.S. funding agency representation
- Health economics experts
- Global Health Security Agenda representation

The group agreed to meet in August during the World Melioidosis Congress. They pledged to address key concerns and carry the goals of the RCN into its next phase of sustainable implementation.