



Armed Forces Research Institute of Medical Sciences Department of Enteric Diseases

1. Summary: The Department of Enteric Diseases at the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand has a long history of conducting collaborative research, epidemiology, and preclinical and clinical trials on enteric diseases. AFRIMS and the Department of Enteric Diseases can conduct both preclinical trials and clinical trials meeting US regulatory standards. The Department of Enteric Diseases has ready access to active field sites in Thailand, Nepal, and Cambodia as well as the capability to develop additional sites. The Department of Enteric Diseases maintains well-equipped and fully-staffed laboratories at AFRIMS in Bangkok and at the AFRIMS satellite laboratory in Nepal.

2. Personnel: The Department of Enteric Diseases at the Armed Forces Research Institute of Medical Sciences (AFRIMS) has a staff of 35 including 4 doctoral level scientists, 15 masters level technicians, and 3 nurses. Four of the masters' level technicians are currently completing doctoral programs. The Department also employs both full-time GLP and GCP specialists to ensure regulatory compliance for human and animal studies. AFRIMS has over 400 staff including full-time safety, occupational health, regulatory affairs, information management, biomedical maintenance, and grants management personnel.

3. Facilities: The Department of Enteric Diseases is located within Main Research Building of the Armed Forces Research Institute of Medical Sciences (AFRIMS) in Bangkok, Thailand on the grounds of the Pramongkutlao Medical Center and across the street from the Faculty of Tropical Medicine of Mahidol University. Aside from the usual laboratory, library, administrative and support facilities at AFRIMS; AFRIMS has the fully-staffed modern AFRIMS Clinical Trial Center for the conduct of outpatient studies at Bumrungrad Hospital in downtown Bangkok as well as the accredited Veterinary Medicine Facility with over 600 rhesus macaques on a separate campus for the conduct of preclinical trials. In addition, the Vaccine Trial Center with a 20-bed ward specifically designed and constructed by WHO for the conduct of enteric vaccine trials is located at the Mahidol University Faculty of Tropical Medicine across the street from AFRIMS. The Department of Enteric Diseases also has microbiology and molecular biology laboratories at the AFRIMS facility in Kathmandu, Nepal.

4. Equipment: The Department of Enteric Diseases has within the department well-equipped microbiology, immunology, and molecular biology laboratories. Equipment within the department includes multiple real-time PCR machines, Luminex machine, column sequencer, ELISPOT reader, automated plate-washer, low-density microarray reader, ultracentrifuges, incubators, freezers, etc. The department also has access to additional shared equipment within AFRIMS to include multi-channel flow cytometers with cell sorting capability, multicolumn sequencers, high-pressure liquid chromatography, etc. The Biomedical Maintenance Section coordinates and documents periodic maintenance, repair, and calibration of equipment at AFRIMS.

5. Field Sites: The Armed Forces Research Institute of Medical Sciences (AFRIMS) currently has active field sites with full-time staff in Thailand at Kamphaeng Phet in central Thailand and in rural Sangklaburi on the Thai-Burmese border; in rural northwestern Cambodia near the Thai-Cambodian border; and at two sites in the Philippines. In addition, the AFRIMS satellite

laboratory in Nepal occupies a four-story building with laboratories and a staff of 25 available to support the conduct of studies within Nepal. The Department of Enteric Diseases has or is conducting studies at these sites and others in Thailand, Cambodia, Nepal, and Vietnam.

6. Vaccines: The Department of Enteric Diseases participates in the evaluation process for enteric vaccines. The Department employs both full-time GLP and GCP specialists to ensure regulatory compliance for human and animal studies. Recent projects in conjunction with the Department of Veterinary Medicine, the Walter Reed Army Institute of Research, and the National Institute of Allergy and Infectious Disease include development of primate models for shigellosis caused by *Shigella flexneri* and *Shigella dysenteriae*. Primate studies to compare the safety, immunogenicity, and efficacy of the live attenuated *Shigella dysenteriae* vaccine WRSSd1 to four newer vaccine constructs are ongoing. Human studies to evaluate the safety and efficacy of the WRSS1 oral, live attenuated vaccine against *Shigella sonnei* are planned for late 2007.

7. Drugs evaluation: The Department of Enteric Diseases participates in studies of traveler's diarrhea in deploying soldiers. In conjunction with the Naval Medical Research Center, a study on the comparative efficacy of short-course Azithromycin vs. single dose Azithromycin vs. Ciprofloxacin was completed during Operation Cobra Gold 2000-2001. This study clearly demonstrated that short-course Azithromycin significantly shortened return-to-duty time. In conjunction with the Naval Medical Research Unit No. 3 in Cairo and the Naval Medical Research Center, a study of diarrhea prophylaxis of the non-absorbable antibiotic Rifaximin is planned for Operation Cobra Gold 2008-9 in Thailand and at Incirlik Air Base in Turkey.

8. Diagnostics: The Department of Enteric Diseases actively participates in the development and evaluation of new diagnostics for diarrheal diseases. The Department has developed realtime polymerase chain reaction assays for the bacterial pathogens *Shigella*, *Salmonella*, enterotoxigenic *E. coli* (ETEC), *Campylobacter*, and *Vibrio* as well as the hard to diagnose Noroviruses and the parasites *Cyclospora* and *Cryptosporidia*. The Norovirus assay has been incorporated into the surveillance efforts. Several of these assays are currently under evaluation for the U.S. government's Joint Biological Agent Identification and Diagnostic System.

9. Surveillance: The Department of Enteric Diseases conducts surveillance on diarrhea etiology and antimicrobial susceptibility patterns in soldiers, travelers, and children in countries in the region such as Cambodia, Vietnam, Nepal, Thailand, and the Maldives. Completed studies from the past several years include a travelers' study in Nepal, an adult study in expatriates and Thai nationals in Bangkok, and children's studies in Hanoi, Vietnam and Phnom Penh, Cambodia. In addition, the Department conducted diarrheal disease surveillance in US forces deploying to Thailand for Operation Cobra Gold from 1987 through 2004. Ongoing studies include a multisite diarrhea surveillance project at regional and provincial medical centers in Thailand and a diarrhea surveillance project at three sites in Nepal. Relevant findings include widespread highlevel quinolone (Ciprofloxacin) resistance in *Campylobacter* species in Southeast Asia; the recognition of Norovirus as an increasingly common diarrheal pathogen; and the onset of macrolide (Azithromycin) resistance in *Salmonella* isolates from patients in Thailand.

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