Introduction and Update Organization to Department of Virology USAMC-AFRIMS

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Chief of Virology Department

13 January 2016
Department of Virology

MISSION:
Develop and evaluate biomedical products and collect epidemiologic data to protect the Soldier from viral infectious diseases

To support these efforts we engage in:

- Clinical Trials
- Field site development and capacity building
- Epidemiological studies and public health sample characterization
- Building and sustaining collaborative relationships
Department of Virology

Personnel:
- Chief: COL Louis Macareo
- Total staff: 89
- Bangkok: 3 US military, 49 Thai, 1 US contractor, 1 Filipino contractor
- Kamphaeng Phet field unit: 16 Thai
- Philippines field unit: 19 Filipino

Field sites:
1. Kamphaeng Phet Virology Research Unit (KAVRU) started since 1980, and formally established in 2003
   - Vaccine trials, receive samples from provincial hospital, public health clinics, school district, include studies on JE, dengue, hepatitis, leptospirosis, and influenza
2. Philippines AFRIMS Virology Research Unit (PAVRU) established in 2004
   - Dengue vaccine trial, dengue and other disease surveillance, and influenza reference laboratory
Longstanding collaboration and mature field sites capable of US FDA trials (accomplished for licensure of hepatitis A and JE vaccines in the past)

- Dengue
  - Participation in vaccine trials:
    - Phase III, Sanofi Pasteur vaccine in KAVRU and PAVRU
    - Phase II, NIH vaccine in Bangkok
  - Vaccine evaluation (animal, human)
  - Epidemiology (clinical, molecular, serologic)
  - Pathophysiology studies (hospital-based)
  - Diagnostic services (public health)
Major Activities

- **Influenza/ Respiratory Illnesses**
  - Surveillance and outbreak investigation that includes support to all of the regional embassies
  - Epidemiology (clinical, molecular, serologic)
  - Diagnostic services (public health)

- **Japanese encephalitis, Chikungunya, Zika, Hepatitis E viruses, and other respiratory virus pathogens**

- **Pathogen identification**
Geographic Area of Responsibility

- Thailand
  - Bangkok
  - Kamphaeng Phet
- Philippines
  - Manila
  - Cebu
- Nepal
- Bhutan
Cooperative between AFRIMS & PHL (Bhutan)
AFRIMS provides training to PHL staff

- To provide training included lecture, observation, and hands on training for the following assays:

1) Viral RNA Extraction by QIAamp Viral RNA Mini Kit
2) Qualitative rRT-PCR Assay for Detection Characterization of influenza viruses
3) Detection of Dengue Virus Genome by nested RT-PCR
4) Detection of MERS-CoV by rRT-PCR
5) Detection of Influenza A subtype H7N9 by rRT-PCR

- Establish the following competency assessment programs:

1) Competency Assessment of Lab Personnel on influenza Real Time RT-PCR
2) Competency Assessment of Lab Personnel on dengue nested RT-PCR
AFRIMS Competency Assessment

• Purpose:
  ➢ Ensure that laboratory personnel is **competent** to perform laboratory testing
  ➢ Assure the testing results performed by laboratory personnel at the USAMD-AFRIMS, Department of Virology, **field sites** and collaborative sites

• Procedure:
  ➢ **Samples**: 10 blinded samples per panel.
  ➢ Perform **2 independent experiments** over a two-day period (1 samples panel/day) to determine laboratory and laboratory personnel variability
  ➢ Perform on the **same testing method** i.e. Qualitative Real-Time RT-PCR Assay for Detection and Characterization of Influenza Viruses Using the Rotor-Gene Thermal Cycler System (SOP No. VIR-ML-017)
Competency Assessment, cont.

- **Results evaluation:**
  - Compare with the known results pre-established at Molecular section, Department of Virology, USAMD-AFRIMS
  - Meet acceptance criteria: The result concordance $\geq 80\%$, false negative $\leq 20\%$, and no false positive

- **Frequency of assessment:** Annually

- PHL, Bhutan participated in the competency assessment program for **Influenza qPCR** (since 2011) and **Dengue RT-PCR** (since 2014)
Study: Sentinel Human Surveillance for Influenza in Bhutan (WRAIR#1599)

- Annual Training (to comply with the US and Local Regulation)
  - Citi Training
  - Protocol Training
- Laboratory training at AFRIMS and PHL in Bhutan (Influenza PCR, Dengue PCR)
- Laboratory specimens: Agreement for transferring and sharing the respiratory specimen (advance testing eg. Virus isolation, Sequencing, HAI)
- Laboratory and Clinical data: Sharing data by webbase
- Lab Supplies (Reagent, VTM, QuickVue etc)
- Funding for the activities under this protocol
Background

- AFRIMS have been asked to provide free diagnostic testing of public health surveillance samples for defining disease epidemiology throughout the region (e.g. Thailand, Philippines, Nepal, Bhutan).

- AFRIMS aim to standardize the repository at Department of Virology, USAMD-AFRIMS.
Department of Virology Specimen Repository (WRAIR #1957)

• General Procedure
  ➢ Obtain a letter (AFRIMS can store and utilize specimens for future research)
  ➢ Attempt to obtain signed individual consent forms (Informed consent cannot be obtained in some public health circumstances e.g. outbreak)
    • If such a consent form disagrees to this, then destroy specimen
  ➢ No future research can be performed unless such a letter is obtained
  ➢ De-identify specimen and data as per SOP and archive in the repository
Annex C

Public health surveillance samples submission and permission for future use form

*Instructions: Read and complete the following form by providing the requested information.*

1.1. Date:

[Date of Submission: DD/MMM/YYYY]

1.2 Specimen Description

[Identify the originating and purpose of which the specimens were collected.]

1.3 Institutional Affiliation

[Identify the institution from which the specimens came.]

1.4 Specimen point of contact

[Name of the individual who will be providing specimens to AFRIMS]
[Work address for specimen point of contact]
[E-mail address for specimen point of contact]
[Work phone number for specimen point of contact]

1.5 Number of specimen submit for testing

[Provide the number of samples that will be submitted to AFRIMS for testing.]

1.6 Request for testing

[Identify laboratory or assay request for testing at AFRIMS. Identify whether required testing will be used in support of a United States Food and Drug Administration (FDA) submission or licensure or not.]

1.7 Specimen labeling.

[Describe specimen labeling]

*Please note that AFRIMS prefer coded samples. Samples submit with identifier information will be coded and archived per AFRIMS’s SOP.*
1.8 Informed Consent

[Identify whether informed consent were obtained when these specimens were collected. If informed consent cannot be obtained in some circumstances, please specify reason.]

I have read the above submission request and agree to these samples being included in the Department of Virology Specimen Repository where they may be used for future research.

Name

Requestor/authorize person's printed name and position: 

Signature: 

Date: 

FOR Department of Virology only:

Department of Virology obtained "submission and permission for future use form" from the host institution to store and utilize samples for future research.

Chief, Department of Virology's printed name: 

Signature: 

Date: 

Dept of Virology tracking No. ___ ___/ ___ ___
Consent Form for Sample Donation
(Version 3.0, Date 22 October 2012)

Title: Department of Virology Specimen Repository

Purpose of Document: This document gives you information to decide whether you want to donate your sample for future research by the Department of Virology.

Statement: Department of Virology, Armed Forces Institute of Medical Sciences (AFRIMS) provides free diagnostic work on samples received from health agencies. The project is supported by the U.S. Department of State (DOS) and the U.S. Department of Defense (DOD). Possible sample types could include blood or blood components, cerebral spinal fluid, respiratory specimens, and body fluid or tissue. Once the results have been transmitted, your samples will be destroyed unless you give us permission to store samples at the Department of Virology. These archived samples may then be used for evaluating new diagnostic tests or infectious disease research. With your permission, additional testing may be considered but only after the review and approval of Ethical Review Committees.

Confidentiality: The personal data will be removed from your sample and the Department of Virology data when diagnostic laboratory result is completed. When the results of the research are published or discussed, no information will be included that would reveal your identity.

Risk and Benefit: Your possible risk for sample donation is breach of confidentiality. There is no other benefit except results of diagnostic testing will be provided to your attending physician.

If you have any questions about this study and your right, please contact:

Name: Mr. Sonam Wangchuk
Public Health Laboratory, Department of Public Health,
Ministry of Health, Thimphu, Bhutan
Phone: 975-2-323317 Fax: 975-2-332464 E-mail: sonamphl@health.gov.bt

Name: Walter Reed Army Institute of Research Institutional Review Board
(C/O Human Subjects Protection Branch)
503 Robert Grant Avenue
Silver Spring, MD 20910-7500, USA
Phone: (301) 319-8940 (during duty hours) Fax (301) 319-9961

Agreement: Your sample will be stored at AFRIMS and has been coded to remove any personal information. Donation of sample is voluntary and you will not be paid for your donation. You will not receive the results of any future testing. Your decision to donate your sample for additional research WILL NOT affect your medical benefit or the free testing.

By signing this form you wish to (please sign one):

| donate my sample for future research with approval from appropriate ethical review committees. |
| Patient/Guardian/Parent Signature: ______________ Date: __________ (DD/MMM/YYYY) |
| Printed Name: ___________________________ |

| not donate my sample for future research. |
| Patient/Guardian/Parent Signature: ______________ Date: __________ (DD/MMM/YYYY) |
| Printed Name: ___________________________ |

Witness Signature: ___________________________
Printed Name: ___________________________ Date: __________ (DD/MMM/YYYY)
བོད་ཡིག་གི་ལམ་དཔེར་བཤད་

ཡིག་ཕན་

བོད་ཡིག་གི་ལམ་དཔེར་བཤད་

དཔེར།

བོད་ཡིག་གི་ལམ་དཔེར་བཤད་

འོར་སྦྱོར་བཤད་

བོད་ཡིག་གི་ལམ་དཔེར་བཤད་

འོར་སྦྱོར་བཤད་
Laboratory and Clinical Data
Overall Summary

- Two modes of collection
  - Protocol collected samples (2970 samples): since August 2011
  - Service samples (4391 samples): since October 2008
Age Distribution

Protocol Study

Frequency

Age in Years

0 10 20 30 40 50 60
Age Distribution

Service

Frequency

Age in Years

0 10 20 30 40 50 60 70 80

0 5 10 15 20 25 30 35
Date of Sample Collection

Protocol Study

Number of samples

Collection Date

Date of Sample Collection
PCR Results (Protocol)

Protocol Study

- FLU B
- FLU A/PDM H1
- FLU A/H3
- ANON.SUBLTYPABLE
- > 1 SUBTYPE

Date of Collection

# of Samples Collected

% Influenza Positive (smoothed)
PCR Results (Service)
% Selected for Isolation

<table>
<thead>
<tr>
<th>Service samples</th>
<th>Protocol samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1294/4391 (42%) were sent for isolation</td>
<td>987/2970 (33%) were sent for isolation</td>
</tr>
</tbody>
</table>
## Viral Isolation vs. PCR (Protocol)

<table>
<thead>
<tr>
<th>Isolation</th>
<th>&gt; 1 SUBTYPE</th>
<th>A/NON-SUBTYPABLE</th>
<th>FLU A/H3</th>
<th>FLU A/PDM H1</th>
<th>FLU B</th>
<th>NEGATIVE</th>
</tr>
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<td>2</td>
<td>59</td>
<td>63</td>
<td>53</td>
<td>1820</td>
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<tr>
<td>A H3</td>
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<td>0</td>
<td>49</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A H3 TX</td>
<td>1</td>
<td>0</td>
<td>66</td>
<td>0</td>
<td>0</td>
<td>2</td>
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<tr>
<td>Adenovirus</td>
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<td>0</td>
<td>0</td>
<td>14</td>
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<td>0</td>
<td>21</td>
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<td>0</td>
<td>69</td>
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<td>5</td>
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</tr>
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<td>1</td>
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<td>71</td>
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## Viral Isolation vs. PCR (Service)

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<thead>
<tr>
<th>Isolation</th>
<th>&gt; 1 SUBTYPE</th>
<th>A/ NON-SUBTYPABLE</th>
<th>FLU A/ H1</th>
<th>FLU A/ H3</th>
<th>FLU A/ PDM H1</th>
<th>FLU B</th>
<th>NEGATIVE</th>
</tr>
</thead>
<tbody>
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<td>Not isolated</td>
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<td>38</td>
<td>61</td>
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<tr>
<td>A H3</td>
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<td>1</td>
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<tr>
<td>A H3 TX</td>
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<td>0</td>
<td>10</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Adenovirus</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>6</td>
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<tr>
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<tr>
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<td>0</td>
</tr>
<tr>
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<td>0</td>
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<td>0</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>B Wisconsin</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
</tr>
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<td>1</td>
<td>3</td>
<td>11</td>
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<td>0</td>
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<td>0</td>
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<td>Neg</td>
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<td>31</td>
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<td>0</td>
</tr>
<tr>
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<td>7</td>
</tr>
<tr>
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<td>0</td>
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<td>0</td>
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<td>2</td>
</tr>
<tr>
<td>Parainfluenza 3</td>
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<td>0</td>
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<td>0</td>
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<td>3</td>
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<td>0</td>
<td>0</td>
<td>289</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

43 CPE+
## Drug Resistance

### Service samples
- 292 were tested for drug resistance by pyrosequencing
- No drug resistance against Neuraminidase inhibitors (Oseltamivir) was detected yet

### Protocol samples
- 129 were tested for drug resistance by pyrosequencing
- No drug resistance against Neuraminidase inhibitors (Oseltamivir) was detected yet
Clinical Symptoms
Symptoms (Protocol)

Yearly Influenza Symptom Profile (Protocol Study)

-2011
-2012
-2013
-2014
-2015

- breathdiff
- injectedpharynx
- diarrhea
- injectedtympanic
- cough
- sorethroat
- fever
- runny nose
- genpain
- malaise
- chill
Symptoms (Service)
Summary of Symptoms (Protocol)

- NA’s indicate missing/unknown data

<table>
<thead>
<tr>
<th>subject.gender</th>
<th>subject.occupation</th>
<th>symp.breathdiff</th>
<th>symp.chill</th>
<th>symp.cough</th>
<th>symp.diarrhea</th>
<th>symp.fever</th>
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<tr>
<td>NA's: 11</td>
<td>UNEMPLOYED</td>
<td>NA's: 48</td>
<td>NA's: 111</td>
<td>NA's: 33</td>
<td>NA's: 255</td>
<td>NA's: 75</td>
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<td></td>
<td>AGRICULTURE RELATED: 251</td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td></td>
<td>NONE</td>
<td>N :250</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(Other)</td>
<td>:637</td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>NA's</td>
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<td></td>
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<td>symp.fever.date</td>
<td>symp.genpain</td>
<td>symp.headache</td>
<td>symp.injectedpharynx</td>
<td>symp.injectedtympanic</td>
<td>symp.malaise</td>
<td></td>
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<tr>
<td>Mean :2014-04-15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>3rd Qu.:2015-04-10</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Max. :2017-03-03</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA's: 163</td>
<td></td>
<td></td>
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<tr>
<td>symp.runny nos e</td>
<td>symp.sore throat</td>
<td>temp. oral</td>
<td>vacc.YesNo</td>
<td>VTM.Specimen Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y :2292</td>
<td>Y :2680</td>
<td>Min. :3.60</td>
<td>Y :15</td>
<td>Nasal</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>N :632</td>
<td>N :254</td>
<td>1st Qu.:38.00</td>
<td>N :2480</td>
<td>Nasal swab, Throat swab: 1</td>
<td></td>
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<tr>
<td>NA's: 46</td>
<td>NA's: 36</td>
<td>Median :38.50</td>
<td>NA's: 475</td>
<td>Nasopharygeal</td>
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<tr>
<td>Mean :38.66</td>
<td>3rd Qu.:39.60</td>
<td>Throat</td>
<td>NA's</td>
<td>2886</td>
<td></td>
<td></td>
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<tr>
<td>Max. :48.60</td>
<td>Max. :731</td>
<td>NA's</td>
<td>32</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Medical Histories (Protocol)

- 5% (128/2577) took Antibiotics; 393 unknown
- 28% (731/2574) took Antipyretic; 396 unknown
- 2.8% (72/2581) took Antiviral; 389 unknown
- 1.3% (32/2544) reported underlying disease; 426 unknown
- Admission: 16/2970 were inpatients
Exposure History (Protocol)

- 13% (369/2858) close contacted person with similar symptoms
  - 112 unknown
- 2.9% (83/2886) contacted sick/dying swine or poultry
  - 84 unknown
- 5.3% (154/2910) had travelled within the last seven days
  - 60 unknown
Publication
Published in 2013

Influenza surveillance from November 2008 to 2011; including pandemic influenza A(H1N1)pdm09 in Bhutan.

Wangchuk S, Thapa B, Zangmo S, Jarman RG, Bhoomboonchoo P, Gibbons RV.

Abstract
OBJECTIVE: Describe the influenza A(H1N1) pandemic in Bhutan.

DESIGN: Observational study from sentinel surveillance sites.

SETTING: Bhutan remains isolated, with only one to two flights a day at the lone airport, no trains, and only three major roads that enter from India.

MAIN OUTCOME MEASURES: PCR positive human respiratory samples.

RESULTS: The first case of A(H1N1)pdm09 infection was detected in Bhutan in July 2009, 3 months after the virus was first reported in Mexico in April 2009. During the official WHO pandemic period (11 June 2009 to 8 August 2010), a total of 2149 samples were collected and tested by RT-PCR of which 22.7% (487) were confirmed A(H1N1)pdm09; H3N2, H1N1, and B were positive in 2.2%, 1.1%, and 7.2%, respectively. The highest rate of A(H1N1)pdm09 cases (57.4%) was detected in the 6-20 year-old age group. Importantly, Bhutan increased from 3 sentinel sites in April 2009 to 11 a year later, and in April 2010 established PCR capability for influenza.

CONCLUSIONS: Despite relative isolation, the A(H1N1)pdm09 reached Bhutan within 3 months of identification in Mexico. The H1N1 pandemic has made Bhutan more prepared for epidemics in the future.

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In Writing Process

- Study of CPE positive (with PCR negative, isolation negative) in this region to identify the unknown pathogen using Next-Generation Sequencing (NGS)
Regulatory / Study Requirements
WRAIR IRB requirements

• Walter Reed Army institute of Research Institutional Review Board
  (WRAIR IRB)

• WRAIR Human Subjects Protection Branch (HSPB)
  Responsible for providing administrative support to the WRAIR
  Institutional Review Board (IRB).

• Category of protocol
  • Human Subject Research (Minimal Risk, Greater Than Minimal Risk)
  • Non Human Subject Research or Research Not Involving Human Subject
  • Exempt Human Subject Research
  • Project does not qualify as a research activity
WRAIR IRB requirements

• Protocol are reviewed by WRAIR IRB prior to submission to host nation IRB(s).

• Scientific review and approval is required

• Approvals
  • WRAIR IRB
  • WRAIR commander approval authorization

• Submit local EC approval(s) to WRAIR IRB/HSBP before WRAIR IRB grant approval.
WRAIR IRB requirements

• Agreement
  The WRAIR AFRIMS POC has the responsibility to obtain all business agreement prior to initiate any work with partner/collaborators

Current Agreement:
COOPERATIVE RESEARCH AND DEVELOPMENT AGREEMENT Between Armed Forces Research Institute of the Medical Sciences (AFRIMS), a foreign detachment of the Walter Reed Army Institute of Research (WRAIR) And Public Health Laboratory, Department of Public Health, Ministry of Health, Royal Government of Bhutan

• Human Subject Protection Training (CITI certificate)

• FWA
  - The Federalwide Assurance is the only type of assurance accepted and approved by Office for Human Research Protections (OHRP).
  - A commitment by the institution to comply with the requirements of 45 CFR part 46.

• WRAIR IRB Roster
  The WRAIR IRB has not supplied copies of official membership roster to researchers/sponsors. The HSPB maintains a past and current listing of all members.
WRAIR IRB Requirement

• WRAIR site assistant visit
  • Routine monitoring of human subjects research conducted by the WRAIR IRB.

• WRAIR will assess whether human subjects research is being conducted in compliance with governing federal regulations, WRAIR policy, IRB approved protocol and other applicable regulations

• Annual visit
CONTINUING REVIEW REPORT (CRR)
IRB(s) Continuing Review Report

CRR

WRAIR IRB

Host Nation IRB(s)

Completion of study
CRR Submission to WRAIR IRB and Local IRB

• Continuation Review Report (CRR) is required to be submitted and approved for all protocols at least once per year.

• Submit CRR and Associated Documents to:
  • WRAIR IRB (c/o HSPB)
  • Local IRBs (some local IRBs have their own template)
CRR Submission to WRAIR IRB and Local IRB

CRR Submission Package and Required Documents:

• Continuing Review Report (signed and dated by both the Detachment Commander and PI/POC)
• Copies of the most currently approved versions of the protocol
• Copies of the most currently approved versions of the consent form
• Human Subjects Protection Training Certificates for the Principal Investigator (current within the last three years)
CRR Submission Timeline Guidance:

- Submit CRR to the WRAIR IRB 60-90 days before the established continuing review expiration date to ensure that CRR will be reviewed and approved within timeline.
- Track all IRB approvals (in case there are two or more IRB reviews) to ensure that they are all submitted in a timely manner.
- If CRR approval (by WRAIR IRB or local IRB) is not received on time, all research activities must stop (unless required for subject safety).
CRR Submission to WRAIR IRB and Local IRB

CRR Approval Date:

- CRR must be approved prior to the preceding CRR expiry date.
- However, per OHRP guideline, IRBs cannot approve CRR more than 30 days prior to effective date. If this happens, WRAIR IRB will deem that the local IRB meeting date is the effective date of CRR approval.
- Period of IRB approval must be no more than 12 months.
CRR Submission to WRAIR IRB and Local IRB

If CRR is not approved prior to expiration date, then there is a lapse in protocol approval.

- **Enrollment** of new subjects and contact with existing subjects cannot occur during the lapse in approval.
- **All research activities must stop** (including laboratory testing and data analysis).
- Lapse should be reported to IRB

* The only exception to this is when stopping research activities would compromise subject safety
  (this exception must be acknowledged by the IRB)
Study Staff Requirements
Study Staff Training/Requirement

Study staff’s document requires, at minimum, the following:

• Curriculum Vitae (CV)
• Human Subjects Protection Training (CITI Training): Require for WRAIR IRB
• GCP Training (Require for Clinical Trial or as per each IRB requirement)
• Training Documents Specific Study:
  - Protocol Training
  - SOPs/SSPs Training

These documents should be filed and available for monitoring
Curriculum Vitae(CV)

- CVs must be dated, signed by the study staff to verify that the information is accurate
- For AFRIMS staff: Require review/update annually, according to AFRIMS SOP No. CMD-AD-003 Contents, Maintenance, and Review of Training Files
- For Study staff (not AFRIMS) involved in the protocol: Require review/update every 2 years as per WRAIR IRB requirement
- If there is no change to the CV, the CV may be signed and dated again under the previous signature/date

CVs use standard CMD-AD-003-F1 format
CITI Training

The Collaborative Institutional Training Initiative (CITI Program): web-based training for Human Subjects Protection

- **Who is required to take the CITI training:** All Research Personnel must complete the online CITI Training Program
  - **Key Research Personnel:** is defined as the Principal Investigator, other investigators and research personnel who are directly involved in conducting research that have interaction/intervention with human subjects
  - **Research Support Personnel:** person who involved in the research with no direct contact with subjects or identifiable data/specimens (e.g., laboratory technicians and project scientists)

http://www.wrairhspb.army.mil/HSPBTraining.aspx

Link for CITI Program:
https://www.citiprogram.org/index.cfm?pageID=14

Instruction on how to register CITI
CITI Training

These groups are for initial CITI training (based on WRAIR Education Policy (July 2008)):

- **Group 1** – Biomedical IRB chairs, IRB members, IRB staff, HRPP Staff
- **Group 2**: Biomedical Dept Chairs, IPT Managers, Division Directors
- **Group 3**: Biomedical Investigators, Key Study Personnel, Medical Monitors (who involves the interaction/intervention with human subjects **(19 modules)**)
- **Group 4**: Biomedical Research Support Personnel **(4 modules)**
- **Group 5**: Institutional Officials
- **Group 6**: Ombudsman
- **Group 7**: SBR IRB chairs, IRB members, IRB staff, HRPP Staff
- **Group 8**: SBR Investigators, Key Study Personnel, Medical Monitors
- **Group 9**: SBR Dept Chairs, IPT Managers, Division Directors
- **Group 10**: SBR Research Support Personnel (Administrative personal, Data entry personal) **(4 modules)**

**Require passing score of 80% on each module**
CITI Training

CITI training must be renewed “every 3 years” refer to AFRIMS SOP No. CMD-AD-005, Initial and Continuing Education for Human Subjects Research Protection

CITI Refresher Course

- **Group 21:** Refresher for Research Support Personnel *(3 modules)*
- **Group 22:** Refresher for Investigators, Key Study Personnel *(6 modules)*

Instruction on how to refresh CITI

Require passing score of 80% on each module

- Most users complete the Basic training in approximately 4 hours or less.
- You are not required to complete the training all at once.
- You may stop and start anytime.
- Just remember your user name and password.
Good Clinical Practice (GCP): A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

- Attend training class
- Online GCP course

https://www.citiprogram.org/index.cfm?pageID=90
Training for Specific Study

✓ Protocol Training
  • Initiate Site
  • Protocol Amendment
    - Major change -> Lecture/Class Training
    - Minor change -> Self reading

✓ Standard Operating Procedure (SOP)

✓ Study Specific Procedure (SSP)

PI must ensure that study staff have trained all these before start study activities

Record in Training Attendance Record Form (CMD-AD-003-F3)

Attendance Record Form (CMD-AD-003-F3)
Study Staff Assignment

• Prior to assigning staff responsibility, PI or Site PI will ensure the staff are qualified by training and have qualifications to perform their jobs.

• As per AFRIMS SOP “Staff Responsibility Assignment Process and Documentation in Clinical and/or Regulated Human Subjects Research” SOP No. CMD-QP-004, PI or Site-PI will assign and document Roles and Responsibilities of staff by using forms below:
  ✓ Study Roles and Responsibilities Assignment Legend, CMD-QP-004-F1
  ✓ Study Roles and Responsibilities Assignment Log, CMD-QP-004-02
# Study Staff Assignment

## Study Roles and Responsibilities Assignment Legend, CMD-QP-004-F1

<table>
<thead>
<tr>
<th>Protocol ID:</th>
<th>Study Site/No. (if applicable):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal/Site Investigator Name:</td>
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</tbody>
</table>

**NOTE:** Use this legend to complete the Responsibility column. For each individual listed in the Name column, enter the Number(s) (e.g., 1, 2, 3) from the legend below corresponding to their protocol-related duties in the Responsibility column. If there are significant protocol-related duties that are not already included in the legend, add them in the empty space provided below.

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1.</td>
<td>Subject recruitment</td>
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<td>2.</td>
<td>Obtaining informed consent</td>
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<td>3.</td>
<td>Obtaining medical history</td>
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<td>Physical examination/ clinical assessment</td>
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<td>Subject eligibility confirmation</td>
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<td>Vital sign measurement</td>
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<td>Venipuncture/ performing specimen collection for laboratory testing</td>
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<td>Laboratory specimen preparation</td>
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<td>Laboratory specimen transportation/ Processing/ Storage</td>
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<td>10.</td>
<td>Biological sample testing (microscopy, urine pregnancy test and biochemistry blood test, etc.)</td>
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<td>11.</td>
<td>Study drug/ investigational product administration</td>
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<td>12.</td>
<td>Study drug/ investigational product management (receipt, storage, dispense, accountability and disposition)</td>
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<td>Quality Control</td>
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<td>Safety or unanticipated problem documentation and report</td>
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<td>Adverse event causality assessments</td>
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<td>Medical care (treatment for adverse events)</td>
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<td>Source document record</td>
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<td>CRF completion and correction</td>
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<td>Reviewing and signing off on CRFs (must be principal investigator or key site investigator)</td>
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<td>20.</td>
<td>Coordination with study site</td>
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<td>TIMF maintenance</td>
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<td>Communication with IRBs</td>
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<td>Data entry into database and correction</td>
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<td>Database monitoring and verification</td>
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<td>Study outcomes analysis and final study report</td>
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Principal/Site Investigator Signature (sign at site closure): _____________________________ Date: __________

Instructions: Entire form, except 'Signature,' and 'Date,' can be filled electronically.

CMD-QP-004-F1

Page ___ of ___

FOR OFFICIAL USE ONLY

25 Oct 12
Study Staff Assignment

Study Roles and Responsibilities Assignment Log, CMD-QP-004-02

<table>
<thead>
<tr>
<th>Study Personnel (Print Name)</th>
<th>Role</th>
<th>Responsibilities (see legend)</th>
<th>Initials</th>
<th>Signature</th>
<th>Date of Responsibilities Start Date</th>
<th>End Date</th>
<th>Remark</th>
<th>PI/PI’s initials or signature (at time of assignment)</th>
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Principal/Site Investigator Signature (sign at site closure): ____________________________ Date: ____________________

Instructions: Entire form, except ‘Initials,’ ‘Signatures,’ ‘End Date,’ ‘Remark,’ can be filled electronically.

CMD-QP-004-F2

Page __ of ___ 25 Oct 12

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Study Staff Assignment

Updating and Maintenance of Staff Responsibilities Assignment Log

- The CRC/designee will maintain the Study Roles and Responsibilities Assignment Log in the Trial Master File
- The CRC/designee will ensure the forms are updated when changes occur

Change(s) of individual’s assignment

- For Minor changes: document change in the “Remark” column of the Roles and Responsibilities Assignment Log. PI / Site-Pi initials and dates each changed item
- For Major changes, add a new line for update of assignment. Then enter end date for the obsolete assignment and specify reason in the “Remark” column
Informed Consent Process and
Informed Consent Form
INFORMED CONSENT
Requirements

- 45 CFR 46.116, 117: Informed Consent
- 32 CFR 312.60: Investigator Responsibilities
- 21 CFR 50 Subpart B: Informed Consent of Human subjects
- ICH GCP E6 section 4 Investigator Responsibilities
- IRB requirements
- Local regulations
INFORMED CONSENT

• A process by which a subject voluntarily confirms his/her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject’s decision to participate.

• Informed consent is documented by means of a written, signed and dated informed consent form.

• Assent is a term used to express willingness to participate in research by persons who are by definition too young to give informed consent but who are old enough to understand the proposed research.
INFORMED CONSENT (General Requirements)

- The **language** used in the oral and written information about the trial, including ICF, should
  - be as **nontechnical** as practical
  - be **understandable** to the subject and the impartial witness

- Provide **ample time** and opportunity to inquire about details of the trial and to decide to participate

- ICF should be **signed and personally dated** by the subject and by the person who conducted the informed consent discussion.

- If a subject is unable to read, an **impartial witness** should be present during the entire informed consent discussion.
INFORMED CONSENT (General Requirements: GCP)

- Investigator/designee should fully inform the subject of all pertinent aspects of the trial including the written information given approval/favorable opinion by the IRB/IEC.

- Provide approved ICF and other written information to subject.

- ICF and other written information should be revised when new information becomes available that may be relevant to the subject’s consent.
Obtaining Informed Consent

• For those ≥ 6months - 6years: need parent or legal guardian’s permission, sign and date on consent form

• For minor those ≥ 7-17 years: parent or legal guardian’s permission, sign and date on consent form, child also has to sign and date on the assent form

• For those ≥ 18 years: sign and date on consent form
Version of Informed Consent Forms

- Study explanation and consent form for parent and guardian (Version 6.0 dated 16 July 2015)
- Study explanation and consent form for child age 7-17 years old (Version 6.0 dated 16 July 2015)
- Study explanation and consent form for adult (Version 6.0 dated 16 July 2015)
INFORMED CONSENT (FINDINGS)

- Wrong version of ICF used
- Signature not date/date on behalf of person signing
- Signatures and dated after consent process taken place/backdated
- Incomplete signature and/or date
- Unauthorized person conducted consent discussion
- Study procedure done before consent sign
- Amendment consent not obtained/not in timely manner
- Witness/Impartial witness
- Inadequate documentation of IC process in subject’s chart
Informed Consent Form for Parent and Guardian

(Example)

Consent for Participation by signing below:

1. I agree that I have read the information provided above regarding your child's participation in this study.

2. I also agree that I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction.

3. I will be given a copy of this form.

4. I may choose not to allow my child to participate without penalty or loss of benefits to which my child is otherwise entitled.

5. I give permission to the investigators to use my child's sample for the testing approved in this study and furthermore: DO / DO NOT (circle one) give permission for my child's sample to be used for additional research studies.

Name of participant: [Name]

Name of Parent/Guardian: [Name]

Signature of Parent/Guardian: [Signature] Date of consent: [Date]

Name of Clinician/representative: [Name]

Signature of Clinician/representative: [Signature] Date: [Date]

Name of Witness: [Name]

Signature of witness: [Signature] Date: [Date]

For participants who cannot read and write will affix their thumb print on the above box after the clinician/representative has read the content of this form.

[Signature]

Page 1 of 3

Sentinel Human Surveillance for Influenza in Africa [WRAF1159] Version 0.0 dated 10 July 2015

UNCLASSIFIED
Assent Form for Child age 7-17 Years old

(Example)

Future use of your samples used in this study:
After this study any samples from the samples you gave as could be used for other studies. This would
not benefit you directly but could help further medical science in general. You do not have to allow your
samples to be used in this future. You will not be notified of future use or use of your donated samples.
They would only be used (if approved by a review committee with your permission). I do not want my samples
used in future research. If you have any questions regarding your rights as a research volunteer please call
the Research Ethics Board for Ethics, Ethics and Public Policy and Planning Division, Ministry of Health.
Arthur, Bahamas, Phone: 952-2-222412, Fax: 952-2-222494.

ASSENT: By signing your name below, you agree that the doctor or nurse has been explained to you and
you have send the information provided about the study. You also agree you have been given time to ask
questions and all of your questions have been answered to the best of you ability. You may drop out of the study at
any time and no one will mind and nothing will change about your medical care other than not being in the
study. Please talk with the doctor that asked you to enter the study if you have any questions or still
unsure about anything.

Department of Health, Health, Bahamas, Phone: 952-2-222412, Fax: 952-2-222494.
A copy of this form will be given to you and your parents.

Name of participant: [Blank]

Signature of participant: [Blank]
Date of consent: [Fill in 09/05/2016]

Permanent Address: [Blank]

Town and street: [Blank]

INDIVIDUAL OBTAINING ASSENT: I certify that I have explained the above individual the nature
and purpose of the study, potential benefits, and possible risks associated with participation in the study.
I have answered any questions that have been raised.

Name of closest representative: [Blank]

Signature: [Blank]
Date: [Blank]

WITNESSES: I have witnessed the explanation of the research study to the participant. The participant
was given an opportunity to ask questions, and the participant’s questions, if any, were answered.

Name of witness: [Blank]

Signature or witness: [Blank]
Date: [Blank]

For participants who cannot read and write will make their right thumb print on the box below after the
designated representative has read the content of this form.

Page 2 of 2

Central Human Surveillance for Influenza in Bahama (AHFIRS) Version 8.0 dated 20 July 2015
Informed Consent Form for Adult

(Example)

Consent for Participation is stated below.

1. I agree that I have read the information provided above.
2. I also agree that I have been given an opportunity to ask questions and all of my questions have been answered to my satisfaction.
3. I will be given a copy of this form.
4. I may choose not to participate without penalty or loss of benefits to which I am otherwise entitled.
5. I give permission to the investigator to use my samples for the testing approved in this study and $DO/DO NOT$ (circle one) give permission for my samples to be used for additional research studies.

Name of Participant: [Name]
Signature of Participant: [Signature]
Permanent Address: [Address]
Name of Clinician/representative: [Name]
Signature of Clinician/representative: [Signature]
Name of Witness: [Name]
Signature of witness: [Signature]

For participant who cannot read and write will affix their right thumbprint on the box below after the clinician/representative has read the contents of this form.

Page 3 of 3

U N C L A S S I F I E D

AFRIMS
Sentinel Human Surveillance for Influenza in Soldiers #IMBAR/209
Version 6.0 dated 16 July 2015

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General Issue Discussion