Research Institute for Tropical Medicine
A model facility for safe and secure handling of high-risk pathogens

REMIGIO M. OLVEDA, MD
Director IV
What is RITM?

- **History**
  - 1981: Japanese ODA through JICA established research laboratories and a 50-bed hospital for research and service
  - 1985: Animal laboratory
  - 1989: Training center / residence hall
  - 2002: National Tuberculosis Reference Laboratory

- **Functions**
  - Main research arm of DOH for infectious and tropical diseases (1981)
  - National Reference Laboratories for infectious disease including emerging pathogens (2000)
  - Designated Referral Hospital for Emerging and Reemerging Infections (2004)

- **Repository of isolates** - from research, reference laboratory, surveillance activities
RITM Research Programs

1981 Research Projects

• Acute respiratory infections
• Diarrheal diseases
• Schistosomiasis

2008 Multidisciplinary Research Groups

• Acute respiratory infections
• Diarrheal disease
• Schistosomiasis
• Dengue
• Filovirus
• Hepatitis
• HIV/AIDS
• Leprosy
• Malaria
• Rabies
• TB
• Orphan infectious diseases
RITM National Reference Laboratories

Department Order 393-E, November 2000

- Dengue
- Influenza
- Measles and other viral exanthems
- Enteroviruses
- Bacterial enteric diseases
- Antimicrobial resistance
- Mycology
- Tuberculosis and other Mycobacteria
- Malaria and other parasites
- Emerging Diseases
- NRL for confirmatory testing of blood donors and blood units
- Rabies (2009)
- Japanese encephalitis (2010)
Laboratory based surveillance

• Influenza (WHO recognized National Influenza Center)
• Measles and other exanthems (in support of Philippine Measles Elimination Campaign/PMEC)
• Enteroviruses from Acute flaccid paralysis/AFP surveillance (WHO recognized National Polio Laboratory)
• Dengue
• JE and other causes of meningitis and meningoencephalitis
NEC OUTBREAK INVESTIGATIONS
Diarrheal disease outbreak investigations

- 2007 outbreaks of Shigella flexneri resistant to Ampicillin, Co-trimoxazole, Chloramphenicol
  - January – Bohol
  - April – Cotabato
  - July – Cavite

- 2008 outbreaks of Salmonella typhi
  - January – Nueva Viscaya
  - March – Laguna and Samar
  - April – Misamis Oriental
Diarrheal disease outbreak investigations

- EIEC/EPEC
- P. shigelloides
- S. typhi
- S. aureus
- V. parahaemolyticus
- Other Vibrios
- Shigella
- Aeromonas
- Non Typhoidal Salmonella
- V. cholerae Ogawa
Emerging Infections*: RITM Response

- 2009: H1N1/ Leptospirosis
- 2009: Ebola in pigs and humans
- 2005: Laboratory Preparedness to Avian Influenza Virus
- 2004: Meningococcemia outbreak in CAR
- 2003: SARS Outbreak
- 2002: West Nile Virus Pseudo outbreak (RITM as Referral Laboratory)
- 2001: Bioterrorism threat using Bacillus anthracis as biological weapon
- 1998: Serological Surveillance ABLV
- 1989: Outbreak of Ebola Reston Virus

* Pathogens are of interest to terrorists because of the fear, panic, anxiety and terror they may cause, aside from the great economic losses.
RITM served as Reference Laboratory for SARS-specific diagnostic tests, special tests to rule out other causes of atypical pneumonia and for specimen/tissue banking for future tests.

RITM was able to confirm SARS infection in eight patients by molecular detection and/or ELISA.
Meningococcemia in CAR
Nov 2004 – Dec 2005

RITM role
Culture (+) for *N. meningitidis* Serogroup A:
145 (34.6%) of 419 cases with clinical samples

Role of WHO Collaborating Center
Further characterization by Typing, Subtyping, PFGE & MLST:
Type 4, serotype P1.9 sequence type 7 & ST-5 complex

*Garnotel et al.; WHO Collaborating Center for Meningococcal Disease Marseilles, France*
Number of Specimen Positive for Seasonal Influenza and Pandemic A(H1N1), Philippines, January - December 2009

2009

Source: NIC-RITM Website weekly update (http://www.influenzasurveillancephilippines.org/content/weekly-updates)
BIOSECURITY RISK ASSESSMENT
Strategy

• It is impossible to eliminate all risk; risk can only be managed.

• Risk-based, graded protection strategy at the RITM facility

• Undesired events judged to present the highest risk to a facility receive the highest level of protection.
RITM Biosecurity Risk Prioritization Methodology
Joint Sandia National Laboratory and RITM teams
January 2007

• Evaluating the assets
• Evaluating the potential adversaries
• Creating scenarios
• Evaluating the vulnerabilities
• Evaluating the risk (threat potential and consequences) of those scenarios occurring.
BIOSECURITY RISK FLOWCHART

Evaluating the risk

BIOSECURITY RISK

Evaluating the risk

THREAT POTENTIAL

Evaluating the potential adversaries

Adversary attributes = motive, means, opportunities

Agent task complexity = acquisition, development, dissemination

Evaluating the potential adversaries

CONSEQUENCES

Population, economic, psychological and operational impact

Site vulnerability = physical, personnel, information, transport security, MCA, program management

Evaluating the vulnerabilities

Evaluating the assets
## Biological assets at RITM

<table>
<thead>
<tr>
<th>Species</th>
<th>Biosafety Risk Group</th>
<th>Why Screened</th>
<th>Biosecurity Risk Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dengue</td>
<td>2 or 3</td>
<td>Mosquito-borne, difficult to disseminate</td>
<td>Low Risk</td>
</tr>
<tr>
<td>E. coli O157</td>
<td>3</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>Ebola Reston</td>
<td>4</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>HIV</td>
<td>2 or 3</td>
<td>Difficult to disseminate</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>3</td>
<td>Mosquito-borne, difficult to disseminate</td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>M. tuberculosis</td>
<td>3</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>S. aureus</td>
<td>2</td>
<td>Very common worldwide, opportunistic pathogen</td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>N. meningitidis</td>
<td>2</td>
<td>Common worldwide, most infections are inapparent</td>
<td>Low Risk</td>
</tr>
<tr>
<td>P. falciparum</td>
<td>2</td>
<td>Common, difficult to disseminate, Mosquito-borne</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Polio</td>
<td>2</td>
<td></td>
<td>Low Risk</td>
</tr>
</tbody>
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### Biological assets at RITM

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<th>Biosecurity Risk Group</th>
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<tr>
<td>Rabies</td>
<td>2 or 3</td>
<td>Common in many areas of the world; difficult to disseminate (aerosol transmission documented only under unique circumstances)</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Rhinovirus spp</td>
<td>2</td>
<td>Ubiquitous in environment; opportunistic pathogen, mild illness</td>
<td>Low Risk</td>
</tr>
<tr>
<td>Parainfluenza</td>
<td></td>
<td>Ubiquitous in environment; mild illness</td>
<td>Low Risk</td>
</tr>
<tr>
<td>RSV</td>
<td>2</td>
<td>Ubiquitous in environment; opportunistic pathogen, mild illness</td>
<td>Low Risk</td>
</tr>
<tr>
<td>S. typhi</td>
<td>2 or 3</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>SARS</td>
<td>3</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>S. dysenteriae</td>
<td>2</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>Snake venom toxins</td>
<td></td>
<td>Stored as crystals; difficult to disseminate</td>
<td>Low Risk</td>
</tr>
<tr>
<td>V. cholerae</td>
<td>2</td>
<td></td>
<td>Moderate Risk</td>
</tr>
<tr>
<td>Influenza A</td>
<td>2</td>
<td>Common worldwide, most infections are mild in healthy adults</td>
<td>Low Risk</td>
</tr>
</tbody>
</table>
## Assets and potential adversaries

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Perpetuator</th>
<th>Level of security risk</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SARS virus</strong></td>
<td><strong>Insider</strong></td>
<td><strong>High</strong></td>
</tr>
<tr>
<td></td>
<td>terrorist group colluding with an insider</td>
<td>Moderate to high</td>
</tr>
<tr>
<td></td>
<td>terrorist group or single terrorist</td>
<td>Moderate</td>
</tr>
<tr>
<td><strong>MDR-TB</strong></td>
<td><strong>Insider terrorist</strong></td>
<td>Moderate to high</td>
</tr>
<tr>
<td></td>
<td>terrorist group colluding with an insider,</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>terrorist group or single terrorist</td>
<td></td>
</tr>
<tr>
<td><strong>Ebola Reston virus</strong></td>
<td><strong>Insider, terrorist group colluding with an insider,</strong></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>terrorist group or single terrorist</td>
<td>Low to moderate</td>
</tr>
<tr>
<td><strong>M. tuberculosis</strong></td>
<td><strong>Insider or terrorist group colluding with an insider</strong></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>terrorist group or single terrorist</td>
<td>Low to moderate</td>
</tr>
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</table>
Site vulnerability - Physical security

• Site perimeter secured.
• Locking doors to laboratories at night
• Access control procedures are very weak and for the most part ineffective.
• Guard force provides some level of security, but even this is ineffective given the openness of the campus. The general public can be found virtually anywhere on the campus during normal working hours and their presence is not questioned by the guards.
• Some CCTV cameras are installed in certain locations; however, the guard responsible for monitoring the cameras has other duties and is usually preoccupied by other attentions.
Site vulnerability – Program management

• No formal biosecurity plan or official who oversees biosecurity.

• No security training to staff when hired or on a regular basis. Some awareness of security practices are explained and reinforced within the specific laboratory but not at an institutional level.

• No formal SOPs or guidance for institutional security and in many areas the security practices seem to be limited due to funding constraints.
Site vulnerability – Personnel security

RITM permanent staff

- Staff are hired based on applications that include biodata, transcripts, and certifications or licenses where applicable. NBI clearance is required.
- Orientation program for new hires which includes policies and procedures on administration and overall RITM policies.
- Laboratory supervisor is responsible for all hands on training within the lab.
- Upon termination of employment, all employees go through a clearance process.
- Badges are required based on policies, but in practice are rarely worn.
- A list of authorized personnel is given to the guards for collection of keys.
- The guard force manages all the keys within RITM and logs in and out who has each key.
- Overtime protocol requires approval and documentation, but this practice is not strictly enforced. The guards do not challenge laboratory staff if they are in the lab after hours – they assume it is allowed, and do not ask for verification of identity or overtime approval.
- Permanent employees sign in and out of the building.
Site vulnerability – Personnel security

Contractual staff

• Staff are hired based on applications that include biodata, transcripts, and certifications or licenses where applicable. No NBI clearance is required.
• Not provided with badges, but do have ID cards.
• They do keep daily time records which are signed by the project lead.
• The foundation provides a general orientation but the project lead is required to provide and safety training and laboratory instruction.
• The exit process for foundation staff includes a clearance process and the final pay check is withheld until this clearance process has been completed.
Site vulnerability – Material control and accountability

• RITM has no system for accurate material control and accountability – a high-risk pathogen could be stolen.

• Each laboratory maintains its own schedule for conducting inventories, with few having recent and complete inventories.
Site vulnerability – transportation security

- Receive requests for isolates from research laboratories and even students
- Current procedures for refilling liquid nitrogen dewars entail transporting the containers to the outside business to be refilled.
- IATA guidelines when shipping samples internationally.
- No established protocols regarding shipment of samples within the Philippines, though there is a process.
- Samples are delivered by courier directly to the laboratory or are received by the guards, who take them to the appropriate laboratory themselves. This occasionally results in the gate or guard post being left unmanned.
- Samples are left unattended in the laboratory anteroom when no laboratory personnel are available to receive them.
Site vulnerability – information security

• There is little information of high value from a biosecurity standpoint on the RITM network.
• However, the network is generally wide open and any form of sensitive data would not be adequately protected on this network.
• RITM does have some information protection guidance. This is focused on patient confidentiality and media interactions in response to outbreaks. After the SARS outbreak, a chain of command for media interactions was formed, and people known to be in violation of breaking this communications chain have been informally reprimanded. Laboratory results regarding HIV status are treated confidentially.
Target of mitigation – decrease the risk
RISK MITIGATION
RECOMMENDATIONS AND ACTIONS
Physical security

Recommendation
• Secure the pathogens in the warehouse by restricting access to this building and by installing simple locks on freezers containing high-risk pathogens.

RITM action with Sandia support
• A portion of the warehouse has been enclosed with bars to house Risk Group 2 and 3 pathogens.
Physical security

Recommendation

- Installation of specific biosecurity equipment and technologies

RITM action with Sandia support

- A security system with automated access control, intrusion detection and 16 CCTVs for alarm assessment, all integrated with a Central Alarm Station, has been installed.

- Currently, used for investigations as no permanent personnel can be assigned to the station.
Recommendation: Access control to other laboratories should also be improved.

WE DEFINED OUR FACILITY BY ASSETS THAT WE KEEP.

PROPERTY PROTECTION AREAS - LOW RISK ASSETS
- Grounds
- Public access offices

LIMITED ACCESS AREAS
- Laboratory Research Wing
- Vaccine Production Areas

RESTRICTED AREAS - Moderate risk assets
- Virology Annex
- Microbiology Laboratory
- ARS Laboratory
- Veterinary Research Department (Experimental Animal Facility)
- BCG Vaccine Production Area
- Freezer Room

HIGHLY RESTRICTED AREAS - High risk assets
- TB Culture Laboratory, NTRL Building
- Rabies and Special Pathogens Laboratories
- TB Unit, Microbiology Laboratory
- Biosafety Level 3 Laboratory
- Select area with freezers with high risk pathogens, Isolate and Sample Bank
PHYSICAL SECURITY SIMPLE MEASURES

LIMITED ACCESS AREAS

Laboratory Research Wing
Vaccine Production Areas

RESTRICTED AREAS

Virology Annex
Microbiology Laboratory
ARS Laboratory
Veterinary Research Department (Experimental Animal Facility)
BCG Vaccine Production Area
Freezer Room

HIGHLY RESTRICTED AREAS

* TB Culture Laboratory, NTRL Building
*Rabies and Special Pathogens Laboratories
*TB Unit, Microbiology Laboratory
Biosafety Level 3 (2+) Laboratory
Select area with freezers with high risk pathogens, Isolate and Sample Bank, Warehouse

*PIN for access and alarm system (sensors inside)
Physical security

• Upgrading of facilities
  - isolate the laboratory research wing
  - access to main door to laboratory – one entry and one exit
PROGRAM MANAGEMENT

Recommendations

• Long-term biosecurity plan that documents all necessary Standard Operating Procedures and incident response plans,

• Biosecurity training for RITM staff that is directly relevant to their specific job functions.

Achieved so far at RITM

• SOP on Security in place for protection of physical facility, personnel, patients

• Some biosecurity orientation/training for laboratory staff.

• Coordination between the policy-maker (Biosafety and Biosecurity Officer) and the program implementation officer (Administrative Officer) is on-going.
Personnel Security

Recommendations
• Standardized screening process should be in place for all personnel working within the laboratories.
• Practices regarding badging should be standardized.

Achieved so far
• A standardized screening process is in place for newly hired permanent and contractual personnel working within the laboratories.
• Identified laboratory personnel with access and PIN to TB Culture, Special Pathogens and Rabies, BSL3 laboratories
• Permission for OT after 5pm is secured from the Admin Officer.
Personnel Security

What still needs to be done?

• SOPs for research contract personnel
  Principal investigators and researchers to provide list of contractuals, duties and responsibilities to AO/ Personnel Department for orientation and monitoring.

• Personnel IDs/badges and biometrics for logging in and out and time keeping will be upgraded with access and information on duration of access to the facility
Personnel security

Practices regarding badging will be standardized.

1. Persons with authorized access to the laboratories should wear their badges so that they are clearly visible, except in situations where this could compromise safety.

2. Badges will be provided for contractors as well as visitors to the lab areas.

3. Ideally, badges will reflect the level of access authorized for the wearer.

4. Persons not wearing proper badges will not be permitted entry into restricted access areas.
Material Control & Accountability

Recommendation

Establish a complete, current inventory of pathogens

Achieved so far:

1. Each laboratory maintains its own schedule for conducting inventories.
2. Bar coding of new samples and isolates is being done.
3. Each laboratory has identified authorized individuals who can access the samples and the data.
4. SOPs for conducting routine inventory of stocks and for determining when to dispose of isolates or samples
Still to be done

• RITM will establish a complete, centralized computer based inventory of pathogens.

• Establish SOPs for sharing and tracking isolates within the facility.

• Proposed National Survey for Inventory of isolates and samples
Transportation Security

Recommendations
- RITM needs its own supply of liquid nitrogen, from which the staff can refill individual dewars themselves, particularly those that contain high-risk organisms.

Achieved so far
- Standard SOPs for shipping security and handling in transport in place
- Setting up large filling dewars or tanks to supply liquid nitrogen to individual dewars, particularly those that contain high-risk organisms will be required as part of a contract for services regarding provision of LN.
Risk mitigation recommendations

Information Security

• RITM program management needs to create standard information policies which include sensitive personal information and biosecurity-related information.

• RITM network users should be required to maintain a minimum level of security on computers and data
Safe and secure laboratories

1. Ensure the containment of hazardous infectious substances in laboratories
2. Maintain citizens’ confidence in the activities of the bioscience research community
3. Increase transparency to investors in the biomedical and biotechnology industries
4. Protect valuable research and commercial assets
5. Reduce the risks of crime and bioterrorism
THANK YOU!