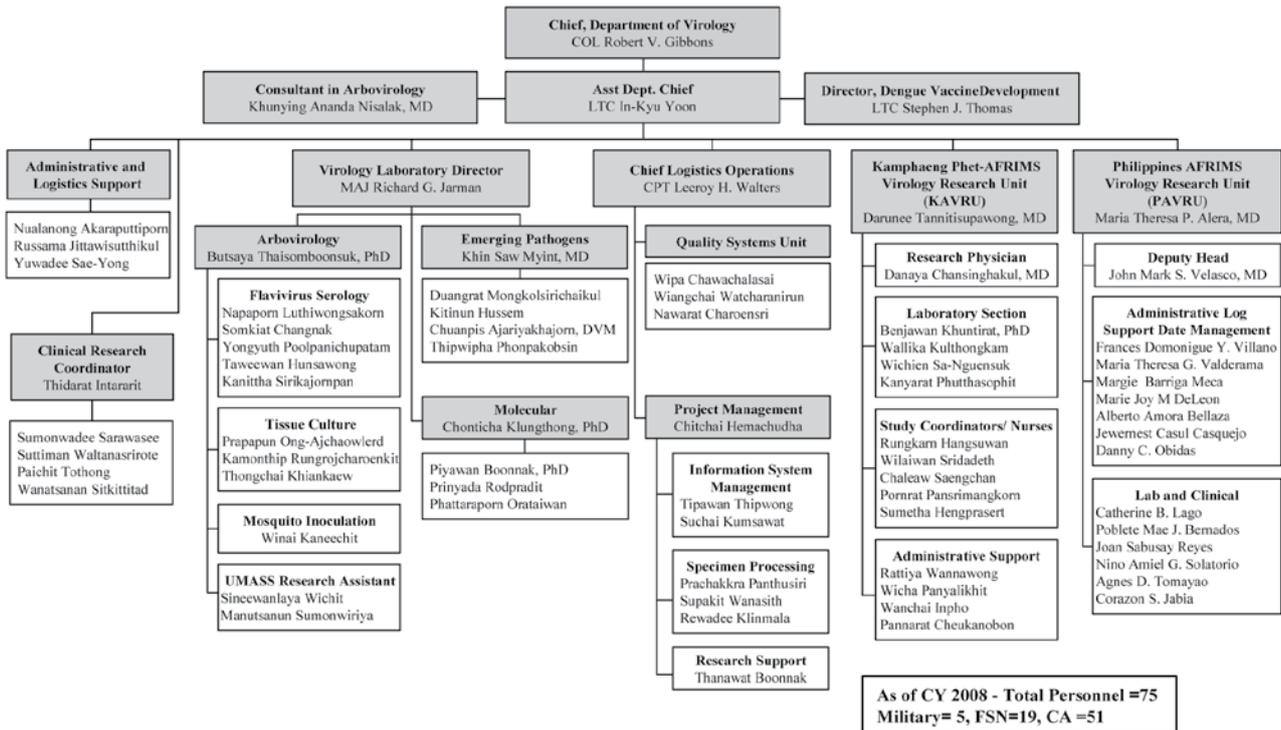


## DEPARTMENT OF VIROLOGY

### DEPARTMENT MISSION

To develop and evaluate products, and collect epidemic data to protect the Soldier from infectious diseases

### PERSONNEL



### IN-HOUSE TRAINING PROGRAMS AND OUTSIDE TRAINING OF PERSONNEL

#### In-House Training

- Epidemiology, Symptoms and Treatment of Tularemia, GEIS
- Safety Training (Hazard and Regulated Medical Waste, Hazard Communication, Fire Prevention and Protection, Blood-borne Pathogen Exposure Control, Safety Risk Assessment, Safety Equipments Usage, Chemical Safety)
- Occupational Health Training (Fit Test, Laboratory Waste Management, Respiratory Protection Program)
- Contracting, Logistics
- SOP Writing Workshop, QAU
- Weapons of Mass Destruction Preparedness, DS/WMD Countermeasures Division, US Department of State
- Performance Management Policy for US Supervisor, US Embassy



- Intermediate Medical Acquisition Course (IMAC), Office of the Principal Assistant for Acquisition, USAMRMC
- Human Subject Researchs: Ethics and Regulations (Thai) RAFT #3024, QAU
- WRAIR Information Management System (WMIS), Randolph J. Ford/ Calvin Ashcraft, WRAIR
- Nanophotometer for Molecular Research
- Sample Size Calculation and Detailed Descriptions of Statistical Methods for Development of Diagnostic Tests
- New CRADA Policy, Dr. Claudia Golenda, WRAIR
- Working with SRSP to Develop Proposals for Extramural Funding, Dr. Peter D'Arpa, Director of Sponsored Research Support Program
- Dr. Aum's Life Support, RTA
- Friendly Fire Infectious Disease: Novel Biomarker and Therapeutic Targets for Life-Threatening Infections, Dr. Kevin C. Kain
- Ergonomic Application for Working Employee, Virology Department
- Good Clinical Practice (GCP) (Refresher), QAU
- Good Clinical Laboratory Practice, QAU

#### **Outside Training**

- 8th International Advance Course on Vaccinology in Asia-Pacific Regions, International Vaccine Institute, Seoul, South Korea
- National Institute of Allergy and Infectious Diseases (NIAID), NIH Grants Policy and Management Training, Bangkok, Thailand
- Emerging Infectious Diseases Program, University of Iowa, USA
- MassTag Training, Columbia University, NY, USA
- Travel Regulations for Uniformed Personnel, JFTR Vol 1 (TDY), Graduate School, USDA, Sandiego, USA
- The 3<sup>rd</sup> Asia-Pacific Biosafety Association Conference, Asia-Pacific Biosafety Association, Bangkok
- Standard Course in Clinical Trials, Faculty of Medicine, Chulalongkorn University, Thailand
- Transport of Biomedical Material Course, USACHPPM, Camp Humphreys, Korea
- The 8th International in Clinical Research, Medicine Faculty, Chiangmai University, Chiangmai
- Improving Analytical Quality Management, Association of Medical Technologists of Thailand, Chulalongkorn University, Thailand
- The 2nd International Conference on Dengue and Dengue Haemorrhagic Fever, Ministry of Public Health, Phuket, Thailand
- Virology Association Conference, Virology Association, Bangkok, Thailand
- Clinical Data Management, Faculty of Allied Health Sciences, Thammasat University, Thailand

#### **AWARDS**

None



## ACCOMPLISHMENTS

### 1. Prospective Study of Dengue Virus Transmission and Disease in Primary Schools and Villages in Kamphaeng Phet, Thailand

**School cohort study:** The number of subjects approved for the school-based component was approximately 2000 at any time during each dengue surveillance season not to exceed a cumulative total of 4000 during the life of the study. In the study, there were 2095, 2088, 2086 and 2060 at the beginning of each dengue season in 2004, 2005, 2006, and 2007 respectively. The cumulative total of subjects enrolled in the school component during the entire study was 3526. The total number of subjects who withdrew from the study during all 4 years was 183. The major reason for withdrawal was relocation out of the study area. Thirty-three subjects withdrew due to objections to blood draws. During the 4 years of active surveillance (2004-2007), 2606 acute illnesses with fever on evaluation or report of fever within the prior 7 days underwent blood draws. Of these illnesses, 186 were serologically positive for dengue (12 acute primary dengue infections, 168 acute secondary dengue infections and 6 recent secondary dengue infections) out of which 148 were dengue PCR positive. DEN-1 was the most common serotype making up 47% of PCR positive cases. Forty children from the school component were hospitalized with confirmed dengue: 31 with dengue fever, 3 with DHFI, 3 with DHFII, and 3 with DHFIII. All hospitalized subjects were eventually discharged with complete recovery.

**Village-based study:** During the entire study, a total of 103 cluster investigations were performed: 51 positive clusters (involving 816 child contacts) based on dengue PCR positive index cases and 52 negative clusters (involving 783 child contacts) based on dengue PCR negative index cases. A total of 3182 blood specimens were drawn. During the entire study, there were a total of 51 positive clusters and 52 negative clusters. Between day 0 and day 15 evaluations, 116 of 816 contacts within the positive cluster investigations were serologically confirmed to have dengue infection of which 42 were dengue PCR positive on day 0. Six of 783 contacts within the negative cluster investigations were serologically confirmed to have dengue infection of which 2 were dengue PCR positive on day 0. In the positive clusters, there were 22 acute primary dengue infections, 80 acute secondary dengue infections and 14 recent dengue infections between day 0 and 15. In the negative clusters, there was one acute primary dengue infection and 5 acute secondary dengue infections between day 0 and 15. On day 15, 11 contacts within the positive clusters were dengue PCR positive (6 DEN-1 and 5 DEN-4) while one contact within the negative clusters was dengue PCR positive (DEN-4). Seven subjects from all the cluster investigations were hospitalized with confirmed dengue: 5 with dengue fever, 1 with DHFI and 1 with DHFII. All seven were discharged from the hospital with complete recovery. As part of the entomological study, 24 of 3238 *Aedes aegypti* mosquitoes collected from cluster investigations were positive by dengue PCR (eleven DEN-1, three DEN-2, two DEN-3 and eight DEN-4). Twenty-three of these positive mosquitoes were collected from positive clusters and the dengue serotypes of these mosquitoes were the same as that of their respective positive index cases. Only one positive mosquito was from a negative cluster.

#### **Future Plans:**

No further contact with study subjects will take place. The human use portion of the protocol is complete. Data analysis is ongoing; presentations and manuscripts are being formulated to be presented at various international venues and journals.



## **2. The Dengue Hemorrhagic Fever Project III: Continued Prospective Observational Studies of Children With Suspected Dengue**

There were 10 positive PCR cases in this report period (DEN 1 = 5; DEN 2 = 0; DEN 3 = 5, DEN 4 = 0). There were 9 Negative PCR cases. All subjects had ultrasound evaluation for plasma leakage. A subset (n = 7) of dengue positive cases had interstitial fluid sampling done. One subject was withdrawn due to fever over 72 hours. No serious adverse events occurred.

### **Future Plans:**

The study is scheduled to stop enrollment on December 2008. Long-term clinical follow-up is ongoing for prior years of enrollment. Analysis for markers that predict disease severity (NS1 protein/antibody levels, immune activation markers), that indicate plasma leakage is or will occur, and that indicate immunity will be done. Statistical analysis of DHF resulting from primary versus secondary DV infections with regard to the role viral serotype, viral burden and virus-antibody complexes plays on resulting disease severity is planned. Characterization of the dengue specific T cell response with regard to the magnitude of T cell expansion during infection and the functional characteristics of these cells is also planned. Measurements of makers of endothelial cell activation are planned. Investigators will submit the amendment protocol request extending the study period for a total of 5 years (31 DEC 2013), 3 years to complete clinical follow up appointments and 2 additional years to complete data analysis.

## **3. A Phase I/II Trial of a Tetravalent Live Attenuated Dengue Vaccine in Flavivirus Antibody Naive Infants**

Results from the primary vaccination series (doses #1 and 2) demonstrate the WRAIR/GSK vaccine candidate to be safe and immunogenic. A significant proportion of the cohort develops neutralizing antibodies to all four dengue virus types following two doses of vaccine. Long term follow up reveals no evidence vaccine recipients have an increased incidence of dengue compared to controls in the period remote from vaccination. There were no overt safety signals in the subset of volunteers receiving a third dose of dengue vaccine remote from the primary vaccination series. Final safety and immunogenicity analyses are pending.

### **Future Plans:**

Clinical activities and final data analysis will be completed in late 2009.

## **4. A Phase I/II, Open, Five-Year, Clinical Follow-Up Study of Thai Children Who Participated in Dengue-003 ("A Phase I/II Trial of a Tetravalent Live Attenuated Dengue Vaccine in Flavivirus Antibody Naive Children") With Evaluation of a Booster Dose Given One Year After Primary Dengue Vaccination Series**

Seven subjects were enrolled since February 2005 (Year - 1) and all subjects were administering a booster. The protocol amendment 1 was approved and allow for acquire peripheral blood mononuclear cells (PBMCs) and sera to characterize cell-mediated immunity responses to vaccination and correlate these with N antibody titers at year 3 follow-up. The clinical follow-up visit 8 (Year - 4) has been completed since FEB 08. The last follow-up visit will be scheduled in FEB 09 (Year -5). There were no subject withdrawals from the study till this report period. There is no Serious adverse event (SAE) till date. Laboratory testing for neutralizing antibodies is complete.



**Future Plans:**

Clinical activities will be end in FEB 09. Investigators will complete testing of samples to fulfill the study objectives and endpoints. Data analysis will continue. The final report will be generated. Scientific manuscripts will be drafted.

**5. Phase II, Randomized, Double-Blind, Single Center, Controlled Study of the WRAIR Live Attenuated Tetravalent Dengue Vaccine Compared to a Placebo Control, Administered on a 0-6-Month Schedule, to Healthy Adults**

A total of 120 volunteers were enrolled and randomized to receive one of two dengue vaccine formulations or placebo in April 2007. 116 subjects received dose 2 and complete study visit. There are 4 subjects lost to follow up (3 subjects after 1st dose and 1 subject after 2nd dose). The final study visit occurred 14 February 2008. There are 3 SAEs reported (1 abdominal hernia, 1 ectopic pregnancy and 1 appendicitis) none of which were deemed related to study vaccine. There are 2 pregnancy cases reported. There are 2 pregnancy reported during this report period. There were no volunteers which met clinical or laboratory criteria for suspected dengue and no alert lab values. Laboratory testing for JE PRNT was done at AFRIMS in NOV 08.

An interim safety analysis performed on cleaned data collected for 31 days after the first study vaccine dose (days 0-30 post dose 1) in the entire cohort (2 vaccine and 1 placebo group). The summary results showed the vaccine was well tolerated in a highly primed adult population.

**Future Plans:**

Lab testing for Q-PCR will be done at AFRIMS in JAN 09. The specimens will be sent to test at location as specified in the protocol in JAN 09. The assays supporting immunogenicity objectives and endpoints will be complete. Completion of the data analysis and filing of the final study report is expected to occur in CY2009.

**6. A Phase II, Prospective, Randomized, Double Blind, Placebo Controlled Field Efficacy Trial of a Candidate Hepatitis E Vaccine in Nepal WRAIR# 749, HSRRB Log# A-9117.1**

The clinical phase of the trial has been successfully completed according to the protocol amendment 9. The DSMB unblinded 111 cases of suspected hepatitis following SOP provided by GSK on 23 June 2004. The study results were reported in the HEV Symposium of the American Society of Tropical Medicine and Hygiene (ASTMH) annual meeting in December 2005 as well as in the New England Journal of Medicine in March 2007. The clinical portion of the study was completed in January 2004. A final clinical study report was submitted to the Food and Drug Administration on 21 August 2006.

**Future Plans:**

The WRAIR protocol # 749 reached five year term in October 2006. Memorandum requesting extension of this protocol for 18 months was submitted to Office of Research Management (ORM) on 12 January 2007. The study remains open in order to complete the plan to inform volunteers about the results of the study and the formulation (placebo or vaccine) they received. As of 18 November 2008, letters of appreciation and result of the study to 916 volunteers has been distributed and acknowledgement received. A total of 555 undelivered letters have been returned by Shree Birendra Hospital. Acknowledgement of 200 letters provided to Shree Birendra Hospital for distribution has not been received. The source document in all subject folders at



WARUN and the Regulatory Documents at AFRIMS have been scanned and secured. The electronic files have also been secured off-site. Hard copy source documents and regulatory documents at WARUN has been forwarded to Archivist, Division of Regulated Activities and Compliance U.S. Army Medical Research & Material Command, 1452 Campus Drive, Fort Detrick, MD 21702 and received on 29 September 2009.

### **7. Japanese Encephalitis Surveillance in Nepal**

In this reporting between 26 October 2007 and 7 November 2008, 1605 blinded clinical encephalitis samples were provided by National Public Health Laboratory (NPHL) in Nepal to AFRIMS for JE IgM-capture ELISA. Overall, we detected JE IgM in 12.8% (205 samples) of the 1603 available samples.

#### **Future Plans:**

Continuation of testing of samples provided by NPHL, analysis of the data collected to date; discussion of the data with investigators at WARUN and NPHL; and manuscript writing. Remaining negative samples will be tested for other possible pathogens of encephalitis.

### **8. Influenza Surveillance in Southeast Asia**

AFRIMS works in close collaboration with the US and Thai CDCs, the Thai Ministry of Public Health, public health officials in Nepal, Bhutan and the Philippines, and with NAMRU-2. The influenza surveillance is divided into individual country projects each for Thailand, Nepal, U.S. Embassies in the region, Bhutan and the Philippines. Provision of staff, equipment, infrastructure development, and training is well underway at all sites. AFRIMS has already set up training on molecular diagnostics in Kathmandu, Kamphaeng Phet, and in the Philippines. The infrastructure of a dedicated respiratory pathogens laboratory is already completed in these sites. This will allow immediate processing of influenza samples, and ensure on-time reporting. Construction of a BSL-3 laboratory is complete and pending certification. The respiratory laboratory will be equipped with a real-time PCR machine, serology set up, viral isolation, computers for data entry, and capabilities for specimen storage and archiving.

Progress on influenza surveillance in U.S. citizens at U.S. Embassies/Consulates in Asia: subject enrollment started since the protocol was approved by HURC on Feb 2006. There are now a total of 14 medical units/clinics from 13 countries in Asia participating in this study - Thailand (Bangkok), Burma (Rangoon), Bangladesh (Dhaka), India (New Dehli), Pakistan (Islamabad), Mongolia, Laos (Vientiane), Malaysia (Kuala Lumpur), Sri Lanka (Colombo), Vietnam (Hanoi and Ho Chi Minh City), Nepal (Kathmandu), China (Beijing), and Philippines (Manila). Total number of subjects enrolled since the study started until Dec 08 is 129; majority was from the U.S. Embassy Medical Unit in Bangkok. Rapid diagnostic tests performed on site showed the following: 18 (13.9%) FLU A, 4 (3.1%) FLU B and 5 (3.8%) FLU A+B. Real-Time PCR for Influenza A/B performed at AFRIMS showed the following: 9 (6.9%) FLU A/H1, 27 (20.9%) FLU A/H3 and 15 (11.6%) FLU B. Virus isolation results were available on 96 specimens: 16 (12.4%) Influenza A, 8 (6.2%) Influenza B, 1 (0.7%) Parainfluenza 2, 2 (1.5%) Parainfluenza 3, 1 (0.7%) herpes simplex virus, and no respiratory virus was isolated in 68 (52.7%).

Progress on influenza surveillance in Nepal: During the period from initiation of the study until 30 November 2008, 918 specimens were received from active sentinel surveillance sites and outbreaks in Nepal. Rapid diagnostic test showed 206 (22.5%) FLU A and 50 (5.5%) FLU B out of 917 specimens. Real-time PCR done at AFRIMS reported 296 (32.6%) as FLU A/H1, 59 (6.5%) FLU A/H3, 1 (0.1%) (1) FLU A/H3 + FLUB, 3 (0.3%) FLUA/Un-subtype and



96 (10.6%) FLU B out of 907 specimens. Viral isolation performed at USAFSAM showed 261 (32.2 %) FLU A, 68 (8.4 %) FLU B, 4 adenovirus (0.5%), 2 Coxsackie B (0.2%), 1 Echo virus (0.1%), 4 Enterovirus (0.5%), 5 Parainfluenza-1 (0.6%), 2 Parainfluenza-2 (0.2%), 4 Parainfluenza-3 (0.5%), 1 Mumps virus (0.1%) and 4 Herpes Simplex Virus (0.5%) out of 810 specimens. No A/H5N1 has been isolated to date. Real time PCR assays for the detection of influenza A & B viruses and their subtypes have been initiated at AFRIMS's lab in Nepal (WARUN).

Progress on influenza surveillance in the Philippines: A total of 569 influenza-like illness (ILI) cases were investigated from the following sites in the Philippines: 1) 5 barangay health center (BHC) sentinel sites, Cebu City 2) Armed Forces of the Philippines Medical Center (AFPMC), Quezon City, and 3) U.S. Embassy Medical Unit, Manila. Male to female ratio of the ILI cases was 1.1 and with age range of 6 months to 63 years old. Majority of the ILI cases were from the 6 months to 4 years old age group and 5 to 9 years old age group at 63% and 23%, respectively. Influenza real time PCR was performed on 425 specimens with 132 (32%) positive for influenza. Breakdown of the influenza PCR results are as follows: 65 (15%) Influenza A/H3, 50 (12%) Influenza B, 15 (4%) Influenza A/H1, 4 (1%) Influenza A (un-subtyped), and 290 (68%) were negative. One specimen was positive for both Influenza A/H3 and Influenza B. Virus isolation results were available for 332 of the specimens: 50 (15%) Influenza A, 28 (8%) Influenza B, 14 (4%) Parainfluenza 1, 13 (4%) Parainfluenza 3, 13 (4%) Adenovirus, 6 (2%) Coxsackie B, 3 (1%) Parainfluenza 2, 2 (1%) Enterovirus, and no respiratory virus was isolated in 199 (60%) of the specimens. Single samples of each of the following viruses were also isolated: Echovirus, Herpes Simplex Virus, Respiratory Syncytial Virus, and a specimen with concurrent infection of Influenza A and B.

Progress on influenza surveillance in Thailand: Total number of subjects enrolled from Kamphaeng Phet and Sangkhlaburi since the study started in April 2007 until temporary halt in March 2008 was 604. Oseltamivir (O) resistance was assessed at the US CDC on four H1N1 viruses isolated from specimens collected in Nov 2007 in Kamphaeng Phet. One of the four H1 strains was found to be O-resistant.

A total of 151 cases that fit the ILI criteria were collected from an ILI outbreak in Sangkhlaburi (Jan-Feb 2008). Nasal swabs were taken to test with QuickVue and throat swabs for the diagnostic panel (viral isolation, RT-PCR and characterization). The outbreak was determined to be FLUB-Malaysia-like. Thirty-seven percent were positive for FLU B by the rapid QuickVue test (done on site). Eighty-eight (58%) were positive for Flu B by RT-PCR, 2 (1%) FluA/H3 by RT-PCR, 75 (50%) were isolation positive for flu B and were characterized as B-Malaysia-like by molecular sequencing. Five of these were sent to the US CDC for HAI testing against B-Malaysia antiserum. Isolation also revealed the following from the outbreak specimens: 2 Adenovirus, 1 Coxsackie B, 2 Echo Virus, 1 Enterovirus, 1 HSV, 1 Parainfluenza 1, 52 (34%) unknown.

Progress on influenza surveillance in Bhutan: AFRIMS has established a relationship with Bhutan Public Health Laboratory and Bhutan Ministry of Health to enhance the country's capabilities to perform influenza and other emerging pathogen surveillance by significantly increasing laboratory and information technology infrastructure and through the provision of training. Influenza-like illness specimens are collected from Thimphu, Punakha and Paro with expansion to Phuentsholing, Gelephu, and Mongar in later phases of the study. Thimphu is the capital city of Bhutan with an estimated population of 80,000, the highest in the country. Paro and Punakha are two districts frequented by tourists and are located close to Thimphu. Three hospitals (Jigme Dorji Wangchuck National Referral Hospital, Thimphu; Punakha Hospital; Paro Hospital) are initially involved in the study.



Twenty five ILI service specimens were collected from Bhutan from Oct - Dec 2008. Influenza real-time PCR subtyping done at AFRIMS showed the following results: 15 (60%) positive for influenza A (H3), and 2 (8%) positive for influenza B. No respiratory virus was detected in 8 (32%) of the specimens tested.

**Future Plans:**

- a. To expand surveillance sites in Nepal, Bhutan and the Philippines.
- b. To expand surveillance to other countries in the region.
- c. BSL-3 facility at AFRIMS to be certified.
- d. Set up Real-Time RT-PCR in Bhutan.

**9. Sentinel Surveillance for Emerging Diseases Causing Hospitalized Dengue-Like Illness in Cebu, Philippines (SEDC)**

From January to December 2008, 176 patients were enrolled into the study. There were 14 lost to follow-up and 2 withdrawals. No Serious Adverse Events (SAEs) were reported. AFRIMS JE/ dengue EIA and/ or dengue RT-PCR data was available on 135 of the subjects. One hundred nineteen (88%) out of the 135 subjects were laboratory confirmed dengue infections. Demographics of the laboratory confirmed dengue cases are as follows: age range of 2 to 32 years old with majority (96%) with age less than 15 years old; male to female ratio was 1.25. One hundred seven (90%) subjects were diagnosed as acute secondary infections and only 4 (3%) cases were diagnosed as acute primary infections. The remaining cases were either suggestive of secondary dengue infection (6%) or it unable to be differentiated whether it was a secondary or primary dengue infection (1%). Specific breakdown of the clinical diagnosis of the laboratory confirmed dengue cases as follows: 53 (45%) DHF gr 2, 31 (26%) DHF gr 1, 29 (24%) DSS (DHF gr 3/gr 4), 4 (3%) DF, and 2 (2%) systemic viral infection. Serotype data was available on 68 subjects with all 4 serotypes documented to be circulating with DEN-3 (82%) predominating. Confirmatory laboratory testing is still being done for the 14 non-dengue cases.

**Future Plans:**

Subject recruitment and clinical follow-up will continue as outlined in the approved protocol. The demographics/ base line data will be analyzed for those enrolled during CY 2008.

**10. Use of Geographic Information System (GIS) to Establish a Community-Based Biosurveillance Infrastructure in Cebu City, Philippines**

As of December 2008, a total of 9,985 households in Guadalupe and Banawa have been interviewed representing 45,151 individuals. This corresponds to a population coverage of approximately 94% of the individuals (as compared to the 2007 population census). Average household size was calculated at 4 members per household. Male to female ratio was reported as 0.94 with majority of the population reported as either single or legally married at 26,004/ 45,151 (56%) and 14,663/ 45,151 (32%), respectively. Majority of the population belonged to the 20-29 and 30-39 years old age groups at 21% and 14%, respectively. Projected health facility utilization data of adults and children for a hypothetical fever was elicited from 9,896 households while actual health facility utilization during the past year for a febrile illness was determined from 6,776 households. Out of 9,896 households, 6,422 (65%) indicated that a member of their household had a fever during the past year. The total number of individual household members who reported having had a fever during the past year was 11,679 (26%).



Out of 9,852 households who answered the question whether they plan to transfer or move out of their present residence in the near future, only 211 (2%) answered in the affirmative while 2,129 (22%) were unsure or answered “don’t know.” Mobile phone ownership by any member of the household was significantly higher with 8,078/ 9,884 (82%) households versus telephone landline ownership which was reported at 3,549/ 9,884 (36%). Ownership of pets or animals was reported among 3,945/ 9,891 (40%) households.

#### **Future Plans:**

Addition of other data layers from various publicly available data sources such as those collected by local health centers and hospitals (i.e. Field Health Service Information System (FHSIS) and Philippine Integrated Disease Surveillance and Response (PIDSRS)), local AFRIMS projects, as well as other collaborative research projects will be done once the database has been finalized and appropriate checks have been instituted. This database will be used to estimate and create models of spatial and temporal disease spread, transmission, and clustering as applied to other succeeding projects.

### **11. Electronic Disease Surveillance Project**

This project is in collaboration with the Johns Hopkins University - Applied Physics Laboratory (JHU-APL), Global Emerging Infections System (GEIS) and the National Epidemiology Center (NEC) of the Philippines Department of Health. This aims to strengthen the disease surveillance activities of the NEC and support the Philippine Integrated Disease Surveillance and Response System (PIDSRS). As of January 2009 sixteen desktops, 2 laptops, and computer software has been turned over to the NEC. Two additional personnel will be hired to support the collaborative study. A hybrid system consisting of the PIDSRS software with an integrated automated alert and reporting system is currently being developed by JHU-APL and is proposed to be piloted in Cebu City.

### **12. Prospective Studies of Avian Influenza Transmission in Cambodia and Thailand**

In Thailand, 800 cohort subjects were enrolled in the three year surveillance study of avian influenza transmission. The enrollment started in April 2008 and completed in October 2008. As of 31 December 2008, four cohort subjects were withdrawn from the study. Three subjects were withdrawn due to death and one subject was withdrawn due to inability to comply with the study protocol.

During the year 2008, 26 ILI investigations were conducted. Sixteen ILI investigations were found to be positive for influenza virus by RT-PCR testing; the remaining ten were negative for influenza virus. Twelve of 16 ILI cases were positive for influenza A (H1 = 7, H3 = 5), three were positive for influenza B, and one was positive for influenza A (H3) and B. Thirteen family transmission studies were conducted; 30 case contact subjects were enrolled. It was later found out that two case contact subjects did not meet the enrollment criteria (did not live under the same roof as the cohort index subjects). These two case contact subjects were subsequently withdrawn from the study. Of the remaining 28 case contact subjects, four had ILI symptoms and all were positive for influenza A virus (H1 = 3, H3 = 1) with the same subtype as the respective index cohort subjects.

#### **Future Plans:**

Weekly and Annual Follow-ups, ILI investigation, and Family Study of Influenza Transmission of the 796 Cohort Subjects Will be Continued.



### **13. Epidemiological Study of Dengue Virus Infection in Children and Adults, Guadalupe, Cebu City, Philippines**

A population-based fever surveillance study for dengue infection is planned for the community of Guadalupe in Cebu, Philippines. A community of 30,000 residents will be included as potential subjects with evaluation and blood draw being performed on those who present with a febrile illness. This study is partly intended to develop a field site for possible future vaccine studies.

### **14. Development and Accreditation of the AFPMC/ VLGH Institutional Review Board (IRB)**

The AFPMC/ VLGH IRB was developed and acquired a Federal Wide Assurance (FWA) number. This will facilitate and streamline AFRIMS studies involving the Armed Forces of the Philippines (AFP).

## **PUBLICATIONS**

1. Ananworanich J; Phanuphak N; Souza MD; Paris R; Arroyo M; Trichavaroj R; Sirivichayakul S; Shikuma C; Phanuphak P; Kim JH. **Incidence and characterization of acute HIV-1 infection in a high-risk Thai population.** J Acquir Immune Defic Syndr 2008; 49(2): 151-5.
2. Blacksell SD; Mammen MP Jr; Thongpaseuth S; Gibbons RV; Jarman RG; Jenjaroen K; Nisalak A; Phetsouvanh R; Newton PN; Day NP. **Evaluation of the Panbio dengue virus nonstructural 1 antigen detection and immunoglobulin M antibody enzyme-linked immunosorbent assays for the diagnosis of acute dengue infections in Laos.** Diagn Microbiol Infect Dis 2008; 60(1): 43-49.
3. Briese T; Renwick N; Venter M; Jarman RG; Ghosh D; Kondgen S; Shrestha SK; Hoegh AM; Casas I; Adjogoua EV; Akoua-Koffi C; Myint KS; Williams DT; Chidlow G; van den Berg R; Calvo C; Koch O; Palacios G; Kapoor V; Villari J; Dominguez SR; Holmes KV; Harnett G; Smith D; Mackenzie JS; Ellerbrok H; Schweiger B; Schonning K; Chadha MS; Leendertz FH; Mishra AC; Gibbons RV; Holmes EC; Lipkin WI. **Global distribution of novel rhinovirus genotype.** Emerg Infect Dis 2008; 14(6): 944-7.
4. Chinnawirotpisan P; Mammen MP Jr; Nisalak A; Thaisomboonsuk B; Narupiti S; Thirawuth V; Putnak R; Zhang C. **Detection of concurrent infection with multiple dengue virus serotypes in Thai children by ELISA and nested RT-PCR assay.** Arch Virol 2008; 153(12): 2225-32.
5. Chuenchitra T; Wasi C; de Souza M; Nitayaphan S; Louisirootchanaikul S; Suttent R; Brown AE; Birx DL; Polonis VR. **Serum levels of MIP-1beta and RANTES in HIV-1 subtype CRF01\_AE infected patients with different rates of disease progression.** Southeast Asian J Trop Med Public Health 2008; 39(5): 856-62.

