Award Number:

W81XWH-11-2-0148

TITLE: National Biocontainment Training Center

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CONTRACTING ORGANIZATION: University of Texas Medical Branch at Galveston
Galveston, TX 77555-5302

REPORT DATE: October 2016

TYPE OF REPORT: FINAL

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT:

Approved for public release; distribution unlimited

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE *(DD-MM-YYYY)*	**2. REPORT TYPE**	**3. DATES COVERED** *(From - To)*
October 2016	Final	15Jul2011 - 14Aug2016

4. TITLE AND SUBTITLE
National Biocontainment Training Center

5a. CONTRACT NUMBER
W81XWH-11-2-0148

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
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5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

University of Texas Medical
Branch at Galveston
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Galveston, TX 77555-5302

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Medical Research and Materiel Command
Fort Detrick, MD 21702-5014

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Scientific investigations, product development, and response to threats of endemic diseases and emerging pathogens are undertaken to reduce the risk of infection and lessen the impact of naturally occurring or man-made pathogens to humankind. If, however, proper precautions are not taken and safe practices are not utilized there is a risk that these interventions could contribute to increase the potential exposure of individual scientists and technical staff, as well as surrounding communities, to dangerous infectious diseases. The threat is perhaps greatest within the international laboratory community where these dangerous pathogens are routinely manipulated and investigated. This award supports critical training and hands-on experience to predominantly international scientists working with especially dangerous pathogens that require special biocontainment facilities for their safe and secure handling.

15. SUBJECT TERMS

Nothing listed

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			USAMRMC
U	U	U	UU	98	**19b. TELEPHONE NUMBER** *(include area code)*

W81XWH-09-2-0148 (NBTC2) Final Report July 2011 – July 2016

Introduction

Through the generous support of award number W81XWH-11-2-0148, and its partner award number W81XWH-09-2-0053, the National Biocontainment Training Center (NBTC) has provided customized training to individuals working on dangerous pathogens under biocontainment for the past 7 years. Trainees came from not only the campus of the University of Texas Medical Branch, home to the Galveston National Laboratory, but also from biocontainment facilities around the world. Our training program has introduced foreign partners to best practices in the safe and secure conduct of research at all levels of biocontainment, including at biological safety level 4 (BSL4), the highest degree of biocontainment.

In addition, the NBTC has assisted experts from around the world as they strive to ensure that their own biocontainment laboratories are operated at the highest level of safety and security and that their maintenance programs meet the rigorous standards that have been established in the United States. This training is absolutely unique in that no other program offers such an extensive hands-on experience to building engineers and operations personnel using a fully operational BSL4 facility as their training grounds.

The training and experiences offered by the NBTC are especially valuable today, both here in the United States as well as abroad. Given the dramatic proliferation of biocontainment laboratories around the world, it is essential that the personnel using these facilities be appropriately introduced to the critical skills needed to work safely and securely with dangerous pathogens. Historically, only a few laboratories around the world had the capabilities to safely handle Ebola and other viral hemorrhagic fevers; however, today China has two BSL4 laboratories nearly operational, India has one already being used, and many, many countries have BSL3 laboratories in use, and the global outbreak of Ebola virus has resulted in this deadly virus being more widely available than ever before.

The work that the NBTC has done to introduce both the scientific and engineering personnel of these new biocontainment facilities to best practices in safety, security and operations is essential and an investment that will pay dividends for many years to come. But the situation is dynamic, with new staff coming on board every day as others move on; thus, there is a constant demand for the kind of expert training offered by the NBTC.

Unfortunately, funding for the NBTC has expired and our international training efforts, as well as the free training of non-UTMB personnel, must cease. At a time when even our most prestigious institutions in the United States are suffering from laboratory incidents leading to damaging headlines and potentially life-threatening exposures to workers, it is especially concerning to see such a valuable training program close.

Over the last two years, UTMB personnel supported by this grant, along with others working for the university, have diligently searched for and applied for funding to continue the training center activities. Formal grant proposals have been submitted to federal and state agencies, collaborations have been explored with military organizations, professional associations, other health care institutions and state agencies, talks have been held with elected officials at both the state and federal level, and personnel have participated in important review panels and have provided testimony to Congress regarding laboratory safety issues. While these efforts have done much to elicit accolades for the program, they have been unsuccessful in securing funding to continue this important work.

Staffing

The National Biocontainment Training Center at UTMB benefits from an experienced team of Environmental Health and Safety Professionals, scientists, engineers and technicians to provide unique biosafety training to students, faculty and other professionals who work in biocontainment laboratories. Trainers deliver customized one-on-one training after providing individualized assessments of each student. Currently there are 14 individuals who have received all or part of their salaries from this grant and who participate in the biosafety training for domestic and international scientists and personnel. In addition, to the individuals listed below, there are other staff from UTMB who assist with training, marketing, administrative support, or report generation. Supported staff include:

James W. Le Duc is the principal investigator for the training center and is responsible for oversight of all program initiatives, institutional collaborations, fiscal management and project reporting.

Dennis Bente provides mentored training to international scientists, including visiting scientists, who are working within the biocontainment laboratories as part of collaborative projects and fellowships. His work focuses on arboviruses, the unique insectaries at the GNL, and filoviruses such as Crimean-Congo Hemorrhagic Fever.

Sophie Brocard provides didactic and mock-laboratory training and is a principal trainer involved in international training in support of the NBTC and other collaborative efforts.

Christopher Gibbs assists in the training of operations personnel, including engineers from domestic and international facilities who benefit from hands-on experience ensuring the safe use, maintenance, and certification of biological safety cabinets.

Miguel Grimaldo assists biocontainment facilities around the world with operational expertise and represents the GNL on the Operations Committee of NIAID's National and Regional Biocontainment Laboratory Network. He is a regular lecturer on the topic of biocontainment engineering and operations.

Jason Hardcastle provides training for the BSL2 Training course, PAPR Training course, and the Class III BSC Training course. He also assists with the ABSL2 Training course, BSL3 Training course, and ABSL3 Training courses.

Vickie Jones is responsible for providing biological and chemical safety training to individuals from academia and industry, including site-specific training.

Tom Ksiazek has more than 30 years of experience in biocontainment research and is one of the world's foremost experts on filoviruses. He is the Director of Biocontainment for the GNL and provides mentored training to all BSL4 trainees.

Sheri Leavitt provides ABSL training to graduate students, faculty and staff who will work in the ABSL laboratories. She is involved in training of new Animal Resource Center staff as well as visiting scientists from around the world.

Je T'aime Newton provides biosafety and facility training for the BSL-4 laboratory and Emerging Infectious Disease (EID) training for healthcare professionals.

Belinda Rivera is the in-vivo training consultant providing oversight and training for ABSL2, ABSL3, ABSL4, and NHP courses for both US and international trainees. As needed, she assists with BSL2 and BSL3 in-vitro training courses. She is frequently a presenter at ABSA and AALS meetings.

Nate Schueller provides training for the BSL2 Training course, ABSL2 Training course, and the ABSL3 Training course and assists with curriculum manual updates and training metrics.

Sharon Walters handles scheduling and administrative duties for all training that is provided through the NBTC.

Dee Zimmerman monitors developments in biosafety and training and ensures that all training courses include the most up to date biosafety protocols and procedures.

NBTC Training

Through the years, UTMB's National Biocontainment Training Center has offered a portfolio of courses and individualized mentorship training experiences that are enhanced based on expanding information, the needs of the students, and as new equipment, procedures and regulations are put into place. All trainees are assessed for existing knowledge and skill prior to the beginning of their training. With this assessment, training is based on individual needs.

The Biosafety Training Courses were designed to provide initial training for laboratorians and research scientists preparing to enter BSL2 through BSL4 labs, as well as provide refresher training for experienced biocontainment laboratory professionals and specialized, customized training for specific situations and experienced scientists and lab professionals.

Mentorship

A mentorship program is an important part of the training process. During mentorship the trainee is supervised at all times by an experienced Principal Investigator or lab professional. The duration of the mentorship phase is based on each institution's requirements and takes into consideration the ability of the trainee to adapt to the environment.

Course List

The following courses comprise the core courses within the laboratory training program as of the end of the grant period. This list has grown throughout the grant period based on the interests and needs of trainees. In addition to these offerings, specialized courses on equipment and procedures (Autoclaves, Aerobiology, Real Time Plethysmography, Assay Development) have been made available.

Biosafety Level 2 Theoretical class

Biosafety Level 2 Theoretical and Practicum classes

Class III Cabinet Training

Biosafety Level 3 Theoretical class

Biosafety Level 3 Theoretical and Practicum classes

Biosafety Level 4 Training

Animal Biosafety Level 2 Theoretical class

Animal Biosafety Level 2 Theoretical and Practicum classes

Animal Biosafety Level 3 Theoretical class

Animal Biosafety Level 3 Theoretical and Practicum classes

Animal Biosafety Level 4 Training

Non-Human Primate Theoretical class

Non-Human Primate Theoretical and Practicum classes

Personal Protection for Health Care Personnel

Biocontainment Facility Engineering Training Program

The Biocontainment Facility Engineering Training Program is a specialized course that provides critical insight and a thorough overview of the basic demands and ongoing requirements of biocontainment operations engineering and management.

The course is taught by engineers and facility operations personnel and offers instruction in the milestone and day-to-day activities involved in the commissioning of a new or renovated containment laboratory facility, as well as information on the ongoing operation, maintenance and validation of these laboratories.

Experienced instructors work alongside trainees, with specific instruction provided by engineers, research scientists, facilities maintenance personnel, equipment vendors/contractors, and biosafety officers. This one to two-week course has been popular with international students in countries where biocontainment facilities are being built.

Topics covered in the training include:

- Laboratory Facilities and Primary Containment Requirements
- Primary Containment Equipment
- Filtration Systems
- Liquid and Solid Waste Decontamination
- Mechanical Systems - Ventilation and Controls
- Laboratory Facility Adjustment and Testing
- Decontamination Methodologies and Procedures
- BSL4 Specialized Equipment & Other Laboratory Equipment
- BSL4 Suits - Setup, Maintenance and Usage
- Annual Maintenance Shutdowns and Record Keeping
- Special Topics on Biocontainment Operations

Specific Aims

NOTE: With the expiration of the NBTC 1 Grant (W81XWH-09-2-0053) in December 2014, Aims within this program were expanded to address the needs of both international and domestic trainees. Progress on both programs is reported for the period July 2015 – July 2016.

Aim 1. To provide standards-based biological containment laboratory safety knowledge to international partners.

NBTC trainers Jason Hardcastle, Vickie Jones, Sheri Levitt, Belinda Rivera and Nate Schueller provided theoretical and hands-on training in the mock training lab at the NBTC and within the facilities of the Galveston National Laboratory to a large number of students, faculty, Animal Resource Center personnel and others during 2016. Dr. Donald Bouyer coordinated mentorship for BSL3, and Dr. Tom Ksiazek coordinated mentorship for BSL4. Corrie Ntiforo and Jet Newton focus on training individuals to work in the BSL4 labs. A chart showing training and mentorship numbers appears on page 10 of this report. Additional training efforts were detailed in the quarterly reports submitted in October 2015, January 2016 and April 2016.

Boston University – National Emerging Infectious Diseases Laboratories (NEIDL)

The NBTC staff has been working with Animal Resource Center and Biosafety staff from the NEIDL at Boston University to provide both training and mentorship. In July 2015, Dr. Jim Levin completed his 100 hours of BSL4 mentorship. He worked with NBTC trainers Corrie Ntiforo and Jet Newton, as well as Dr. Curtis Klages, the former chief veterinarian for the GNL. In addition, Dr. John Tonkiss returned to Galveston throughout the year to continue his 50 hour BSL4 mentorship. Other staff from Boston University have received training from NBTC staff in preparation for working in the high containment labs at the NEIDL.

Jagiellonian University, Krakow, Poland – In November, Belinda Rivera traveled to Poland to provide theoretical and practical training for working with mice in research experiments conducted in a high containment environment. The laboratory at Jagiellonian University is the only BSL3 facility in Poland. This facility is scheduled to go online in 2016, and there are plans to work with MERS, SARS, and West Nile Virus.

In addition to this training, which took place between Nov. 13 and Nov. 23, 2015, it is anticipated that additional collaborations with this facility will take place as the facility commissions and prepares to open and as additional staff are hired.

Shown in the ABSL3 lab in Krakow are (left to right): Aleksandra Milewska, Krzysztof Pyrc (director), Katarzyna Kosowicz, and Inga Drebot. Also participating in the training but not in photo was Monika Majchrak-Gorecka.

Texas Department of State Health Services and William Beaumont Army Medical Center - Staff from the NBTC provided both theory and laboratory training to the Emergency Preparedness Team Leader from the Texas Department of State Health Services and the Deputy Chief of Microbiology from the Army Medical Center in El Paso, Texas.

In addition, a large group from the Texas Department of State Health Services toured the Galveston National Laboratory following a regional emergency preparedness meeting in Galveston. The group is shown here after the tour, which was conducted by Corrie Ntiforo, a senior EHS Consultant and one of the BSL4 trainers for the NBTC. The state of Texas is very interested in the training capabilities of the NBTC staff and the high containment capabilities of the Galveston National Laboratory.

University of Saskatchewan, Canada – Three trainees from the Vaccine and Infectious Disease Organization – International Vaccine Centre (VIDO – InterVac) attended a full week of ABSL3 training in Galveston in March 2016.

The three participants work in the animal care group, which has BSL2 laboratories and a BSL3 Ag facility. The trainees had prior experience working with small animals at BSL2 and large animals at BSL3, but there are plans for future work with small animals at level 3.

Belinda Rivera provided the full course of training and ensured that they would be prepared to work with small animals at the vaccine center.

U.S. Food and Drug Administration Training – Marisa Hickey, D.V.M., MPH, attended training in Galveston from Feb. 29 – March 4th, 2016, completing the full ABSL3 course with NBTC trainer Belinda Rivera. Dr. Hickey is a Biosafety Manager at the FDA's White Oak campus. She will be responsible for training personnel at the FDA's Center for Biologics Evaluation and Research, which works to protect and enhance the public health through the regulation of biological and related products including blood, vaccines, allergenics, tissues and cellular and gene therapies.

The theoretical and hands-on training provided by Ms. Rivera was designed specifically to assist Dr. Hickey in learning what she needed to know to train other researchers to work with ferrets in Highly Pathogenic Avian Influenza (HPAI) studies.

Dr. Marissa Hickey of the FDA is shown here with Belinda Rivera of the NBTC during her week-long training in Galveston.

George Mason University, Fairfax, Virginia – A laboratory supervisor and a manager for animal care at the Biomedical Research Laboratory (BRL) at George Mason University, spent a week in Galveston Oct. 19 – 23, 2015, training with NBTC trainers on critical aspects of working with nonhuman primates. The BRL supports research programs in the National Center for Biodefense and Infectious Diseases, and the BRL is equipped with facilities to house multiple animal species, including nonhuman primates. NBTC Trainers provided both theoretical instruction and hands-on animal training. George Mason University is part of NIAID's Biodefense Laboratory Network, and NBTC trainers regularly provide instruction to colleagues within the network. It is anticipated that additional training will be provided to personnel working in this facility as part of an ongoing collaboration.

The Biomedical Research Laboratory (BRL) at George Mason University is a part of the NIAID Biodefense Laboratory Network.

Baylor College of Medicine, Baylor University – From January 25 -29, 2016, Belinda Rivera provided theoretical and practical training for Lynn Bmiler, a Department of Immunology graduate student from Baylor College of Medicine. Ms. Bimler is studying influenza and sought training to prepare to work on her graduate project, which will include working with influenza with small animals. In addition, three graduate students from the Baylor College of Medicine and one Training and Project Manager completed ABSL2 training in the NBTC Mock Training Lab facilities. The students were trained by NBTC trainers Nate Schueller and Sheri Leavitt. The students will be working on projects with rodents infected with HIV-1 and Influenza (H1NI and H3N2 strains), and the training manager will be training all animal care staff assigned to ABSL2 facilities. To meet the needs of the students, training was customized to include training on the writing of Standard Operating Procedures.

NBTC trainers (Belinda Rivera in photo at left and Nate Schueller and Sheri Leavitt in photo at right) worked with students from Baylor College of Medicine.

Training Numbers – National Biocontainment Training Center

Training Course/Module	May-Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-Dec 2013	Jan-Dec 2014	Jan-Dec 2015	Jan-Mar 2016	Apr-Jul 2016	Total
BSL2 theoretical	107	144	251	160	133	165	158	19	68	1,205
BSL2 hands-on	64	76	92	117	102	134	219	13	36	853
ABSL2 theoretical	N/A	1	79	149	284	116	172	28	55	884
ABSL2 hands-on	N/A	1	40	76	105	116	148	30	40	556
BSL3 theoretical	45	119	100	135	86	125	48	29	33	720
BSL3 hands-on	45	101	94	76	57	49	71	20	35	548
BSL3 mentorship	36	41	24	18	14	26	15	4	6	184
Class III cabinet theoretical (New course)	N/A	N/A	N/A	N/A	N/A	2	N/A	N/A	N/A	2
Class III cabinet hands-on (New course)	N/A	N/A	N/A	N/A	N/A	2	N/A	N/A	N/A	2
ABSL3 theoretical	29	55	47	73	76	36	89	13	20	438
ABSL3 hands-on	29	50	46	37	53	29	34	13	12	303
ABSL3 mentorship	N/A	N/A	38	19	26	34	7			124
BSL4 Training, orientation and mentorship	9	28	59	47	41	59	26	4	2	275
ABSL4 program	N/A	N/A	N/A	N/A	N/A	18	22	0	14	54
Non-human primate theoretical	16	15	60	41	20	24	9	9	3	197
Non-human primate, hands-on	N/A	N/A	90	41	28	23	20	0	7	209
Non-human primate annual refresher	N/A	N/A	37	114	89	108	120	N/A	N/A	468
Animal handling certificates	N/A	N/A	22	75	39	27	16	9	8	196
Graduate Program	39	36	32	13	18	25	44	0	8	215
Introduction to Microbiology	18	0	6	4	0	0	0	1	N/A	29
Aerobiology	19	5	2	8	0	2	0	0	0	36
Autoclave	195	27	46	30	25	14	0	0	0	337
High Throughput Safety training	8	11	3	2	17	12	0			53
PAPR (respirator training)	N/A	10	49	52	78	82	28	12	16	327
ABSA/AfBSA courses*	84	175	87	207	181	137	184	18	80	1,153
Agent specific training	N/A	N/A	N/A	N/A	186	141	0	N/A	N/A	327
Specialized Biosafety course	N/A	N/A	N/A	N/A	N/A	71	113	N/A	N/A	184
Ebola response training/ Healthcare training	N/A	N/A	N/A	N/A	N/A	177	206	32	75	490
Total trained	**743**	**895**	**1,304**	**1,494**	**1,658**	1,754	1491	**254**	**518**	**10369**

Aim 2: To provide the information and education necessary for a critical global discussion on the biosecurity, biosurety and related policy issues involved in the operation and maintenance of biocontainment facilities.

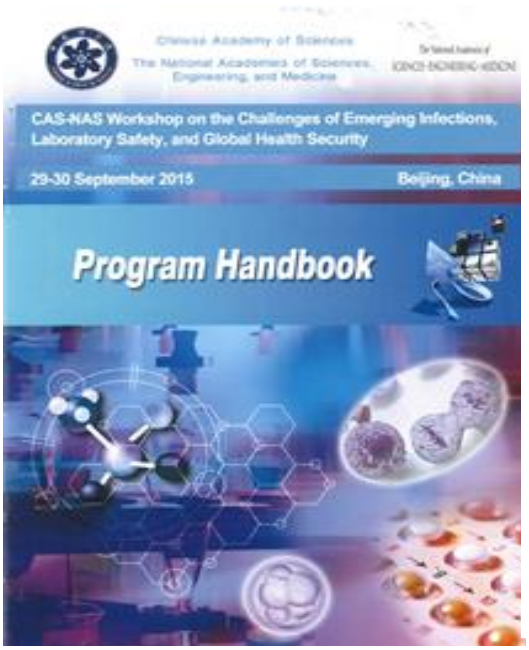
GAO Audit and Deactivation Protocol Discussions - Representatives from the General Accountability Office in Washington, D.C. visited the Galveston National Laboratory and the National Biocontainment Training Center in July 2015 as part of a national audit of biocontainment facility biosafety practices and deactivation protocols. Five auditors participated in the visit, which involved more than a dozen biosafety professionals and principal investigators who work in high containment at UTMB. The GAO team also visited the NBTC mock training lab. Response to the training and the facilities in Galveston was overwhelmingly favorable. A formal report was to be prepared by the GAO.

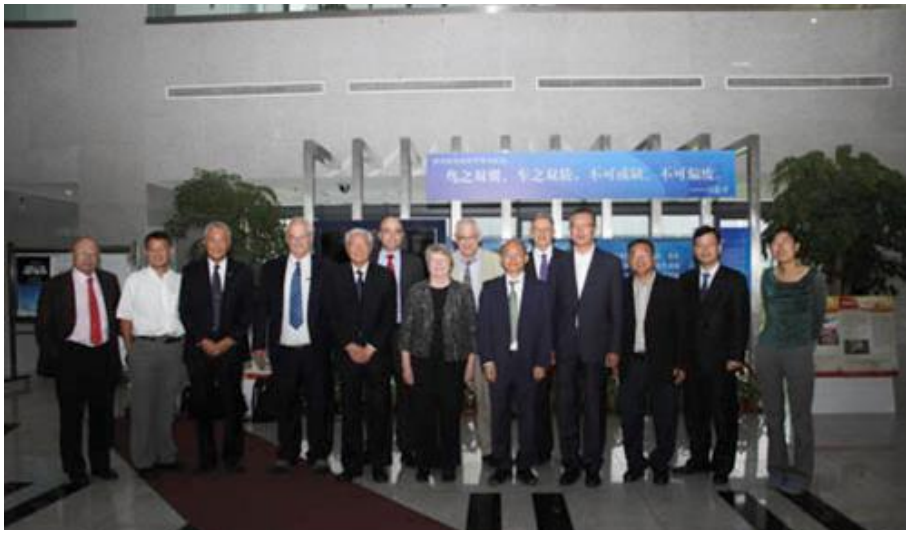
Brazilian Biosafety Conference – Mr. Miguel Grimaldo traveled to Brazil for the IX Brasilian Biosafety Congress at Porto Alegre, Brazil from Sep 29 to Oct 1, 2015. While there he presented a lecture focused on the engineering principles needed to construct and operate a biocontainment laboratory. He also taught a day-long class that covered the topic more in-depth. A large audience of engineers and biosafety professionals was in attendance and the information was very well-received. Both the lecture and the course have generated significant interest and follow-up from attendees and has led to further consulting and collaboration by Mr. Grimaldo with developing operations in Brazil and other parts of South America.

Texas A&M University and Department of Homeland Security - The NBTC is a collaborator with Texas A & M University on a DHS funded grant "From the Bench to the Shop: Creation and Implementation of a Scientific Business Development and Management Program to Transition High-Consequence Livestock Disease Research and Development Technologies for Commercialization," also referred to as "Technology Transition 101: to the Global Marketplace." Early stage conversations and planning have been held in preparation for assisting A&M with this project. Dr. James Le Duc, Dr. Sophie Brocard, and Ms. Dee Zimmerman are leading this collaborative effort for the NBTC, and other staff trainers from the NBTC are expected to become engaged in the project as it gets underway.

CAS-NAS Workshop on the Challenges of Emerging Infections, Laboratory Safety, and Global Health Security. Dr. Tom Ksiazek, Director of Biocontainment Operations at UTMB, traveled to Beijing China Sept.29-30 as the Chair of the Ebola and Beyond track of this workshop sponsored by the Chinese Academy of Sciences and the National Academies of Sciences, Engineering and Medicine. In addition to organizing the track on emerging infectious diseases and participating in panel discussions, he presented one talk on Ebola and another on High Containment Laboratories and the requirements for ensuring global health security and laboratory safety. As China continues to develop its biocontainment laboratory capabilities and infectious disease research programs, other discussions and visits have occurred between Chinese and UTMB personnel. Participation in this program was a continuation of ongoing discussions and assistance between the NBTC and scientists, laboratory personnel and regulatory authorities in China.

A follow up to the CAS-NAS Workshop will be held in 2016 at the Wuhan Institute of Virology of the Chinese Academy of Sciences in Jiangxia, Wuhan. The first national BSL4 laboratory in China is now under construction and is positioning for important research in emerging infectious diseases. WIV has 266 employees, and training is a top concern. Dr. Han Xia, who completed a two-year Fellowship at UTMB as a part of this grant, has returned to China and is a key contributor to the development of important standards for biosafety, facility operations and training.





Dr. Tom Ksiazek (center), Director of Biocontainment for the Galveston National Laboratory and a mentor in the BSL4 training programs of the NBTC, was a key participant in the CAS-NAS Workshop in China.

National Science Advisory Board for Biosecurity – Dr. Jim Le Duc has contributed to a NSABB committee focused on the communication of risks associated with Dual Use Life Sciences Research. Specific questions addressed as part of this committee work included:

- What are the strengths and limitations of the risk and benefit assessments?
- Which gain-of-function (GOF) studies are of greatest concern, if any? Which are of less concern?
- Are the assumptions, approaches and findings about risks and benefits associated with GOF studies comprehensive and sound?
- Are there specific risks or benefits that are over-or understated in the risk and benefit assessments?

This group advises the U.S. Government on strategies for the effective oversight of dual use life sciences research. The findings of this committee are often used by international biosecurity organizations to set policies. It is yet another example of the involvement of NBTC leadership in scientific issues of international concern.

NIAID Biodefense Laboratory Network Annual Meeting – Representatives of the Galveston National Laboratory and National Biocontainment Training Center participated in the annual meeting of the NIAID Biodefense Laboratory Network, held in Boston at the National Emerging Infectious Disease Laboratory and Boston Medical School April 10 – 12, 2016.

More than 70 participants from 14 universities were in attendance and participated in two days of discussions regarding safety, security and regulatory concerns facing the National Biocontainment Laboratories and Regional Biocontainment Laboratories that have been funded by the National Institutes of Health.

NBTC representatives led discussions among their peers from the following universities:

- Boston University
- Colorado State University
- Duke University
- George Mason University
- Rutgers University
- Tufts University
- Tulane University
- University of Alabama at Birmingham
- University of Chicago
- University of Louisville
- University of Missouri
- University of Pittsburgh
- University of Tennessee
- University of Texas Medical Branch

In addition to providing an opportunity for personnel from these biodefense labs to have focused discussions on operations, maintenance, biosafety, security and veterinary services, guest speakers from the National Institutes of Health, the Federal Bureau of Investigation, and the U.S. Centers for Disease Control & Prevention shared information about current national level discussions and initiatives that will impact biosafety and biosecurity at high containment laboratories throughout North America.

NAS Committee on Biosafety in Microbiological and Biomedical Laboratories (BMBL) – Dr. Tom Ksiazek was asked by the National Academies of Science to participate on a committee convened at the request of the U.S. Centers for Disease Control & Prevention and the National Institutes of Health to review the biosafety protocols and procedures in the BMBL. Dr. Ksiazek attended meetings and requested input from scientists at UTMB and other institutions. The result of the committee's work has been published by NAS.

Aim 3. To Develop and implement a dedicated program to facilitate the establishment, maintenance and administrative oversight of operations of biocontainment facilities.

Biocontainment facilities are unique in their mechanical, security and safety infrastructures, and there are very few educational programs available that prepare professionals for their operational requirements. Today, with more international laboratories being constructed, the Galveston National Laboratory has taken on the role of sharing expertise on the unique engineering,

maintenance and administrative challenges of running a safe biocontainment operation. The goal: to help ensure that all labs that deal with infectious pathogens operate safely and securely.

While every facility is unique in the research being conducted and the pathogens being handled, there are general principles that must be followed. As a national resource with a large variety of research projects underway, the GNL is in a unique position to share its expertise and lessons learned. Whether providing tours, one-on-one consultations, or formal training programs, the staff at the GNL is constantly sharing relevant, hands-on experience with the next generation of biocontainment industry leaders. An expanding list of the essential tools, skills and procedures critical to the safe and secure operations of a biocontainment laboratory is being compiled, documented, and shared to ensure that the best practices for fiscal stability, security, utility management, and equipment needs are available to biocontainment laboratories around the world.

Consulting: The Central Veterinary Institute of Wageningen UR (the Netherlands) – The goal of the Central Veterinary Institute is to support the mission of Wageningen University, which is the only university in the Netherlands focused specifically on "healthy food and healthy environment." The CVI is the national reference laboratory that is focused on the health of both animals and humans. They provide research for government and commercial entities on animal diseases that threaten the food supply, as well as those that have the potential to form a threat in humans. The High Containment Unit, located in Lelystad, is the only one of its kind in the Netherlands. Mr. Douwe Kuperus, the CVI's Biosafety Officer, has been in consultation with Mr. Miguel Grimaldo, Biocontainment Engineer at the GNL, to discuss issues pertaining to duct work and exhaust systems and material considerations for HVAC in high containment, testing and regulations.

The Central Veterinary Institute (CVI), right, resides on the campus of Wageningen University on the Dutch side of the Lower Rhine in The Netherlands.

Doherty Institute – Melbourne, Australia – Miguel Grimaldo continues his consultations with the Peter Doherty Institute for Infection and Immunity. This is a joint venture between the University of Melbourne and the Royal Melbourne Hospital and combines research, teaching, public health and laboratory services for diagnostics and clinical care. Mr. Grimaldo has been working with the high containment operations and engineering staff on a recurring basis, providing insight into maintenance and operations efficiency.

Below: Doherty Institute for Infection and Immunity.

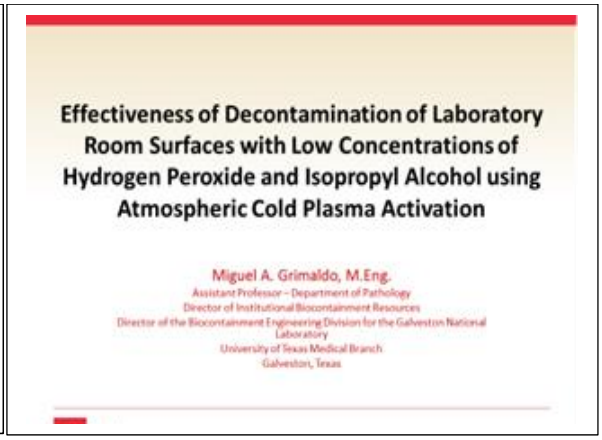
National Institute for Communicable Diseases: South Africa --Mr. Grimaldo has also been collaborating with engineering and biosafety professionals at the National Institute for Communicable Diseases (NICD), the national public health institute for South Africa. He provided a peer review of their Engineering Policy and Implementation Strategy in March 2016. The National Institute provides reference microbiology, virology, epidemiology, surveillance and public health research to support the South African government's response to communicable disease threats. The NICD works closely with public health organizations internationally, including the CDC, NIAID and NIH in the U.S.

LAB OPERATIONS CONSULTING AND PLANNING FOR FUTURE TRAINING

American Hospital – Instanbul, Turkey – The American Hospital has previously consulted with biocontainment engineering and operations staff at the Galveston National Lab regarding the construction of high containment laboratories. With completion of their facilities nearing, they have requested training pograms for their laboratory personnel and operations staff. Mr. Miguel Grimaldo is working with the training staff of the NBTC to develop a training program that can be provided at a fair price.

Biosafety experts and facility engineers from Brazil, Colombia and Mexico joined Mr. Miguel Grimaldo (right) in Galveston in June 2016 for a week-long training session focused on biocontainment facility maintenance and operations.
Ongoing consulting and future scientific collaborations.

International Veterinary Biosafety Workgroup -- Miguel Grimaldo was a speaker at the IVBW17 conference in Geelong, Victoria, Australia on November 3, 2015. His presentation covered laboratory decontamination procedures. The mission of the International Veterinary Biosafety Workgroup is to promote best practices in microbiological biocontainment and safety in veterinary labs that have national responsibility for the health of large animals, and which operate at BSL3 and BSL4. Members come from agencies all over the world.



Aim 4. To develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

As in previous years, training continues on a regular basis within the laboratories at the GNL. New equipment that is purchased requires new training. Training on microscopy and telemetry equipment was a highlight for 2016. Dr. Rick Pyles also provides training on a regular basis in his Assay Development Core on the use of advanced high throughput diagnostic equipment, which has become increasingly important in light of the Zika virus outbreak.

American Biological Safety Association (ABSA) Annual Meeting - Ms. Dee Zimmerman, EHS Consultant, co-taught a day-long class on "BSL-3 Operations and Management" during the ABSA Annual meeting in October. The course reviewed the operation of a BSL-3 facility from two points of view; management of the facility and the daily operations. In addition to covering basic training needs, the course focused on maintenance support, occupational health issues; waste management, HVAC maintenance, facility systems checks and emergency planning for failures, entry and exit procedures, and Personal Protective Equipment (PPE). It also provided information on developing Standard Operating Procedures, ensuring the secure operations of novel equipment, and overall biocontainment safety standards.

Also at ABSA, Ms. Belinda Rivera taught an 8 hour class on "Advanced Principles and Practices of Working in an ABSL-3," focused on the unique requirements for animal care, research staff, and safety personnel. This course provided information for individuals who audit or train personnel to work in ABSL-3 facilities. It focused on the unique hazards faced by animal care staff, researchers, and biosafety professionals, as well as ways to ensure proper risk assessments and management of risks, training, and species-specific handling procedures. Discussions covered PPE, equipment, husbandry procedures, caging options, waste management, and emergency response procedures.

Aim 5. To develop and implement policies, procedures and training programs for the safe and secure conduct of preclinical studies to be undertaken within biocontainment at biosafety laboratory levels 2, 3 and 4 (BSL-2, 3, 4) in compliance with the U.S. Food and Drug Administration (FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

As mentioned in previous years, a growing number of projects in the biocontainment laboratories at the GNL are for the purpose of developing diagnostic tests, drugs and vaccines that will eventually go into FDA human trials.

The University of Texas Medical Branch Office of Regulated Nonclinical Studies continues to validate SOPs, procedures, and equipment to comply with 21 CFR Part 58, commonly referred to as Good Laboratory Practices. Training for members of this team is continuing, with mentoring in progress for one BSL4 researcher and lower level biosafety training being provided to a new equipment repair technician.

Quality Assurance and documentation practices that meet GLP regulations are a major focus at the Galveston National Laboratory, and Melissa Eitzen, Director of Regulatory Services for UTMB has been involved in a national group to develop training and "recommendations for scientists" on good documentation practices that will aide in reproducibility of experiments.

The FDA/UTMB Course on Quality Assurance, which has been highlighted in previous annual reports, was presented in Bethesda, Maryland in late April 2016. The focus is to share information on the necessary requirements for validating SOPs, procedures, and equipment to comply with 21 CFR Part 58, commonly referred to as Good Laboratory Practices.

CONCLUSION

Prior Year Results and Progress toward the Specific Aims

Since the beginning of this program, quarterly reports covering each of the five Aims listed above have been reported, and each year a summation of the information is provided in an annual report.

What follows are the annual reports dating back to the start of the program. While these reports do not document every training activity that has been undertaken within the National Biocontainment Training Center, they offer a well-rounded look at the breadth of reach that has been made since the start of this program.

Taken together, the information on these pages provides a representative look at the consistent efforts of a team of dedicated and highly talented professionals. It is important to note that, without exception, the relationships that have been created through these training efforts do not end when the students leave Galveston or when the trainers return home. These relationships continue in a consulting capacity. The benefit of the training has multiplied, as many of the students highlighted in these pages have returned to their home countries or institutions and shared what they have learned. Many have formalized their training through SOPs or new training programs. The training provided by the trainers of the National Biocontainment Training Center has undoubtedly made biocontainment operations around the world safer.

INTRODUCTION

At the time this report is being written, concerns over laboratory safety at the growing number of biocontainment laboratories in the U.S. and around the world are being proclaimed by elected officials, regulatory agencies, and high profile media. Investigations and hearings are being held to discuss laboratory mistakes, the potential for dangerous exposures, and concerns over transfers of biological agents between laboratories.

At the same time, the need for infectious disease research in high containment laboratories is greater than ever before as scientists push to understand the pathology and develop diagnostics, vaccines and therapeutics for deadly diseases like Ebola. Human mobility means that epidemics that occur in other parts of the world can quickly become problems elsewhere. Ensuring adequate training for the scientists who work in laboratories where dangerous pathogens are studied is the goal of the National Biocontainment Training Center.

Through the aims identified in this project, the NBTC shares [illegible] operation of the Galveston National Laboratory (GNL) with others involved in laboratory research. Training the scientists who work in the GNL, and more than five years of operation, have provided unique and valuable expertise that is taught through formal, customized didactic and hands-on training with laboratory personnel, scientists and operations personnel from across the U.S. and around the world.

This annual report describes the training that has been provided between 15 July of 2014 and July 30 of 2015. Training supported by this program since January 2015 has included both domestic and international training, picking up where the companion award (W81XWH-09-2-0053), which expired at the end of 2014, left off. The work described herein supports a coordinated effort to provide critical hands-on training and mentored experience to both national and international scientists who work with dangerous pathogens in biocontainment facilities.

Staffing report:

The National Biocontainment Training Center at UTMB benefits from an experienced team of Environmental Health and Safety Professionals, scientists, engineers and technicians to provide unique biosafety training to students, faculty and other professionals who work in biocontainment laboratories. Trainers deliver customized one-on-one training after providing individualized assessments of each student. Currently there are 16 individuals who have received all or part of their salaries from this grant and who participate in the biosafety training for domestic and international scientists and personnel. They include:

James W. Le Duc is the principal investigator for the training center and is responsible for oversight of all program initiatives, institutional collaborations, fiscal management and project reporting.

Dennis Bente provides mentored training to international scientists, including Dr. Han Xia, who are working within the biocontainment laboratories as part of collaborative projects and fellowships. His work focuses on arboviruses, the unique insectaries at the GNL, and filoviruses such as Crimean-Congo Hemorrhagic Fever.

Sophie Brocard provides didactic and mock-laboratory training and is a principal trainer involved in international training in support of the NBTC and other collaborative efforts.

Christopher Gibbs assists in the training of operations personnel, including engineers from domestic and international facilities who benefit from hands-on experience ensuring the safe use, maintenance, and certification of biological safety cabinets.

Miguel Grimaldo assists biocontainment facilities around the world with operational expertise and represents the GNL on the Operations Committee of NIAID's National and Regional Biocontainment Laboratory Network. He is a regular lecturer on the topic of biocontainment engineering and operations.

Jason Hardcastle provides training for the BSL2 Training Course, PAPR Training Course, and the Class III BSC Training Course. He also assists with the ABSL2 Training Course, BSL3 Training Course, and ABSL3 Training Courses.

Vickie Jones is responsible for providing biological and chemical safety training to individuals from academia and industry, including site-specific training.

To**m Ksiazek** has more than 30 years of experience in biocontainment research and is one of the world's foremost experts on filoviruses. He is the Director of Biocontainment for the GNL and provides mentored training to all BSL4 trainees.

Sheri Leavitt provides ABSL training to graduate students, faculty and staff who will work in the ABSL laboratories. She is involved in training of new Animal Resource Center staff as well as visiting scientists from around the world.

Mary Milazzo has 18 years of experience in biocontainment research and is the Assistant Director for the GNL's BSL4 laboratory. She supports all aspects of high containment training, from SOP development to *in vivo* and *in vitro* training of scientists and other support staff.

Je T'aime Newton provides facility training for the BSL-4 laboratory and Emerging Infectious Disease(EID) training for Healthcare.

Belinda Rivera is the *in-vivo* training consultant providing oversight and training for ABSL2, ABSL3, ABSL4, and NHP courses for both US and international trainees. As needed, she assists with BSL2 and BSL3 *in-vitro* training courses. She is frequently a presenter at ABSA and AALS meetings.

Nate Schueller provides training for the BSL2 Training Course, ABSL2 Training Course, and the ABSL3 Training Course.

Sharon Walters handles scheduling and administrative duties for all training that is provided through the NBTC.

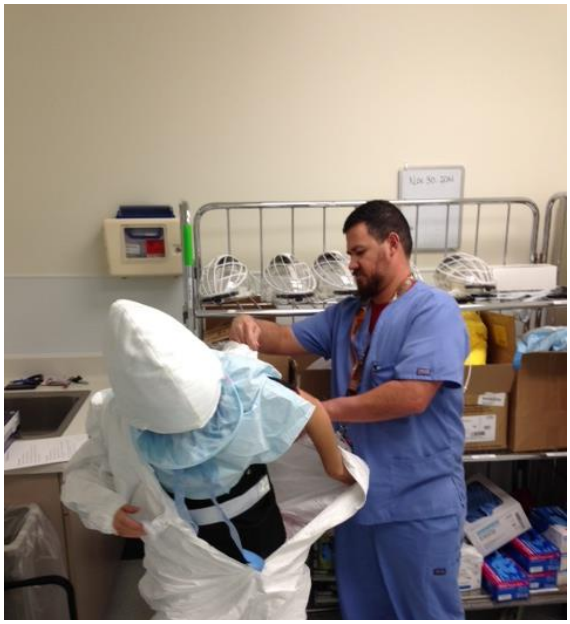
Han Xia is a post-doctoral fellow from China who is in training with Dr. Dennis Bente under NBTC Aim 3.

Dee Zimmerman monitors developments in biosafety and training and ensures that all training courses include the most up to date biosafety protocols and procedures.

Background

UTMB's National Biocontainment Training Center offers a portfolio of courses and individualized mentorship training experiences that evolve based on expanding information, the needs of the students, and as new equipment, procedures and regulations are put into place. All students are assessed for existing knowledge and skill prior to the beginning of their training. With this assessment, each student can be trained based on his or her individual needs. This report highlights the training that has been provided to both national and international students throughout this year, including representatives from within the NBL-RBL Network, UTMB students, and representatives from other biocontainment laboratories and regulatory organizations.

The progress detailed here is part of a continuous training process that provides unique training for scientists and laboratory personnel. The overall goal of the NBTC is to enhance global biosecurity and biosafety by ensuring that those who work with dangerous pathogens are well-educated and prepared to work safely in biocontainment facilities.



Initial training of students occurs in the specially designed mock training lab at the National Biocontainment Training Center at the University of Texas Medical Branch in Galveston. Mentored training may be done at UTMB or at a student's home institution.

Aim 1. To provide standards-based biological containment laboratory safety knowledge to international partners.

Ongoing collaborations with institutions around the world are common occurrences for the trainers at the National Biocontainment Training Center at the University of Texas Medical Branch. Training is focused on providing support to personnel who work in facilities that are involved in the study of infectious diseases and research. The unique nature of the NBTC attracts scientists, engineers, and laboratory personnel from institutions and organizations worldwide. In addition to international students, through this Aim, trainers from the NBTC are also working with partner institutions in the United States. Progress on this Aim is reported below:

Center for Technological Development in Health, Brazil -- Engineering Director Miguel Grimaldo and his team continue to communicate and consult with the team of engineers and scientists who are responsible for the BSL3 laboratories that are being designed, constructed, and validated at the Center for Technological Development in Health (CTDS) at Fiocruz, Brazil. Individuals from Brazil completed a week-long training program in Galveston in July 2014, and ongoing consultations to assist with their efforts have continued on a regular basis. This organization is working on translational projects that bring scientific research together with manufacturing and production partners. Ongoing consultations have focused on efforts to install and validate specialized equipment, develop protocols and SOPs for safe laboratory and facility operation, and to expand operational knowledge among the team of technical and engineering personnel at the Center.

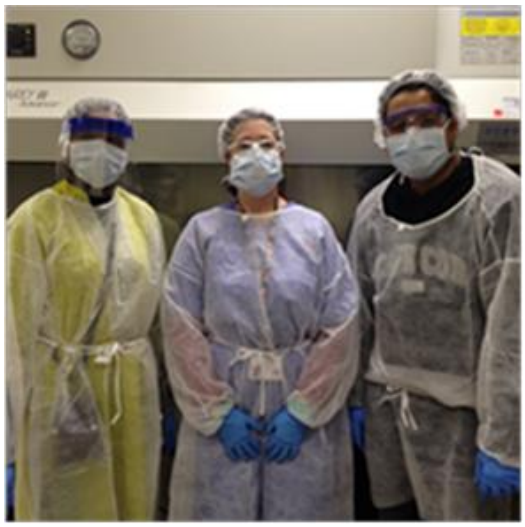
Victorian Infectious Disease Reference Laboratory, Melbourne, Australia – Two staff members from the Victorian Infectious Diseases Reference Laboratory (a division of the Doherty Institute at the University of Melbourne), attended training at the National Biocontainment Training Center in Galveston in preparation for working in BSL4 laboratories at the facility. This laboratory provides services to the Department of Health Victoria, Victorian hospitals and clinics, the Commonwealth Department of Health, and the World Health Organization. Additional training on-site in Melbourne, specific to the Personal Protective Equipment and laboratory set-up, is scheduled to take place prior to the opening and commissioning of the new BSL-4 laboratories there.

One Health Summer School – Sokoine University, Morogoro, Tanzania -- Dr. Anne-Sophie Brocard was invited to participate in the Southern African Centre for Infectious Disease Surveillance (SACIDS) 3rd One Health Summer School week in August 2014, focusing on biosafety for high containment laboratory personnel. The course took place at the Sokoine University in Morogoro, Tanzania and involved 25 students representing ten African countries. Those countries included the Democratic Republic of Congo, Kenya, Tanzania, Ethiopia, Uganda, Malawi, South Africa, Zambia, Mozambique, and Mali. Instructors assisting Dr. Brocard with the training came from the United Kingdom, South Africa and Tanzania. This opportunity to train those who will train others provided significant leverage in biosafety training that should have a huge impact on laboratories throughout Africa as those who participated go back to their facilities and train others.

BELOW: Dr. Anne-Sophie Brocard, Director of the National Biocontainment Training Center, is seated front left with representatives of the faculty and the students who were trained at the 3rd SACIDS One Health Summer School on Biosafety in Morogoro, Tanzania August 25th – 30th, 2014.

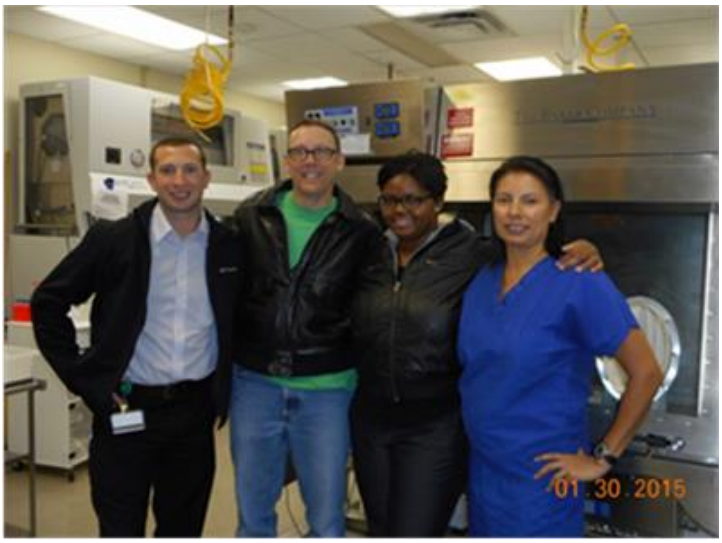
American Biological Safety Association (ABSA) Biosafety Conference – Trainers from the NBTC taught courses at the annual Biosafety Conference, sponsored by ABSA in October 2014. The event was held in San Diego, California, and consisted of three days of education and several pre-conference seminars. High containment and select agent issues were the subject of the international session, which was held on October 5, 2014. In addition, three sessions were led by NBTC personnel: Dr. Anne-Sophie Brocard on "Advanced Risk Assessment," Ms. Belinda Rivera on "Advanced Principles and Practices of Working in an ABSL3 Laboratory," and Mr. Miguel Grimaldo on "Lessons Learned in the Operation of BSL3/BSL4 Laboratory Facilities." Information provided in these sessions assists both domestic and international high containment laboratory personnel in advancing their education. The contents of the sessions also become ABSA resources for sharing with individuals both in the U.S. and abroad.

International Trainees from Pakistan – The NBTC welcomed two students from Aga Khan University who traveled to Galveston in January 2015 to receive nearly three weeks of personalized training at UTMB's National Biocontainment Training Center. The students – a senior technologist and an assistant laboratory manager -- participated in BSL2 and BSL3 training (both theory classes and hands-on training in the mock laboratory), as well as theoretical and practicum training for working with animals at Biosafety Level 2 (ABSL2). They also received PAPR training. The students worked with UTMB trainers Jason Hardcastle, Vickie Jones, Sheri Leavitt, and Belinda Rivera.



BSL and ABSL Safety Training *-- A senior technologist and an assistant manager from Aga Khan University in Karachi, Pakistan, attended training at UTMB during January 2015. The students are shown here with trainer Sheri Leavitt.*

Gulf Coast Consortium Postdoctoral Veterinary Training Program - A clinical veterinarian from the Center for Comparative Medicine at Baylor College of Medicine in Houston and a veterinarian from the University of Texas Health Science Center in Houston who are participating in the Gulf Coast Consortium Postdoctoral Veterinary Training Program focused on Laboratory Animal Medicine and Science, attended PAPR training led by Jason Hardcastle and ABSL3 training led by Belinda Rivera and Nate Schueller. This training, which took place in January 2015, was well received and is anticipated to produce more students from the same program.



Baylor College of Medicine – In early 2015, collaboration continued with the Baylor College of Medicine in Houston, with students from that university attending training at the NBTC. In February, two postdoctoral researchers from Baylor's Department of Pediatrics attended BSL2 training led by NBTC's Jason Hardcastle. Later in the same month, an Assistant Professor and a Research Assistant from the National School of Tropical Medicine at Baylor and two clinical veterinarians from the Center for Comparative Medicine at Baylor attended PAPR training led by Jason Hardcastle and ABSL3 training led by Nate Schueller and Belinda Rivera.

Weill Cornell Medical College, Qatar – From March 3 – March 5, 2015, a Director from the Weill Cornell Medical College in Qatar attended BSL2 training at UTMB. This alliance is anticipated to grow, as the university is focused on delivering a world-class medical education, strongly enhanced by hands-on research experience in their laboratories. They are focused on accessing the best biosafety training available and have turned to the NBTC to assist their faculty and students with that endeavor.

Standards-based biological safety training involves hands-on practice, as shown by this student who traveled to Galveston from Qatar and the Weill Cornell Medical College.

University of Texas El Paso – In March 2015, UTMB welcomed the Director of Veterinary Services and a Research Assistant from the University of Texas at El Paso (UTEP) for BSL3 training led by Jason Hardcastle. UTEP, which is located on the border between Texas and Mexico, is a center of excellence for research on many of the emerging diseases that are impacting the animal and human populations in Mexico. The UTEP staff members returned to Galveston later in the month to complete PAPR training with Mr. Hardcastle and ABSL3 training with Belinda Rivera and Nate Schueller. They were joined by a veterinarian from Baylor College of Medicine who was participating in the Gulf Coast Consortium Postdoctoral Training Program in Laboratory Animal Medicine and Science.

UTMB Trainers Nate Schueller (left) and Belinda Rivera (right) with trainees from University of Texas El Paso and Baylor College of Medicine.

University of Wisconsin – Madison - An Associate Professor and PI from the Pediatrics Department at the University of Wisconsin – Madison in Madison, Wisconsin, attended three days of BSL3 training to prepare her for work at BSL3. Her training was led by NBTC trainer Vickie Jones. The training was customized for the researcher and designed to prepare her to safely perform research that will contribute to the knowledge of pediatric illnesses and that will benefit pediatric patients around the world. It focused on appropriate use of personal protective equipment and biosafety cabinets, as well as safe practices and procedures when working with BSL3 agents. The goal of the training was to provide her with the knowledge to share safe practices with her staff.

NIAID National Biocontainment/Regional Biocontainment Network Partners – Periodic training has been ongoing for a biosafety professional and the attending veterinarian from the Boston University National Emerging Infectious Disease Laboratories. The focus of this training has been on ensuring readiness for BSL4 safety, with training being provided by Corrie Ntiforo and Jet Newton, with support from the Galveston National Laboratory's attending veterinarian Dr. Curtis Klages. Both trainees completed ABSL4 training with Belinda Rivera and are in the process of completing 100 hour mentorships in the BSL4 facilities with the UTMB EHS and ARC staffs.

In April 2015, following the annual NBL/RBL Network meeting in Galveston, the Biosafety Officer from the Regional Biocontainment Laboratory at Colorado State University in Fort Collins, Colorado, attended ABSL3 training led by Belinda Rivera. The focus for her training was to familiarize her with the functions that laboratory personnel are performing in the labs with animals to help with her understanding of safety concerns and biocontainment procedures that are of critical importance. The training was designed to assist her in working with the ARC staff at Colorado State to ensure appropriate training and safety for all lab personnel.

From July 27 – July 31, 2015, the Senior Research Associate and a Research Analyst from Duke University's Regional Biocontainment Laboratory participated in ABSL3 training with Ms. Rivera. Their training was focused on preparing them to work with ferrets in BSL2 and BSL3 labs for influenza strain research that is about to commence at Duke. The trainees received comprehensive training that covered daily husbandry procedures and safe handling of ferrets, as well as technical training and hands-on practice with ferrets that ranged from tissue sampling and bleeding to necropsies.

Dr. Charles McGee, (left) Senior Research Associate from Duke University's RBL, and Christopher Sample, Research Analyst at Duke are shown with Belinda Rivera following their five day intensive ABSL training at the NBTC.

United Arab Emirates (UAE) Second Biosafety Conference – From April 27 to April 29, 2015, Dr. Anne-Sophie Brocard was in Abu Dhabi as an instructor for that nation's major biosafety conference, which was attended by biosafety professionals from throughout the UAE. Dr. Brocard led a preconference session on laboratory safety and Personal Protective Equipment, as well as a one-day worship for 40 researchers and laboratory directors. The conference was sponsored by the Ministry of Environment & Water in the UAE, as well as the Global Virus Network. *(Photo above.)*

Miscellaneous Training of Domestic Academic and Industry Professionals - Demand for training of domestic biocontainment laboratory professionals remains high, both at academic institutions throughout the United States and at industry laboratories. During the final quarter of this reporting period, several additional domestic training efforts were completed. They include:

May 5-May 7: Two PhD students from the University of Houston, Houston, Texas, attended BSL2 training led by Jason Hardcastle, with a focus on basic biosafety principles and the use of biosafety cabinets and PPE.

May 11- May 15: Vickie Jones traveled to Buffalo, New York, to provide BSL3 training to industry laboratory personnel, including one intern and three scientists from Calspan-University of Buffalo Research Center (CUBRC). The training was customized to ensure safe utilization of the equipment in their laboratories. This lab specializes in Chemical, Biological & Medical Sciences.

May 11- May 15: Belinda Rivera traveled to Indiana University in Bloomington, Indiana, where four laboratory animal resource personnel completed the ABSL3 course (theory and practicum) and twenty-four trainees from various departments completed the ABSL3 Theory Course.

June 30-July 2: An Analytical Development Scientist from Biotest Pharamceuticals Corporation (BPC), Boca Raton, Florida, attended BSL2 training at the NBTC, led by Jason Hardcastle.

Aim 2: To provide the information and education necessary for a critical global discussion on the biosecurity, biosurety and related policy issues involved in the operation and maintenance of biocontainment facilities.

Students, staff, and faculty, as well as those working in the biocontainment field around the world share an interest in growing the knowledge base and the understanding of existing and developing policies in biosecurity, biosurety and policy issues as they relate to the operation and maintenance of biocontainment facilities. Representatives of UTMB and the Galveston National Laboratory continue to participate in national and international committees, providing leadership and information that contributes to the growing knowledge in the field.

External Advisory Committee, CDC - Dee Zimmerman, Biosafety Officer and Director of the Environmental Health and Biosafety Regulations and Requirements Core at the University of Texas Medical Branch, was selected to participate in a special external advisory committee charged with reviewing issues that occurred at the CDC laboratories in June 2014, with the goal of creating corrective protocols, safeguards, and training initiatives that can be implemented at biocontainment laboratories around the world. The group met periodically throughout 2014 and 2015, and recommendations from the group will be implemented in laboratories around the world.

World Health Organization, Emergency Committee on Ebola – Dr. James Le Duc participated as a member of the WHO's international committee that not only monitored the growing threat of Ebola in West Africa but that provided recommendations to government leaders in West Africa in hopes of slowing the spread of the current epidemic. Recommendations from this committee covered policy as well as safety and security suggestions and procedures. Dr. Le Duc also shared his insights and recommendations with U.S. government officials, elected officials on the state and federal level, and the general public through media interviews, guest editorials and presentations. International coverage of these activities was widespread.

West African Ebola Outbreak Outreach – Dr. Thomas Ksiazek spent six weeks in Sierra Leone in August and September 2014 leading a contact tracing team for the U.S. Centers for Disease Control and Prevention. Prior to, during his deployment, and since his return from Sierra Leone, his advice and counsel have been sought by national and international media and professional groups to help domestic and international health care professionals and policy makers increase their understanding of both the clinical and biocontainment requirements for dealing with Ebola. In addition, Dr. Ksiazek presented a lecture about the situation in Sierra Leone and the CDC's efforts to curtail the epidemic that was broadcast live on the internet as well as videotaped and placed on YouTube. Information about the video was shared with colleagues at biocontainment labs, regulatory agencies and response organizations. This outreach has continued throughout the year.

Topics in Biosecurity Seminar Series – In September 2014, Dr. Kavita Berger, Associate Director of the Center for Science, Technology and Security Policy for the American Association for the Advancement of Science in Washington, D.C., presented a lecture as part of this ongoing biosecurity seminar series, adding to the knowledge of scientists from around the world about how national and international science policy is created. She specifically focused on select agent rules, scientific funding, insider threats, and future policies under development, encouraging scientists to provide input that helps make science policies more effective a realistic.

Dr. James Le Duc presents a Certificate of Appreciation to Dr. Kavita Berger, of Washington, D.C. -based American Association for the Advancement of Science, who delivered a lecture entitled "Leveraging Science for Security: From Research to Diplomacy" to more than 100 students, faculty, and staff representing more than a dozen countries. Dr. Tara O'Toole, shown with Dr. Le Duc in the photo to the left, discussed major biosecurity issues that will face our nation and the world in coming years.

The December 2014 Topics in Biosecurity seminar featured Dr. Tara O'Toole (photo at right), a professional who is a major part of the inner workings in Washington. Dr. O'Toole served as the Under Secretary for Science & Technology in the Department of Homeland Security under President Barack Obama from 2009 - 2013. She currently works with a major venture financing firm that links high technology companies to federal security agencies to provide new technologies that meet expanding security needs. Dr. O'Toole's presentation offered an interesting look at how biology and science will help to solve many of the biosecurity and healthcare-related problems that will face our nation in the coming years. In a private lunch with graduate students, she also provided insight into alternative careers for scientists.

Texas Task Force on Infectious Disease Preparedness and Response – Dr. Le Duc and Dr. Ksiazek were appointed by Texas Governor Rick Perry to a special task force charged with creating policies and recommendations for enhancing Texas' capabilities for preparing for and responding to pandemic disease, such as Ebola. The committee is charged with creating a strategic emergency response plan to deal with the biosecurity, public health, and medical issues involved in preparing for, responding to, and recovering from a public health threat. While the work of this group is state-specific, the policies and actions they recommended will have a wide-spread, national and international impact on policy development in the areas of infectious disease and public health protection and response.

VIP Visit to the Galveston National Laboratory – Texas Governor Rick Perry

*Texas Governor Rick Perry, far right, converses with BSL4 Lab Manager Terry Juelich (in bio**c**ontainment suit), Dr. Brett Giroir of Texas A&M University, and Dr. Curtis Klages of UTMB about the in-depth training required to work with dangerous pathogens. Governor Perry visited the Galveston National Laboratory in October 2014 to tour the facility and to discuss the Texas Task Force on Infectious Disease Preparedness and Response, which provides policy*

International Federation of Biosafety Associations -- Mr. Miguel Grimaldo, facilities engineer for the Galveston National Laboratory, traveled to Barcelona, Spain in late October 2014 at the invitation of the International Federation of Biosafety Associations. There he visited the Ciesa Laboratory at the Universitat Autonoma de Barcelona (UAB) to review operational procedures and provide suggestions for improvements. While in Spain, he also made a presentation to the growing association membership on the development of autoclave cycles for decontamination of laboratory waste and animal carcasses. The continued interest by members of the International Federation of Biosafety Associations is anticipated to lead to future training on site in Galveston for representatives from several member laboratories.

University of Melbourne – Collaboration and consultations continue with the University of Melbourne as the BSL4 laboratory being constructed there nears completion. Engineers and facility maintenance personnel from the University of Texas Medical Branch continue to consult with and advise their counterparts in Australia on best practices for the operation and maintenance of the high containment laboratory facilities where specimens from hemorrhagic fever within Australia will be brought for analysis and study. Additional collaborations and support are anticipated throughout 2015.

Global Outbreak Alert and Response Network (GOARN) – UTMB continues to be an active participant in GOARN, currently focused on the Ebola crisis in West Africa. Representatives of the Galveston National Laboratory and the NBTC have provided leadership and counsel focused on ensuring the safety of laboratory workers, healthcare workers, military personnel, and volunteers who are working with patients and in research laboratories where laboratory samples are handled and analyzed.

USDA Training Course – Baltimore, MD – Mr. Miguel Grimaldo was an instructor at the 3rd USDA Agricultural Research Service International Biosafety and Biocontainment Symposium held in Baltimore, Maryland, in February 2015. He was one of five instructors who taught curricula during two pre-conference courses: Facility Operational Biosafety and Research and Diagnostic Facility Biosecurity: Operational Challenges and Solutions. Exposure at events such as this often lead to future collaborations and queries regarding customized training or participation in NBTC training programs. In this case, as a result of his teaching during this symposium, UTMB received an inquiry from the FDA Center for Biologics Evaluation & Research asking for personalized assistance in establishing protocols for shut-downs of animal facilities for HVAC inspections. Mr. Grimaldo is working with Dr. Marisa Hickey of the FDA in response to this request.

Victorian Infectious Disease Reference Laboratory – Melbourne, Australia – The Victorian Infectious Disease Reference Laboratory is another example of an institute with an ongoing collaboration with the University of Texas Medical Branch and the National Biocontainment Training Center. From March 30 – April 2, 2015, NBTC trainers and EHS consultants Corrie Ntiforo and Jet Newton traveled to Australia to provide a biosafety peer review and consultation on this newly constructed BSL4 facility. While there, they provided staff members with site specific BSL4 training.

Jet Newton (second from left) and Corrie Ntiforo (second from right) have developed an ongoing relationship with staff in Melbourne, Australia, who appreciate their expertise in BSL4 laboratory biosafety and operations.

National and International Policy Discussions – In recent months, with several high profile issues involving select agents making the news, professional organizations and committees have convened to develop strategies and plans for ensuring the ongoing safety of personnel, training of laboratory professionals, documentation of procedures and myriad other issues. Dr. Le Duc has been an active participant in many forums, ranging from NIAID's National Biocontainment/Regional Biocontainment Network to the National Academy of Sciences and the National Science Advisory Board for Biosecurity. These meetings will continue in both domestic and international forums, including a meeting in India in August 2015.

Aim 3. To Develop and implement a dedicated program to facilitate the establishment, maintenance and administrative oversight of operations of biocontainment facilities.

Biocontainment facilities are unique in their mechanical, security and safety infrastructures, and there are very few educational programs available that prepare professionals for their operational requirements. Today, with more international laboratories being constructed, the Galveston National Laboratory has taken on the role of sharing expertise on the unique engineering, maintenance and administrative challenges of running a safe biocontainment operation. The goal: to help ensure that all labs that deal with infectious pathogens operate safely.

While every facility is unique in the research being conducted and the pathogens being handled, there are general principles that must be followed. As a national resource with a large variety of research projects underway, the GNL, through the National Biocontainment Training Center, is in a unique position to share its expertise and lessons learned. Whether providing tours, one-on-one consultations, or formal training programs, the staff at the GNL is constantly sharing relevant, hands-on experience with the next generation of biocontainment industry leaders. An expanding list of the essential tools, skills and procedures critical to the safe and secure operations of a biocontainment laboratory are being compiled, documented, and shared to ensure that the best practices for fiscal stability, security, utility management, and equipment needs are available to biocontainment laboratories around the world.

Standards Development – Miguel Grimaldo participated on the American Biological Safety Association's Committee for the development of the 2014 ANSI Z9.14 Standard for the Performance verification of ventilation systems for BSL3 and ABSL3 Laboratories.

NBTC Fellowship - Dr. Han Xia – Dr. Xia is a graduate of the Chinese Academy of Sciences and came to UTMB from the Wuhan Institute of Virology. Dr. Xia's focus is on Crimean-Congo hemorrhagic fever, working under the mentorship of Dr. Dennis Bente. As she nears the end of her Fellowship, Dr. Xia continues to work with Dr. Bente in the BSL4 laboratory on the viral replication and pathogenicity *in vitro* and *in vivo* of CCHFV. She continues to receive ongoing training in high level biocontainment, as well as individualized training on the management of a high containment laboratory and oversight responsibilities and training requirements for personnel. She plans to use her operational knowledge upon her return to China. In October 2014, Dr. Bente and Dr. Xia traveled to the Wuhan Institute of Virology in China to share information on the work taking place in Galveston on Ebola and other filoviruses and to provide an update on Dr. Xia's work on Crimean-Congo hemorrhagic fever.

Dr. Han Xia, a second year NBTC Fellow (shown in both pictures to the right) works with her mentor Dr. Dennis Bente on documentation for equipment and other operational issues encountered during research being done in the BSL-4 lab at UTMB. Dr. Xia has been involved in groundbreaking work on Crimean-Congo Hemorrhagic Fever.

Mr. Miguel Grimaldo , an expert on biocontainment engineering, is shown here at the podium during his presentation to the Mexican Biological Safety Association in June 2015.

Mexican Biological Safety Association (AMEXBIO), Mexico City – In June 2015, Mr. Grimaldo participated at the 7th International Symposium of Biosafety and Biosecurity where he taught an 8-hour class at the Pre-Symposium activities on "Critical Elements in the Operation on a BSL3 Laboratory." During the Symposium, Mr. Grimaldo provided a talk about the new ANSI Z9.14 Standard for Testing and Performance Verification Methodologies for Ventilation Systems for BSL3 and ABSL3 Laboratories.

Gorgas Memorial Research Institute, Panama – Mr. Grimaldo traveled in May 2015, and then again in July 2015, to participate in meetings with members of the Institute to discuss and advise about future infrastructure needs. The Gorgas Institute has a longstanding scientific collaboration with UTMB, and deteriorating infrastructure at the Institute in Panama has hampered administrative and research operations for the facility. Representatives from Gorgas will be working to implement recommendations provided by Mr. Grimaldo to ensure ongoing safety and security at the facility.

The Instituto Nacional de Enfermedades Virales Humanas, Argentina – The NBTC has an ongoing relationship with this Institute, which first sent personnel for facilities engineering and operational training to Galveston in late 2013. In 2014 and 2015, they continue to rely upon the expertise of the GNL's engineering staff for instruction and advice. Miguel Grimaldo consulted with research and engineering personnel from the Institute to assist with autoclave cycle validation studies based on standards developed and proven at the GNL. This support assists the Institute with its work on diagnostics, treatments, investigations and preventative measures for combatting infectious diseases, particularly chikungunya, denge and hemorrhagic fevers. In July 2015, the collaboration continued with discussions on validation of autoclave decontamination cycles.

International training efforts result in ongoing collaborations with colleagues from around the world. Miguel Grimaldo (far right) consults regularly with his Argentinian colleagues. This photo was taken at the Instituto Nacional de Enfermedades Virales Humanas. Professionals there continue to seek direction from GNL staff.

Universidad Autonoma De Nuevo Leon, Monterrey, Mexico – Mr. Grimaldo visited the Department of Virology and Immunology in Monterrey, Mexico, as a follow-up to the training classes that were previously conducted for Nuevo Leon personnel at UTMB. His goal for the visit was to review the completed remodeling of a BSL3 laboratory, as well as to review and consult on the BSL3 and BSL4 cabinet labs that are currently under construction. While there, Mr. Grimaldo made additional recommendations for the laboratory build-outs. It is anticipated that future collaborations will include the sharing of SOPs and additional safety training for new personnel, which will be covered under Aim 1 of this award.

Institute of Medical Biology, Chinese Academy of Medical Sciences, Kunming, China – Dr. Curtis Klages, a veterinarian at the Galveston National Laboratory, and Mr. Miguel Grimaldo were invited to review the animal facilities at the Chinese Academy of Medical Biology and present information on BSL4 technical specifications and performance requirements. In addition, they were asked to provide training on Laboratory Management, Facility Operations and Facility Personnel Training. The pair traveled to China Sept. 2- 8, 2014. Collaborations continued throughout the year, with a focus on the specialized maintenance needs of high containment laboratories. Staff members from Kunming also traveled to Galveston in January 2015 for specialized engineering training.

Personnel from the Chinese Academy of Medical Sciences are shown here with Mr. Miguel Grimaldo and Dr. Curtis Klages in Kunming, China in September 2014. The consultations being provided to the Chinese are helping to ensure that solid engineering and stable operational practices are in place for this BSL4 laboratory.

National Institutes of Health Committees – Miguel Grimaldo is participating in a committee focused on updating the NIH's Design Requirements Manual (DRM), which addresses best practices and design standards for high containment laboratory facilities. Both national and international institutions involved in the design and construction of high containment laboratories will utilize this manual as a valuable resource.

Standards Development and Implementation Guidelines – NBTC representatives continue to be called upon by both national and international colleagues for assistance in interpreting the implementation requirements for new standards for maintenance and operation of high containment laboratories. In particular, the 2014 ANSI Z9.14 Standard for Performance verification for ventilation systems for BSL3 and BSL4 laboratories continues to raise questions for maintenance and operations personnel.

National Biocontainment Laboratory/Regional Biocontainment Laboratory Network Meeting - Miguel Grimaldo participated in the steering committee and planning efforts for the two-day NBL/RBL Network Meeting, which was held in Galveston in April. His goal is to continue to provide leadership to regional biocontainment laboratories located at universities around the United States and the world, sharing best practices in operations and maintenance.

Representatives from 13 National and Regional Biocontainment Laboratories, NIAID, the NIH, the FBI, and the CDC converged in Galveston in April 2015 for an annual meeting focused on the safe operation of biocontainment laboratories.

Consulting - Mr. Grimaldo received a request to provide information on the waste decontamination for a children's Ebola isolation unit from Children's Hospital in Houston. He shared has expertise on autoclave operation with staff there.

China Center for Disease Control – Representatives from the Chinese equivalent of the US Centers for Disease Control & Prevention traveled to Galveston to meet with several representatives of the Galveston National Laboratory. Mr. Grimaldo spent several days working with the representatives to provide insight into the safe operation of high containment laboratories.

Aim 4. To develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

New instrumentation continues to make its way into biocontainment laboratories where highly dangerous pathogens are studied. At UTMB, as new instrumentation is utilized in high containment labs, special circumstances are documented with the goal of sharing it with students from the U.S. and international locales. Our team is continually documenting the use of new instruments and special precautions or concerns that come with using them in a high containment laboratory. For example, decontamination of novel instrumentation for service and maintenance remains a major challenge, as many vendors will not work on equipment once it has been in a BSL4 laboratory. Over the last year, the progress documented on the following pages was made on this Aim.

Doherty Institute, University of Melbourne, Australia – Engineering professionals from Sinclair Knight Merz (SKM)/Jacobs Engineering in Melbourne, Australia, spent time at the Galveston National Laboratory in July 2014 learning about the specialized air filter systems that ensure air quality and safety. Since that time, Mr. Grimaldo has provided Colin Sakinofsky and Jim Hargreaves of SKM, who are designing systems for the new biocontainment laboratories in Melbourne, with additional documentation and site information. In turn, Mr. Sakinofsky and Mr. Hargreaves have presented the information to other SKM employees, as well as to personnel from the laboratory and administrative staffs at the University of Melbourne. In October 2014, Mr. Leo K. Fincher-Johnson, a Construction Manager for Major Projects and Project Delivery with the University of Melbourne, and Mr. Neil Walz, an independent consultant working on the Standard Operating Procedures for the University of Melbourne's BSL4 laboratories, met with Mr. Grimaldo and his team in Galveston to receive assistance and instruction in conducting laboratory audits.

Both BSL3 and BSL4 laboratories are housed in this new multi-story facility located on the University of Melbourne campus. The newest BSL4 lab in the building will be used to diagnose hemorrhagic fever.

Biocontainment Training of IT Support Personnel – During this year, professionals from the NBTC and UTMB developed a training program for Information Technology personnel who work on equipment found in high containment laboratories. Training IT professionals to work on equipment inside the labs will save time and money and should eliminate the necessity of disposing of computer equipment when it is in need of repair. Information on this training program has been added to the operational training guides and is being shared with international personnel in charge of the operation and ongoing maintenance of high containment facilities.

Real-Time PCR Training – The UTMB Assay Development Services Division, in conjunction with the NBTC and the Galveston National Laboratory, sponsored a Real-Time PCR training session hosted by vendor Life Technologies on Oct. 1, 2014. The purpose of the session was to provide an introduction to Real-Time PCR to students, postdocs and staff working in the high containment laboratories. 15 participants, including international trainees, participated in this session, which reviewed applications for working with DNA, RNA and protein analysis. Trainees were introduced to procedures for mutation detection, single nucleotide polymorphisms, and high resolution melt, as well as the analysis of RNAs and gene expression.

Course Updates -- On an ongoing basis, as new instrumentation is adopted for use in biocontainment laboratories, information is documented so that it can be shared with students and trainees from both U.S. and international laboratories. Courses are constantly updated with information about new instrumentation and novel laboratory equipment. Reviews of all course outlines were made during this reporting period.

American Biological Safety Association – Dee Zimmerman taught a course at the ABSA conference in Charleston, South Carolina, on principles and practice of biological safety. The event was held Feb. 23 – 27, 2015, and was attended by 40 students from both the U.S. and other countries around the world.

Real-Time Plethysmography Training – While working on research projects within the BSL2 laboratories at the Galveston National Laboratory, scientists are documenting concepts and real world situations that are shared with students who will have the opportunity to work with this novel laboratory instrumentation. Dr. Johnny Peterson and Dr. William Lawrence support the efforts of the NBTC staff by providing their expertise on working with this novel instrumentation. They are sharing this information with trainees as opportunities arise.

Aim 5. To develop and implement policies, procedures and training programs for the safe and secure conduct of preclinical studies to be undertaken within biocontainment at biosafety laboratory levels 2, 3 and 4 (BSL-2, 3, 4) in compliance with the U.S. Food and Drug Administration (FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

As mentioned in prior reports, a growing number of projects in the biocontainment laboratories at the GNL are for the purpose of developing diagnostic tests, drugs and vaccines for use in the recognition, treatment and prevention of biological terrorism threats and emerging infectious diseases. Major attention continues to be focused on Ebola due to the West African epidemic and concerns throughout the world.

The University of Texas Medical Branch's Office of Regulated Nonclinical Studies continues to validate SOPs, procedures, and equipment to comply with 21 CFR Part 58, commonly referred to as Good Laboratory Practices. As these processes are conducted, information is being captured for inclusion in training programs that will be used with students to help ensure their understanding of the requirements for compliance with the FDA's Good Laboratory Practice (GLP) regulations.

Clinical & Translational Research Forum – On March 11, 2015, staff from the NBTC attended the 3rd Annual Clinical & Translational Research Forum hosted by the Institute for Translational Sciences at UTMB. The forum offered an opportunity for researchers to display the broad spectrum of research being performed at UTMB and to promote the resources available to facilitate their work. Staff from the NBTC set up a booth and provided information to researchers about the training they provide to support biosafety preparedness and to ensure the safe and secure conduct of studies taking place at biosafety laboratory levels 2, 3 and 4 in compliance with FDA GLP regulations.

UTMB/FDA Training – On April 28, 2015, 52 federal regulatory staff members attended the 3rd Annual UTMB/FDA Practical Exercise in a Mock BSL4 Training lab. The objectives of the course were to demonstrate practical differences between BSL2 and BSL4 laboratory environments. Participants took part in exercises involving laboratory procedures and focused on the intricacies of donning/doffing personal protective equipment specific to BSL2 and BSL4. The BSL2 portion was led by Vickie Jones and the BSL4 portion of the practical exercise was led by Corrie Ntiforo and Jet Newton.

CONCLUSIONS

Providing individualized training to both domestic and international biocontainment professionals who work in laboratories or who are responsible for operations and maintenance remains a key to ensuring national security. Our goal is to ensure that scientific pursuits and the development of diagnostics, vaccines and therapies to prevent or cure infectious diseases are conducted in a safe and secure fashion. We continue to work to build this international culture of trust, collaboration, and transparency that enhances biosecurity around the world.

W81XwH-11-2-0148 (NBTC2) Annual Report July 2013 – July 2014

INTRODUCTION

Perhaps at no time in recent history has it been so evident that the study of infectious diseases, naturally-occurring agents and emerging pathogens is needed. Recent events have also underscored the need for rigorous training of professionals who work in modern biocontainment laboratories where this type of research takes place. Scientific investigations, product development, and response to threats of endemic diseases or bioterrorism are critically important on a global scale. To do the work required to increase scientific and medical understanding and to develop the diagnostics, therapeutics, and vaccines necessary to combatting disease and other threats, scientists and technical staff must be specially trained in proper precautions, safe practices, personal protective barriers, standard operating procedures, laboratory design, facility operations and more.

The threat is perhaps greatest within the international laboratory community where these dangerous pathogens may be routinely manipulated and investigated under less than ideal conditions by individuals who may lack adequate training or experience. While historically, this work was concentrated in a small number of research or government facilities where a limited number of highly trained investigators worked within appropriately equipped laboratories, today this type of investigation, research and development has become a global enterprise. Unfortunately, some of the individuals and their parent organizations attempting to conduct this work do not have in place adequate facilities, nor the training and administrative oversight to ensure the safety of the investigations, protection of the personnel, and the safe evaluation of the projects underway.

Through the aims identified below, we are sharing the valuable experiences we have gained at the Galveston National Laboratory (GNL) with others throughout the world who are involved in laboratory research. Our state-of-the-art facilities and the experience and knowledge we have gained from years of biocontainment laboratory operations have led to the development of thorough training programs that have been successfully implemented with our own scientists and personnel. We are pleased to share our expertise with biocontainment laboratory scientists and program directors around the world through the National Biocontainment Training Center's (NBTC) expanded scope of work.

The progress reported here complements activities summarized separately in a companion project (Award Number W81XWH-09-2-0053, also titled National Biocontainment Training Center). Together these awards support a coordinated effort to provide critical training and hands-on experience to U.S. and international scientists working with especially dangerous pathogens that require special biocontainment facilities for their safe and secure handling.

BODY

Research accomplishments associated with each specific aim are summarized on the following pages. This report covers July 2013 – July 2014.

Staffing - *The NBTC draws upon the expertise of a number of professionals who work at the University of Texas Medical Branch. The professionals listed below have been integrally involved in some aspect of fulfilling the NBTC's mission during the last 12 months.*

James W. LeDuc serves as principal investigator for the training center and is responsible for oversight of program initiatives, fiscal management and progress reporting.

Dennis Bente is directly involved in mentoring and supervising the research of international research fellows whose work takes place in the biocontainment laboratories.

Anne-Sophie Brocard is the LBTP director, manages the training facility, develops training programs for the NBTC, and is involved in training on-site at the NBTC, at conferences, and at collaborative partner locations around the world.

Christopher Gibbs assists in the training of building engineering fellows and provides hands-on guidance, especially in the care, maintenance and certification of the biological safety cabinets used in virtually every laboratory that handles pathogens.

Miguel Grimaldo directs the building engineering fellowship and provides lectures and hands-on guidance to fellows within the program. He also represents the program at meetings and events dedicated to biocontainment engineering.

Connie Holubar assists in the preparation of reports, organization and implementation of guest lectures, and general communications of program activities. She also monitors relevant policy issues and communicates those throughout the system.

Aaron Miller assists with the efforts to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

John Morrill provides assistance in the training of students in the care, use and handling of laboratory animals within BSL-3 and BSL-4 biocontainment laboratories.

Ronald Veselenak also works to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Sheri Leavitt assists senior trainers with the training of students specializing in in-vivo techniques at ASBL-2 and assists the in-vitro trainers.

Mary Milazzo assists in the mentored training of students and staff in the BSL-4 biocontainment laboratory. She also assists in mentored training and the administration of tracking the status of approved users in the BSL-4 containment laboratories.

Belinda Rivera is a senior trainer who provides biosafety training for specializing in in-vivo techniques at ABSL-2 to ABSL-4, and she is involved in training on site, at conferences, and at collaborative partner locations around the world.

Nathaniel Schueller assists senior trainers with the training of students specializing in in-vivo techniques at ABSL-2 and assists with other training as needed.

Dee Zimmerman is the Biosafety Officer and Director of the Environmental Health and Biosafety Regulations and Requirements Core at UTMB. She oversees all aspects of safety training and is a member of the newly appointed external laboratory safety group advising the CDC.

Specific Aims

Aim 1. To provide standards-based biological containment laboratory safety knowledge to international partners.

Background

There continues to be a huge need for training in biosafety and biosecurity on an international level. To address this need and to reduce the potential impacts on national security, we continue to successfully expand our efforts to engage international partners in educational programs that are structured around the same principles and practices we use at the National Biocontainment Training Center at the University of Texas Medical Branch in Galveston.

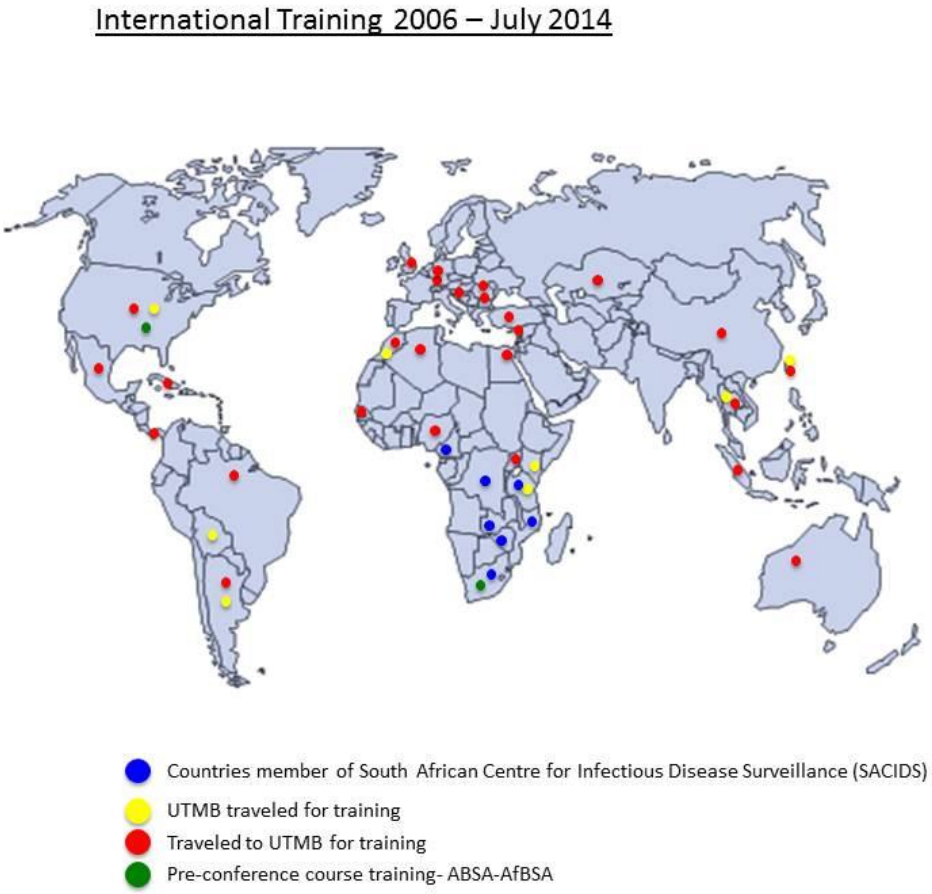
Our focus is on identifying and providing training to personnel from international biocontainment facilities that are involved in the diagnosis and/or research and development of infectious diseases. Over the last year our international training efforts have continued to expand and grow, with many of our efforts extending beyond a specific quarter as collaborations evolve. The training of individuals from around the world is conducted both in Galveston and at international locations where it can be tailored to meet the facility's specific environmental, capacity and staff needs. In addition to providing individual training, we focus on opportunities to "train the trainer," leveraging our efforts as our students return to their countries to provide training within their own facilities and beyond.

We continue to work with a growing network of national and regional organizations that are focused on biosafety, biosecurity and related fields of interest, providing our leadership and expertise, in conjunction with other professional groups, to expand collaborative efforts that enhance training efforts. Through this aim we are providing standards-based biological containment laboratory safety knowledge in a hands-on manner with international scientists and laboratory personnel. Our efforts are focused on enhancing this important aspect of public health, safety, research and development as relates to infectious diseases.

Progress

We are building collaborative working relationships with professional organizations throughout the world. As the map below shows, we continue to expand our biosafety training in response to growing needs and the international recognition of our unique abilities. We not only seek opportunities but also respond to requests for assistance to ensure that biosafety personnel around the world are professionally and thoroughly trained and that those with responsibility for training others have the tools and education they need.

BSL2-BSL3-ABSL3-BSL4 Training
Algeria
Argentina
Australia
Bolivia
Brazil
Bulgaria
Cameroon
China
Cuba
Egypt
Hawaii
Israel
Kazakhstan
Kenya
Mexico
Morocco
Mozambique
Nigeria
Panama
Romania
Senegal
Singapore
Slovenia
Switzerland
Taiwan
Tanzania
Thailand
Turkey
Thailand
Uganda
Ukraine
United Kingdom
USA
Zambia
Zimbabwe



Biocontainment Engineering Working Group, International Federation of Biosafety Associations (IFBA).

In an ongoing effort, Mr. Miguel Grimaldo, a GNL biocontainment engineer with the training center, continued this year to participate in the development of risk-management based guidelines for biocontainment laboratories as a member of the Biocontainment Engineering Working Group of the International Federation of Biosafety Associations (IFBA). These guidelines will eventually be endorsed by international organizations such as World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the Office International des Epizooties (OIE), the World Organization for Animal Health.

Central American Regional Biosafety Group. Mr. Grimaldo participated in a biosafety meeting for the region encompassing Central America, South America, the Caribbean and Panama in August 2013. The purpose was to discuss the creation of a Regional/Sub Regional biosafety association. More than 40 individuals from 13 countries participated in the planning and assessment meeting. Throughout the year, Mr. Grimaldo has continued to participate with this group and has lent his biocontainment engineering expertise to efforts to build a formal association. This participation has also led to training sessions with contacts made, both at the NBTC and abroad.

American Biological Safety Association. The 56th Annual meeting of the American Biological Safety Association (ABSA) conference was held in Kansas City, Missouri, October 17-23, 2013. NBTC trainers facilitated sessions during the event and also presented pre- and post-conference educational sessions that were attended by both domestic and international conference attendees. Presenters included:

- Ms. Belinda Rivera taught an eight-hour class entitled "Advanced Principles and Practices of Working in an ABSL-3." The course provided information to individuals that are currently working in, plan on working in, or who audit ABSL-3 facilities. The course covered the unique hazards of working in an ABSL-3 facility and covered personal protective equipment (PPE), animal handling procedures, husbandry procedures, caging options, waste management, and emergency response procedures. Institutions with ABSL-3 facilities need to involve safety personnel, animal care staff, and researchers to ensure proper work procedures and safety protocols are in place and followed to maintain a safe and productive work environment.

- Ms. Dee Zimmerman taught an eight-hour class on "BSL-3 Operations and Management." The course covered the most important aspects of a BSL-3 facility from two points of view: management of the facility and daily operations. She covered the unique management aspects of BSL-3 operations, such as hiring and training of lab workers, maintenance support, occupational health concerns, waste management, maintenance and monitoring of the physical facility, and emergency management plans. The course covered operations issues, including the selection and use of Personal Protective Equipment, waste handling, facility cleaning, equipment maintenance procedures. It also covered the development of manuals, SOPs, and training.

- Dr. Anne-Sophie Brocard co-taught an eight-hour class on "Advanced Risk Assessment."
  Through a case study approach, attendees learned how to follow a research project as it evolves over time from basic to multifaceted in vitro and in vivo scenarios based on actual research protocol submissions. The course covered risk assessments that build upon each other from the discovery of a novel virus to

determining the efficacy of experimental vaccines in humans. Dr. Brocard covered risk assessments and risk mitigation strategies.

- Mr. Miguel Grimaldo taught an advanced eight-hour class on "Advanced BSL-3 Facility Operations." This course focused on detailed aspects of biocontainment operations of BSL-3, ABSL-3 and enhanced BSL-3 laboratories. It covered risk assessments for biocontainment equipment, facility operations and maintenance SOPs, as well as training requirements for maintenance personnel. The course covered the facility verification process in detail, including recommended test methodologies, solid and liquid waste decontamination equipment and procedures, ventilation control methodologies and equipment configurations, documentation and recordkeeping.

Mr. Miguel Grimaldo's class on Advanced BSL-3 Facility Operations was well attended at the 2013 ABSA Annual Conference in Kansas City.

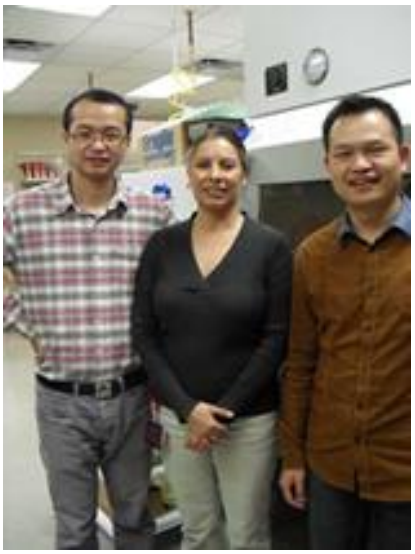
Sokoine University of Agriculture (SUA), Tanzania. NBTC trainer Dr. Anne-Sophie Brocard has continued her involvement with the One Health Summer School at Sokoine University of Agriculture in Morogoro, Tanzania. This program is part of the Southern African Centre for Infectious Disease Surveillance. Over the last 12 months, the NBTC has provided training and education to 24 individuals and has developed and presented material on biosafety and biosecurity as part of a master's degree program for students studying molecular biology. In addition, a training agreement was signed between UTMB and SUA to provide lab safety training to all SUA laboratorians. Dr. Brocard has remained involved in the curriculum development process and will travel to Tanzania in August 2014 to teach coursework for the program focused on biosafety. The enormous concern over infectious diseases in Africa underscores the importance of this program, which is being designed to train a new generation of African researchers to address the heavy burden and threat of emerging infectious diseases in Africa. The aim is to help generate discoveries that can potentially be translated into diagnostics or control methods to improve human and animal health.

ABOVE: Tanzania Training -- Dr. Gerald Misinzo, Senior Lecturer, SUA, and Principal Investigator, Global Emerging Infections Surveillance (GEIS); Professor Mark Rweyemamu BVSc, PhD, FRCVS, Executive Director of the Southern African Centre for Infectious Diseases and Surveillance (SACIDS), SUA; Dr. Brocard; Professor Meck Mattee of Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania; and Dr. Christopher Kasanga, Virologist, SACIDS, SUA. *Pictured bottom right: Martha Betson, an instructor at Sokoine from the Royal Veterinary College of London and Dr. Brocard.*

Institute of Medical Biology in Kunming, China. Dr. Longding Liu, a scientist, and Qing Dai, an engineer (pictured below, right), traveled to the GNL to participate in an intensive two-week NBTC biocontainment engineering fellowship. They worked alongside GNL biocontainment engineer Miguel Grimaldo to review comprehensive aspects of facility operation and management in preparation for the opening of a new biocontainment laboratory under construction at their Institute in Kunming. The training program was customized to the needs of the two individuals and included:

- Laboratory Facilities and Primary Containment Requirements
- Primary Containment Equipment
- Filtration Systems
- Liquid and Solid Waste Decontamination
- Mechanical Systems - Ventilation and Controls
- Laboratory Facility Adjustment and Testing
- Decontamination Methodologies and Procedures
- BSL4 Specialized Equipment & Other Laboratory Equipment
- BSL4 Suits - Setup, Maintenance and Usage
- Annual Maintenance Shutdowns and Record Keeping
- Special Topics on Biocontainment Operation

The collaboration with the Institute of Medical Biology continued later in the year when Dr. Jiandong Shi and Dr. Lei Guo participated in BSL-2 and BSL-3 training at the NBTC in Galveston with trainer Belinda Rivera. The training was provided in preparation for the opening of the new biocontainment laboratory being constructed in Kunming.



Dr. Jiandong Shi and Dr. Lei Guo with BSL-2 trainer Belinda Rivera in Galveston.

Global Outbreak Alert and Response Network. Representatives of the NBTC continue their involvement in this important international network. Dr. Thomas Ksiazek attended the GOARN Steering Committee meeting in Switzerland in December on behalf Dr. Jim LeDuc, and Dr. LeDuc participated in an emergency meeting of the Steering Committee held in early June, focused on the Ebola crisis in Western Africa and worldwide efforts to combat and contain it. As a follow-up to the meeting, Dr. Tom Ksaizek has agreed to lead a team of experts in support of the U.S. Centers for Disease Control and Prevention and will deploy to Sierra Leone for 30 days to provide his expertise in containment of the Ebola epidemic.

Federal University of Vicosa, Brazil. The NBTC has established a new collaboration with the Federal University of Vicosa (UFV) and the Center for Regional Technological Development of Vicosa (Center). Mr. Grimaldo was invited to provide a presentation on the "Requirements for successful construction and operation of BSL-3 and BSL-4 laboratories" at the workshop for Innovation and Technology in Biological Agents and Biosafety, March 27-28, 2014. UFV has been an active collaborator with UTMB in the area of rickettsial diseases research, and Center and UFV are planning a new technological center for Biological Agents and Biosafety at their new Technological Park located in Vicosa, Minas Gerais, and Brazil.

Tradeline, Inc. Scottsdale, Arizona, USA. In April 2014, Mr. Grimaldo was invited to speak at the 2014 International Conference on Biocontainment Facilities. The title of the presentation was "If I only knew then, what I know now: Operating Lessons Learned for Biocontainment facilities". Over 125 participants composed of Facility Directors, Engineers and Architects from Institutions in the United States and around the world participated on this year's conference. Mr. Grimaldo's presentation was voted as the top rated general session presentation.

Center for Technological Development in Health (CDTS) at Fiocruz, Brazil. Dr. Claudio Manuel Rodrigues spent a week in Galveston July 21st through July 25th attending the ABSL-2 training program. During his week he was provided with customized training based on an initial assessment of his knowledge and skills. He also participated in a module on Autoclave Operations and Cycle Validation. Upon completion of his training, he expressed plans to return to Brazil to develop training programs specific to what he had learned to share with his colleagues and the personnel involved in laboratory research at the CDTS.

Dr. Claudio Manuel Rodrigues (center) spent a week at the NBTC working with ABSL-2 trainers. He plans to take what he learned back to the CDTS in Brazil to share with other scientists and laboratory personnel. Shown with Dr. Rodrigues are Miguel Grimaldo and Dr. Jim LeDuc.

Aim 2. To provide the information and education necessary for a critical global discussion on the biosecurity, biosurety and related policy issues involved in the operation and maintenance of biocontainment facilities.

Background

Students, staff, and faculty, as well as those working in the biocontainment field here and abroad have an interest in understanding more about existing and developing policies in biosecurity, biosurety and other issues. The base of knowledge is still developing, providing an opportunity for education and discussion that helps build the foundation for the safe and secure operation and maintenance of biocontainment facilities.

We continue to contribute to the growing foundation of knowledge on this topic through the execution of our "Topics in Biosecurity Symposia Series, " which features distinguished experts from government, academic, and corporate entities. We also continue to engage with national and international partners to share information, stimulate discussion, and develop solutions to emerging and shared concerns. Our participation in the ongoing efforts of the U.S. National Academy of Sciences, the World Health Organization and other organizations continue to focus on topics of international concern, including the creation and safe operation of biocontainment facilities in Europe, Central Asia, Asia, the Americas, Australia and in Africa. Our goal is to engage national and international leaders to develop and implement evidence-based policy discussions and eventual agreements that will enhance the security of biocontainment facilities around the world, including in areas where no biosecurity infrastructure currently exists. This is being accomplished by participation in national, regional and international meetings and conferences and ongoing outreach efforts. Numerous collaborative studies and investigations, personnel exchanges and fellowships, and educational programs are contributing to the advancement of this aim.

Progress

Topics in Biosecurity Symposia Series. Distinguished guest speakers continue to participate in the "Topics in Biosecurity Symposia Series" held at the Galveston National Laboratory. Seminars throughout the year were presented to several hundred participants. Guest speakers who traveled to Galveston to present topics of national and international interest included:

- September 2013: Tom Slezak, a bioinformatics expert with Lawrence Livermore National Laboratory. A trailblazer in the field, Tom pioneered the use of "bioinformatics" in DNA physical mapping. He and his pathogen bioinformatics team built the BASIS System to provide wide-area monitoring for bioterrorism and he was instrumental in the creation of the nation's BioWatch System.

- October 2013: Dr. Roger Breeze, president of Centaur Science Group in Washington, DC and former director of the USDA Agricultural Research Service Plum Island Animal Disease Center. He currently advises the Defense Threat Reduction Agency (DTRA) within the U.S. Department of Defense on ways to reduce the biological weapons threat in the former Soviet Union. Dr. Breeze is also aligned with the Lawrence Livermore National Laboratory.

In his seminar session he presented a compelling topical discussion on looking ahead in a world of biological threats.

- November 2013: Dr. Francisco Pinheiro, an expert on viral diseases with the Program of Communicable Diseases in the Division of Disease Prevention and Control at the Pan American Health Organization, presented "Reflections of a Brazilian Virologist on Arboviruses and Other Viruses in Latin America," which included historical perspectives and insight into laboratory biosafety.

Dr. Pinheiro is pictured alongside students and faculty from Brazil who are in residence at UTMB, as well as the GNL's Dr. Jim LeDuc.

- May 2014: Peter Jahrling, PhD, the Chief Scientist at the National Institutes of Health's NIAID Integrated Research Facility provided a seminar in May. He serves as chief of the Emerging Viral Pathogens Section at NIAID and spoke on "Perspectives on Building and Activating a Unique BSL-4 Laboratory."

- June 2014: Michael T. Osterholm PhD, MPH, director of the Center for Infectious Disease Research and Policy (CIDRAP), director of the NIH-supported Center of Excellence for Influenza Research and Surveillance within CIDRAP, professor in the Division of Environmental Health Sciences, School of Public Health, and an adjunct professor in the Medical School, University of Minnesota gave a lecture on the topic of "Emerging Infectious Diseases Worldwide."

Planning for the Fall 2014 seminars is underway, with confirmed speakers Dr. Kavita Berger, Associate Director of the Center for Science, Technology and Security Policy for the American Association for the Advancement of Science; Dr. Tara O'Toole, former Under Secretary for Science and Technology at the U.S. Department of Homeland Security; and Dr. Robert Miceli of the U.S. Department of Defense Intelligence Agency.

CDC External Laboratory Safety Group -Recent events at laboratories in the U.S. have underscored the need for the development and implementation of national policies on the vital topics of biosecurity, biosurety and related policy issues that form the foundation for the safe and secure operation and maintenance of biocontainment facilities. Personnel from UTMB and the NBTC have been tapped to assist on several levels. Domenica (Dee) Zimmerman, Biosafety Officer, NBTC

Instructor, and the Director of the Environmental Health and Biosafety Regulations and Requirements Core for UTMB has been appointed to serve on an external laboratory safety workgroup of the Advisory Committee to the Director of the CDC to assist in developing corrective actions for the CDC laboratories.

Aim 3. To develop and implement a dedicated program to facilitate the establishment, maintenance and administrative oversight of operations of biocontainment facilities.

Background

Biocontainment facilities are unique in their mechanical, security and safety infrastructures, and there are very few educational programs available that prepare professionals for their operational requirements. Today, with more international laboratories being constructed, the Galveston National Laboratory has taken on the role of sharing expertise on the unique engineering, maintenance and administrative challenges of running a safe biocontainment operation. The goal: to help ensure that all labs that deal with infectious pathogens operate safely. While every facility is unique in the research being conducted and the pathogens being handled, there are general principles that must be followed. As a national resource with a large variety of research projects underway, the GNL is in a unique position to share its expertise and lessons learned. Whether providing tours, one-on-one consultations, or formal training programs, the staff at the GNL is constantly sharing relevant, hands-on experience with the next generation of biocontainment industry leaders. An expanding list of the essential tools, skills and procedures critical to the safe and secure operations of a biocontainment laboratory are being compiled, documented, and shared to ensure that the best practices for fiscal stability, security, utility management, and equipment needs are available to biocontainment laboratories around the world.

Progress

NBTC Fellowship - Dr. Aysen Gargili. Program fellow Dr. Aysen Gargili completed a fellowship with the NBTC in the fall of 2013 and returned to her native Turkey. Since that time, she has continued her collaboration with the GNL and NBTC, with a project focused on Crimean-Congo hemorrhagic fever, which is fast-emerging in Turkey and Central Asia. She also has continued tick collection efforts as part of a CCHFV collaborative project with USAMRIID, and she has been planning design and construction for a new BSL-3 laboratory for Koc University. She also participated in a Global Virus Network fellowship, where she visited Colorado State University, CDC and USDA National Wildlife Center in Fort Collins. At CSU she gave a talk about what she had learned about ticks and tick-borne diseases in her native Turkey, and at the CDC and NWRC, she met with the researchers and had the chance to observe their field study techniques and equipment. In addition, the knowledge she gained while at the University of Texas Medical Branch and Galveston National Laboratory was put to use training a group of 24 biocontainment laboratory workers in Turkey in January 2014. Dr. Gargili is a wonderful example of the success of the train-the-trainer strategy. Her efforts are ensuring well-trained personnel for the BSL-2 and BSL-3 laboratories in the Pendik

Veterinary Control Institute, which is a national research laboratory under the Turkish Ministry of Food, Agriculture and Livestock. In summarizing her experience at the GNL, Dr. Gargili wrote:

> *"Overall, this fellowship provided me with an amazing opportunity to meet with an impressive array of researchers and begin laying the groundwork for collaborations in the near future. It was an invaluable chance to improve my understanding and current knowledge about the tick-borne studies that we're planning as part of our work in Turkey and to exchange practices that I believe host institutions will find most useful."*

Photo of participants in a week long training course in biosafety and biosecurity organized by Dr Aysen Gargili (first row, center) for laboratory staff of the Pendik Veterinary Control Institute, a national research laboratory under the Turkish Ministry of Food, Agriculture and Livestock.

NBTC Fellowship – Dr. Han Xia. Dr. Xia came to Galveston from the Wuhan Institute of Virology in Wuhan, China. She is a graduate of the Chinese Academy of Sciences, where she received her

doctorate degree in biochemistry and molecular biology. She arrived during the summer of 2013 to focus on research in the areas of viruses, diagnostic assay method of diseases, vaccine research, gene function, genomic and evolution analysis and epidemiology. Over the last several months Dr. Xia has completed theoretical BSL-3 training and laboratory training under Dr. Dennis Bente's mentorship. The U.S. Department of Justice cleared Dr. Xia for research work with select agents in late 2013, and in January 2014 she began her BSL-4 training, again working with Dr. Bente. She also participated in a BSL-4 facility training program alongside trainees from the Institute of Medical Biology in Kunming, China. From a research standpoint, Dr. Xia has made tremendous progress on her Crimean-Congo hemorrhagic fever project – in collaboration with U.S. Centers for Disease Control and Prevention (CDC) – in which parts of the genome are being cloned. She is also being trained by UTMB's Dr. Naomi Forrester to set up a next-generation sequencing pipeline for Crimean-Congo hemorrhagic fever virus. As reported last quarter, Dr. Xia continues to make excellent progress in developing her scientific projects. She has constructed the CCHFV (Crimean-Congo hemorrhagic fever virus) M segment with Nanoluciferase marker based on a rescue system developed by scientists at CDC and shared with UTMB. Working with Dr. Bente in the BSL-4 laboratory, studies are underway on the viral replication and pathogenicity in vitro and in vivo of this labeled recombinant virus. Dr. Xia's research is leading to important new knowledge at the molecular level regarding CCHFV transmission between ticks and vertebrate hosts. Through her fellowship, Dr. Xia is not only receiving ongoing training in high level biocontainment laboratories, but she is learning about the oversight and administrative responsibilities of operations while also conducting important research.

Amerikan Hastanesi (American Hospital) in Istanbul, Turkey. In May 2014, Mr. Grimaldo provided a week long training on BSL-3 Biocontainment Operations to Esra Kora (Project Manager), Muhammet Ali Süngü (Mechanical Engineer), and Birkan Kankatan (Arquitect). The American Hospital is in the process of completing the construction of a new BSL-3 Laboratory.

Representatives of the Amerikan Hastanesi in Instanbul learned essential components of BSL-3 operations while at the NBTC.

International Veterinary Biosafety Workgroup in Pirbright, England. In June, Mr. Grimaldo participated in and presented at the 16th Workshop of the International Veterinary Biosafety Workgroup in Pirbright, England. Mr. Grimaldo did a presentation on "Primary Containment Challenges for Medium Size Animals in ABSL-4 Facilities". The meetings were held at the Pirbright Institute. The International Veterinary Biosafety Workgroup is made up of high and maximum containment facility safety officers and biocontainment engineers with the purpose of cross-training and the exchange of experiences in the operation of these types of laboratories. Mr. Grimaldo has been a member of this working group since 1998; he has served as secretary of the group in the past and serves currently as the America's representative.

Latin American Laboratories, Mexico. In June 2014, Mr. Grimaldo provided a week-long training on BSL-3 Biocontainment Operations to a Latin-American group of scientists, engineers and biosafety officers. Jairo Betancourt from University of Miami, Cesar Esquivel from Universidad de Monterrey - UDEM, Mexico, and from Universidad Autonoma de Nuevo Leon - UANL, Mexico, Lenin Espinosa, Beatriz Lopez, Cristina Padilla, Lydia Rivera and Jose Vasquez.

Trainees from University of Miami, Universidad de Monterrey - UDEM, Mexico, and Universidad Autonoma de Nuevo Leon - UANL, Mexico trained at the NBTC in June 2014.

Center for Technological Development in Health (CDTS) at Fiocruz, Brazil. The goal of the CDTS is to fuse individual research projects with industrial production partners and to play a prominent role in Brazil's developing science, technology, and public health policies. As part of a developing partnership between UTMB/NBTC and the CDTS, senior engineer Marcos Denicio Da Silva De Souza traveled from Brazil to Galveston in July to work with Miguel Grimaldo and his team at the GNL. Mr. De Souza spent a week learning about facility design, specialized equipment, maintenance schedules, administrative record-keeping and other operational procedures. He planned to return to Brazil to share what he learned with other engineers and personnel, as well as with other laboratories and scientific organizations.

Marcos Denicio Da Silva De Souza (center) spent a week training with Miguel Grimaldo (left) and his staff on facility design, maintenance, and operations issues specific to biocontainment laboratories. His customized training was recognized with a certificate presented by Dr. James LeDuc (right) and will be utilized in his position with the Center for Technological Development in Health in Brazil.

Sinclair Knight Merz (SKM)/Jacobs Engineering, Melbourne VIC, Australia. Research facility design professionals Colin Sakinofsky and Jim Hargreaves visited the facilities of the Galveston National Laboratory in July to learn about specialized engineering concerns for air quality and safety from GNL engineers and facility operation experts. A customized training session was provided to assist them with design issues for laboratories being constructed in Australia.

Aim 4. To develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Background

The rate of change in laboratory instrumentation and adaptation of novel technologies to the laboratory setting is progressing rapidly. Routine laboratory procedures are becoming more and more automated, saving technicians and investigators time and effort. Technologies that once were so costly as to limit their use to only a few facilities are now affordable for many laboratories. For example, the sequencing of a pathogen or host that once required months or even years of specialized investigation and costly outsourcing, now can be provided in a matter of hours through the use of automated, high throughput instruments never before available to the research community.

As these modern advances make their way into biocontainment laboratories where highly dangerous pathogens are studied, it is not always clear what safety concerns might exist. For instance, many automated pieces of equipment such as flow cytometry include procedures that could generate an infectious aerosol during wash steps or other routine operations. This could place laboratory workers at risk of accidental infection if appropriate precautions are not utilized. Decontamination of such instrumentation for service and maintenance is another major challenge. In addition, modern imaging equipment is now finding greater application within the research community. Both in vivo and in vitro imaging techniques and equipment are becoming available for use within the biocontainment laboratory environment for use in pathogenesis studies involving

live animals or cell cultures infected with especially dangerous agents. Further, it is now possible to grow relatively large volumes of pathogens using modern bioreactor technology. The development of safe operating procedures, guidelines for product processing, and training on the safe use of each piece of equipment necessary for the production, processing and storage of the resultant product is required. There is an urgent need to develop well-validated procedures to safely and securely conduct these important studies while ensuring the safety of investigators and the surrounding environment.

Progress

Under this aim, personnel have been focused specifically on testing and documenting the use of instruments involved in the BSL-2 laboratories, while also examining their use within the BSL-3 and BSL-4 laboratories. In particular, standard operating procedures for use of instruments with processes that might generate infectious aerosols when live pathogens are investigated and decontamination procedures have been studied and documented. As with all procedures at the Galveston National Laboratory, a focus of this effort is on the development of specialized safety interventions to be used to protect workers at all levels of biocontainment.

Assay Development. Over the last several months, the assay development services division (ADSD) has continued to provide training, optimization and validation of much needed assays at lower containment for export to the BSL-3 and BSL-4 facilities. Such training includes basic methodologies as well as service and maintenance of the equipment that often is designed to be partially or completely automated. The ADSD has also developed and validated methods to eliminate infectivity while preserving the quality and quantity of nucleic acids. Such disinfecting methods have been exported to both BSL-3 and BSL-4 level containment through staff training and collaboration, ultimately providing safe egress of samples to the ADSD laboratory where automated and well-controlled processing can take place. A goal has been to reduce the amount of high maintenance equipment in the higher level containment laboratories. Downstream applications of the processed material include deep sequencing of disinfected pathogen genomes, transcriptional profiling of both the pathogen and the host species and basic proteomic evaluations.

Training has been completed for 4 research staff, 3 medical fellows, 2 PhD students, and several post-doctoral fellows involved in collaborative projects that can be or have been exported to higher containment. Additional training is underway. We have evaluated the integrity and sequence composition of nucleic acid stocks of several BSL-4 viral pathogens, training lab members in the process.

Specific instrumentation includes the Pyromark 96ID (Qiagen) and Ion Torrent PGM platforms (from Life Technologies). The ADSD group has also assisted and trained personnel from several laboratories on PCR-based array technologies utilizing the Tecan EVO liquid handling system to create pre-plated qPCR and qRT-PCR arrays for pathogens and underserved small animal host

species (e.g. guinea pig). They also have developed methods to evaluate human microbiomes in clinical samples. These materials are created at low containment and can then be transferred to higher containment, reducing time and labor in the higher containment lab. This work has included training of researchers on the method and providing raw materials for completing work at distant sites, while testing both shipping and storage methods.

The ADSD, in collaboration with the division of clinical cytopathology, has developed tools to analyze nucleic acids from archived human tissue in the form of fine needle aspirates, paraffin embedded tissues and other biopsy materials. These nucleic acids can be interrogated for the presence of specific pathogens and host responses to these infections in material that is at least 10 years old and has been sub-optimally stored. For these assays we have been able to detect specific host polymorphisms that may contribute to susceptibility or inability to clear infections. Importantly, this may contribute to increased transmission during epidemic events. These same materials can also be subjected to sequencing to establish haplo-groupings for the human host from which the material was collected. Work with specialized instrumentation for purposes of developing standard operating procedures and improving safety conditions continues.

Real Time Plethysmography. New instrumentation and software that accurately measures actual inhaled volumes in non-human primates is being tested and will be implemented in the aerosol biology labs at the GNL. The system, called "real time plethysmography," has shown promising results for measuring lung capacity during studies conducted with the assistance of the manufacturer. The GNL's aerosol biology lab personnel are currently writing new standard operating procedures for using the system in animal studies, and software implementation should be completed during the next quarter.

Select Agent Inventory Management. A new automated system for managing select agent inventories is being piloted within the laboratories at the GNL. Training for those in the pilot program will be underway during the next quarter. More information on this technology will be provided in future reports.

Aim 5. To develop and implement policies, procedures and training programs for the safe and secure conduct of preclinical studies to be undertaken within biocontainment at biosafety laboratory levels 2, 3 and 4 (BSL2, 3, 4) in compliance with the U.S. Food and Drug Administration(FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

Background

There is a growing requirement for the development of diagnostic tests, drugs and vaccines for use in the recognition, treatment and prevention of biological terrorism threats and emerging infectious disease agents. Bioterrorism threats are among the most dangerous infectious pathogens known to humankind, and their safe and secure handling must be done within the confines of specially constructed biocontainment laboratories. The level of biocontainment needed is specific to each particular pathogen and is layered from the lowest level, BSL-2, to "high containment" found in BSL-3 facilities, to "maximum containment" found only in BSL-4 laboratories.

In order to be formally approved for use in humans, products developed for potential application in humans must be evaluated for safety and efficacy during preclinical studies using laboratory animals under safe conditions of biocontainment prior to undergoing clinical safety and efficacy testing in human clinical trials. In addition, in certain cases where efficacy testing in humans is logistically or ethically impractical, products may be approved under the FDA's "Animal Rule" which allows for efficacy to be demonstrated in appropriate animal models. Preclinical safety and animal rule efficacy studies must be conducted by appropriately trained personnel under standardized conditions using well defined procedures and validated equipment as described in 21 CFR Part 58, commonly referred to as Good Laboratory Practices. Each of these studies is likely to encompass activities across multiple levels of in vitro and animal biocontainment and, to date; few organizations have undertaken carefully regulated studies on these highest threat pathogens. Processes and procedures needed for formal GLP studies in biocontainment have generally not been created or have not been tested in actual working biocontainment facilities.

Progress

Representatives of the GNL and NBTC were integrally involved in 2014 FDA-sponsored "Achieving Data Quality and Integrity in Maximum Containment Laboratories" course, which was held at the Natcher Conference Center on the campus of the National Institutes of Health from April 28 – May 2, 2014. Personnel from the GNL, UTMB's Institutional Office of Regulated Nonclinical Studies (ORNcS) and the NBTC served as faculty for the course. Trainees also had the chance to visit the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) and the National Institutes of Health Integrated Research Facility (IRF). Continuing Education Units (CEUs) were awarded to attendees who completed the four and one-half day course, which covered topics such as:

- Regulatory Mechanisms for Development and Approval of Medical Countermeasures
- Communications with the FDA
- The Animal Rule
- Data Quality and Integrity
- Case studies and Practical Experiences in a BSL-4 Lab

The ORNcS and GNL leadership have continued to develop a Study Director-centric model for the conduct and oversight of regulated studies that occur as precursor studies to fully compliant GLP studies. Advancement of medical countermeasure products requires carefully planned and administered studies under a quality system based on the principles of the FDA GLP regulations. Additional information on progress toward these goals will be provided in future reports.

Key Research Accomplishments

Significant progress has been made in addressing each of the Aims identified for study. The level of international engagement with laboratory scientists, engineers, biosafety officers, and growing organizations around the world has continued to expand. The demand for and acceptance of the training we are offering continues to grow. The trainers involved in these efforts have been warmly received by colleagues from around the world who have appreciated and embraced the training provided in both laboratory procedures and biocontainment building maintenance and operations. The opportunity to expand training and influence the safe and secure operations of biocontainment laboratories around the world is virtually unlimited. We are confidently providing a critically important link in the continued safe and secure operations of biocontainment laboratories and continue to be at the forefront of developing and sharing best practices.

Reportable Outcomes

Important partnerships and exchanges have been established both with international biosafety associations and with the individual leadership of international biocontainment laboratories. Key individuals from respected organizations around the world have benefited from extensive training on site at UTMB or at their home facility. These are significant steps towards helping to ensure safety and security at facilities where important research on infectious diseases and dangerous pathogens is being conducted. We are helping to develop highly trained and educated leaders in the field of biocontainment. This will provide the foundation for the continued dissemination of best practices to a much wider international audience.

Conclusions

Providing one-on-one training to international biocontainment professionals is a key to ensuring national security. The leadership and expertise that is being provided through training and the sharing of standards not only provides goodwill but helps to ensure that our counterparts throughout the world are able to move forward with scientific pursuits in a safe and secure manner. The collaborations that are being forged are building a foundation for long-term cooperation, as well as an international culture of trust and transparency that directly enhances global security.

W81XWH-11-2-0148 (NBTC2) Annual Report July 2012 – July 2013

INTRODUCTION.

Scientific investigations, product development, and response to threats of endemic diseases and emerging pathogens are all undertaken in modern research biocontainment laboratories to reduce the risk of infection and lessen the impact of naturally occurring or man-made pathogens to humankind. There is, however, a risk that these activities could contribute to increase the potential exposure of individual scientists and technical staff, as well as surrounding communities, to dangerous infectious diseases if proper precautions are not taken and safe practices are not utilized in laboratories where this work is undertaken.

The threat is perhaps greatest within the international laboratory community where these dangerous pathogens may be routinely manipulated and investigated under less than ideal conditions by individuals who may lack adequate training or experience. Historically, this work was concentrated in a few research or governmental facilities where appropriate biocontainment existed and where a limited number of highly trained investigators conducted the research. Today, the investigation of emerging infectious diseases, the development of novel products to diagnose these infections, prevent infection and treat those who have become ill, has become a global enterprise. Unfortunately, some of the individuals and their parent organizations attempting to conduct this work do not have in place adequate facilities, training or administrative oversight to ensure that this important research and development is undertaken in the safest possible fashion, or that the products under development are evaluated safely.

Through the aims identified below, we are sharing the experiences gained as we operate the unique facilities of the Galveston National Laboratory (GNL) with others involved in laboratory research. Our experiences and lessons learned in the administration, investigation and effort to develop formal regulated studies were gained from years of biocontainment laboratory operations and from training the scientists who work within them. This unique and valuable experience is being shared with other biocontainment laboratory scientists and program directors around the world through the National Biocontainment Training Center's (NBTC) expanded scope of work.

The progress reported here complements activities summarized separately in a companion project (Award Number W81XWH-09-2-0053, also titled National Biocontainment Training Center). Together these awards support a coordinated effort to provide critical training and hands-on experience to U.S. national and international scientists working with

especially dangerous pathogens that require special biocontainment facilities for their safe and secure handling.

BODY.

Research accomplishments associated with each specific aim are summarized below. This annual report covers July 2012 – July 2013.

Staffing Report.

James W. LeDuc serves as principal investigator for the training center and is responsible for oversight of program initiatives, fiscal management and progress reporting.

Christopher Gibbs assists in the training of building engineering fellows and provides hands-on guidance, especially in the care, maintenance and certification of the biological safety cabinets used in virtually every laboratory that handles pathogens.

Miguel Grimaldo directs the building engineering fellowship and provides lectures and hands-on guidance to fellows within the program. He also represents the program at meetings and events dedicated to biocontainment engineering.

Aaron Miller assists with the efforts to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

John Morrill provides assistance in the training of students in the care, use and handling of laboratory animals within BSL-3 and BSL-4 biocontainment laboratories.

Alisha Prather assists in the preparation of reports, in the organization and implementation of guest lectures and with general communications of program activities. She also monitors relevant policy issues related to international biosafety and biosecurity.

Ronald Veselenak works with Aaron Miller to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Specific Aims

Aim 1. To provide standards-based biological containment laboratory safety knowledge to international partners.

Background: There is a massive unmet need for training in biosafety and biosecurity on an international level, which could ultimately stand to impact national security. To address this need we are expanding our efforts to engage international partners in an educational program that is structured around the same principles and practices as those currently in use within our existing funded NBTC, but focused on trainees from international centers possessing a biocontainment facility involved in the diagnosis, research and development, or the clinical care of patients suffering from especially dangerous infectious diseases. We strive to provide on-site training so that the instruction is tailored to meet the local facility and environmental needs and capacity of the end users. We focus on opportunities to "train the trainer" so that our efforts may be multiplied within that country. There is a fledgling network of national and regional organizations that are focused on biosafety, biosecurity and related fields of interest, and we are working with these organizations, and other professional groups to help build this network and further enhance this important aspect of research and development as it relates to infectious diseases.

Progress:

Progress during this past reporting year, highlighted by quarter (Q1, Q2, Q3, Q4) includes:

Q1 highlights –

- **Koc University in Istanbul, Turkey.** This quarter we have had two students from Koc University in Istanbul, Turkey come to the NBTC for onsite laboratory biosafety training. These student researchers work at the same institution as one of our NBTC fellows, Dr. Aysen Gargili. The researchers were with us for two weeks and took both the BSL3 and ABSL3 courses.

- Instituto Nacional de Enfermedades Virales Humanas, Argentina. We also trained nine

individuals from the Instituto Nacional de Enfermedades Virales Humanas (INEVH), Argentina at BSL3 and sixteen individuals in BSL2 theory.

- **Centro Nacional de enfermedades tropicales in Bolivia.** Following this training and due to collaborations between UTMB researcher Dr. Aguilar and members of INEVH, NBTC trainers were asked to travel to Centro Nacional de enfermedades tropicales (CENETROP) in Bolivia to train new BSL3 researchers in preparation of the opening of their BSL3 facility. This course was organized by Pan American Health Organization (PAHO). Six researchers participated in our BSL3 course and 11 participated in theoretical BSL3 training. Two consultants from the NBTC travelled to Bolivia to provide theoretical and practical training for a total of 17 staff who will work in the national laboratory in Santa Cruz (pictured above, August 2012). The director, manager, researchers, and staff were trained in biological safety techniques critical for functional operation in a P-3 environment. The participants were very engaged throughout the training often asking questions and posing scenarios. Evidence of achievement by the trainees was demonstrated in successful completion of theoretical and practical assessments. All participants were rewarded with certificates. In addition, local administrators have been in contact with the NBTC about possible future training sessions for a broader laboratory audience in Santa Cruz.

- **International Federation of Biosafety Associations.** Continuing this quarter, Mr. Miguel Grimaldo, a Galveston National Laboratory biocontainment engineer with the training center is participating as a member of the Biocontainment Engineering Working Group of the International Federation of Biosafety Associations (IFBA). One of the goals of the Working Group is to develop risk-management based guidelines for biocontainment laboratories that will eventually be endorsed by international organizations such as World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the Office International des Epizooties (OIE) the World Organisation for Animal Health.

- **European Research Infrastructure on Highly Pathogenic Agents project.** Mr. Grimaldo was also invited to the workshop of the European Research Infrastructure on Highly Pathogenic Agents (ERINHA) project. This activity was an international expert workshop on the evidence-based design on high containment facilities. It was held in London between 25th and 27th of September 2012. Mr. Grimaldo did a presentation on BSL4 Ventilation - Design and Operation. This invitation-only workshop was attended by an international audience of containment experts (facility managers, scientists, architects and engineers) from France, Germany, Italy, Netherlands, Australia, Austria, United Kingdom, Slovakia, Denmark, Greece, Romania, Spain, Portugal, Canada and the U.S.

- **AFRIMS, Bangkok, Thailand.** NBTC trainers Jason Hardcastle and Vickie Jones travelled to Thailand at the end of November 2012 to present a two-week BSL3 course offered to the USAMRMC - AFRIMS (U.S. Army Medical Research and Material Command - Armed Forces Research Institute of Medical Sciences, a U.S. Department of Defense overseas facility) research staff. Simultaneously NBTC trainer Belinda Rivera and GNL biocontainment veterinarian Dr. Curtis Klages travelled with them the first week to offer a different set of individuals Non-Human Primate and ABSL3 training. This was in follow-up to training we offered at UTMB to three members of their staff in early 2012. An update on this training in Thailand follows: Members of the AFRIMS invited NBTC trainers to Bangkok, Thailand to offer BSL3, ABSL3 and NHP training to researchers stationed at their facilities in the region. AFRIMS is home to over 300 staff members who are a highly integrated group of U.S. and Thai military and civilians from both countries. The U.S. Component Commander is on the U.S. Ambassador's Country Team for Thailand and provides advice to the country team on biomedical issues. At AFRIMS, twenty researchers participated in our BSL3 course and 28 participated in theoretical BSL3 training. The Institute's director, manager, researchers, and staff were trained in biological safety techniques critical for functional operation in a BSL3 environment. The participants were very engaged throughout the training, often asking questions and posing laboratory scenarios. Evidence of achievement by the

trainees was demonstrated in successful completion of theoretical and practical assessments. All participants (*pictured previous page, top right*) were rewarded with certificates. Four participants (*pictured previous page, middle right*) completed the ABSL3 training and ten staff participated in the theoretical class. Seven participants completed the NHP training and 11 participated in the theoretical class (*pictured previous page, bottom right*). The veterinarians and staff were trained in biological and animal safety techniques critical for functional operation in their containment animal facilities.

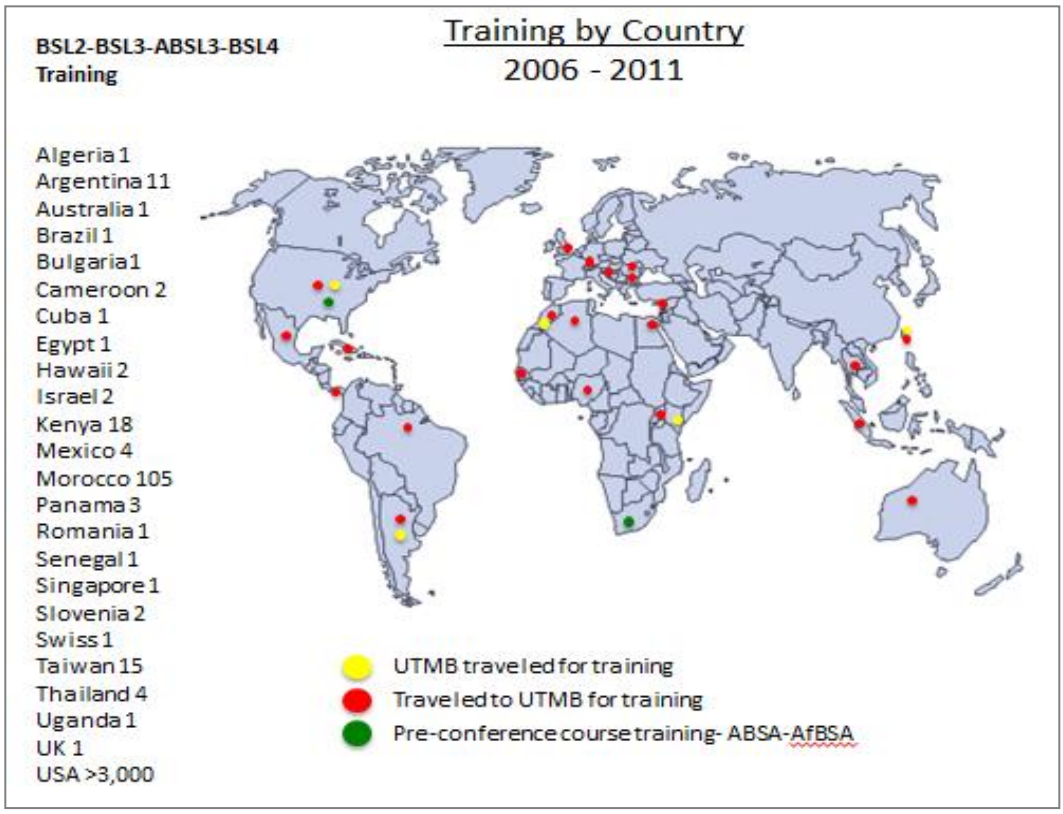
- **SACIDS, Tanzania.** Following the African Biological Safety Association (AfBSA) meeting in Johannesburg in the summer of 2012, the NBTC was asked to offer BSL2 theoretical training to several institutions from East Africa. A consultant from NBTC was invited to Tanzania to provide theoretical training for 11 staff working in laboratories in Tanzania, Democratic Republic of Congo, Mozambique, South Africa, Zambia as part of the Southern African Centre for Infectious Diseases Surveillance (SACIDS). SACIDS is a One Health consortium of southern African medical and veterinary, academic and research institutions involved with infectious diseases of humans and animals in the DRC, Mozambique, South Africa, Zambia and Tanzania in partnership with centers of science in industrialized countries. All these individuals were selected by their respective institutions as key staff with the ability and influence to improve the safety and quality control of their laboratories and institutions. The participants (*pictured above with the NBTC's Dr. Sophie Brocard*) were very engaged throughout the training often asking questions and posing scenarios.

- **Biocontainment Engineering Working Group, International Federation of Biosafety Associations (IFBA).** Continuing this quarter, Mr. Miguel Grimaldo, a GNL biocontainment engineer with the training center is participating in the development of risk-management based guidelines for biocontainment laboratories as a member of the Biocontainment Engineering Working Group of the International Federation of Biosafety Associations (IFBA). These guidelines will eventually be endorsed by international organizations such as World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the Office International des Epizooties (OIE) the World Organization for Animal Health.

- **American Biological Safety Association.** During pre- and post-conference sessions of 2012 American Biological Safety Association (ABSA) conference held in Orlando, Florida in October, Mr. Grimaldo participated on following activities:
  - He represented the NBTC as an Observer Member of the International Federation of Biosafety Associations. As such, Mr. Grimaldo participated on the 2012 ABSA International Forum on Sharing Biorisk Management Success Stories. During this forum, individual discussion where held with participants regarding training opportunities on Biosafety and Laboratory Biocontainment and Maintenance Operations.
  - As member of the Biocontainment Engineering Working Group (BEWG) of the International Federation of Biosafety Associations (IFBA), Mr. Grimaldo participated in a follow-up meeting to the plenary meeting held in South Africa in June 2012. The topics of discussion included the priority items that were identified during the meeting in South Africa, as well as the IFBA Biocontainment Working Group requirement to create a "network of biocontainment engineers" capable of mentoring and supporting those new to the field; and the development of technical guidance for risk-based solutions to containment facilities and equipment. It is expected that the next members' meeting of the IFBA and the BEWG will take place during the preconference sessions of the Asian Pacific Biosafety Association 2013 conference to be held in Kuala Lumpur, Malaysia.
  - Also during preconference of the 2012 ABSA Conference, Mr. Grimaldo participated a meeting to delineate key issues regarding the work-in-progress ANSI Z9.14 standard for the Testing and Performance Verification Methodologies for Ventilation Systems for BSL3 and ABSL3 Laboratories. The meeting included committee members attending the ABSA conference.

- **International Veterinary Biosafety Workgroup, South Africa.** In November, Mr. Grimaldo participated in and presented at the 15th Workshop of the International Veterinary Biosafety Workgroup in Pretoria, South Africa. Mr. Grimaldo did a presentation on "Ventilation Control Modes and Failure Testing" (*pictured right*) as well as presented data and participated in a panel discussion about "Laboratory Pressurization during Fumigation". The meetings were held at the Agricultural Research Council of South Africa. The International Veterinary Biosafety Workgroup is made up of high and maximum containment facility safety officers and biocontainment engineers with the purpose of cross-training and the exchange of experiences in the operation of these type of laboratories. Mr. Grimaldo has been a member of this working group since 1998, he has

served secretary of the group in the past and was elected representative for The Americas at this year's meeting.



Aim 2. To provide the information and education necessary for a critical global discussion on the biosecurity, biosurety and related policy issues involved in the operation and maintenance of biocontainment facilities.

Background: A significant unmet need exists on the part of students, staff and faculty for greater knowledge regarding the origin, development, necessity and implementation of national policies on the vital topics of biosecurity, biosurety and related policy issues that form the foundation for the safe and secure operation and maintenance of biocontainment facilities. We continue to address this need through our ongoing lecture series led by distinguished guest speakers in our "Topics in Biosecurity Symposia Series." It is clear, however, that much more could be done to meet this aim; consequently, we are working to engage a number of national and international partners to educate audiences, to stimulate discussion, and to consider and propose solutions to our biosecurity and biosurety concerns. This effort includes, for example, participation in the ongoing efforts of the U.S. National Academy of Sciences and other organizations, and in other activities associated with the creation and operation of biocontainment facilities such as those in Central Asia, Asia, the Americas and in Africa. Our goal is to engage national and international leaders to develop and implement evidence-based policy discussions and eventual agreements that will enhance the security of biocontainment facilities around the world, including in those areas where little or no biosecurity infrastructure currently exists. This is being accomplished by participation in national, regional and international meetings and conferences and other outreach efforts, the facilitation of collaborative studies and investigations, the support of short- and long-term personnel exchanges to address specific goals in biosecurity, the development of programs suitable for a variety of educational methodologies, including ones that are web-based, and other timely opportunities designed to enhance global biosecurity.

Progress:

- Dr. Jim LeDuc of the NBTC participated in the 2011 Review Conference of the Biological and Toxin Weapons Convention in Geneva, Switzerland during which the U.S. National Academies of Science sponsored a side event to discuss the recently completed report, "*Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories."* Pre-publication copies of the report were provided to the approximately 50 delegates in attendance. Dr. LeDuc participated in the meeting held in Istanbul, Turkey last July that provided the foundation for this report, and he helped in the drafting of the final document (see below). The final report is now available online at the National Academy Press (www.NAP.edu), and a formal release and press conference was held at the National Academies of Sciences Keck Building in June 2012. Dr. LeDuc was one of the three panelists discussing the report.

Dr. James W. LeDuc is pictured at the 2011 Review Conference in Geneva, Swtizerland alongside colleagues discussing the "Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories" National Academies report.

- Based on the findings contained in this National Academy of Sciences report, a follow up meeting was held in Kiev, Ukraine in late April 2012. Dr. LeDuc participated in that meeting and contributed three presentations.
- During the reporting year, Dr. LeDuc also participated in a National Academy of Sciences workshop entitled "*Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories"* held in Istanbul, Turkey with the involvement of 68 international experts representing 32 different countries. *(Right: photo courtesy of Ben Rusek, CISAC.)*

- Members of the NBTC participated as presenters at the American Association for Laboratory Animal Science (AALAS) 62nd National Meeting held October 2-6, 2011 in San Diego, California. The title of their

presentation was *"Biocontainment Training and Access Process for Animal Care and Research Staff."*

- A member of the NBTC participated in a meeting of the Global Virus Network, a fledgling group of leading experts in virology from around the world. This meeting was held on October 7-9, 2011 in Dublin, Ireland during which two formal presentations were made describing opportunities for training offered by the National Biocontainment Training Center and discussions of possible liaison actions with international organizations and other established networks that include biocontainment laboratories.

- A member of the NBTC was an invited expert guest for a meeting of the National Academy of Sciences' Committee on Evaluation of the NBAF Site Specific Risk Assessment. This is a congressionally mandated effort by the NAS to evaluate a 2nd risk assessment on the proposed replacement laboratory for Plum Island Animal Center in Manhattan, Kansas. The evaluation includes the physical facility as well as operational and manpower issues (including training requirements for laboratory staff). The final report from this committee will be released on July 13, 2012.

- West Point cadets Nicholas Tubbs and Whitney Strong spent part of their summers as interns with the NBTC as a part of the Academy's Academic Individual Advanced Development program. Cadet Tubbs, who is in his final year at West Point, did a biocontainment engineering internship with Miguel Grimaldo in the GNL. Cadet Strong, who is in her third year at the Academy, joined the lab of Dr. Alex Freiberg in Keiller for a research internship. Cadet Tubbs shadowed Miguel and Chris Gibbs during his stay, learning the basics of building engineering from air flow and filtration to electronic monitoring systems and routine maintenance. Cadet Tubbs commented, "I have learned a lot on the various biocontainment systems and the necessary workings behind a lab. I didn't really understand the complexities or redundancy of the systems before I came here, but now I am learning the various components to the lab." Cadet Strong was involved in two research projects to learn about different laboratory techniques. She worked on the characterizations of Rift Valley fever virus glycoprotein mutants and of recombinant expressed Nipah virus proteins.

Pictured (l to r): Miguel Grimaldo, Alex Freiberg, Cadet Strong, Cadet Tubbs and Jim LeDuc.

- *Publications from the past reporting year include:*

- Franz, David R. and LeDuc, James W, 2011. Balancing our approach to the insider threat. *Biosecurity Bioterrorism* 9 (3):1-2.
- LeDuc, James W. and Franz, David R, 2012. Genetically engineered transmissible influenza A/H5N1: A call for laboratory safety and security. *Biosecurity Bioterrorism* 10 (3): 153-4.

Aim 3. To develop and implement a dedicated program to facilitate the establishment, maintenance and administrative oversight of operations of biocontainment facilities.

Background: There are unique requirements for the operations of a biocontainment facility that extend beyond the scientific investigations and the safety and security infrastructure. For facilities such as the regional and national biocontainment laboratories constructed with support from NIH, as well as the independent commercial and not-for-profit institutions and foundations that manage biocontainment facilities and the international containment laboratories such as those now under construction in Central Asia under U.S. Department of Defense support, there is a need for a specialized administrative structure and culture. This culture must be sensitive and responsive to local needs and also address the unique operational challenges associated with the conduct of research and development involving highly dangerous infectious pathogens and the specialized business practices that are critical to sustaining the enterprise. These challenges are especially difficult ones that vary by organization with no standard model fully appropriate for all facilities.

There are some general principles that must be followed; however, in many instances the operational environment at each facility is unique and demands specialized attention. We captured these lessons learned as we brought the GNL online and embarked on the full operation of this national resource. We are developing plans to offer short and longer term training opportunities to administrative staff and institutional leadership of containment laboratories, as well as to students interested in careers in this field. Longer term fellowships are being established to provide relevant hands-on experience to the next generation of the biocontainment industry leaders. We are also creating a standardized checklist of essential tools, skills and procedures that are critical to the safe and secure operations of a biocontainment laboratory. This will include best business practices to ensure fiscal stability in the face of the high costs of security, utilities and specialized equipment required for successful operations.

Progress: A researcher from Turkey who is directly involved in both the scientific investigations and oversight of a newly constructed BSL3 laboratory in Istanbul that will

focus primarily on pathogens of agricultural and human health importance began this long-term training program in January 2012. The individual is a DVM, PhD with extensive experience in vector-borne diseases and virology. In addition to her training on containment laboratory operations and management, the scientific focus of her work while at UTMB involves investigations of Crimean-Congo hemorrhagic fever, an important endemic virus disease of growing significance in Turkey and Central Asia. Her work involves virus transmission studies using vector tick colonies that she has helped to establish here at UTMB from material originally collected in Turkey.

Aim 4. To develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Background: The rate of change in laboratory instrumentation and adaptation of novel technologies to the laboratory setting is progressing rapidly. Routine laboratory procedures are becoming more and more automated, saving technicians and investigators time and effort. Technologies that once were so costly as to limit their use to only a few facilities are now affordable for many laboratories. For example, the sequencing of a pathogen or host that once required months or even years of specialized investigation and costly outsourcing, now can be provided in a matter of hours through the use of automated, high throughput instruments never before available to the research community.

As these modern advances make their way into biocontainment laboratories where highly dangerous pathogens are studied, it is not always clear what safety concerns might exist. For instance, many automated pieces of equipment such as flow cytometry include procedures that could generate an infectious aerosol during wash steps or other routine operations, which might place laboratory workers at risk of accidental infection if appropriate precautions are not utilized. Decontamination of such instrumentation for service and maintenance is another major challenge. In addition, modern imaging equipment is now finding greater application within the research community. Both *in vivo* and *in vitro* imaging techniques and equipment are becoming available for use within the biocontainment laboratory environment for use in pathogenesis studies involving live animals or cell cultures infected with especially dangerous agents. Further, it is now possible to grow relatively large volumes of pathogens using modern bioreactor technology. The development of safe operating procedures, guidelines for product processing, and training on the safe use of each piece of equipment necessary for the production, processing and storage of the resultant product is required. There is an urgent

need to develop well-validated procedures to safely and securely conduct these important studies while ensuring the safety of investigators and the surrounding environment.

Under this aim, we are focusing specifically on those processes that might generate infectious aerosols when live pathogens are investigated and on those instruments that will require decontamination prior to service by external personnel who may not be equipped to work in a biocontainment setting. A product of this effort will be the creation of detailed standard operating procedures to ensure the safe analysis of material originating from potentially infectious substances and the development of specialized safety interventions to be used to protect workers at all levels of biocontainment. Our efforts are focused on the BSL2 laboratories where the majority of this equipment is located and where the greatest number of users exists; however, we are also examining these resources when they are in use within BSL3 and BSL4 laboratories.

Progress: Administrative procedures are in progress to establish support for personnel under this aim. The funds have not yet been expended. An update will be provided in future reports.

Aim 5. To develop and implement policies, procedures and training programs for the safe and secure conduct of preclinical studies to be undertaken within biocontainment at biosafety laboratory levels 2, 3 and 4 (BSL2, 3, 4) in compliance with the U.S. Food and Drug Administration(FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

Background: There is a growing requirement for the development of diagnostic tests, drugs and vaccines for use in the recognition, treatment and prevention of biological terrorism threats and emerging infectious disease agents. Bioterrorism threats are among the most dangerous infectious pathogens known to humankind, and their safe and secure handling must be done within the confines of specially constructed biocontainment laboratories. The level of biocontainment needed is specific to each particular pathogen and is layered from the lowest level, BSL2, to "high containment" found in BSL3 facilities, to "maximum containment" found only in BSL4 laboratories (highly complex facilities built with special air handling, waste sterilization and other safety and security protections incorporated into the physical plant and routine operations).

In order to be formally approved for use in humans, products developed for potential application in humans must be evaluated for safety and efficacy during preclinical studies using laboratory animals under safe conditions of biocontainment prior to undergoing clinical safety and efficacy testing in human clinical trials. In addition, in certain cases where efficacy testing in humans is logistically or ethically impractical, products may be approved under the FDA's "Animal Rule" which allows for efficacy to be demonstrated in appropriate animal models. Preclinical safety and animal rule efficacy studies must be conducted by appropriately trained personnel under standardized conditions using well defined

procedures and validated equipment as described in 21 CFR Part 58, commonly referred to as Good Laboratory Practices.

Each of these studies is likely to encompass activities across multiple levels of *in vitro* and animal biocontainment and, to date; few organizations have undertaken carefully regulated studies on these highest threat pathogens. Processes and procedures needed for formal GLP studies in biocontainment have generally not been created or have not been tested in actual working biocontainment facilities.

Progress: We are currently preparing for support of GLP-compliant studies to be performed at BSL3 or BSL4 using laboratories in the GNL and elsewhere on the UTMB campus. The FDA requires that critical drugs and reagents are protected from potential mix-ups or contamination. We are preparing standard operating procedures and associated equipment files for a dedicated regulatory studies support laboratory and general BSL2 laboratory, located on the 6th floor of the GNL.

The dispensary laboratory is intended to provide a dedicated space for critical reagent (e.g. test and control articles) receipt, storage and handling and is equipped with a suite of basic laboratory equipment that has been validated according to a set of general operating parameters for storage and measurement of reagents. Likewise, a general BSL2 laboratory is being established for use on regulated (GLP) and other sponsored studies that require restricted access and/or segregation of laboratory work to meet compliance or contractual requirements. In addition to standard equipment consistent with other GNL BSL2 laboratories, this laboratory will house blood and clinical chemistry analyzers and a Tecan automated plate handling system. These lab spaces can be used to support studies in a GLP compliant manner and, when not in use for a compliant study, will be used to train facility personnel and validate potential test models and supporting procedures.

GNL and UTMB personnel are continuing to develop standard operating procedures and associated documentation to support safe and secure future operations of those laboratories and to facilitate training of study personnel in appropriate performance and documentation of activities that would be performed in those dedicated laboratories. In addition, personnel are working with other GNL cores/divisions, UTMB Environmental Health and Safety, and individual investigators to develop specific procedures for quality assurance unit (QAU) oversight of studies performed in high biocontainment laboratories at UTMB and for validation of significant laboratory equipment, methodologies and information systems infrastructure that may be used in support of future product development-related studies in compliance with FDA regulations for product licensure. This is a long process that will require significant investments of time and effort to develop

the robust program needed to ensure successful regulated studies conducted under biocontainment conditions.

Key Research Accomplishments. Significant progress has been made in addressing each of the Aims identified for study, with the exception of Aim 4, that deals with safety precautions of modern laboratory equipment. The level of international engagement with laboratory scientists and biosafety officers around the world has been exceptional and clearly demonstrates a substantial demand for the training we are offering. We have been especially gratified by the warm reception and very positive comments that we have received from our colleagues dealing with biocontainment building maintenance and operations. This is a critically important link in the continued safe and secure operations of biocontainment laboratories, yet there is virtually no international source of guidance or established best practices. We are proud to be at the forefront of addressing this need.

Reportable Outcomes. Important partnerships and exchanges have been established both with international biosafety associations and with the individual leadership of international biocontainment laboratories. Further, several individuals have benefited from extensive training on site at UTMB or at their home facility. These are significant steps towards developing leaders around the world and will serve as a foundation for future growth and dissemination of best practices to a much wider international audience.

Conclusions. The value of international engagement on a personal level cannot be overstated. The friendships and mutual respect that develops through our training efforts not only enhances the safe and secure operations of containment laboratories around the world, but it also fosters a culture of trust and transparency that directly enhances global seful in generating funding for the NBTC.

W81XWH-11-2-0148 (NBTC2) Annual Report July 15, 2011 – July 14, 2012

INTRODUCTION.

Scientific investigations, product development, and response to threats of endemic diseases and emerging pathogens are all undertaken in modern research biocontainment laboratories to reduce the risk of infection and lessen the impact of naturally occurring or man-made pathogens to humankind. There is, however, a risk that these activities could contribute to increase the potential exposure of individual scientists and technical staff, as well as surrounding communities, to dangerous infectious diseases if proper precautions are not taken and safe practices are not utilized in laboratories where this work is undertaken.

The threat is perhaps greatest within the international laboratory community where these dangerous pathogens may be routinely manipulated and investigated under less than ideal conditions by individuals who may lack adequate training or experience. Historically, this work was concentrated in a few research or governmental facilities where appropriate biocontainment existed and where a limited number of highly trained investigators conducted the research. Today, the investigation of emerging infectious diseases, the development of novel products to diagnose these infections, prevent infection and treat those who have become ill, has become a global enterprise. Unfortunately, some of the individuals and their parent organizations attempting to conduct this work do not have in place adequate facilities, training or administrative oversight to ensure that this important research and development is undertaken in the safest possible fashion, or that the products under development are evaluated safely.

Through the aims identified below, we are sharing the experiences gained as we operate the unique facilities of the Galveston National Laboratory (GNL) with others involved in laboratory research. Our experiences and lessons learned in the administration, investigation and effort to develop formal regulated studies were gained from years of biocontainment laboratory operations and from training the scientists who work within them. This unique and valuable experience is being shared with other biocontainment laboratory scientists and program directors around the world through the National Biocontainment Training Center's (NBTC) expanded scope of work.

The progress reported here complements activities summarized separately in a companion project (Award Number W81XWH-09-2-0053, also titled National Biocontainment Training Center). Together these awards support a coordinated effort to provide critical training and hands-on experience to U.S. national and international scientists working with especially dangerous pathogens that require special biocontainment facilities for their safe and secure handling.

BODY.

Research accomplishments associated with each specific aim are summarized below. This annual report covers July 15, 2011 – July 14, 2012.

Staffing Report.

James W. LeDuc serves as principal investigator for the training center and is responsible for oversight of program initiatives, fiscal management and progress reporting.

Christopher Gibbs assists in the training of building engineering fellows and provides hands-on guidance, especially in the care, maintenance and certification of the biological safety cabinets used in virtually every laboratory that handles pathogens.

Miguel Grimaldo directs the building engineering fellowship and provides lectures and hands-on guidance to fellows within the program. He also represents the program at meetings and events dedicated to biocontainment engineering.

Aaron Miller assists with the efforts to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

John Morrill provides assistance in the training of students in the care, use and handling of laboratory animals within BSL-3 and BSL-4 biocontainment laboratories.

Alisha Prather assists in the preparation of reports, in the organization and implementation of guest lectures and with general communications of program activities. She also monitors relevant policy issues related to international biosafety and biosecurity.

Ronald Veselenak works with Aaron Miller to address Aim 4, to develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Specific Aims

Aim 1. To provide standards-based biological containment laboratory safety knowledge to international partners.

Background: There is a massive unmet need for training in biosafety and biosecurity on an international level, which could ultimately stand to impact national security. To address this need we are expanding our efforts to engage international partners in an educational program that is structured around the same principles and practices as those currently in use within our existing funded NBTC, but focused on trainees from international centers possessing a biocontainment facility involved in the diagnosis, research and development, or the clinical care of patients suffering from especially dangerous infectious diseases. We strive to provide on-site training so that the instruction is tailored to meet the local facility and environmental needs and capacity of the end users. We focus on opportunities to "train the trainer" so that our efforts may be multiplied within that country. There is a fledgling network of national and regional organizations that are focused on biosafety, biosecurity and related fields of interest, and we are working with these organizations, and other professional groups to help build this network and further enhance this important aspect of research and development as it relates to infectious diseases.

Progress:

Progress during this past reporting year includes:

- We participated in the 3rd Biosafety and Biosecurity International Meeting (BBIC) held in Amman, Jordan in September 2011. The meeting was supported by HRH Prince El Hassan bin Talal and HRH Princes Sumayabint El Hassan. The focus of the conference was to continue with the development of biosafety and biosecurity awareness and implementation in the deferent countries on the Middle East and North Africa (MENA) regions. Representatives present from countries within the region included Jordan, Algeria, Yemen, Sudan, Morocco, Kuwait, Pakistan, and Oman. Dr. Brocard presented a talk *(pictured right above)* and 2 posters at the conference (*pictured right below: a photo of Dr. Brocard and HRH princess Sumaya bin El Hassan, she and her father HRH prince El Hassan bin Talal are strong supporters of the biosafety and biosecurity initiative in Jordan*). Immediately following the conference, interested countries could

participate in a workshop to develop their respective national biosafety associations. Dr. Brocard gave a presentation to this group as well. A strong interest that emerged from both the 2nd and 3rd BBIC conferences is the development of national/regional or local training centers in biosafety and biosecurity. Dr. Brocard is a member of the working group dedicated to this effort, which will be further developed over the next year.

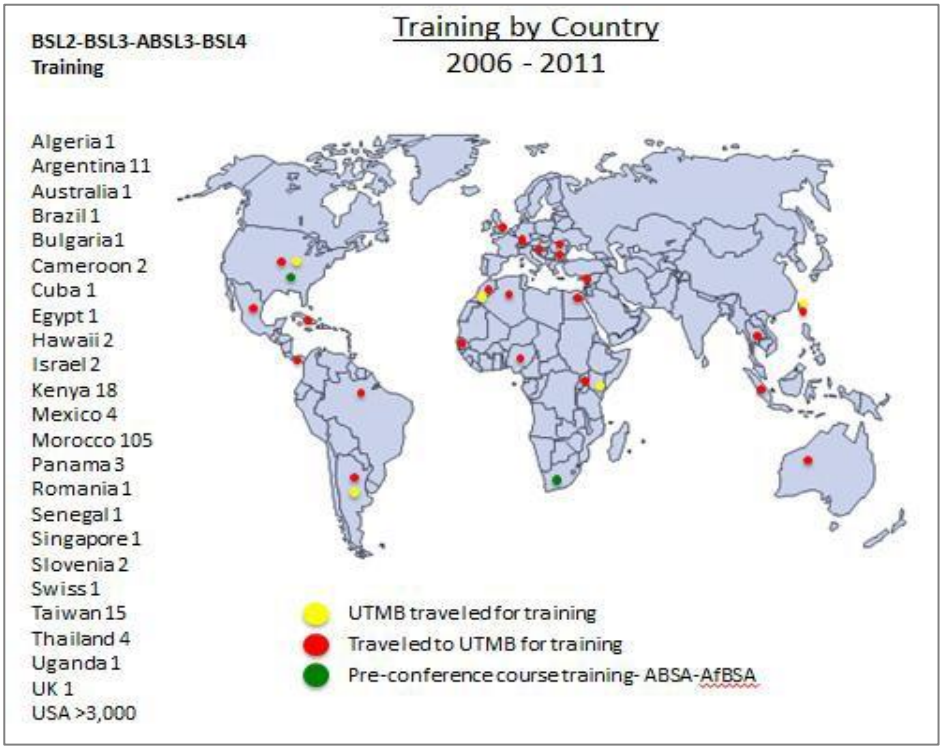
- Following the meeting in Jordan, Dr. Brocard was invited to teach a course on biosafety at the Pasteur Institute in Casablanca, Morocco. The training took place in December 2011 and was attended by 104 individuals representing the majority of the Pasteur Institute research and clinical laboratory staff. The emphasis of the instruction was on theoretical BSL2 practices. The initiative was promoted and supported by the Interim Director of the

institution and the departmental leadership. The trip and coursework were organized over a two-day onsite training session in Casablanca *(pictured above)*. During day one Dr. Brocard toured the entire site which included a research component, clinical laboratories and laboratories for the public health department that oversees food, as well as a tour of water and food processing areas. Dr. Brocard fielded participant questions regarding biosafety as well as waste disposal processes that could be applied to their unique location. There was great awareness of possible health issues and exposure to the general population should biological and chemical waste be disposed of inappropriately. Day two consisted of a full day instructional presentation – in French – by Dr. Brocard that was extremely well attended. Roughly 50-60 people were expected to attend but 104 people ultimately attended, doubling participation and clearly demonstrating their interest in biosafety. Attendees posed thoughtful questions that confirmed the directors' intent to promote and implement good biosafety and waste disposal in the institution. Questions also focused on field work biosafety as many of the samples studied at the Institute are collected in the field. The NBTC will maintain contact with the Pasteur Institute to provide them with information and further training as needed to help them implement their biosafety goals.

- We provided BSL2 training to a research scientist from Monterrey, Mexico in September 2011. The researcher returned to our training center in January 2012 to complete BSL3 training. This researcher is now the manager of the BSL3 facility in Monterrey which was inaugurated in April 2012. Drs. Ann-Sophie Brocard, Janice Endsley and Alfredo Torres were invited by the University of Monterrey, Mexico to be present at their BSL3 grand opening in April 2012. The University invited their UTMB partners to join in the ribbon cutting ceremonies (pictured right). The specialty of the new university lab will be the molecular diagnosis of infectious diseases such as dengue, influenza and tuberculosis. The BSL3 lab was inaugurated by the NBTC's Dr. Anne-Sophie Brocard and Dr. Janice Endsley along with the CDC's Dr. Jeffrey Chang, directors of hospitals in the Mexican Institute of Social Security, and campus researchers and administration.

- We provided BSL3 training to three individuals from USAMRMC-AFRIMS stationed in Bangkok, Thailand. One individual from this laboratory stayed on and completed the ABSL3 training program as well. This person will be moving to a new duty station but indicated that they will strongly recommend that their replacement participate in our training program.

- Per the world map below, we continue to build ties with the Middle East and North Africa (MENA) regions to assist in their development of national and regional biosafety and biosecurity programs. Our training ties continue to expand as the demand for biosafety training grows.



Also during this past reporting year, the training facility's engineering and maintenance team welcomed trainees from the Institutio Nacional de Enfermedades Virales Humanas "Dr. Julio Maiztegui" (INEVH) and the Universidad Technologica Nacional, both located in Argentina. Three trainees participated in the NBTC's Biocontainment Engineering Training Program in October 2011 held in the GNL. Course modules were tailored for the necessities of these particular institutions and included instruction in facility and primary containment requirements, ventilation mechanical systems and controls, facility adjustment and testing, decontamination and filtration systems, and documentation and record keeping among others. Advance paperwork was filed in compliance with 8 USC 1324b (a)(3) which regards training of non-US citizens on the UTMB campus. "It was more than just the training," visiting Engineer Ruben Fassio said about the NBTC coursework. "It was so much more than we expected or hoped for." The group spent 10 days touring the various laboratories, learning best practices and reviewing and solving problems they've encountered at home. They took a wealth of knowledge back to Argentina to improve their laboratories. "After my time here, I know what I'm doing right and where we need to make improvements," Fassio added. "Moving forward, I know the right way to do things and can train others the right way." That shared expertise represents one of UTMB's core values and encapsulates the goals of this unique biocontainment engineering training program. NBTC trainers continued the instruction by travelling to Pergamino, Argentina in May 2012 to provide hands-on instruction in the engineers' and researchers' own laboratory environment. As noted by the Institute's director Dr. Delia Enria, "The course was excellent, not only for the quality of the materials, organization, methodology, but also of the technical expertise of the people and the personal contacts that developed. I hope that the group continues with future projects, thus following the line of a friendship initiated more than 30 years ago in a new generation."

Pictured above: Engineers from Argentina's Institutio Nacional de Enfermedades Virales Humanas "Dr. Julio Maiztegui" and the Universidad Technologica Nacional attended the NBTC's Biocontainment Engineering Training Program at UTMB in October 2011. They are pictured in the lab's mechanical spaces and with GNL Biocontainment Engineer Miguel Grimaldo and also receiving their certificates of completion from Grimaldo and GNL Director Dr. Jim LeDuc.

When NBTC trainers travelled to Pergamino in May 2012, they provided BSL3 training and facility/maintenance engineering training for their staff of 16 individuals. Each received BSL3 theoretical and practical training (one individual received theoretical training only) and 3 individuals received facility training. Each also participated in a BSL2 theoretical class; the course materials were printed in Spanish to facilitate understanding and comprehension.

Mr. Grimaldo, the NBTC's biocontainmen r Gibbs provided training on *"Basic Concepts for the Design, Construction and Operation of BSL3 Laboratories and their necessary aspects for their certification," "Biosafety Cabinet Certification Under the NSF 49 Standard,"* and also performed a site inspection of the INVEH's new BSL3 laboratory under construction.

Pictured on this page (top) are INEVH's team members who took part in the biosafety training provided onsite by the NBTC. Also pictured are Mr. Gibbs (bottom left) and Mr. Grimaldo (bottom right) during the maintenance and engineering instructional portions of the training program at the Pergamino laboratory.

- Mr. Grimaldo was invited to become a member of the **Biocontainment Engineering Working Group of the International Federation of Biosafety Associations (IFBA).** One of the goals of the Working Group is to develop risk-management based biocontainment guidelines for biocontainment laboratories that will eventually be endorsed by international organizations such as WHO/OIE/FAO. During a June 2012 meeting of the IFBA held in Johannesburg, South Africa the NBTC was formally invited to become a member of the group which is committed to fostering collaborations with global organizations to promote and strengthen biosafety and biosecurity worldwide.

- In continuing work with our partners in Africa, Dr. Brocard taught a preconference course *"Building Your Biosafety Capacity – How to Get Started"* at the 3rd African Biological Safety Association (AfBSA) conference in Johannesburg, South Africa in June of 2012. Thirty conference attendees participated in Dr. Brocard's course.

- The NBTC's Belinda Rivera (pictured right) attended the 51st Annual Canadian Association for Laboratory Animal Science (CALAS) Symposium in Vancouver, British Columbia, June 2-5, 2012 and was sponsored by the Laboratory Animal Welfare and Training Exchange (LAWTE). Belinda provided a pre-conference workshop and co-presented with Bruce Kennedy, the current president of LAWTE. The workshop presentations included *"How to Train on Laboratory Animal Allergens"* and *"Training on Biocontainment"* and were attended by 30+ individuals. The 52nd Annual Symposium will be held in Winnipeg, MB, May 4-7, 2013 and will be a joint meeting with CALAS and LAWTE.

Aim 2. To provide the information and education necessary for a critical global discussion on the biosecurity, biosurety and related policy issues involved in the operation and maintenance of biocontainment facilities.

Background: A significant unmet need exists on the part of students, staff and faculty for greater knowledge regarding the origin, development, necessity and implementation of national policies on the vital topics of biosecurity, biosurety and related policy issues that form the foundation for the safe and secure operation and maintenance of biocontainment facilities. We continue to address this need through our ongoing lecture series led by distinguished guest speakers in our "Topics in Biosecurity Symposia Series." It is clear, however, that much more could be done to meet this aim; consequently, we are working to engage a number of national and international partners to educate audiences, to stimulate discussion, and to consider and propose solutions to our biosecurity and biosurety concerns. This effort includes, for example, participation in the ongoing efforts of the U.S. National Academy of Sciences and other organizations, and in other activities associated with the creation and operation of biocontainment facilities such as those in Central Asia, Asia, the Americas and in Africa. Our goal is to engage national and international leaders to develop and implement evidence-based policy discussions and eventual agreements that will enhance the security of biocontainment facilities around the world, including in those areas where little or no biosecurity infrastructure currently exists. This is being accomplished by participation in national, regional and international meetings and conferences and other outreach efforts, the facilitation of collaborative studies and investigations, the support of short- and long-term personnel exchanges to address specific goals in biosecurity, the development of programs suitable for a variety of educational methodologies, including ones that are web-based, and

other timely opportunities designed to enhance global biosecurity.

Progress:

- Dr. Jim LeDuc of the NBTC participated in the 2011 Review Conference of the Biological and Toxin Weapons Convention in Geneva, Switzerland during which the U.S. National Academies of Science sponsored a side event to discuss the recently completed report, "*Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories."* Pre-publication copies of the report were provided to the approximately 50 delegates in attendance. Dr. LeDuc participated in the meeting held in Istanbul, Turkey last July that provided the foundation for this report, and he helped in the drafting of the final document (see below). The final report is now available online at the National Academy Press (www.NAP.edu), and a formal release and press conference was held at the National Academies of Sciences Keck Building in June 2012. Dr. LeDuc was one of the three panelists discussing the report.

Dr. James W. LeDuc is pictured at the 2011 Review Conference in Geneva, Switzerland alongside colleagues discussing the "Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories" National Academies report.

- Based on the findings contained in this National Academy of Sciences report, a follow up meeting was held in Kiev, Ukraine in late April 2012. Dr. LeDuc participated in that meeting and contributed three presentations.
- During the reporting year, Dr. LeDuc also participated in a National Academy of Sciences workshop entitled "*Anticipating Biosecurity Challenges of the Global Expansion of High Containment Biological Laboratories"* held in Istanbul, Turkey with the involvement of 68 international experts representing 32 different countries.

- Members of the NBTC participated as presenters at the American Association for Laboratory Animal Science (AALAS) 62nd National Meeting held October 2-6, 2011 in San Diego, California. The title of their presentation was *"Biocontainment Training and Access Process for Animal Care and Research Staff."*

- A member of the NBTC participated in a meeting of the Global Virus Network, a fledgling group of leading experts in virology from around the world. This meeting was held on October 7-9, 2011 in Dublin, Ireland during which two formal presentations were made describing opportunities for training offered by the National Biocontainment Training Center and discussions of possible liaison actions with international organizations and other established networks that include biocontainment laboratories.

- A member of the NBTC was an invited expert guest for a meeting of the National Academy of Sciences' Committee on Evaluation of the NBAF Site Specific Risk Assessment. This is a congressionally mandated effort by the NAS to evaluate a 2nd risk assessment on the proposed replacement laboratory for Plum Island Animal Center in Manhattan, Kansas. The evaluation includes the physical facility as well as operational and manpower issues (including training requirements for laboratory staff). The final report from this committee will be released on July 13, 2012.

- West Point cadets Nicholas Tubbs and Whitney Strong spent part of their summers as interns with the NBTC as a part of the Academy's Academic Individual Advanced Development program. Cadet Tubbs, who is in his final year at West Point, did a biocontainment engineering internship with Miguel Grimaldo in the GNL. Cadet Strong, who is in her third year at the Academy, joined the lab of Dr. Alex Freiberg in Keiller for a research internship. Cadet Tubbs shadowed Mr. Grimaldo and Chris Gibbs during his stay, learning the basics of building engineering from air flow and filtration to electronic monitoring systems and routine maintenance.

Pictured (l to r): Miguel Grimaldo, Alex Freiberg, Cadet Strong, Cadet Tubbs and Jim LeDuc.

Cadet Tubbs commented, "I have learned a lot on the various biocontainment systems and the necessary workings behind a lab. I didn't really understand the complexities or redundancy of the systems before I came here, but now I am learning the various components to the lab." Cadet Strong was involved in two research projects to learn about different laboratory techniques. She worked on the characterizations of Rift Valley fever virus glycoprotein mutants and of recombinant expressed Nipah virus proteins.

- *Publications from the past reporting year include:*
    - Franz, David R. and LeDuc, James W, 2011. Balancing our approach to the insider threat. *Biosecurity Bioterrorism* 9 (3):1-2.
    - LeDuc, James W. and Franz, David R, 2012. Genetically engineered transmissible influenza A/H5N1: A call for laboratory safety and security. *Biosecurity Bioterrorism* 10 (3): 153-4.

Aim 3. To develop and implement a dedicated program to facilitate the establishment, maintenance and administrative oversight of operations of biocontainment facilities.

Background: There are unique requirements for the operations of a biocontainment facility that extend beyond the scientific investigations and the safety and security infrastructure. For facilities such as the regional and national biocontainment laboratories constructed with support from NIH, as well as the independent commercial and not-for-profit institutions and foundations that manage biocontainment facilities and the international containment laboratories such as those now under construction in Central Asia under U.S. Department of Defense support, there is a need for a specialized administrative structure and culture. This culture must be sensitive and responsive to local needs and also address the unique operational challenges associated with the conduct of research and development involving highly dangerous infectious pathogens and the specialized business practices that are critical to sustaining the enterprise. These challenges are especially difficult ones that vary by organization with no standard model fully appropriate for all facilities.

There are some general principles that must be followed; however, in many instances the operational environment at each facility is unique and demands specialized attention. We captured these lessons learned as we brought the GNL online and embarked on the full operation of this national resource. We are developing plans to offer short and longer term training opportunities to administrative staff and institutional leadership of containment laboratories, as well as to students interested in careers in this field. Longer term fellowships are being established to provide relevant hands-on experience to the next generation of the biocontainment industry leaders. We are also creating a standardized checklist of essential tools, skills and procedures that are critical to the safe and secure operations of a biocontainment laboratory. This will include best business practices to ensure fiscal stability in the face of the high costs of security, utilities and specialized equipment required for successful operations.

Progress: A researcher from Turkey who is directly involved in both the scientific investigations and oversight of a newly constructed BSL3 laboratory in Istanbul that will focus primarily on pathogens of agricultural and human health importance began this long-term training program in January 2012. The individual is a DVM, PhD with extensive experience in vector-borne diseases and virology. In addition to her training on containment laboratory operations and management, the scientific focus of her work while at UTMB involves investigations of Crimean-Congo hemorrhagic fever, an important endemic virus disease of growing significance in Turkey and Central Asia. Her work involves virus transmission studies using vector tick colonies that she has helped to establish here at UTMB from material originally collected in Turkey.

Aim 4. To develop and implement training opportunities that focus on the safe and secure operations of novel laboratory instrumentation being introduced into the biocontainment laboratory environment.

Background: The rate of change in laboratory instrumentation and adaptation of novel technologies to the laboratory setting is progressing rapidly. Routine laboratory procedures are becoming more and more automated, saving technicians and investigators time and effort. Technologies that once were so costly as to limit their use to only a few facilities are now affordable for many laboratories. For example, the sequencing of a pathogen or host that once required months or even years of specialized investigation and costly outsourcing, now can be provided in a matter of hours through the use of automated, high throughput instruments never before available to the research community.

As these modern advances make their way into biocontainment laboratories where highly dangerous pathogens are studied, it is not always clear what safety concerns might exist. For instance, many automated pieces of equipment such as flow cytometry include procedures that could generate an infectious aerosol during wash steps or other routine operations, which might place laboratory workers at risk of accidental infection if appropriate precautions are not utilized. Decontamination of such instrumentation for service and maintenance is another major challenge. In addition, modern imaging equipment is now finding greater application within the research community. Both *in vivo* and *in vitro* imaging techniques and equipment are becoming available for use within the biocontainment laboratory environment for use in pathogenesis studies involving live animals or cell cultures infected with especially dangerous agents. Further, it is now possible to grow relatively large volumes of pathogens using modern bioreactor technology. The development of safe operating procedures, guidelines for product processing, and training on the safe use of each piece of equipment necessary for the production, processing and storage of the resultant product is required. There is an urgent need to develop well-validated procedures to safely and securely conduct these important studies while ensuring the safety of investigators and the surrounding environment.

Under this aim, we are focusing specifically on those processes that might generate infectious aerosols when live pathogens are investigated and on those instruments that will require decontamination prior to service by external personnel who may not be equipped to work in a biocontainment setting. A product of this effort will be the creation of detailed standard operating procedures to ensure the safe analysis of material originating from potentially infectious substances and the development of specialized safety interventions to be used to protect workers at all levels of biocontainment. Our efforts are focused on the BSL2 laboratories where the majority of this equipment is located and where the greatest number of users exists; however, we are also examining these resources when they are in use within BSL3 and BSL4 laboratories.

Progress: Administrative procedures are in progress to establish support for personnel under this aim. The funds have not yet been expended. An update will be provided in future reports.

Aim 5. To develop and implement policies, procedures and training programs for the safe and secure conduct of preclinical studies to be undertaken within biocontainment at biosafety laboratory levels 2, 3 and 4 (BSL2, 3, 4) in compliance with the U.S. Food and Drug Administration(FDA) Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

Background: There is a growing requirement for the development of diagnostic tests, drugs and vaccines for use in the recognition, treatment and prevention of biological terrorism threats and emerging infectious disease agents. Bioterrorism threats are among the most dangerous infectious pathogens known to humankind, and their safe and secure handling must be done within the confines of specially constructed biocontainment laboratories. The level of biocontainment needed is specific to each particular pathogen and is layered from the lowest level, BSL2, to "high containment" found in BSL3 facilities, to "maximum containment" found only in BSL4 laboratories (highly complex facilities built with special air handling, waste sterilization and other safety and security protections incorporated into the physical plant and routine operations).

In order to be formally approved for use in humans, products developed for potential application in humans must be evaluated for safety and efficacy during preclinical studies using laboratory animals under safe conditions of biocontainment prior to undergoing clinical safety and efficacy testing in human clinical trials. In addition, in certain cases where efficacy testing in humans is logistically or ethically impractical, products may be approved under the FDA's "Animal Rule" which allows for efficacy to be demonstrated in appropriate animal models. Preclinical safety and animal rule efficacy studies must be conducted by appropriately trained personnel under standardized conditions using well defined procedures and validated equipment as described in 21 CFR Part 58, commonly referred to as Good Laboratory Practices.

Each of these studies is likely to encompass activities across multiple levels of *in vitro* and animal biocontainment and, to date; few organizations have undertaken carefully regulated studies on these highest threat pathogens. Processes and procedures needed for formal GLP studies in biocontainment have generally not been created or have not been tested in actual

working biocontainment facilities.

Progress: We are currently preparing for support of GLP-compliant studies to be performed at BSL3 or BSL4 using laboratories in the GNL and elsewhere on the UTMB campus. The FDA requires that critical drugs and reagents are protected from potential mix-ups or contamination. We are preparing standard operating procedures and associated equipment files for a dedicated regulatory studies support laboratory and general BSL2 laboratory, located on the 6th floor of the GNL.

The dispensary laboratory is intended to provide a dedicated space for critical reagent (e.g. test and control articles) receipt, storage and handling and is equipped with a suite of basic laboratory equipment that has been validated according to a set of general operating parameters for storage and measurement of reagents. Likewise, a general BSL2 laboratory is being established for use on regulated (GLP) and other sponsored studies that require restricted access and/or segregation of laboratory work to meet compliance or contractual requirements. In addition to standard equipment consistent with other GNL BSL2 laboratories, this laboratory will house blood and clinical chemistry analyzers and a Tecan automated plate handling system. These lab spaces can be used to support studies in a GLP compliant manner and, when not in use for a compliant study, will be used to train facility personnel and validate potential test models and supporting procedures.

GNL and UTMB personnel are continuing to develop standard operating procedures and associated documentation to support safe and secure future operations of those laboratories and to facilitate training of study personnel in appropriate performance and documentation of activities that would be performed in those dedicated laboratories. In addition, personnel are working with other GNL cores/divisions, UTMB Environmental Health and Safety, and individual investigators to develop specific procedures for quality assurance unit (QAU) oversight of studies performed in high biocontainment laboratories at UTMB and for validation of significant laboratory equipment, methodologies and information systems infrastructure that may be used in support of future product development-related studies in compliance with FDA regulations for product licensure. This is a long process that will require significant investments of time and effort to develop the robust program needed to ensure successful regulated studies conducted under biocontainment conditions.

Key Research Accomplishments. Significant progress has been made in addressing each of the Aims identified for study, with the exception of Aim 4, that deals with safety precautions of modern laboratory equipment. The level of international engagement with laboratory scientists and biosafety officers around the world has been exceptional and clearly demonstrates a substantial demand for the training we are offering. We have been especially gratified by the warm reception and very positive comments that we have received from our colleagues dealing with biocontainment building maintenance and operations. This is a critically important link in the continued safe and secure operations of biocontainment laboratories, yet there is virtually no international source of guidance or established best practices. We are proud to be at the forefront of addressing this need.

Reportable Outcomes. Important partnerships and exchanges have been established both with international biosafety associations and with the individual leadership of international biocontainment laboratories. Further, several individuals have benefited from extensive training on site at UTMB or at their home facility. These are significant steps towards developing leaders around the world and will serve as a foundation for future growth and dissemination of best practices to a much wider international audience.

Conclusions. The value of international engagement on a personal level cannot be overstated. The friendships and mutual respect that develops through our training efforts not only enhances the safe and secure operations of containment laboratories around the world, but it also fosters a culture of trust and transparency that directly enhances global security.