Infectious Diseases and Military Operational Medicine (Environmental Health, Injury Prevention, Physiological Health and Psychological Health)

US Army Medical Research and Materiel Command

19 April 2016
Panel Members

- COL Michael P. Kozar (Co-Chair) – Science & Technology
- LTC Bryan T. Gnade – Advanced Development
- LCDR Christopher Steele (Co-Chair) – Science & Technology
- Mr. Steve Hawbecker – Advanced Development

The views expressed in this presentation are those of the author(s) and may not reflect the official policy or position of the Department of the Army, Department of Defense, or the U.S. Government.
Infectious Diseases

Colonel Michael P. Kozar, Ph.D
Director, Military Infectious Diseases Research Program
US Army Medical Research and Materiel Command
19 April 2016
Infectious Disease Panel Members

- Colonel Michael P. Kozar – Science & Technology
- Lieutenant Colonel Bryan T. Gnade – Advanced Dev
Mission
To conduct for the Department of Defense, a focused and responsive world class infectious diseases research and development program leading to fielding of effective, improved means of protection and treatment to maintain maximal global operational capability with minimal morbidity and mortality

- Force Health Protection
- Naturally occurring, known, predictable threats
- Requirements driven
Mission and Functions

Plan, coordinate and oversee a DOD Science and Technology (S&T) program that develops effective and improved countermeasures to minimize the impact of naturally occurring endemic infectious diseases upon the warfighter.

**Prevention**

- Infectious diseases adversely impact military operations. Vaccines are the long-term solution.

**Diagnostics**

Early diagnosis (human and vector) facilitates prompt, appropriate treatment and aids commanders in the field.

**Treatment**

New drugs are continually required to overcome evolving drug resistance.

**Insect Vector Control**

Most militarily relevant infectious diseases are transmitted by biting insects and other arthropods.
What Makes the MIDRP Unique?

- Focused on FDA/EPA approved products for adult indications
  - Enhance global health security
  - Enhance stability operations

- USAMRMC organized like a pharmaceutical company
  - Product development oriented organizational structure and processes
  - Decision Gate System integrates best industry business practices
  - Historical success of vaccines/therapeutics

- Core research program embedded in Military labs with uniformed researchers
  - Discipline and mission focus
  - Global research platform – Host nation partners
  - Unique overseas clinical trial sites
Infectious Diseases Countermeasure Development Strategy

**Prevention**
- Pre Exposure/Pre-Deployment
  - Provide Immunity Before Exposure
- Understand Epidemiology, Pathophysiology, and Immunity
  - Develop and Test Candidate Products

**Field Interventions**
- Deployed in the Field
  - Reduce Risk of Exposure to Pathogens
  - Reduce Risk of Illness (LDD)
  - Identify Agents
- New Drugs
  - Vector Control Products
  - Blood Screening Tools
  - Human Diagnostics – Vector Detection

**Long Term Treatment/Management**
- MTF/Definitive Care
  - Reduce Exposure to Nosocomial Pathogens
  - Identify Agents of Wound Infections
  - Optimize Wound Infection Management
- New Drugs and Biologics
- Diagnostics
- Environmental Decontamination Products
- Bio-Marker Discovery

**Products**
- Malaria Vaccine
- Dengue Vaccine
- ETEC Vaccine
- HIV Vaccine
- HFRS Vaccine
- Improved Bed Net
- Tafenoquine
- IV Artesunate
- Non-DEET Repellants
- Topical Paromomycin
- Leishmania Rapid Diagnostic Device
- Anti-Microbial Human Skin Substitute
- Sideromycins - Antibacterial Delivery Systems
- Arbekacin
- MDRO Real-time Diagnostics
**Investment Strategy**

**Tier 1 - High user need, High operational risk**

<table>
<thead>
<tr>
<th>Disease</th>
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<tbody>
<tr>
<td>Malaria (all types)</td>
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<tr>
<td>Diarrhea - bacterial</td>
</tr>
<tr>
<td>Dengue fever</td>
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<tr>
<td>Chikungunya/Onyong-nyong, Ross River Fever</td>
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<tr>
<td>Norovirus</td>
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<tr>
<td>Mers-CoV and other Emerging Inf. Diseases</td>
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<tr>
<td>MDR Bacteria</td>
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<tr>
<td>Ebola hemorrhagic fever/Marburg</td>
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<tr>
<td>Influenza</td>
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**Tier 2 - Medium user need, Medium operational risk**

<table>
<thead>
<tr>
<th>Disease</th>
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<tbody>
<tr>
<td>HIV/AIDS</td>
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<tr>
<td>Leishmaniasis - cutaneous and mucosal -visceral</td>
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<tr>
<td>Hantavirus hemorrhagic fever with renal syndrome/pulmonary syndrome</td>
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<tr>
<td>Adenovirus</td>
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<tr>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Schistosomiasis</td>
</tr>
<tr>
<td>Typhoid/paratyphoid fever</td>
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<tr>
<td>Meningococcal meningitis</td>
</tr>
<tr>
<td>Rabies</td>
</tr>
<tr>
<td>Crimean-Congo hemorrhagic fever</td>
</tr>
<tr>
<td>Q fever</td>
</tr>
<tr>
<td>Lassa fever</td>
</tr>
<tr>
<td>Rift Valley fever</td>
</tr>
<tr>
<td>Melioidosis</td>
</tr>
<tr>
<td>Tuberculosis w/MDR included</td>
</tr>
<tr>
<td>West Nile fever</td>
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</tbody>
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**Conduct of Chemical And Biological Defense Program**

50 U.S.C. § 1522 (d)(2) “Funding requests for the program may not be included in the budget accounts of the military departments."
Intramural Overseas Research Laboratories

Critical Resource in Global Infectious Disease Research

USAMRIID, Fort Detrick

WRAIR/NMRC, Silver Spring

NAMRU-3, Cairo

AFRIMS, Bangkok

NAMRU-6, Lima

USAMRU-K, Nairobi

USAMRU-G, Tbilisi

NMRC-Asia, Singapore/NAMRU-2, Cambodia
<table>
<thead>
<tr>
<th>Program Portfolio</th>
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</thead>
<tbody>
<tr>
<td><strong>Research Effort</strong></td>
</tr>
</tbody>
</table>
| Parasitic Diseases | - Malaria drug (CDD)  
- Malaria vaccine (CDD)  
- Leishmaniasis | - Intravenous Artesunate (CPD)  
- Tafenoquine  
- Topical Paromomycin drug (CPD) | - Atovaquone/Proguanil (Malarone®, 2000)  
- Doxycycline (Vibramycin®, 1992)  
- Halofantrine (Halfan®, 1992)  
- Mefloquine (Lariam®, 1989)  
- Sulfadoxine-Pyrimethamine (1983)  
- Chloroquine-Primaquine Tablets (1969)  
- Primaquine (1952) |
| Viral Diseases | - Dengue (CDD)  
- Hemorrhagic fevers  
- scrub Typhus  
- HIV Global (CDD)  
- Acute respiratory disease research  
- Chikungunya vaccine development | - Dengue Tetravalent (CDD)  
- HIV Regional (CDD) | - Adenovirus 4 & 7 (1980) – (2011)  
- Japanese Encephalitis - cell based (2009)  
- Japanese Encephalitis (1992)  
- Hepatitis B (1981) |
| Diagnostics Development | - Point-of-need devices (CDD)  
- Biofire Filmarray NGDS assay development  
- ESKAPE pathogens | - Biofire Filmarray NGDS - Malaria, Dengue, Chikungunya | - Malaria Rapid Diagnostic Test (2007)  
- Leishmania Rapid Diagnostic Device (2014)  
- 5 hour antimicrobial susceptibility testing transitioned to industry (Accelerate Diagnostics) Expect FDA approval in 2017 |
**Program Portfolio**

<table>
<thead>
<tr>
<th>Research Effort</th>
<th>Advanced Development</th>
<th>Fielded Products</th>
</tr>
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</table>
| • Clinical studies using current antibiotics for the prevention of infection post surgery  
  • Intrasite vancomycin  
  • Bismuth-thiol                                                                   | • Rapid Microbiological Diagnostics for MDRO Quantitative Identification              | • Antimicrobial Prescribing Practices - Prevention of Infections Associated With Combat-Related Injuries (series of publications. *J. Trauma* 2011) |
| • Preclinical studies with novel therapeutic agents for the treatment of wound infections  
  • Broad-spectrum conjugate vaccine  
  • Gallium citrate  
  • Antifungal (VT-1598)  
  • Recombinant interleukin-12  
  • Activated adult mesenchymal stem cells                                             |                                                                                      | • Arbekacin (FDA-approved for Single site study at Walter Reed National Military Medical Center) |
| • Preclinical studies with novel anti-infective delivery systems for the treatment & prevention of wound infections  
  • Anti-infective human skin substitute  
  • Antimicrobial nanoemulsion (NB-201)                                               |                                                                                      | • Recognition and Comprehensive Management of Invasive Fungal Infections in War Wounds - *JTTS Clinical Practice Guideline* approved 1 Nov 2012 |
| • Diarrhea (CDD)                                                                  |                                                                                      | • Meningococcus (A, C, Y, W-135) (1981)                                            |
| • Repellents/Insect control                                                        |                                                                                      | • Oral Live Typhoid Ty21A (1989)                                                    |
| • Insect identification                                                            |                                                                                      | • Sentrex BioSponge™ - added to FSS 1 Apr 2015                                      |
| • Arthropod-Vector Detection Device (CDD)                                           |                                                                                      | • Combined Camo Face Paint (2013)                                                  |
| • Bednet                                                                         |                                                                                      | • Alternate Repellent System (2013)                                                |
| • CO2 Generator Mosquito Trap                                                     |                                                                                      | • Arthropod Vector Rapid Detection Device for Dengue (2012)                        |
| • AV-RDD Chikungunya Virus                                                        |                                                                                      | • Rift Valley Fever virus Vector Detection Assay (2011)                            |
| • West Nile Virus detection Kit (2001)                                             |                                                                                      | • West Nile Virus detection Kit (2001)                                             |
| • Amifostine (Ethylol®, 1995)                                                      |                                                                                      | • Amifostine (Ethylol®, 1995)                                                      |
| • DEET-based Insect Repellent (1946)                                               |                                                                                      | • DEET-based Insect Repellent (1946)                                               |
Success Continues Today

USAMRMC PLAYS KEY ROLE IN THE CURRENT LEADING VACCINES DEVELOPMENT

- **HIV**
  (TIME 2009 - Top 10 Medical Breakthroughs)

- **Malaria**
  (Time 2011 - Top 10 Medical Breakthroughs)

- **Dengue**

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**Protection Against Malaria by Intravenous Immunization with a Nonreplicating Sporozoite Vaccine**

The PfSPZ Vaccine (cryopreserved radiation-attenuated sporozoites)
- Safe, very well tolerated
- 100% protection in the subjects that received the highest vaccine dose

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**GSK’s malaria candidate vaccine, Mosquirix™ (RTS,S), receives positive opinion from European regulators for the prevention of malaria in young children sub-Saharan Africa.**

Early clinical development was done in collaboration with WRAIR.
Army and Defense Health Program Task Areas

**Army**

- Parasitic Diseases Research
  - Anti-Parasitic Drug Development
  - Malaria Vaccine Research
- Viral Diseases
  - Flavivirus Vaccine Research
  - Lethal Virus (Hantann, Puumala) Countermeasures
- Bacterial Diseases
  - Prevention of Diarrheal Diseases
  - Rickettsial Diseases
- Vector Control
  - Identification and Control of Insect Vectors of Infectious Diseases
- Diagnostic Systems
  - Diagnostic Systems for Infectious Diseases (far forward, rapid & easy to use point-of-care tests)

**DHP**

- Antimicrobial Countermeasures
- Wound Infection Prevention and Management (applied & translational product development)
- Diagnostic Systems for Infectious Diseases (integrated platform with multiple ID panels at role 3 and higher)
- Acute Respiratory Diseases/Emerging Infectious Diseases
  - Military HIV Research Program*
  - Combatting Antimicrobial Resistance Pgm*
  - Deployed Warfighter Pgm*

* DHP Named Programs under JPC2
Strategic Science & Technology Research Gaps

- Hantann/Puumala Virus DNA Vaccine – Co-Development Partner
  - A Phase 2a Randomized, Double-Blind, Dose-Optimizing Study to Evaluate the Immunogenicity of Hantaan/Puumala Virus DNA Vaccine Administered to Healthy Adult Volunteers Using the TDS-IM Electroporation Delivery Device for Prevention of Hemorrhagic Fever With Renal Syndrome

- Detect, prevent, and manage combat wound infections and biofilm formation – Focus on IND enabling studies
  - Emphasis on Multi-Drug Resistant Organisms (MDROs) and invasive fungi/molds
  - Novel countermeasures and innovative treatment approaches – chelators, antibody therapy, phage, anti-microbial peptides, quorum-sensing inhibitors, host immunomodulation/immunotherapies, etc.
  - New chemical chemotypes/classes and biologics – antibiotics? vaccines?

- Novel drug delivery technologies for treatment/prevention of infectious disease
  - Sustained release or reduce toxicity
  - Passive prophylaxis – eliminate individual compliance issues with an emphasis on anti-malarials

- Broad spectrum antiviral drugs
  - Agents that are clinically effective for treating multiple viral families, including the potential for "designer" applications that would allow for selection of combinations of agents based on geographic deployment.
Treatment for Cutaneous Leishmaniasis (CL) in development

- Topical (skin) treatment for uncomplicated CL
- 2 pivotal, Phase 3 studies complete (Tunisia and Panama)
- Product down-select anticipated in April 2016
- Gap: Long-term commercial/co-development partner and final product manufacturer not yet identified
Working with MIDRP


• Broad Agency Announcement - http://www.grants.gov
  ➢ On the Grants.gov homepage, click the tab "SEARCH GRANTS";
  ➢ In the "Funding Opp #" block, enter W81XWH-16-R-BAA1

• Peer Reviewed Medical Research Program http://cdmrp.army.mil/prmrp/
  ➢ $278.7 million in FY16
  ➢ 39 topic areas including: Emerging Infectious Diseases, Malaria, and Vaccine Development for Infectious Diseases
Military Operational Medicine Research Program Overview

LCDR Christopher Steele, PhD
Deputy Director, MOMRP
US Army Medical Research and Materiel Command
19 April 2016
Military Operational Medicine Panel Members

LCDR Christopher Steele – Science & Technology
Deputy Director, MOMRP

Mr. Steve Hawbecker – Advanced Development
Project Manager, Medical Support Systems
US Army Medical Materiel Development Activity
MOMRP is an extremely diverse program

~90% of MOMRP projects are linked to knowledge products that are central to the DoD Total Force Fitness (TFF) and Army Human Dimension concepts.

Supports performance sustainment, health protection and operational readiness of the Joint Warfighter across the Range of Military Operations and Service member life-cycle

R&D to understand novel mechanisms and develop focused solutions at the group and individual level for Precision Operational Medicine
Develop effective medical countermeasures against operational stressors and prevent physical and psychological injuries during training and operations in order to maximize the health, performance and fitness of Service members and their Families.
MOMRP ARMY/DHP Total Program Distribution (FY17-23)

Army Program Tasks ($414M)
- PSYCH: $90K (22%)
- ENVIRO: $105K (25%)
- PHYSIO: $80K (19%)
- INJURY: $139K (34%)

DHP (JPC-5) Program Tasks ($246M)
- PSYCH: $35K (14%)
- ENVIRO: $58K (24%)
- PHYSIO: $67K (27%)
- INJURY: $86K (35%)
MOMRP research touches every Service member, every day.

DEVELOPING AND MAINTAINING A FIT AND READY FORCE

- Influencing Policy, Leadership, and Training & Education
- Knowledge Products: Regulations, Standards, Guidelines, Decision Support Tools
  - Materiel Products: COTS/GOTS, New Devices
MOMRP Gaps

Environmental Health & Protection (1 of 2)

Heat Exposure
- Performance and injury predictions
- Return to duty criteria following heat injury
- Microclimate cooling
- Technologies for optimal hydration status management

Altitude/Hypoxia Environments
- Performance and injury predictions
- Technologies to support sustained operations

Multi-environmental Stressors

Arctic Operations

Panel Discussion – Performance Sustainment and Health Protection in Operational Environments
Environmental Health & Protection (2 of 2)

Toxicant Exposure

- Accurate dose information for exposure to industrial chemical mixtures and material hazards
- Technologies and wearable devices to track chemical/toxic hazard exposures

Biomarker Panels to Assess SM Impact

- Toxicant environmental health hazards
- Industrial chemical mixtures found in dense urban environments

Acute and Chronic Health Effects Linked to Response-Biomarkers

Panel Discussion – Performance Sustainment and Health Protection in Operational Environments
Training and Operational Environments

- Improved understanding of the physiological mechanisms underlying musculoskeletal injuries
  - Advanced technologies for real-time assessments outside of the clinic

- Physical fitness training strategies to reduce the risk of injury from load, jolt, vibration, etc.

- Countermeasures to mitigate injury risk potential for exploitation in training environments
Injury Prevention & Reduction (2 of 2)

Training and Operational Environments

- Development of injury criteria for Personal Protection Equipment against blunt, blast and ballistic trauma threats

- Injury criteria and medical performance standards to protect against hearing loss, vestibular injury, and ocular facial injury

- Standards and criteria to identify when Warfighters are capable to Return-to-Duty (RTD), fully able to perform demanding tasks

Panel Discussion – Performance Sustainment and Health Protection in Operational Environments
Fatigue Mechanisms and Countermeasures

- Novel mechanisms in understanding/manipulating sleep for performance and health

- Sleep quality assessment that is objective but not necessarily tied to actigraphy/polysomnography – *What are we currently measuring and what are we currently missing?*

- Non-pharmacological manipulation of alertness and sleep

- Use of VALIDATED wearables for Sleep as an indicator/predictor of performance, safety and health

- Management of Circadian rhythms
Physiological Health & Performance (2 of 3)

Nutrition Solutions, Countermeasures and Strategies

- Nutrition solutions to optimize recovery and sustain the Joint Warfighter under extreme conditions
- Nutritional interventions for mission reset and injury recovery -- countermeasures for physical and cognitive degradation following military operations
- Protection strategies to mitigate operational stress
- Tailored, modular ration components to improve readiness
Physiological Basis of Resilience and Cognitive Readiness

- **Sustain robust cognitive function** in Service members under acute operational psychological/physiological stressors

- **Promote adaptability to novel, militarily-relevant demands** and improve cognitive function in Service members over the course of a training cycle or career
Psychological Health & Resilience (1 of 2)

Service Member Resilience

- Evidence-based individual and group interventions and technologies to promote Resilience
- Resilience training that incorporates key behavioral health outcomes
- Biomarkers of resilience

Behavioral Health

- Tools and technologies to better prevent, diagnose, and treat mental health issues such as suicide and substance abuse
Psychological and Behavioral Health

- Non-self report assessment technologies of psychological well-being and status

- Telemedicine and mental/behavioral health approaches that overcome barriers/challenges

- Identification/validation of biomarkers for Post Traumatic Stress Disorder (PTSD)

- Translational efforts on the diagnosis and treatment of PTSD
National Research Action Plan (NRAP) to coordinate psychological health research across DoD, VA and NIH (NIMH/NIDA/NIAAA)

Army Study to Assess Risk and Resilience in Service Members (Army STARRS and STARRS-Longitudinal Study (STARRS-LS))

Consortium to Alleviate PTSD (CAP)

Joint review and analyses of integrated psychological health research programs across DoD, VA and NIH (NIMH/NIDA/NIAAA)

FY13 Joint Program Announcement, “Substance Abuse Prevention and Health Promotion”, with NIDA/NIAAA/NCCAM
Every Service Member, Every Day
Advanced Development

RESEARCH → ADVANCED DEVELOPMENT → FIELDED PRODUCT

- Prototyping (Durability/Packaging)
- Manufacturing Evaluation
- Validation and Verification
- Logistics Analysis/Planning
- Integration with User Representatives
- User Evaluation
- Transition/integration to other PEOs/Services

DoD 5000

Materiel Solution Analysis → Technology Maturation and Risk Reduction → Engineering and Manufacturing Development → Deployment → Operations and Sustainment

Bridging the Valley of Death
For additional questions after the conclusion of the conference, send an email message to usarmy.detrick.medcom-usamrmc.mbx.mmpd@mail.mil