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14. ABSTRACT The National Biocontainment Training Center (NBTC) provides standards-based theoretical and practical training to trainees and professionals preparing for work in biocontainment laboratories where especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL-2), BSL-3 and BSL-4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee.					
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W81XWH-09-2-0053 (NBTC1) Final Report May 2009 – December2014

Table of Contents	1
Introduction	2
Body	
Staffing Report	2-4
NBTC Training	4
Specific Aims 1-6	4-8
Table 1. Summary of Courses/Participants	9
Key Research Accomplishments	10
Reportable Outcomes	10
Conclusions	11
Quarterly Report submitted October 2014	12
Annual Report submitted June 2014	20
Annual Report submitted June 2013	52
Annual Report submitted June 2012	81
Annual Report submitted June 2011	103
Annual Report submitted June 2010	125

INTRODUCTION

Since 2009, the National Biocontainment Training Center at UTMB has relied on a team of Environmental Health and Safety professionals, scientists, engineers and technicians to provide student assessments and customized training to professionals working in the field of biocontainment.

Through the years the team has worked collaboratively to design and deliver training with a staff that has generously shared its expertise with students and other trainers, collectively creating a team that is considered to be among the most experienced biocontainment training teams in the United States. The information on the following pages summarizes the activities of this staff and other UTMB colleagues who have worked together within this grant to provide training to students from the U.S. and around the world.

Moving forward, the staff of the National Biocontainment Training Center will continue to use their expertise not only to train professionals to work in biocontainment laboratories, but also to provide critical training to clinical professionals who work with infectious diseases. The need for this type of training became apparent during the “Ebola” crisis in 2014, and the staff of the NBTC and UTMB were called upon for their expertise to provide guidance and training at health care clinics, to EMTs and emergency responders, and for hospitals in Texas and beyond.

It is important to note that this grant has provided the opportunity to create a biocontainment training team with depth and expertise that is truly exceptional.

BODY

TATRC’s financial support for the NBTC formally began on May 22, 2009 and this submission comprises our final report for this initiative. This support has allowed for the expert trainers at UTMB’s NBTC to provide more than 7,800 units of training.

Staffing

Staffing Report.

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. Below is a summary of the individuals supported in part by the TATRC award over the past reporting year and their roles in the operation and management of the NBTC.

Dr. Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr. Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr. Ksiazek also oversees the BSL4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL4 environment.

Dr. Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr. Anne-Sophie Brocard, an accomplished virologist and experienced biosafety trainer who has directed the

training center courses since their inception. Dr. Brocard provides both theoretical and practical training to trainees and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms. Je T'aime Newton. Dr. Brocard is ably assisted by Ms. Je T'aime Newton, a highly experienced instructor with extensive expertise in biocontainment. Ms. Newton provides specialized training at all levels of containment, but is specifically responsible for preparing trainees for BSL4 investigations, focusing her efforts on the proper care, use and maintenance of the protective "space suits" used in the BSL4 laboratory and other aspects of work in this highly specialized environment.

Ms. Vicki Jones. Ms. Jones is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera. Ms. Rivera is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical animal training modules.

Mr. Jason Hardcastle. Mr. Hardcastle is a trainer and assists Ms. Jones and Rivera with the training of students, specializing in *in-vitro* techniques.

Ms. Dee Zimmerman. Ms. Zimmerman is the director of the University's biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Mr. Rodrigo Marques dos Santos. Dr. Santos works with ticks and tick borne pathogens, mainly tick-borne encephalitis virus. He has worked with ticks and BSL4 agents within the maximum containment laboratories. He has completed mentored BSL4 training and now has independent access to the BSL4 laboratories.

Ms. Sharon Walters. Ms. Walters serves as the business coordinator for the NBTC and is involved in the outreach program as well as registration process for all external trainees, nationally and internationally.

Dr. Janice Endsley. Dr. Endsley is an assistant professor on the UTMB faculty. Dr. Endsley is an expert in tuberculosis and works with XDR-TB. Dr. Endsley will complete her fellowship in June, 2014. She has gained important experience and has mastered skills needed to work in this environment.

Dr. Han Xia. Dr. Xia Joined the NBTC fellowship program in October, 2013 as part of an agreement with the Wuhan Institute of Virology in Wuhan, China – part of the Chinese Academy of Sciences – where she is a research assistant.

Dr. Dennis Bente. Dr. Bente is a BSL4 research scientist with the GNL at UTMB. He is an assistant professor in the Department of Microbiology & Immunology and he serves as a BSL4 scientific mentor for the NBTC. Dr. Bente's research concentrates on understanding how viruses cause disease with special focus on the pathogenesis of Crimean-Congo hemorrhagic fever virus and its transmission by tick vectors.

Dr. James LeDuc. Dr. LeDuc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr. LeDuc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions and he has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

Through the years there have been other research scientists, research fellows, faculty and staff of UTMB involved in training efforts. Their names and contributions are included in the various reports corresponding to their efforts. They include Gary Bowick, Paige Camess, Lee Thompson, Joan Geisbert, Tom Geisbert, Aysen Gargili, and Sarah Ziegler.

NBTC Training

As previously stated in quarterly and annual reports, the NBTC has developed a highly successful system for training individuals who will work in biocontainment. Since the inception of the University of Texas Medical Branch's Laboratory Biosafety Training Program in 2005, more than 8,500 training units have been provided. Each year the number of training courses and people trained has grown. Those who have received training specifically since the start of this training grant are summarized in the chart on page 9. Throughout the tenure of this program, the team at UTMB has been focused on the following Specific Aims:

Specific Aims

***Aim 1:** To provide standards-based, high containment laboratory safety knowledge.*

***Aim 2:** To provide standards-based, high containment laboratory hands-on training.*

***Aim 3:** To provide topic-specific training.*

***Aim 4:** To provide a mentorship program for scientists working in BSL3/ABSL3 or BSL4/ABSL4 facilities.*

***Aim 5:** To establish a fellowship program for scientists and building engineers working in BSL3/ABSL3 or BSL4/ABSL4 facilities.*

***Aim 6:** To provide training in Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.*

Progress on these Aims since the last reporting period is summarized below and through page 9. Prior progress on these Aims is included in the detailed reports for each reporting period, as listed in the Table of Contents.

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

In addition to the training detailed in the reports listed above, standard training activities for UTMB staff, students and laboratory personnel from outside the university continue through the present time. The number of individuals trained at each level since the beginning of the training grant is summarized in **Table 1** on page 9.

Prior to training, each trainee is tested to determine their base level of knowledge in biocontainment. All training is individualized based on the needs of the student. The topics covered in the basic training units include basic laboratory safety precautions for laboratory work, including the protocols and regulations that are designed to protect both individuals and the environment from accidental contamination by an infectious microbe. Basic training covers topics like the proper use of a biological safety cabinet, as well as routine cleaning of the work

environment. In addition, training covers appropriate procedures for clean-up and decontamination following a spill, the care and use of autoclaves, essential equipment use, safety factors, and clean-up.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, hands-on training in the laboratory setting. Course content is tailored to include the use of specific equipment and the application of procedures that are likely to be a part of routine laboratory work. The training is customized for the individual or group being trained. Those destined to work in a specific type of lab, such as a virology laboratory, will receive training focused on those protocols that are most appropriate for use in a virology laboratory. Individuals who will work with bacteria will learn protocols for working with bacteria. There are, of course, common practices used in any biocontainment laboratory, and training on the safe conduct of these procedures is the foundation of the coursework. The ratio of instructor to student is always maintained at a low level, such as 1:1 or 1:2. All training continues to be based on personalized interaction between the instructor and the trainee. Procedures that are essential to day-to-day laboratory work are practiced under the close supervision an instructor. Training procedures involve the use of indicator dyes that allow clear recognition of contamination. Trainees are able to quickly grasp the key teaching points and rapidly master safe laboratory practices. Training is offered in the fully equipped training laboratory under “mock” circumstances.

Aim 3: To provide topic-specific training.

Autoclave Operations. We continue to provide training on the proper use of autoclaves, which is an important skill for all persons working in containment laboratories. Through the years, topic-specific training on autoclave operation has been a part of the orientation for all individuals who will work in the Galveston National Laboratory. In addition, we have provided autoclave training to individuals from other laboratories, universities, and military institutions. More than 300 people have received autoclave training since the start of this training grant.

Aerobiology. Scientific research relies on aerobiology for effective and safe exposures and challenge studies when working with pathogens in the laboratory. As the Aerobiology Service Division at the Galveston National Laboratory has continued to develop experience, members of that team have developed specific training modules and topics that have been provided to students going through the ABSL training courses. New SOPs have been drafted and training has been provided for UTMB students, staff and trainees from around the country. During the last quarter, two UTMB research scientists have been working on acquiring the required number of mentored hours to receive independent access to the ABSL4 Aerobiology Lab. They are Dr. William Lawrence and Dr. Satheesh K. Sivasubramani.

High Through-Put Screening. Specialized training in high through-put screening is provided on a regular basis, primarily to medical students and visiting scientists. Staff take advantage of new trainings by vendors to learn about emerging technologies and the use of new equipment. In addition, as the NBTC training program has developed with this grant, training has been added that provides instruction on conducting data analysis for different assays and diagnostic systems used in research.

BSL4 Training. Training to work in a high containment laboratory can take anywhere from six months to two years on average. Much depends on the dedication and time commitment of the trainee, as well as the schedules of the safety team and individual mentors. At the end of 2014, there were eight new trainees who had gained independent access to the BSL4 labs. One took approximately seven months, and most took over a year. The process for independent status is complex. In 2014, 17 individuals began their training, and 12 others moved into the mentored training phase.

ABSL2/3 Training. Training to work in animal laboratories is difficult to find, and the programs that have been created as a result of the NBTC grants are unique as well as comprehensive. There are both theoretical and hands-on training opportunities, and many of the instructors have years of experience working in animal research. In Feb. 2015, Dr. Curtis Klages, chief veterinarian for the Galveston National Laboratory and one of the leaders in our animal training program was named Veterinarian of the Year by the Texas Branch of the American Association of Laboratory Animal Science. The ABSL2 and ABSL3 programs are open to both UTMB and non-UTMB staff. Currently, these classes are offered monthly or as needed both internally and externally. There is an increasing demand for this type of training both nationally and internationally.

Non-Human Primate (NHP) Training. The NBTC is one of the few places where trainees can receive NHP training. The programs that have been created and offered through this training grant include both intensive, personalized training program. Individuals who qualify for the Non-Human Primate Training receive extensive one-on-one attention and mentorship. The training includes animal handling and regulatory components, and as new issues arise in this area they are added to the NHP program.

Specialized Classes. Specialized courses are both developed and delivered to individuals as needed to meet their occupational needs. Special training courses might include agent-specific training to complement specific research going on in the UTMB laboratories to ensure that individuals are familiar with the biological agents currently under study on the UTMB campus. Expertise in course design allows training to focus on unique requirements to prepare trainees to work with specific agents or to address the signs and symptoms of exposure. Emergency response training also can be specialized based on the specific work of a laboratory or the individual needs of a research professional or laboratory employee.

External Training Highlights. Training of individuals who are not affiliated with UTMB occurs regularly and is in high demand. We receive requests from some of the nation's most prominent research facilities. During the last quarter of 2014, we began work with two professionals from Boston University's NBL, NEIDL. These individuals took basic training in December and returned to Galveston in early 2015 to begin mentorship of 100 hours. This training is taking place after the expiration of the training grant and is an example of the continued need for the type of specialized training that has been developed with the NBTC grant over the last several years. The last quarter of 2014 included:

- ABSL2 training (theoretical and practicum):
MD Anderson (1 individual for theory and practicum)
Baylor College of Medicine (1 individual for theory and practicum)

- ABSL3 training: training done at their institutions
Baylor College of Medicine (7 individuals for theory, 4 individuals for practicum, for skill certificate training- at BMC)
- BSL2 training
Microbial discovery group (11 individuals for theory, 6 for practicum- at MDG location)
City of Houston- HHS (1 individual for theoretical and practicum)
UT Health Science Center – Houston (1 individual for theoretical and practicum)
Baylor College of Medicine (1 individual for theory and practicum)
- BSL4 training, as mentioned above:
NEIDL-Boston (2 individuals completed facility and suit training- they will be returning in 2015 to UTMB for mentorship training for independent access: one for BSL4, 1 for ABSL4)

Aim 4: To provide a mentorship program for scientists working in BSL3/ABSL3 or BSL4/ABSL4 facilities.

Mentored training typically extends beyond a given reporting quarter. The BSL3 and BSL4 mentorship program provides a hands-on training experience under the tutelage of a senior staff scientist (mentor) with guidance from other experienced laboratorians in the real-world environment of a functioning biocontainment laboratory. The experience includes an orientation to the laboratory environment by a senior scientist working at that level of biocontainment and then hands-on experience with tasks germane to the proposed tasking of the person being mentored.

Through the years, as the GNL laboratory has taken on a robust portfolio of research projects, the experience of our scientists and staff has grown, providing unprecedented opportunities for mentoring that are hard to find not only in this country but around the world. Over the course of the NBTC grant, 259 individuals have benefitted from a customized mentoring program. This number has grown each year, from just nine in 2009 to 59 individuals in 2014.

Aim 5: To establish a fellowship program for scientists and building engineers working in BSL3/ABSL3 or BSL4/ABSL4 facilities.

High and maximum containment fellowship program for scientists. The high and maximum containment fellowship program for scientists is in place. The university receives regular inquiries and interest in these fellowships, both from students in the United States and those abroad. Throughout the years there have been several individuals who have benefitted from this unique opportunity. They are detailed in the reports that follow. As of the end of 2014, one individual remains in fellowship through this program: Dr. Han Xia. Extensive information on the research of Dr. Xia has been detailed in previous reports. In the summer of 2014, Dr. Janice Endsley completed her training and is now working independently in the laboratories at UTMB conducting important research on TB/HIV coinfection using a unique humanized mouse model.

Dr. Xia's work on Crimean-Congo hemorrhagic fever virus and her collaborations with her home university in China will continue to be documented in our companion project report – Award Number W81XWH-11-2-0148, National Biocontainment Training Center, even as this award closes out.

Laboratory Containment Operations Training Program. This program, which formerly operated as a fellowship has been retitled the Biocontainment Facility Engineering Training Program. It has evolved into a sought-after one week intensive course that is offered twice each year by the National Biocontainment Training Center. This program was designed to offer unique and individualized training for engineers covering the basic requirements of commissioning, operation, maintenance, and ongoing validation of Biosafety Level (BSL) 2, 3, and 4 laboratories. There were four professionals who received training in October 2014, and the most recent training session was held in January 2015 for two engineering professionals from China. Detail on that training will be covered in a future quarterly report for the companion grant that continues to support the National Biocontainment Training Center.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Topics in Biosecurity Symposia Series. As part of our participation in the national dialogue on biosecurity – and as a service to the research community – this grant has supported a distinguished speaker series that has been offered for several years. The *Topics in Biosecurity Symposia Series* completed 2014 with a Dec. 2 event attended by more than 100 scientists and graduate/post-doc students. The lecture by Dr. Tara O'Toole, former Under Secretary for Science and Technology in the Office of Homeland Security, was entitled "Policy Implications of the Life Sciences Revolution." It offered an eye-opening look toward the future and discussions about how science and science policy will impact the changing demographics, biosecurity concerns, and other issues that will arise. This popular seminar series has become a favorite of the local science community. Presenters give of their time without honorarium, and in addition to their lectures, they spend time with graduate students and research professionals discussing important issues and creating ties that have proven valuable in furthering long-term collaborations.

Dr. James Le Duc presents Dr. Tara O'Toole with a certificate of appreciation and a coin depicting the Galveston National Laboratory after her Dec. 2, 2014 lecture at UTMB.



Table 1: Comprehensive Training Numbers – 2009 through 2014

Training Course/Module	May-Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-Dec 2013	Jan-Dec 2014	Total
BSL2 theoretical	107	144	251	160	133	165	960
BSL2 hands-on	64	76	92	117	102	134	585
ABSL2 theoretical	N/A	1	79	149	284	116	629
ABSL2 hands-on	N/A	1	40	76	105	116	338
BSL3 theoretical	45	119	100	135	86	125	610
BSL3 hands-on	45	101	94	76	57	49	422
BSL3 mentorship	36	41	24	18	14	26	159
Class III cabinet theoretical (New course)	N/A	N/A	N/A	N/A	N/A	2	2
Class III cabinet hands-on (New course)	N/A	N/A	N/A	N/A	N/A	2	2
ABSL3 theoretical	29	55	47	73	76	36	316
ABSL3 hands-on	29	50	46	37	53	29	244
ABSL3 mentorship	N/A	N/A	38	19	26	34	167
BSL4 Training, orientation and mentorship	9	28	59	47	41	59	244
ABSL4 program	N/A	N/A	N/A	N/A	N/A	18	18
Non-human primate theoretical	16	15	60	41	20	24	176
Non-human primate, hands-on	N/A	N/A	90	41	28	23	182
Non-human primate annual refresher	N/A	N/A	37	114	89	108	348
Animal handling certificates	N/A	N/A	22	75	39	27	163
Graduate Program	39	36	32	13	18	25	163
Introduction to Microbiology	18	0	6	4	0	0	28
Aerobiology	19	5	2	8	0	2	36
Autoclave	195	27	46	30	25	14	337
High Throughput Safety training	8	11	3	2	17	12	53
PAPR (respirator training)	N/A	10	49	52	78	82	271
ABSA/AfBSA courses*	84	175	87	207	181	137	871
Agent specific training	N/A	N/A	N/A	N/A	186	141	327
Specialized Biosafety course	N/A	N/A	N/A	N/A	N/A	71	71
Ebola response training	N/A	N/A	N/A	N/A	N/A	177	177
Total trained	743	895	1,304	1,494	1,658	1,754	7,848

KEY RESEARCH ACCOMPLISHMENTS:

- Our comprehensive, standards-based training program was continued and expanded to prepare individuals for work at all levels of biocontainment.
- Advanced, mentored training was provided to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL4 level.
- Our unique fellowship was continued to provide training to the next generation of containment laboratory facility operations professionals to prepare them to oversee the safe operations of these complex facilities.
- As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we continued to offer our unique seminar series, *Topics in Biosecurity*. Sessions offered continue to be attended by large crowds and draw positive attention and feedback. Planning is underway to continue the series in 2015.

REPORTABLE OUTCOMES 2013-2014:

- Since the inception of UTMB's Laboratory Biosafety Training Program, prior to the TATRC funding award in 2009, nearly 8,500 training units have been provided covering safe research practices and operations in biocontainment laboratories. The vast majority of these trainees have taken part in the program since 2009 when TATRC funding allowed for significant growth of the program.
- Requests for external biosafety training continue to be received in increasing numbers providing clear evidence of the strong demand for high quality training in biosafety and biosecurity.

CONCLUSIONS:

While the traditional means of support for the work described in this document is coming to a close, there is no doubt that the important accomplishments that were the aims of this program must continue on. Demand for the training described above is only increasing, and new inquiries are received on a regular basis. For example:

- In the wake of the Ebola crisis in October 2014, the NBTC received daily calls from hospitals, clinics, and EMT organizations that realized they were not trained to deal with the safety concerns in their jobs.
- The Texas Task Force on Infectious Disease and Preparedness helped to create a higher profile for the NBTC and its efforts and requested a training video for state hospital and healthcare workers. This project may go forward if funding can be secured. Options are being pursued.
- The Development team at UTMB has taken an increased interest in the important work of the NBTC in keeping laboratory scientists and the communities where biocontainment laboratories reside safe. In Galveston, the university's development staff has been responsible for introducing private foundation representatives to the work of the NBTC. In February 2015, a major gala in Galveston has designated the NBTC as the beneficiary of its proceeds and will recognize five UTMB research scientists as their gala's honorees.

In the wake of these new opportunities, the staff of UTMB also recognizes the need to continue to provide established training modules for students at all levels of biocontainment. There also is commitment to continue to invite distinguished leaders in the field of biosecurity to participate in the ongoing symposia series. Everyone involved remains committed to focusing on ensuring both domestic and international aspects of biosecurity.

The following pages include previously filed reports.

QUARTERLY REPORT June – September 2014

10. Comments on administrative and logistical matters.

Staffing report. The National Biocontainment Training Center at UTMB relies on a team of Environmental Health and Safety professionals, scientists, engineers and technicians to provide the customized, one-on-one training and assessments for students and professionals working in the field of biocontainment. The team remains very active, and during this quarter, Melary Jones joined the team to provide administrative support, replacing an employee who left during the prior quarter.

11. Use additional page(s), as necessary, to describe scientific progress for the quarter in terms of the tasks or objectives listed in the statement of work for this assistance agreement.

As previously stated in quarterly and annual reports, the NBTC has been operating for many years, with a portfolio of courses in place and a successful system for training individuals who will work in biocontainment. Since the inception of the NBTC, the team has delivered more than 7,700 training units. A summary of the efforts made and training provided during the current reporting period is located within this report. Activities and accomplishments are organized by each specific aim as they were presented in our original proposal.

The progress reported here complements activities summarized separately in a companion project (Award Number W81XWH-11-2-0148, also titled National Biocontainment Training Center). Together these awards support a coordinated effort to provide critical training and hands-on experience to national and international scientists working with especially dangerous pathogens that require special biocontainment facilities for their safe and secure handling.

Specific Aims:

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the quarter. The number of individuals trained at each level is summarized in **Table 1** below. The topics covered in the basic training units include basic laboratory safety precautions, including the protocols and regulations that are designed to protect both individuals and the environment from accidental contamination by an infectious microbe, the use of a biological safety cabinet, as well as routine cleaning of the work environment. In addition, training covers appropriate procedures for clean-up and decontamination following a spill, the care and use of autoclaves, essential equipment use, safety factors, and clean-up.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, hands-on training in the laboratory setting. Course content is tailored to include the use of specific equipment and the application of procedures that are likely to be a part of routine laboratory work. The training is customized for the individual or group being trained. Thus, those destined to

work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL2 laboratory, and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals. This allows for personalized interaction between the instructor and the trainee. Procedures that are essential to day-to-day laboratory work are practiced under the close supervision an instructor. Training procedures involve the use of indicator dyes that allow clear recognition of contamination. Trainees are able to quickly grasp the key teaching points and rapidly master safe laboratory practices. Training is offered in the fully equipped training laboratory under “mock” circumstances.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in the containment laboratories is the need to be able to properly operate the autoclaves. A dedicated training session (and/or refresher training session) is offered to all individuals as a standard and separate element of their orientation to the Galveston National Laboratory (GNL) and this training is also offered to individuals working in other laboratories using the same or similar equipment. The number of autoclave trainees during the current reporting quarter is also noted in the table below.

Aerobiology. The Aerobiology Service Division has continued to develop experience performing aerosol challenge studies in the GNL BSL4 aerobiology facility this past quarter. Challenges and agents have included Ebola Zaire virus and Nipah virus. The aerobiology team has also conducted aerosol exposures to *Yersinia pestis* and *Burkholderia pseudomallei* in the ABSL3 facility, which provided additional training for the group.

Drs. Johnny Peterson, William Lawrence and Jason Comer have drafted a formal qualification plan for validating the BSL4 Biaera AeroMP platform. Qualification has begun in the UTMB Office of Regulated Nonclinical Studies (ORNCs) with formal review of the plan. This work is focused on validation of the BSL4 aerosol system used in the GNL BSL4 facility. Drs. Lawrence and Satheesh Sivasubramani have completed their biosafety training with NBTC trainers. Dr. Sivasubramani is an aerosol scientist who was recruited from the Tulane Primate Center. He has made tremendous progress in training in the aerobiology facilities. Aerosol challenge studies have been performed in collaboration with Dr. Curtis Klages, the GNL biocontainment veterinarian. Dr. Lawrence has completed exploratory studies with Dr. Klages using the GNL PET-CT radiographic equipment with non-infected animals. Work is currently underway to develop biocontainment device to enable scans of infected animals.

High Through-put Screening. During this reporting period, two Pediatric residents, a Pathology resident and a second year medical student received training in high through-put screening. In addition, both a research scientist and undergraduate student visiting from the Oak Crest Institute of Science were trained in a number of our specialized molecular protocols. The three residents and the medical student were trained in nucleic acid extraction protocols and received instruction and validation for quantitative real-time PCR (qPCR). Further, one of the Pediatric residents was instructed in the use and design of pyrosequencing assays using our PyroMark ID96 platform. The visiting scientists from Oak Crest received instruction in automated DNA

extractions and qPCR methodologies that culminated in their performing a qPCR validation run. All trainees received instruction on conducting data analysis for their respective assays and all training was provided by our senior trainers utilizing the GNL's 96-well format system for validation tests at the completion of their training. Training functions focused on research use only diagnostic systems.

BSL4 Training. Seven individuals matriculated from the mentored training program to independent user status for the BSL4 labs. In addition, our biocontainment engineering staff provided BSL4 facility training to one new scientist and provided one facility training session as a refresher course for one individual.

ABSL2/3 Training. During this quarter, we continued to offer the ABSL2 theoretical and hands-on training program. The ABSL2 theoretical training was offered to 50 individuals, 49 of whom also completed the practicum portion of the course. The ABSL3 theoretical program was offered to 11 individuals and an additional 8 people completed the practicum portion of the training. The ABSL2 and ABSL3 programs are open to both UTMB and non-UTMB staff. Currently, these classes are offered monthly or as needed both internally and externally.

Non-Human Primate Training. During this quarter, we continued to offer the NHP training, which includes both theoretical coursework and an intensive, personalized training program. Six individuals completed the theoretical training program, and five individuals were involved in one-on-one mentored training to prepare them to work with NHPs.

Specialized Classes. Specialized courses are delivered to individuals as needed to meet their occupational needs. During this quarter, nine individuals received instruction in the use of positive air purifying respirators (PAPR) and animal handling techniques at ABSL2/ABSL3/ABSL4. Nineteen individuals received general biocontainment equipment training. Thirty-one people received the required biocontainment laboratory facility training.

- We also offer **agent-specific training** to all of the UTMB Animal Resource Center personnel. This training covers biological agents currently under study on the UTMB campus (ABSL2 - ABSL4) including zoonotic agents. Classes focus on unique aspects of each agent, signs and symptoms of exposure and emergency response. Comprehensive assessments are provided at the end of each session. Classes are offered on a monthly basis to cover the large number of agents being researched at UTMB. This reporting quarter, we offered one additional classes and covered 24 agents. Total attendance in agent-specific training this reporting quarter was 15 individuals. This was the last offering for this training as all infectious agents handled on campus have been covered.

External Training Highlights. Of note during this reporting quarter was NBTC training provided to individuals at the following domestic external institutions/corporations:

- ABSL2 training (theoretical and practicum):
 - University of Houston (2 individuals)
 - MD Anderson (2 individuals)
 - Baylor College of Medicine (1 individual)
- ABSL3 training: training done at their institutions
 - University of Texas El Paso (17 individuals for theory, 4 for practicum)
 - University of Texas Southwestern (14 individuals for theory, 3 for practicum)
 - MD Anderson (2 individuals)

- BSL3 training:
 - University of Houston (3 individuals)
 - University of Texas Southwestern (17 individuals for theory, 8 for practicum) training done at UT Southwestern
 - Georgia Southern University (1 individual for theoretical and practicum)
- PAPR training:
 - Georgia Southern University (1 individual)

Community/External Outreach. During this reporting quarter distinguished guests both visited the training center and were also provided information on the NBTC through various forums. Highlights of these activities follow:

- In January 2014, staff from the University of Texas System's Office of Federal Relations visited the GNL/NBTC. Included in the visit was Ms. Angela Godby, the UT System's Associate Vice Chancellor for Federal Relations; the newly appointed Dr. Michelle Atchison, Associate Vice Chancellor for Federal Relations; and Jana Lozano, Coordinator for Federal Relations (*pictured right*). The group was briefed on the NBTC programs and outreach activities. They also had the opportunity to visit the biosafety training mock-laboratory where a BSL4 demonstration.



- Also in January 2014, NBTC trainer Jason Hardcastle delivered a presentation on the NBTC and his training efforts to the Galveston Rotary Club. This local group of prominent Galveston representatives requested the presentation in an effort to stay abreast of collaborative programs – such as the NBTC – that are underway at the UTMB.

Table 1. Summary of training courses offered and number of participants in each course, May 2009 – August 2014.

Training Course/Module	May- Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-Dec 2013	Jan 2014	Feb- May 2014	Jun-Aug 2014	Total
BSL2 theoretical	107	144	251	160	133	3	39	98	837
BSL2 hands-on	64	76	92	117	102	3	29	69	486
ABSL2 theoretical	N/A	1	79	149	284	8	31	53	555
ABSL2 hands-on	N/A	1	40	76	105	11	29	49	262
BSL3 theoretical	45	119	100	135	86	5	89	23	582
BSL3 hands-on	45	101	94	76	57	6	34	8	416
BSL3 mentorship	36	41	24	18	14	3	7	4	143
Class III cabinet	N/A	N/A	N/A	N/A	N/A	N/A	2	0	2

Training Course/Module	May- Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-Dec 2013	Jan 2014	Feb- May 2014	Jun-Aug 2014	Total
theoretical (New course)									
Class III cabinet hands-on (New course)	N/A	N/A	N/A	N/A	N/A	N/A	2	0	2
ABSL3 theoretical	29	55	47	73	76	0	8	11	288
ABSL3 hands-on	29	50	46	37	53	1	6	8	222
ABSL3 mentorship	N/A	N/A	38	19	26	2	7	4	92
BSL4 Training, orientation and mentorship	9	28	59	47	41	0	24	0	208
Non-human primate theoretical	16	15	60	41	20	0	9	6	161
Non-human primate, hands-on	N/A	N/A	90	41	28	1	7	5	167
Non-human primate annual refresher	N/A	N/A	37	114	89	0	0	0	240
Animal handling certificates	N/A	N/A	22	75	39	4	21	5	161
Graduate Program	39	36	32	13	18	0	0	11	138
Introduction to Microbiology	18	0	6	4	0	0	0	0	28
Aerobiology	19	5	2	8	0	0	0	1	35
Autoclave	195	27	46	30	25	1	7	1	332
High Throughput Safety training	8	11	3	2	17	3	9	0	53
PAPR (respirator training)	N/A	10	49	52	78	0	9	9	198
ABSA/AfBSA courses*	84	175	87	207	181	0	0	40	734
Agent specific training	N/A	N/A	N/A	N/A	186	50	76	15	312
Total trained	743	895	1,304	1,494	1,658	101	445	416	6654

Aim 4: To provide a mentorship program for scientists working in BSL3/ABLS3 or BSL4/ABSL4 facilities.

Mentored training typically extends beyond a given reporting quarter. The BSL3 and BSL4 mentorship program provides a hands-on training experience under the tutelage of a senior staff scientist (mentor) with guidance from other experienced laboratorians in the real-world environment of a functioning biocontainment laboratory. The experience includes an orientation to the laboratory environment by a senior scientist working at that level of biocontainment and then hands-on experience with tasks germane to the proposed tasking of the person being mentored.

As the GNL laboratory was brought online and the Shope laboratory continues to operate, our cadre of experienced BSL3 and BSL4 scientists and scientific staff continues to expand. This is actually decreasing the individual burden of training as it is now spread across a larger number of scientists and staff. The numbers of staff that have passed through the BSL3 and BSL4 mentorship program is presented in **Table 1**.

An extensive listing of the number of all individuals trained during the reporting quarter can be found in **Table 1**.

Aim 5: To establish a fellowship program for scientists and building engineers working in BSL3/ABSL3 or BSL4/ABSL4 facilities.

High and maximum containment fellowship program for scientists. The high and maximum containment fellowship program for scientists is in place. We have two fellows now in training and two fellows who have transitioned from the program. Of the fellows who have completed the program, one moved on to a permanent UTMB faculty position involving BSL4 pathogen research and the second returned to her home country of Turkey to continue her research and assume management of a BSL3 laboratory facility.

There are two fellows currently participating in the program – Dr. Janice Endsley and Dr. Han Xia. Their quarterly updates are below.

Dr. Janice Endsley's fellowship program update. Dr. Endsley is an expert in tuberculosis and is engaged in work with XDR-TB. We anticipate that Dr. Endsley will continue in the fellowship as she gains critical experience and masters skills needed to work in this environment. She is in training in the high and maximum containment fellowship program for scientists for research in the BSL3, ABSL3, and BSL4 laboratories in the GNL. She is principle investigator of the tuberculosis laboratory in the Galveston National Laboratory. She further provides immunology consult for investigators working in BSL3 and BSL4 containment, especially specific to cellular immunology assay planning, performance, and interpretation. In this role she assists other investigators in planning immunology studies for grant development and provides letters of support for application packages.

She is additionally the director of the Flow Cytometry and Cell Sorting Core Facility and advises on flow cytometry equipment issues within biocontainment. Dr. Endsley provides hands on training for all personnel working with BSL3 level mycobacterium including *Mycobacterium tuberculosis (M.tb)* and performance of mycobacterial infections in animal models. This includes graduate students and research technicians from the Endsley lab and other PI (Dr. Jai Rudra, UTMB, Dr. Omonike Olaleye, Texas Southern University) labs desiring to expand their research programs in TB vaccine development and drug discovery. Recently she completed training Ms. Rebecca Nusbaum in the BSL3 for work with mycobacteria and Ms. Nusbaum is now working independently. She is currently training Mr. Matthew Huante for Animal BSL3 (ABSL3) work with mycobacterial and burkholderia infections.

She is also providing direct mentorship for graduate student Brent Chesson in the BSL3 Tuberculosis lab. She additionally works in collaboration with Dr. Alfredo Torres to develop mouse models of aerosol-acquired Mellioidosis due to *Burkholderia pseudomallie* (Tier 1 select

agent) infection. She has developed, optimized, and/or adapted several new techniques for study of *M.tb* or *B. pseudomallei* in the BSL3/ABSL3 including confocal microscopy-based bacterial viability detection, *in vivo* imaging of bacterial infection in live animals, multi-color flow cytometry, multi-plex ELISA, and *in vitro* HIV/TB co-infection assays. Her lab recently published a manuscript detailing the development of an *in vitro* model for screening antimycobacterial and antiretroviral drug compounds for use in people with TB/HIV co-infection (Vijayakumar, et al., 2013, *Tuberculosis*).

Dr. Han Xia's fellowship program update. Dr. Xia joined the NBTC as a fellow in late 2013. She joined the program as part of an agreement with the Wuhan Institute of Virology in Wuhan, China – part of the Chinese Academy of Sciences – where she is a research assistant. Dr. Xia's research interests include viruses, diagnostic assay methodology for infectious diseases, vaccine research, gene function, genomic and evolutionary analysis and epidemiology. She graduated from the Chinese Academy of Sciences and received her doctoral degree in biochemistry and molecular biology. Since then, she has been working on the development of a mini genome system and epidemiological investigations for Crimean-Congo hemorrhagic fever virus in Western China. She completed an epidemiological survey of CCHFV in Yunnan, China in 2008 (*International Journal of Infectious Diseases*, 07/2011; 15(7): e459-63). She is interested in a range of emerging arboviruses but mainly in tick-borne bunyaviruses.

In the current reporting quarter Dr. Xia is continuing her work in the lab of Dr. Dennis Bente in the Galveston National Laboratory. Her research focus is on Crimean-Congo hemorrhagic fever virus (CCHFV) and related nairoviruses. Dr. Xia completed the facility training workshop under NBTC trainer and engineer Miguel Grimaldo in December. She is currently in the midst of BSL3 training with an eye toward progressing on to BSL4 training immediately upon completion – this advancement to BSL4 training should occur this month. She is also working/training with UTMB's Dr. Naomi Forrester on how to analyze new viruses by next-generation sequencing. Additionally, she has joined a collaborative project currently underway working with Dr. Eric Bergeron on a reverse genetics system for Crimean-Congo hemorrhagic fever virus.

A full accounting of her research and fellowship will continue to be included in our companion project report – Award Number W81XWH-11-2-0148, also titled National Biocontainment Training Center.

Laboratory Containment Operations Training Fellowship Program. The biocontainment laboratory building operations and engineering fellowship is unique and is, to the best of our knowledge, the only one of its kind. The program – typically requiring a minimum of two-weeks – promises to set a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, most individuals entering biocontainment facility operators will require a more structured course of study. Consequently, we have identified twelve distinct modules to be covered over the course of the fellowship. These structured modules cover an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, annual certification of laboratories, testing of HEPA filter housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping.

There has been no change in current trainees or supporting information since the previous quarterly report.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over this past reporting period we have continued our active participation in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology, the American

2014 TABLE OF CONTENTS	1
Introduction	2
Body	2
Staffing Report	3-4
Teaching Laboratory Facilities	4-5
Overview of NBTC training	5
BSL2 and BSL3 training	6
Animal BSL2/3 training	7
BSL4 training	7
Specific Aims 1-6	8-24
Table 1. Summary of Courses/Participants	25-28
Figure 7. Total number of courses administered	29
Annually – May 2005 - December 2013	
Figure 8. Job distribution of trainees	30
Annually – May 2005 – December 2013	
Key Research Accomplishments	33
Reportable Outcomes	33
Conclusions	33
References	33

INTRODUCTION

The **National Biocontainment Training Center (NBTC)** provides standards-based theoretical and practical training to students and professionals preparing for work in biocontainment laboratories where infectious agents, possibly including especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL2), BSL3 and BSL4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee. Advanced coursework includes hands-on mentored training in the containment laboratories, including consecutive training at BSL3 and BSL4 levels of containment should that be required by the researcher's needs. Specialized training in the handling of laboratory animals is also offered. Sponsored mentored training is available to scientists embarking on a career focused on high hazard pathogens at the BSL4 level through a dedicated fellowship. Fellows in this program work under the close supervision of an established mentor while addressing a research topic of their own choosing. Mentored scientists and fellows progress to full independent access to the BSL4 laboratory only when their mentor and laboratory director are fully confident of the individual's skills and abilities to work independently in this environment.

The NBTC also offers a unique training opportunity for facility operations specialists interested in pursuing a career as a biocontainment operations manager. To the best of our knowledge, this is the only such training program in the world. This program is designed as a series of modules which address specific aspects of the construction, maintenance and safe operation of a biocontainment laboratory. The coursework is tailored to the specific needs of the individual trainee and involves both didactic training and mentored hands-on work using the Galveston National Laboratory (GNL) as its classroom. Over the course of the training period the fellow(s) will be directly involved in the maintenance of the laboratory, decontamination of specific laboratories, monitoring and replacement of filters, fans and control units, understanding the Building Automation System (BAS), and a wealth of other duties routinely seen in the operations of typical biocontainment facilities.

BODY

TATRC's financial support for the NBTC formally began on May 22, 2009 and this submission comprises our annual report for the period **June 2013 to June 2014** for this initiative. The Laboratory Biosafety Training Center at The University of Texas Medical Branch was established and operational prior to receiving TATRC funding; consequently, the course structure and procedures were already in place and allowed the NBTC to implement enhanced training operations almost immediately. From inception to date, the NBTC has provided training to nearly 7,400 participants since program inception through the various courses offered. Below is a summary of the significant progress made over the preceding year (2013-2014) under TATRC support. Funding and accomplishments are organized by each specific aim as they were presented in our original proposal.

Staffing Report.

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. Below is a summary of the individuals supported in part by the TATRC award over the past reporting year and their roles in the operation and management of the NBTC.

Dr. Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr. Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr. Ksiazek also oversees the BSL4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL4 environment.

Dr. Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr. Anne-Sophie Brocard, an accomplished virologist and experienced biosafety trainer who has directed the training center courses since their inception. Dr. Brocard provides both theoretical and practical training to trainees and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms. Je T'aime Newton. Dr. Brocard is ably assisted by Ms. Je T'aime Newton, a highly experienced instructor with extensive expertise in biocontainment. Ms. Newton provides specialized training at all levels of containment, but is specifically responsible for preparing trainees for BSL4 investigations, focusing her efforts on the proper care, use and maintenance of the protective "space suits" used in the BSL4 laboratory and other aspects of work in this highly specialized environment.

Ms. Vicki Jones. Ms. Jones is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera. Ms. Rivera is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical animal training modules.

Mr. Jason Hardcastle. Mr. Hardcastle is a trainer and assists Ms. Jones and Rivera with the training of students, specializing in *in-vitro* techniques.

Ms. Dee Zimmerman. Ms. Zimmerman is the director of the University's biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Mr. Rodrigo Marques dos Santos. Dr. Santos works with ticks and tick borne pathogens, mainly tick-borne encephalitis virus. He has worked with ticks and BSL4 agents within the maximum

containment laboratories. He has completed mentored BSL4 training and now has independent access to the BSL4 laboratories.

Ms. Sharon Walters. Ms. Walters serves as the business coordinator for the NBTC and is involved in the outreach program as well as registration process for all external trainees, nationally and internationally.

Dr. Janice Endsley. Dr. Endsley is an assistant professor on the UTMB faculty. Dr. Endsley is an expert in tuberculosis and works with XDR-TB. Dr. Endsley will complete her fellowship in June, 2014. She has gained important experience and has mastered skills needed to work in this environment.

Dr. Han Xia. Dr. Xia Joined the NBTC fellowship program in October, 2013 as part of an agreement with the Wuhan Institute of Virology in Wuhan, China – part of the Chinese Academy of Sciences – where she is a research assistant.

Dr. Dennis Bente. Dr. Bente is a BSL4 research scientist with the GNL at UTMB. He is an assistant professor in the Department of Microbiology & Immunology and he serves as a BSL4 scientific mentor for the NBTC. Dr. Bente's research concentrates on understanding how viruses cause disease with special focus on the pathogenesis of Crimean-Congo hemorrhagic fever virus and it's transmission by tick vectors.

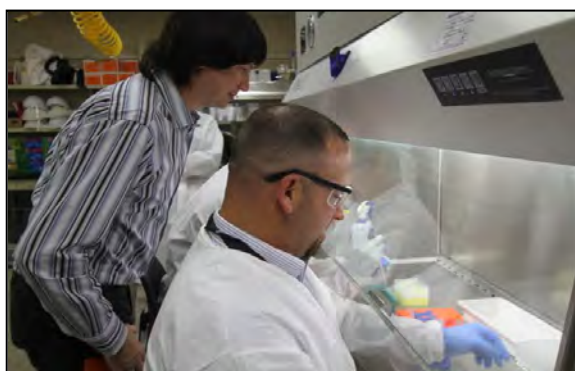
Dr. James LeDuc. Dr. LeDuc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr. LeDuc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions and he has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

Teaching Laboratory Facilities.

The teaching laboratory is a critical asset of the NBTC and it is designed to offer trainees realistic exposure to the conditions and equipment they will typically encounter at each level of biocontainment as they conduct their studies.

At the **BSL2** level, this typically includes a biological safety cabinet where infectious pathogens are handled. (*pictured*). Biological safety cabinets are used at all levels of biocontainment. The teaching laboratory also includes limited specialized equipment, as well as facilities to manage laboratory waste and storage of pathogens. Training for individuals preparing for work in the **BSL3** laboratory includes a dedicated area where individuals master the donning and doffing of protective gear and its proper disposal.

Those trainees going on to prepare for work in the **BSL4** laboratory have specialized instruction in the care and use of the positive pressure encapsulating ensemble or "space suit" that is worn in the most



common type of **BSL4** laboratory in use today (*pictured*). This includes inspection of the suit for any evidence of leaks prior to use, gaining experience and familiarity in the wearing of the suit, use of compressed air hoses, and training in emergency procedures. In order to provide this training under realistic conditions, the training facility has been outfitted with a breathing air compressor and a mock laboratory where trainees can experience wearing the suit and become familiar with working in this unique environment. Some people discover that they experience claustrophobic reactions when wearing a suit; this practical, realistic suit training environment allows them to overcome any such reactions under well-controlled conditions, or decide that this work is not a good fit for them.

Laboratory training is conducted in the mock training laboratory with authentic laboratory equipment utilizing non-infectious materials. Entry into the lab is through a double door anteroom with directional airflow and mock pressure monitors. The laboratory has four class II biological safety cabinets, three of which are constructed with see-through panels which allow the trainer to introduce smoke into the BSC to visualize air movement within the BSC. One BSC class II cabinet also has see-through panels and **BSL4** air connections ports. Two of the BSC cabinets



are equipped with cameras inside that allow for remote demonstrations. The laboratory itself also has two cameras installed for remote demonstrations. The laboratory has two class III biosafety cabinets, incubators, centrifuges, bench top autoclave, refrigerator, -80° freezer, dunk tank, and general laboratory equipment to allow for mock BSL2 to BSL3 and -4 laboratory work. The laboratory is equipped with a compressor and air lines for practice in the suit check examination and use of BSL4 suits within that facility prior to the trainee entering the active BSL4 laboratories. The laboratory also has multiple airline drops allowing the trainee to work throughout the laboratory with the ability to connect and disconnect airlines as needed.

Overview of NBTC Training.

The NBTC provides a series of training modules involving a mixture of didactic instruction and hands-on training to be carried out within an existing mock BSL3/4 training laboratory that is located within the Environmental Health and Safety Office space in the Materials Management Building on the UTMB campus. The intent of the NBTC is to promote good laboratory techniques and safe procedures to be used at all biosafety levels, and to provide consistency in research practices. The program is designed to ensure that all training attendees have the same general biosafety training at BLS2 and -3, and if necessary BSL4, prior to entering an active biocontainment laboratory, thus ensuring that high safety standards are observed and good practice is consistently pursued.

BSL2 and BSL3 Training.

The BSL2 and -3 training provide a multi-phased approach:

- the assessment phase
- the training phase
 - theory
 - hands-on practicum
- final assessment

Each trainee begins with an **assessment phase** that includes a written test focusing on safety related topics, hands-on skills related to protocols based on their research using appropriate biosafety practices and procedures. During the assessment the trainer does not intervene as he/she notes both safety and scientific techniques employed by the trainee. This allows for the determination of experience and level of training that will be required for each trainee. Once the initial assessment is completed the results are reviewed with the trainee, the specific areas of training focus are identified. A written report is then sent to the trainee and their principal investigator or supervisor.



The **training phase** includes a theoretical class which covers the following topics:

- BSL1 through -4 standard microbiological practices, special practices, safety equipment and laboratory facilities.
- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of laminar flow biological safety cabinets (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work, and spill response in the BSC.
- Procedures with the potential for creating infectious aerosols, recognizing aerosol producing devices and learning how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory, BSC, centrifuge, incident response, cleanup, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- Introduction to select agent rules and NIH-Office of Biotechnology Activities guidelines.

The **hands-on practicum** during the training phase compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a non-hazardous environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as scientific issues (e.g. contamination of cultures). The practicum is specific to biosafety and agents to be used (e.g. bacteria, parasites, viruses) by the trainee. This approach also allows the use of specific protocols or facility specific practices that the trainee brings with them. Emergency response and spill mitigation training allows the trainee to visualize and respond to spills and contamination with the use of florescent dye and breakable training lab ware.

The **final assessment** is identical to the initial assessment, with a written exam and hands-on skills assessment. Once the trainee has completed and passed the final assessment, the trainee is provided with a certificate of training for the biosafety level they completed. A report is sent to the principal investigator, the trainee and the laboratory director.

Animal BSL2 (ABSL2), Animal BSL3 (ABSL3), Animal BSL4 (ABSL4) and Non-Human Primate (NHP) Training.

An animal biosafety training program was developed and instituted based on the same concepts as the BSL3 training program. Trainees must have completed BSL3/BSL4 training before commencing ABSL3/ABSL4 training. ABSL2 and NHP training are completed as required by animal specific protocols. Following completion of an animal training program, trainees can return to the program to enhance their animal handling skills for specific techniques and species. All animal use is approved by our institutional animal care and use committee, and our animal holding facilities and procedures have been approved by AAALAC. All aspects of our animal training program have been reviewed and approved by the USAMRMC Animal Care and Use Review Office (ACURO).

The ABSL training phase includes a theoretical class which covers the following topics:

- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the BSC, how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work and spill response in the BSC.
- Procedures with the potential to create infectious aerosols, recognizing an aerosol producing devices and learning procedures to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory or in the BSC, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a safe working environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as animal handling. The practicum is specific to biosafety and animal species to be handled. This approach to training also allows the use of specific protocols or facility specific practices the trainee brings with them.

In the third phase, the final assessment includes a written exam and a hands-on skills assessment. Once the trainee has completed and passed the final assessment the trainee is provided with a certificate of training for the biosafety level they completed.

BSL4 Training.

BSL4 training rests upon a firm adherence to the principles and specific practices of safe BSL-3 research. This practice prevents an over-reliance on the BSL4 suit as a primary means of personal protection, and makes the suit an operationally redundant means of personal

protection, significantly enhancing overall containment. Accordingly, individuals who are selected for BSL4 training will have completed training at BSL3 and have been approved for independent access to the BSL3 laboratories. These individuals would then complete the BSL4 modular training.

Specific Aims.

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the year. The number of individuals trained at each level is summarized in **Table 1** below and the associated figures. As summarized above, the topics typically covered in this introductory training include the principles of basic safety precautions in the laboratory, routine rules and regulations designed to protect the individual and environment from accidental contamination by an infectious microbe, and the care and use of the biological safety cabinet. Also covered are the appropriate procedures of clean-up following a spill, decontamination procedures, principles of the care and use of autoclaves and other essential equipment.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, real-world training in the laboratory setting. Course content is tailored to include those procedures and the use of specific equipment likely to be encountered by the trainee in their routine work. Thus, those destined to work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL-2 laboratory and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals, allowing for intense interaction between the instructor and trainees. By actually doing the procedures essential to their day-to-day laboratory work under the close supervision an instructor (with the use of indicator dyes that allow clear recognition of contamination), the trainee quickly grasps the key teaching points and rapidly masters safe laboratory practices. Training is offered in the state-of-the-art training laboratory described above.

The number of individuals trained under Aim 2 for the NBTC is summarized in **Table 1**.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in containment laboratories is the need to be able to properly operate autoclaves. A dedicated training session is offered to all individuals as a separate element of their orientation to the GNL, and this training is offered to individuals working in other laboratories using the same or similar equipment.



Aerobiology. The GNL contains aerobiology laboratories at both the BSL3 and BSL4 levels of containment. The BSL3 facilities were fully commissioned and approved for use by the CDC and USDA in early 2010, and the GNL BSL4 facilities were approved for full operations in May 2010 with operations beginning in September 2010. These facilities are highly complex and require specialized training not only in the operation of this sophisticated equipment, but also in the proper care and handling of the laboratory animals that will be experimentally infected. Aerobiology personnel receive instruction and specialized training about how aerosols are generated, the safety precautions in place in aerobiology laboratories and how to quantitate virus in aerosol samples.

Gamma Irradiator Training. BSL4 laboratories utilize a number of techniques to inactivate biological materials prior to removal from the containment laboratory. One of the most frequently utilized means of removing materials from the BSL4 laboratory is inactivation by gamma irradiation. In an effort to provide training of individuals that use gamma irradiation at UTMB, a module providing background on radiation biology, radiological and biological safety training, select agent and radiological security training, introductory training on dosage determination and method validation, and practical instruction on the use of the devices used for gamma bombardment was assembled and is offered to staff on an as needed basis.

High Through-Put Screening. We continue to work to develop a systematic training program focused on the safety concerns associated with high through-put screening. We are developing this capability as it represents one of the cutting-edge interfaces between technology and biological sciences and as such potentially creates new challenges for biological safety.

Animal handling skill certificate. Following initial training in ABSL2-ABSL4 individuals return to the training program to continue developing animal handling skills necessary to their research project. Each skill certificate is specific to the species, techniques and biosafety level at which the individual was trained.

Class III Biosafety Cabinet Training. We have in this past quarter developed and taught a new training course that focuses on the use of Class III biosafety cabinet. Class III cabinets have very unique features of design and proper use that differ from the other biosafety cabinets routinely used by researchers. These cabinets are mainly found in aerobiology research and BSL4 cabinet line laboratories.

Aim 4: To provide a mentorship program for scientists working in BSL3/ABLS3 or BSL4/ABSL4 facilities.

Mentored training typically extends beyond a given reporting quarter. The BSL4 mentorship program provides a hands-on training experience under the tutelage of a senior staff scientist (mentor) with guidance from other experienced laboratorians in the real-world environment of a functioning BSL4 laboratory. The experience includes an orientation to the laboratory environment by a senior BSL4 scientist and then working experience with tasks germane to the specific requirement of the person being mentored.

As the GNL laboratory was brought online and the Shope BSL4 laboratory continues to operate, our cadre of experienced BSL4 scientists and scientific staff continues to expand (**Figures 1 &**

2). This is actually decreasing the individual burden of training as it is now spread across a larger number of scientists and staff. The numbers of staff that have passed into and out of the mentorship program is presented in **Table 1**.

An extensive listing of the number of individuals trained during the reporting year can be found in **Table 1**.

Figure 1. Cumulative Number of Independent BSL4 Users – January 2005-January 2014, Galveston National Laboratory

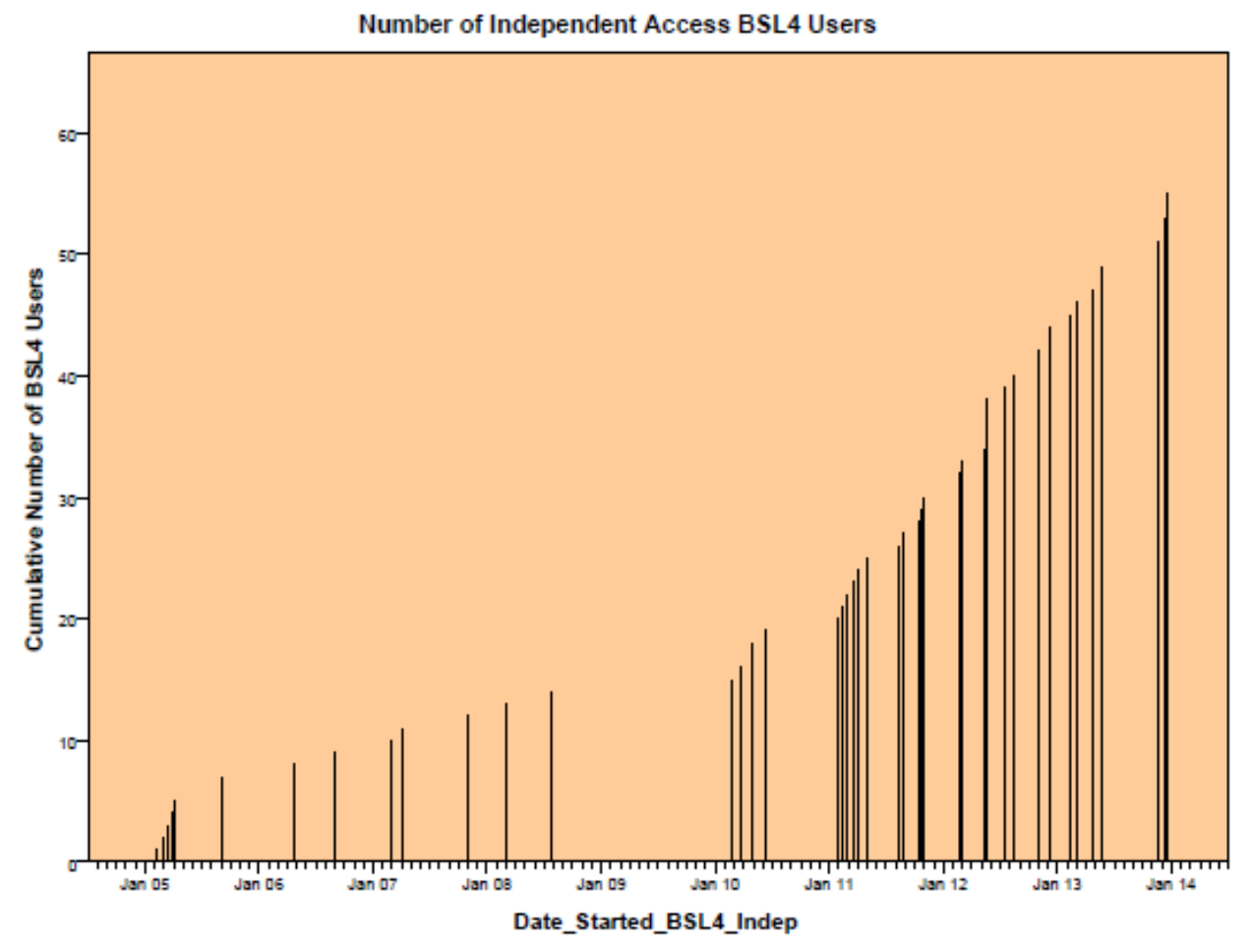
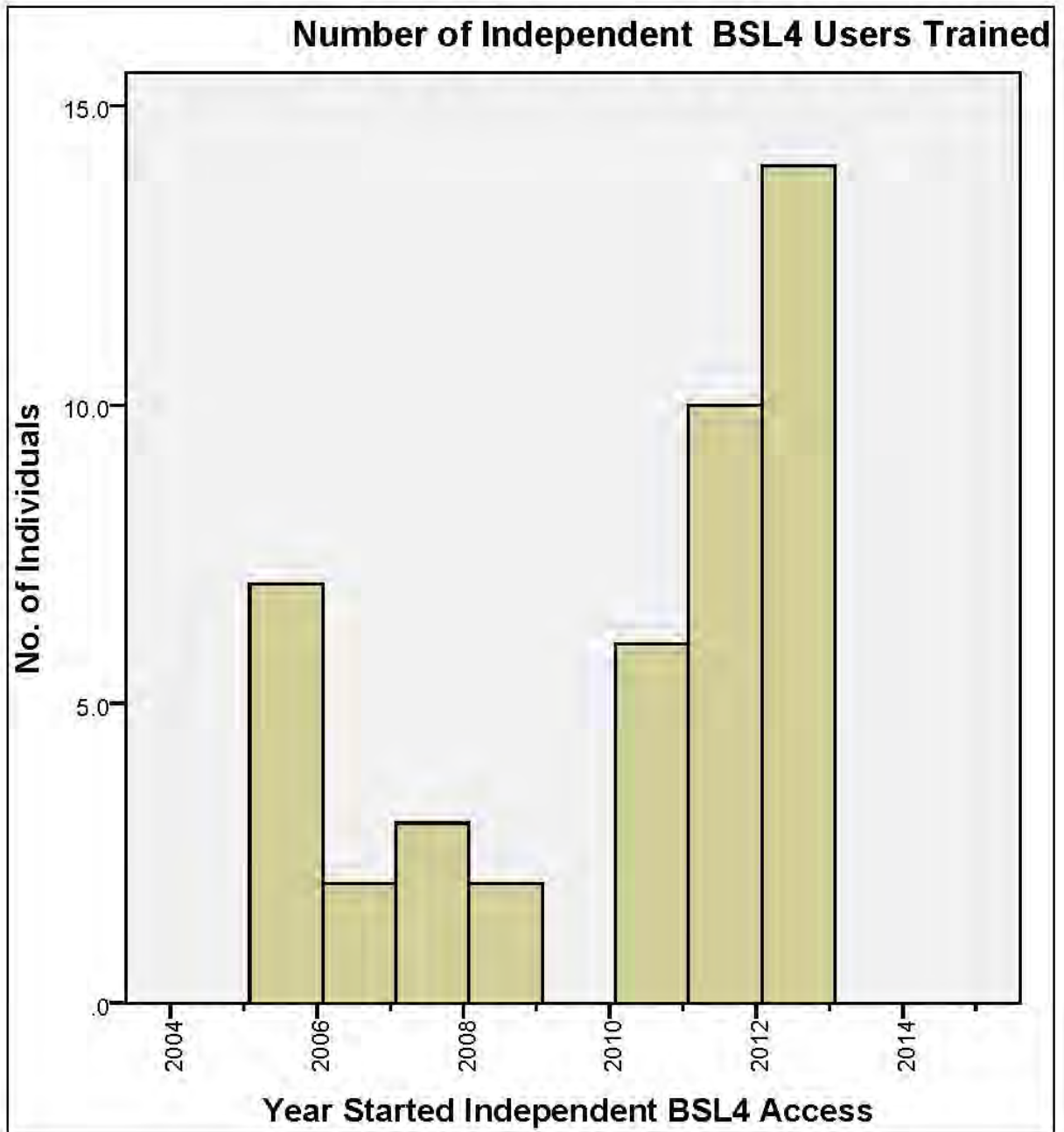


Figure 2. Number of Independent BSL4 Users Trained – 2004-2014, Galveston National Laboratory.



Aim 5: To establish a fellowship program for scientists and facility operations professionals working in BSL3/ABSL3 or BSL4/ABSL4 facilities.

The high and maximum containment fellowship program for scientists is in place. We have two fellows now in training, one fellow who has transitioned from the program to a permanent UTMB faculty position and another who has returned to her native Turkey to lead biocontainment research in that country.

Dr. Endsley' s updates from quarterly reports over the past year detail her progress to May 2014:

Dr. Janice Endsley is a fellow in training in the high and maximum containment fellowship program for scientists for research in the BSL3, ABSL3, and BSL4 laboratories in the GNL. In this role, she provides immunology expertise to investigators working in BSL3 and BSL4 containment, including experimental design, assay performance, and data interpretation. This includes design and interpretation of immunological profiling experiments including performance of Bioplex ELISA, immune recall assays, blood chemistry and blood inflammatory biomarkers, and flow cytometry. As Director of the Flow Cytometry and Cell Sorting Core Facility, she further advises investigators and staff on flow cytometry equipment needs and technical troubleshooting specific to high containment flow cytometers. She is principle investigator of the Tuberculosis Laboratory in the Galveston National Laboratory and has been building a research program in TB Immunology and drug resistance development. In this role, Dr. Endsley is directly responsible for providing hands on, mentored, training for all personnel working with BSL3 level mycobacterium including *Mycobacterium tuberculosis (M.tb)* and performance of mycobacterial infections in animal models in the ABLS3 housing facilities. This includes laboratory technicians, safety officers, and graduate students in need of *M.tb*-specific or general BSL3/ABSL3 training. Through collaboration she is contributing to efforts to develop novel diagnostic platforms to detect drug resistant TB and identification of novel antimicrobial compounds with antibacterial activity against TB (Vijayakumar, et al., Dec. 2013, *Tuberculosis*). She has also developed, optimized, and/or adapted several new techniques for study of bacterial lung infections (*M.tb*, *B. pseudomallei*) in the BSL3/ABSL3 including confocal microscopy-based bacterial viability detection, *in vivo* imaging of bacterial infection and dissemination kinetics in live animals, multi-color flow cytometry, multi-plex ELISA, and *in vitro* infection assays.

Dr. Rodrigo Ivo Marques dos Santos fellowship update, May 2014:

Dr. Santos is a post-doctoral fellow from Brazil working in the laboratory of Dr. Saravanan Thangamani on tick-transmitted pathogens. Under the NBTC fellowship, Dr. Santos completed his BSL3 training and has now gained independent access into the GNL BSL4 laboratories where he is working on the mechanisms of virus transmission by infected ticks. Some of the most dangerous vector-borne diseases are transmitted by ticks, and the Galveston National Laboratory is unique in its ability to maintain and conduct experiments using live vector ticks and the pathogens then transmit under biocontainment conditions, including BSL4. Tick-borne encephalitis (TBE) is an often fatal viral disease transmitted to humans by infected tick bites. According to WHO, tick-borne encephalitis virus (TBEV), a member of the genus *Flavivirus*, is the most important arthropod-borne virus transmitted by ticks in Europe causing severe human infections. TBEV is endemic over a wide area covering Europe and Asia.

TBEV is divided into three subtypes: Central European (TBEV-CE), Siberian and Far-Eastern (TBEV-FE). *Ixodes persulcatus* is the primary vector to TBEV-FE subtype while *Ixodes ricinus* is the primary vector for the Siberian and TBEV-CE. The Central European subtype produces a biphasic disease in 72% of the cases with a first stage in which unspecific symptoms prevail following by the meningoencephalitic stage with mortality of around 5%. The Far-Eastern subtype typically shows more severe monophasic encephalitis with mortality ranging from 30 to 40%, with high levels of sequelae in the survivors. Infectious agents transmitted by ticks are delivered to the vertebrate host together with saliva at the bite site.

Current literature search shows that majority of studies on tick transmitted infections focuses on later state of tick feeding (>24 hours). However, our lab (and a few other labs) has shown that tick borne viruses are transmitted to the host within the first 3 hours of tick attachment. The molecular mechanisms during the earliest stages of tick transmitted TBEV infection are poorly understood. Our lab's research focuses on unraveling the role of tick saliva in creating an immunologically privileged environment and facilitating TBEV transmission and dissemination. Our lab is uniquely positioned to perform these studies, as we have the state-of-the-art BSL-4 laboratory (Galveston National Laboratory), the expertise on tick biology and also the availability of exotic tick colonies from the GNL's insectary services core. We are also the only academic institution that has the capability to conduct research with ticks in BSL-4 laboratory. To this end we have investigated the cutaneous immune response to TBEV infected tick feeding, and have identified tick salivary genes differentially expressed during the feeding process. Our previous work on tick feeding biology showed appreciable neutrophil and macrophage recruitment to the site of tick feeding. Recently, we have shown that macrophage/mononuclear cells at the tick feeding loci are the primary cells infected with TBEV-CE. Though we had observed the recruitment of neutrophils to the feeding site, we could not identify TBEV-CE positive neutrophils. These background data led us to hypothesize that macrophages are the primary target cells for TBEV-CE, and neutrophils facilitate chemotaxis of macrophages to the site of infection/feeding. We are currently investigating the role of macrophages and neutrophils, *in-vitro*, in TBEV infection and

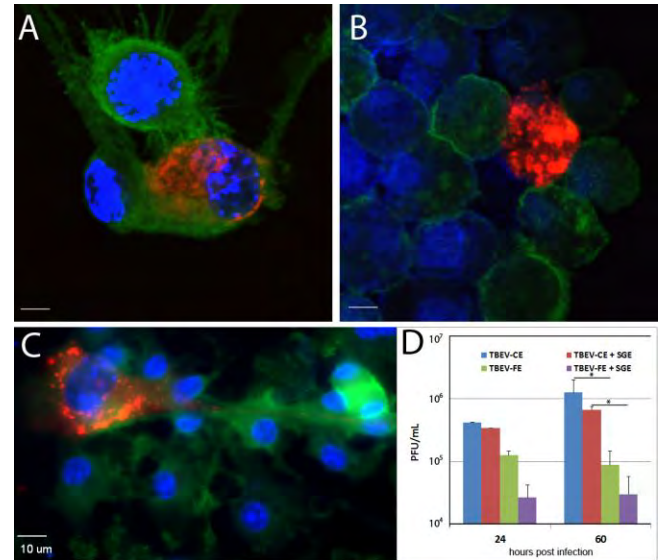


Figure 3: Detection of tick borne encephalitis virus (TBEV) in macrophages. A-C: Immunofluorescence assay for Central European subtype of TBEV (TBEV-CE) and macrophage (F4/80) detection (Fig 1 A); Far-Eastern subtype of TBEV (TBEV-FE) and F4/80 detection (Fig 1B); TBEV-CE and F4/80 (Fig 1C). TBEV-CE and TBEV -FE staining are shown in red (Alexafluor 647), macrophages (F4/80) stains are shown in green (Alexafluor 488), cell nucleus were stained with DAPI (blue). D: PFU assay to determine the susceptibility of macrophages to TBEV-CE and TBEV-FE infection in the presence and absence of tick salivary gland extract (SGE). Statistically significant ($p < 0.05$) data are marked by *. Images were taken at the GNL's imaging core facility.

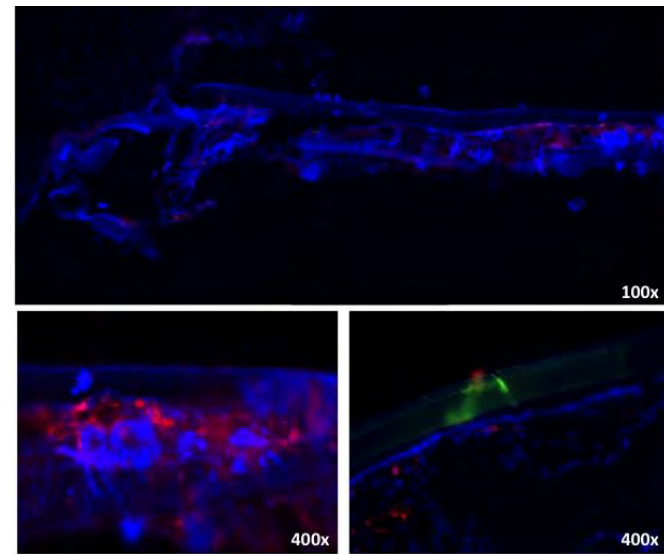


Figure 4: Detection of tick borne encephalitis virus (TBEV) in ticks. Immunofluorescence assay to localize TBEV infection was performed in tick samples using mouse immune ascetic serum generated against Central European subtype of TBEV (TBEV-CE). Cells/tissues with red fluorescence are TBEV-CE positive. These positive tick tissues/cells were used to identify genes that are specifically expressed during the feeding/TBEV infection process. We are currently investigating these genes/proteins for their ability to facilitate TBEV transmission to mammalian hosts.

dissemination and the influence of tick salivary gland extract (SGE). To facilitate this work, we have optimized immunohistochemistry (IHC) and immunofluorescence assay (IFA) protocols for TBEV (Figures 3 and 4) and immune cell detection (Figure 3).

To understand the role of macrophages in TBEV infection and dissemination, macrophages derived from mice bone marrow were infected with TBEV-CE and TBEV-FE with and without tick SGE. At 6, 24 and 60 hours post infection (hpi) supernatant samples were used for virus titration and Bioplex cytokine analysis, while the adherent macrophage cells were used for immunofluorescence assay (IFA). The IFA showed around 5% of infection in TBEV-CE infected macrophages (shown in red in fig 3A and C) and less than 1% in TBEV-FE infected ones (shown in red in fig 3B). TBEV-CE infected macrophages have macropodia as observed in figures 3A and C, meanwhile TBEV-FE infected macrophages are round-shaped (Fig 3 B). The F4/80 antigen expression (macrophage marker showed in green in fig 3A-C) increases in uninfected cells close to infected ones. It also appears that the uninfected macrophages are grouping around infected cells (fig 3A and C). The cell grouping was not observed when macrophages were treated with SGE. The difference between the titers of macrophages supernatant infected with TBEV-CE and TBEV-FE were statistically significant at 60 hpi (Fig 3D). Significant difference was also found between the supernatant of TBEV-CE and TBEV-FE with previous treatment with SGE at the same timepoint (Fig 3D). The Bioplex analysis indicated that SGE has immunomodulatory effect in IL1a, IL1b, IL6, IL10, MIP1a, MIP1b and G-CSF.

Our data indicates that: (1)TBEV-CE preferentially infects macrophages compared to that of TBEV-FE (Fig 3D); (2) SGE does not affect virus production but can affect the ability of macrophage to recognize infected cells. We are currently investigating the role of neutrophils in the chemotaxis of macrophages to the site of infection, and the role of tick SGE in facilitating this process.

Dr. Han Xia's fellowship program update, May 2014:

Dr. Xia Joined the NBTC fellowship program in October, 2013 as part of an agreement with the Wuhan Institute of Virology in Wuhan, China – part of the Chinese Academy of Sciences – where she is a research assistant. Dr. Xia's research interests include viruses, diagnostic assay methodology for infectious diseases, vaccine research, gene function, genomic and evolutionary analysis and epidemiology. She graduated from the Chinese Academy of Sciences and received her doctoral degree in biochemistry and molecular biology. Since then, she has been working on the development of a mini genome system and epidemiological investigations for Crimean-Congo hemorrhagic fever virus in Western China. She completed an epidemiological survey of CCHFV in Yunnan, China in 2008 (International Journal of Infectious Diseases, 07/2011; 15(7): e459-63). She is interested in a range of emerging arboviruses but mainly in tick-borne bunyaviruses. Her supervisor at the Wuhan Institute remarked: "Every year there are about 20-30 PhD students graduating from the institute. Only very few are retained as junior faculty and she is one of them. Her leaving for the U.S. for two years would be a huge loss to the lab, but we understand that this would be better for the long run and hope for her return upon finishing work in the U.S." While an NBTC fellow, Dr. Xia has been working in the lab of Dr. Dennis Bente. During her time in Dr. Bente's lab, Dr. Xia has focused on Crimean-Congo hemorrhagic fever virus (CCHFV) and related nairoviruses.

Dr. Xia completed the facility training workshop under NBTC trainer and engineer Miguel Grimaldo in December, 2013. She is working/training with UTMB's Dr. Naomi Forrester on how to analyze new viruses by next-generation sequencing. Additionally, she has joined a collaborative project currently underway working with Dr. Eric Bergeron, Special Pathogens Branch, CDC, on a reverse genetics system for Crimean-Congo hemorrhagic fever virus.

Dr. Xia's Scientific Activities to May, 2014:

1. Next-generation sequencing (NGS) for CCHFV in tick and animal tissues

We are sequencing samples from ticks and vertebrate host animals collected at different infection stages, then analyzing the viral genome in tick and animal host to interrogate the CCHFV transmitted between ticks and host animals at the virus population at the molecular level. Dr. Xia developed methods of CCHFV cDNA library preparation from infected ticks. It is often difficult to get high quality viral cDNA libraries from CCHFV infect tick samples, since the host genome is very complicated and the viral load is usually much lower than found in cell culture. She has prepared one sample of CCHFV (strain IbAr10200) from an infected tick for Illumina sequencing and obtained about 4 GB of high quality paired-end data which contained almost 15 million reads. These were aligned with CCHFV reference genome (IbAr10200) and the preliminary results show that some SNPs exist in the CCHFV L segment and M segment (Figure 5 below).

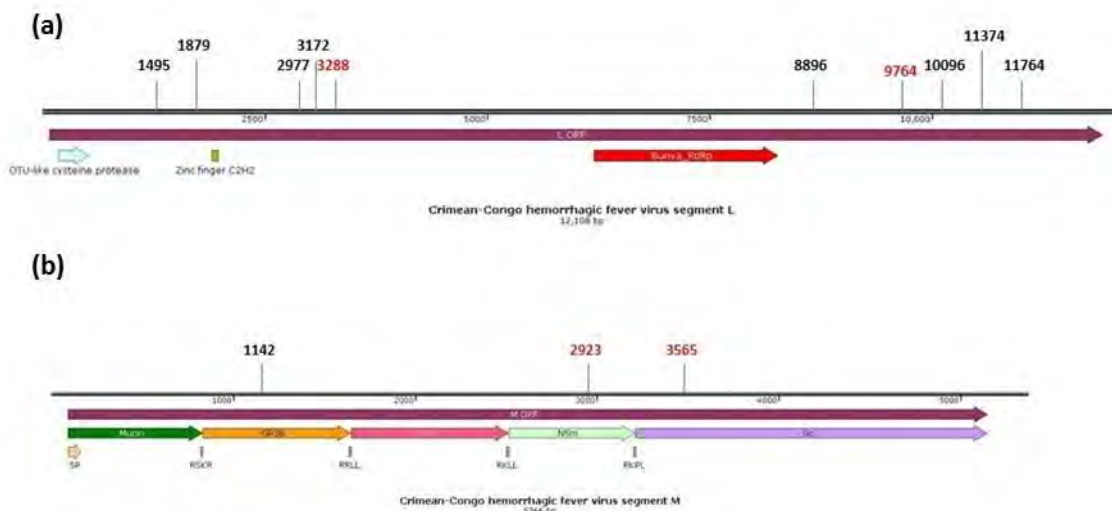


Figure 5. SNPs in CCHFV from an infected tick sample. (a) SNPs positions in L segment. (b) SNPs positions in M segment. The number above the vertical bar indicates the position located in genome; black indicates no change in the coded amino acid; red indicates amino acid changes.

Our plan is to prepare other samples for Illumina sequencing, which includes CCHFV viral tissue culture stock (IbAr10200) and from ticks which have been infected with CCHFV (IbAr10200) for about one year. She will then compare and analyze the data.

2. Nanoluc labeled recombinant CCHFV

Nanoluciferase (Nanoluc) is a newly developed small monomeric luciferase reporter with the brightest bioluminescence reported to date. We hope to create a recombinant CCHF reporter virus (Based on rescue system from our collaborator, Dr. Burgeron, CDC) with Nanoluc which will then be used in our study of viral replication and pathogenicity *in vitro* and *in vivo*. We plan to insert Nanoluc into 3 different positions of M segment (see Figure 6 below), get three transcript plasmids the V0.0 M (SP_Nluc), V0.0 M (Mucin_Nluc) and V0.0 M (GP38_Nluc). To date, Dr. Xia has successfully created the plasmid V0.0 M (SP_Nluc). Our plans is to construct the other two plasmids of M (V0.0 M (Mucin_Nluc) and V0.0 M (GP38_Nluc)) and start the rCCHFV rescue work in BSL-4.



Figure 6. Schematic of the CCHFV M segment fusion with Nanoluc. (a) insert the Nanoluc after the signal peptide, (b) insert the Nanoluc before the RSKR site, (c) insert the Nanoluc before the RRLL site.

3. Mucin and GP38 domain research

Dr. Xia has constructed the eukaryotic expression plasmids which can express mucin with mcherry and GP38 with mcherry and she has constructed the *E.coli* expression system of CCHFV mucin and GP38 domain. Her plan is to use the mcherry marker to detect the position of mucin and GP38 in mammalian cells. She will purify the mucin and GP38 protein to study the role of these two proteins in the progress of viral replication and infection.

A full accounting of her research and fellowship will continue to be included in our companion project report – Award Number W81XWH-11-2-0148, also titled National Biocontainment Training Center.

Dr. Aysen Gargili's fellowship update through May, 2014:

Dr. Gargili completed her fellowship early in this reporting year after spending about 18 months at UTMB. Upon her return to Turkey, Dr. Gargili resumed working at a national biocontainment facility outside Istanbul. While at the GNL, Dr. Gargili accumulated necessary entries and hours in the BSL4 and qualified for independent access. She and her team of researchers conducted studies with the establishment of a CCHF virus infected tick colony in BSL4. Dr. Gargili and her colleagues also designed further infectious studies for the visualization of the virus either in the tick or in infected animals with real-time imaging techniques. They accumulated critical data on the imaging techniques in live ticks/animals and started to use them in BSL4 for the visualization of the virus in the vector and the host. Her team also collaborated with UTMB researcher Dr. Gustavo Valbuena's team and began to infest humanized mice with infected ticks in BSL4 to see the preliminary results of the infection on human skin. On her return to Turkey, Dr. Gargili has continued her work on CCHF virus and additionally, she has instituted a biosafety training program in Turkey modeled after that in place in the NBTC. To date she has trained in excess of 20 individuals from across Turkey who are working in BSL3 laboratories. This successful example of train-the-trainer amplification of our investments in Dr. Gargili is especially gratifying.

The laboratory containment operations fellowship is unique and is, to the best of our knowledge the only one of its kind. The program sets a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists, where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, most entering facility operators require a more structured course of study. Consequently, we have identified fourteen distinct modules to be covered over the course of the fellowship. These structured modules cover basic microbiology, provide an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, select agent regulations, formal Good Laboratory Practices, annual certification of laboratories, testing of HEPA filter housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping.

During the course of their training, fellows directly participate in each of these activities, as well as are personally involved in the planned shut down and decontamination of containment suites, validate decontamination, and conduct and oversee maintenance activities.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over this past year of support we have actively participated in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology and other organizations at the fore of these discussions. We have also participated in ongoing discussions on these topics hosted by the National Science Advisory

Board for Biosecurity (NSABB) and the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.

Biosurety and biosecurity are currently covered in our theoretical training sessions, and we are in the process of developing a structured course to more specifically address biosurety and biosecurity in depth. We anticipate posting this course on our internal website as an educational tool to augment our more formal training opportunities and to complement lectures already offered. Depending upon the success of this internal posting, we will then consider posting the course on our website where it would be available to the general public.

As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established a distinguished speaker series. Our *Topics in Biosecurity Symposia Series* has been offered since 2010. Sessions in the series continue to be of great interest to students, faculty and community members and are consistently attended by large crowds drawing positive attention and feedback.

Summary of Biosurety and Biosecurity training activities this past year:

Topics in Biosecurity Symposia Series.

The GNL's *Topics in Biosecurity* seminar series had an active 2013-2014 season with several distinguished speakers including Tom Slezak (Sept 2013), Dr. Roger Breeze (Oct 2013), Dr. Francisco Pinheiro (Nov 2013), Dr. Peter Jahrling (May 2014) and Dr. Michael Osterholm (June 2014).

Session 13 in the series was held September 17, 2013 and featured **Mr. Tom Slezak**. Mr. Slezak (*pictured right*) is a bioinformatics expert with the Lawrence Livermore National Laboratory. His seminar focused on the history of the federal BioWatch program and its relevancy today. His presentation was entitled **“BioWatch After 10 Years: Why was it built and how is it relevant today?”** Mr. Slezak's insight on the inner workings of the BioWatch program and its current status contributed significantly to ongoing discussions regarding research and biosecurity.



Session 14 in the series was held on October 1, 2013. The session featured **Dr. Roger Breeze** (*pictured right with Dr. Jim LeDuc*). Dr. Breeze is currently the president of the Centaur Science Group in Washington, DC. Centaur Science is a science consulting company specializing in countermeasures against high consequence infections of humans, animals, and plants, some of which are potential biological weapons and others are naturally occurring disease threats in the U.S. and overseas. He also currently advises the Defense Threat Reduction Agency (DTRA) on ways to reduce the biological weapons threat in the former Soviet Union. From 1987 to 1995, he was Director of the USDA Agricultural Research Service Plum Island Animal Disease Center in New York. The title of Dr. Breeze's presentation was **“Looking Ahead in a World of Biological Threats.”** His understanding of the future of biosecurity programs, especially those within the U.S. Department of Defense, contributed to a productive session and fruitful discussion.



Session 15 in the series rounded out the fall season and featured **Dr. Francisco**



Pinheiro (pictured right alongside Dr. LeDuc and graduate students/faculty from Brazil who are in residence at UTMB). Dr. Pinheiro was an advisor in viral diseases in the program of communicable diseases with the Pan American Health Organization's division of disease prevention and control. During his tenure he helped establish several disease surveillance and monitoring programs, improved the blood supply in the face of growing challenges associated with blood-borne pathogens in the region, and coordinated the response to many outbreaks of infectious disease including several major dengue outbreaks. Prior to his post at PAHO, he spent a number of years as the director of the Institute Evandro Chagas virus laboratory in Belem, Brazil. The Institute, once a Rockefeller Network Laboratory, is today a non-profit organization which promotes public health in Brazil and is one of the primary labs for virology in the country. Dr. Pinheiro's *Topics in Biosecurity* session was held on November 12, 2013. His presentation, entitled "**Reflections of a Brazilian Virologist on Arboviruses and Other Viruses in Latin America,**" provided a keen historical perspective on virology as well as insight on evolving laboratory biosafety. The session was very well received and, while on campus, he also had the opportunity to meet with several Brazilian scientists working at UTMB.

Dr. Peter Jahrling speaking in topics in Biosecurity, May 2014.

Dr. Jahrling is the chief scientist at the NIAID Integrated Research Facility and the chief of NIAID's emerging viral pathogens section. He is **formerly the senior research scientist for the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID) Frederick, MD** where he served as the principal scientific advisor on issues related to medical defense against infectious disease threats. He has authored or co-authored more than 160 scientific publications, chiefly in the areas of filovirus and poxvirus research. Subject matter expert and consultant to numerous agencies including NIH, the National Academy of Sciences, the World Health Organization, the Department of State, the National Security Council, and the CDC. On May 2, 2014 he offered a discussion of the role of the NIAID Integrated Research Facility during his visit to the GNL and spent valuable time meeting with UTMB students and faculty discussing technical challenges of applying modern imaging equipment to infectious disease research.



Dr. Michael Osterholm speaking in Topics in Biosecurity, June 2014.

Dr. Osterholm is 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, a professor in the Division of Environmental Health Sciences, School of Public Health, and an adjunct professor in the Medical School, University of Minnesota. He is also a member of the Institute of Medicine (IOM) of the National Academy of Sciences and the Council of Foreign Relations. In June 2005 Dr. Osterholm was appointed by Michael Leavitt, Secretary of the Department of Health and Human Services (HHS), to the newly established National Science Advisory Board on Biosecurity. In July 2008, he was named to the University of Minnesota Academic Health Center's Academy of Excellence in Health Research. In October 2008, he was appointed to the World Economic Forum Working Group on Pandemics. On June 3, 2014 he offered an exceptional talk, "Emerging Infectious Diseases: Looking into the Crystal Ball". His talk was very well attended, and he dedicated considerable time to meet with UTMB faculty and



students to discuss the interface between emerging infectious diseases and biosecurity.

NBTC Website.

Over the past reporting year, the new NBTC website has continued to develop - www.utmb.edu/nbtc and it has become a home base for the program. Course training schedules and staff listings are continuously added to the website. We also updated our staff listing with new members of the training team. Per its intent, this site serves as a hub of information regarding the Center, our goals, and the resources that the NBTC makes available to the biosafety and research communities.



Onsite/Offsite training and related updates from the past reporting year.

External Training Highlights (May 2013- May 2014). Of note during this reporting quarter was NBTC training provided to individuals at the following domestic external institutions/corporations:

May 2013 to February 2014:

- ABSL2 training:
 - Baylor College of Medicine and MD Anderson Cancer Center - 2 veterinarians
 - University of Houston - 2 individuals
- ABSL3 training:
 - Baylor College of Medicine and MD Anderson Cancer Center - 2 veterinarians
 - University of Texas El Paso - 17 individuals for theory, 4 for practicum - training done at UT El Paso
 - University of Texas Southwestern - 14 individuals for theory, 3 for practicum - training done at UT Southwestern
- BSL2 training:
 - NuAir – 1 individual
 - University of Houston – 2 individuals
- BSL3 training:
 - Tulane University Primate Center - 1 individual
 - Baylor College of Medicine - 2 individuals
 - Oklahoma State University – 1 individual
 - Fred Hutchinson Cancer Research Center – 1 individual
 - Dept. of Defense Contractor/Booz Allen Hamilton – 1 individual
 - Arizona State University – 1 individual
 - University of Texas Southwestern - 17 individuals for theory, 8 for practicum - training done at UT Southwestern

- Georgia Southern University - 1 individual for theoretical and practicum
- PAPR training:
 - Tulane University Primate Center - 1 individual
 - Baylor College of Medicine - 2 individuals
 - Oklahoma State University – 1 individual
 - Fred Hutchinson Cancer Research Center – 1 individual
 - Dept. of Defense Contractor/Booz Allen Hamilton – 1 individual
 - Arizona State University – 1 individual
 - Georgia Southern University - 1 individual

External training and instruction was also provided during the 56th Annual meeting of the **American Biological Safety Association (ABSA) Conference** which was held in Kansas City, Kansas (October 17-23, 2013). Several of the NBTC trainers led pre- and post- conference sessions for domestic and international conference attendees. These sessions (and NBTC trainers involved) included:

Ms. Belinda Rivera taught an eight-hour class on **“Advanced Principles and Practices of Working in an ABSL3.”** Twenty-two individuals participated in the course. The following is a course description and a list of course objectives.

This course introduced information to individuals that are currently working, plan on working, or audit ABSL-3 facilities. Working in an ABSL-3 facility has unique hazards. Personnel working in these facilities need to be informed of these hazards and trained to work safely and appropriately with the species being handled. Topics will include 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.

Course Objectives:

- Identify proper PPE and disinfection practices
- Restate the techniques used to manipulate animals safely
- Explain the processes on waste management
- Summarize the knowledge gained regarding emergency and exposure response

Ms. Dee Zimmerman co-taught an eight-hour class on **“BSL3 Operations and Management.”** Thirty-eight individuals participated in the course. The following is a course description and a list of course objectives.

This course reviewed the important aspects of the daily operation of a BSL-3 facility from 2 points of view; management of the facility and daily operations. This assumes that you already have a facility built and have all required authorizations to work in it. The course covered the different aspects you need to consider to operate a BSL-3 facility such as approval of a worker, training of workers and maintenance support, occupational health issues, managing waste, maintenance of the HVAC and physical facility, periodic checks on the facility's systems, and emergencies of different types. It also covered daily operations in a BSL-3 such as understanding when it is safe to enter and when you need to evacuate the facility, what to do when the

ventilation fails, practical aspects of entry and exit procedures, practical tips on selection and use of PPE, safety considerations within the experimental SOPs, waste handling, facility's cleaning, and how to have equipment repaired or serviced. This course will be conducted in a way that allows for interaction and exchange of experiences between participants and instructors. This course did not cover regulatory aspects from specific countries.

Course Objectives:

- Describe elements of annual verification, emergency response, etc.
- Recognize institutional responsibilities from management to user.
- Describe methods to develop manuals, SOPs, and training.

Dr. Anne-Sophie Brocard co-taught an eight-hour class on **“Advanced Risk Assessment.”** The following is a course description and a list of course objectives. Forty-one individuals participated.

In this new, advanced, and interactive course, attendees followed a research project as it evolves over time from basic to multifaceted in vitro and in vivo scenarios based on actual research protocol submissions. Attendees worked together to conduct risk assessments that build upon each other from the discovery of a novel virus to determining the efficacy of experimental vaccines in humans. Multiple systems used in the research progress from cell culture to small animal models using recombinant viral vectors, to macaques, and finally clinical trials. Risk assessments focused on the likelihood of exposure and the severity of consequences from exposure to the multitude of hazards encountered in the increasingly complex research. Course attendees should have a thorough understanding of rDNA work and the linkage between biosafety, risk assessment and risk mitigation.

Course Objectives:

- Analyze complex scenarios by identifying hazards associated with component parts of the plan
- Prioritize risks based on likelihood and consequences of occurrence
- Assess the overall risk and determine mitigation strategies to minimize the risk
- Evaluate mitigation strategies for effectiveness, adjust strategies as warranted

Mr. Miguel Grimaldo co-taught an eight-hour class on **“Advanced BSL3 Facility Operations.”** Thirty-seven individuals participated. Following is a course description and a list of course objectives.

This course is a follow up to the BSL-3 Facility Operations and Management course. This advanced 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; maintenance personnel training requirements; solid and liquid waste decontamination equipment; procedures, validation and cycle development; area decontamination methodologies; procedures and validations; filtration systems and their validation and testing processes; ventilation control methodologies and ventilation equipment configurations; facility ventilation system testing during normal and failure conditions; test documentation; and record keeping.

Pictured right: Mr. Grimaldo's well attended class at the ABSA meeting.

Course Objectives:

- Explain the facility verification process in detail, including recommended test methodologies
- Restate the training requirements for facility personnel accessing the biocontainment areas
- Identify methodologies for decontamination of areas, equipment, filters, and waste
- Describe elements of biocontainment equipment risk assessments



Ms. JeT Newton, Vickie Jones, Dee Zimmerman and Dr. Brocard facilitated additional courses and attended committee meetings during the course of the conference.

Ms. Jones facilitated the following pre-conference courses: **“Implementation of Programs and Procedures for an Effective Biosurety Program for BSL-3 Laboratories”**, **“The Safe Transport of Infectious and Biological Substances”**, **“Developing and Maintaining Roles & Responsibilities for Risk-Based Access to, Control of, and Accountability for Biological Agents and Toxins”**, and **“Fundamentals of Microbiology and Infectious Disease”**.

Ms. Newton facilitated the following pre-conference courses: **“Managing Infection Risk”**, **“Developing and Maintaining Roles & Responsibilities for Risk-Based Access to, Control of, and Accountability for Biological Agents and Toxins”**, **“Implementing Personnel Security Programs in Biomedical and Microbiological Laboratories”**, **“Bioterrorism Awareness for the Animal Health Community”**, and **“How to Develop an Export Management and Compliance Program Including the I-129 for Deemed Exports.”**

Several NBTC trainers play prominent leadership roles within the ABSA organization:

- Ms. Jones is a member of the Pre-conference Course Committee, Membership Committee and Scientific Program Committee.
- Ms. Newton is member of the Membership Committee and Pre-conference Course Committee.
- Ms. Zimmerman is a member of the Pre-conference Course Committee, ABSA-Owned Course Working Group, Membership Committee, and Accreditation Task Force. She has also completed her first year of a three-year term as a council member for ABSA. ABSA’s Council is made up of the current ABSA president, the president-elect, the past president, secretary, financial officer and four council members.
- Dr. Brocard is Co-chair of the Professional Development Team. She is also a member of the Membership Committee, Finance Committee, Member Profile Task Force and Biosafety Graduate Course Task Force.

February 2014 to May 2014:

University of Texas South Western, Dallas, Texas – BSL3 Training was provided for faculty and staff working with *Mycobacterium tuberculosis*. Training was arranged by the grant PI and

Biosafety officer/Facility Director. A total of 8 people, including the PI, were trained in practices consistent for safe entry, use, and exit of their containment facility. Individuals were provided with a one-on-one training experience while establishing biological safe techniques. This training took place in Dallas, Texas. Trainers: Vickie Jones and Jason Hardcastle.

Food and Drug Administration (FDA-CBER) – BSL3 training was provided for faculty and staff transitioning into a newly constructed facility. Training was arranged by the biosafety officer for the entire group of facility users. Theoretical class had 75 participants, and 15 people participated in the full training course. The training took place in the NIH BSL4 training facility in Bethesda, MD. Trainers: Vickie Jones, Belinda Rivera and Jason Hardcastle.

UTMB/FDA-CET – For the past 2 years NBTC trainers have been involved in a joint UTMB/FDA annual course designed to provide FDA inspectors, regulators and personnel involved in oversight of regulated studies with insight on requirements and constraints of conducting regulated research in BSL4 laboratories. The NBTC trainers provided biosafety cabinet technical use awareness for participants in the course titled “Achieving Data Quality and Integrity in Maximum Containment Laboratories”. A total of 16 researchers worked with trainers one-on-one to establish and reinforce safe and aseptic microbiological techniques within a biological safety cabinet in a BSL4 environment. This year the training took place in the NIH BSL4 training facility in Bethesda, MD. Trainers: JeT Newton, Corrie Ntiforo and Vickie Jones.

Methodist Hospital, Houston, Texas–BSL2 training. We provided a highly specialized BSL2 for clinical-pharmacy staff in a ISO Class 7 environment (Compounding Aseptic Containment Isolator). Four individuals directly responsible for the preparation of pharmacy grade intravenous therapeutics were trained in aseptic and fundamentals of biological safety. This training was performed exclusively in a compounding aseptic containment isolator, with special considerations given for the inclusion of vaccines and recombinant material. This training took place in Houston, Texas. Trainers: Vickie Jones and Jason Hardcastle.

Community/External Outreach. During the reporting year distinguished guests both visited the training center and were also provided information on the NBTC through various forums. Highlights of these activities follow:

- In January 2014, staff from the University of Texas System’s Office of Federal Relations visited the GNL/NBTC. Included in the visit was Ms. Angela Godby, the UT System’s Associate Vice Chancellor for Federal Relations; the newly appointed Dr. Michelle Atchison, Associate Vice Chancellor for Federal Relations; and Jana Lozano, Coordinator for Federal Relations (*pictured right*). The group was briefed on the NBTC programs and outreach activities. They also had the opportunity to visit the biosafety training mock-laboratory where a BSL4 demonstration.
- Also in January 2014, NBTC trainer Jason Hardcastle delivered a presentation on the NBTC and his training



efforts to the Galveston Rotary Club. This local group of prominent Galveston representatives requested the presentation in an effort to stay abreast of collaborative programs – such as the NBTC – that are underway at the UTMB.

Table 1 below offers a comprehensive summary of all courses offered and number of participants since 2009. Table 2 gives a summary of the international participants receiving training through the NBTC. Figure 7 provides a record of the growth in the number of trainees participating in NBTC courses by year since 2009, and Figure 8 offers a summary of the typical participant by background for the period May, 2005 to December 2013.

Table 1. Summary of training courses offered and number of participants in each course, May 2009 through April 2013.

Training Course/Module	May- Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-Dec 2013	Jan 2014	Feb- May 2014	Total
BSL2 theoretical	107	144	251	160	133	3	39	837
BSL2 hands-on	64	76	92	117	102	3	29	483
ABSL2 theoretical	N/A	1	79	149	284	8	31	552
ABSL2 hands-on	N/A	1	40	76	105	11	29	262
BSL3 theoretical	45	119	100	135	86	5	89	579
BSL3 hands-on	45	101	94	76	57	6	34	413
BSL3 mentorship	36	41	24	18	14	3	7	143
Class III cabinet theoretical (New course)	N/A	N/A	N/A	N/A	N/A	N/A	2	2
Class III cabinet hands-on (New course)	N/A	N/A	N/A	N/A	N/A	N/A	2	2
ABSL3 theoretical	29	55	47	73	76	0	8	288
ABSL3 hands-on	29	50	46	37	53	1	6	222
ABSL3 mentorship	N/A	N/A	38	19	26	2	7	92
BSL4 orientation and mentorship	9	28	59	47	41	0	24	208
Non-human primate theoretical	16	15	60	41	20	0	9	161
Non-human primate, hands-on	N/A	N/A	90	41	28	1	7	167
Non-human primate annual refresher	N/A	N/A	37	114	89	0	0	240
Animal handling certificates	N/A	N/A	22	75	39	4	21	161
Graduate Program	39	36	32	13	18	0	0	138
Introduction to Microbiology	18	0	6	4	0	0	0	28
Aerobiology	19	5	2	8	0	0	0	34
Autoclave	195	27	46	30	25	1	7	331
High Throughput Safety training	8	11	3	2	17	3	9	53
PAPR (respirator training)	N/A	10	49	52	78	0	9	198
ABSA/AfBSA courses	84	175	87	207	181	0	0	734
Agent specific training	N/A	N/A	N/A	N/A	186	50	76	312
Total trained	743	895	1,304	1,494	1,658	101	445	6,640

Table 2. International Trainee Summary, 2009 to 2014.

2009				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
Academia Sinica, Institute of Biomedical Sciences Taipei, Taiwan *			BSL3 didactic BSL3 practical	9 9
2010				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
Institut National d'Hygiène du Maroc Rabat, Morocco	World Health Organization	Ministry of Health, WHO, European Union, UNICEF, French Cooperation, International Atomic Energy Agency, Italian Cooperation, WHO COPEP, INSERM – CNRST, CDC	BSL3 didactic BSL3 practical	1 1
GIP WHO Global Influenza Programme Geneva, Switzerland	World Health Organization	“ “	BSL3 didactic BSL3 practical	2 2
InDRE Instituto de Diagnostico y Referencia Epidemiologicos Mexico	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Universidad Nacional Autonoma De Mexico Mexico City, Mexico	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
GMI Gorgas Memorial Institute for Health Studies Panama City, Panama	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
IOC/FIOCRUZ Laboratório de Virus Respiratórios e do Sarampo Rio de Janeiro, Brazil	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Cantacuzino Institute Bucharest, Romania	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
INEI Instituto Nacional de Enfermedades Infecciosas “Carlos G. Malbran” Buenos Aires, Argentina	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Instituto de Medicina Tropical “Pedro Kouri” Havana, Cuba	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Institut Pasteur de Dakar Dakar, Senegal	World Health Organization	WHO, Ministry of Foreign and European Affairs, Ministry of Higher Education and Research, Ministry of Health and Sports, The Bill and Melinda Gates Foundation, Wellcome Trust	BSL3 didactic BSL3 practical	1 1
Central Public Health Laboratory Ministry of Health and Population, Cairo, Egypt	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Institut Pasteur in Algeria National Influenza Center Algerian Ministry of Public Health Algiers, Algeria	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1

Chaim Sheba Medical Center Tel Aviv, Israel	World Health Organization	“ “	BSL3 didactic BSL3 practical	2 2
UVRI Uganda Virus Research Institute National Influenza Center Entebbe, Uganda	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1
Ministere de la Sante Publique Laboratoire de Virologie Yaounde, Cameroun	World Health Organization	“ “	BSL3 didactic BSL3 practical	1 1

2011				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
Institute Pasteur Casablanca, Morocco *	Moroccan Ministry of Health	World Health Organization	BSL2 Didactic	104
KEMRI Kenya Medical Research Institute Nairobi, Kenya *	UTMB institutional funds.	Wellcome Trust	BSL3 didactic BSL3 practical	18 18
University of Ljubljana Ljubljana, Slovenia	State funded institution.	European Union, Structural Funds in Slovenia (European Regional Development Fund, European Social Fund), Innovation & Environment Regions of Europe Sharing Solutions (INTERREG)	BSL3 didactic BSL3 practical	2 2
University of Monterey Monterey, Mexico	University of Monterrey	Privately funded institution.	BSL2 didactic BSL2 practical	1 1
USAMRMC – AFRIMS U.S. Army Medical Research and Materiel Command - Armed Forces Research Institute of Medical Sciences (a U.S. Department of Defense facility) Bangkok, Thailand	U.S. Army	U.S. Department of Defense	BSL3 didactic BSL3 practical ABSL3 didactic ABSL3 practical	3 3 1 1
GMI Gorgas Memorial Institute for Health Studies Panama City, Panama	Public institution aligned with the Ministry of Health in Panama.	Research agreements with numerous entities including the U.S. Department of Health & Human Services, Walter Reed Institute of Research and the WHO.	BSL3 didactic BSL3 practical	2

2012				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
INVEH Instituto Nacional de Enfermedades Virales Humanas “Dr. Julio Maiztegui” Pergamino, Argentina*	Argentina Ministry of Health	Country of Argentina	BSL3 practical BSL3 didactic Biocontainment engineering	10 27 5
SACIDS Southern African Centre for Infectious Diseases Surveillance (Democratic Republic of Congo, Mozambique, South Africa, Zambia and Tanzania) Tanzania, Africa*	One Health Commission	Rockefeller Foundation Google Wellcome Trust Nuclear Threat Initiative’s (NTI) Global Health and Security Initiative (GHSI)	BSL2 theoretical	12

USAMRMC – AFRIMS U.S. Army Medical Research and Material Command - Armed Forces Research Institute of Medical Sciences (a U.S. Department of Defense facility) Bangkok, Thailand*	U.S. Army	U.S. Department of Defense	BSL3 practical BSL3 didactic ABSL3 didactic ABSL3 practical NHP training	20 49 26 4 7
University of Monterey Monterey, Mexico	University of Monterey	Privately funded institution.	BSL3 practical BSL3 didactic	1 1
Koc University Istanbul, Turkey	Koc University	Privately funded institution.	BSL3 practical BSL3 didactic ABSL3 practical ABSL3 didactic	1 1 1 1
CENETROP Centro Nacional de enfermedades tropicales (linked with other health institutions in Bolivia, Latin America and Belgium) Santa Cruz, Bolivia*	Pan American Health Organization (PAHO)	Country of Bolivia	BSL3 practical BSL3 didactic	6 6

2013				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
VIDRL Victorian Infectious Diseases Reference Laboratory North Melbourne, Victoria, Australia	State of Victoria	State owned and operated.	BSL4 Training BSL4 Training Biocontainment engineering	2 2 2
SACIDS Southern African Centre for Infectious Diseases Surveillance Sokoine University of Agriculture (Democratic Republic of Congo, Mozambique, South Africa, Zambia, Zimbabwe and Tanzania) Tanzania, Africa*	One Health Commission	Rockefeller Foundation Google Wellcome Trust Nuclear Threat Initiative's (NTI) Global Health and Security Initiative (GHSI)	Introduction to biosafety course.	17
Technical University of Denmark National Veterinary Institute Kalvehave, Denmark	Technical University of Denmark	Technical University of Denmark	Biocontainment engineering	1
The Pirbright Institute Surrey, United Kingdom	Pirbright Institute	Biotechnology and Biological Sciences Research Council (BBSRC)	Biocontainment engineering	1

2014				
International Trainee Organization	Sponsoring Organization	Sponsor Funder	Training Type	Number of individuals trained
Institute of Medical Biology Kunming, China			BSL3 practical BSL3 didactic ABSL2 practical ABSL2 didactic Biocontainment engineering	2 2 2 2 2

Figure 7. Total number of courses administered annually over the history of the biosafety training program – May 2005-December 2013 (Total = 6926). The creation of the NBTC in 2009 has contributed significantly to the exponential growth of the biosafety training program.

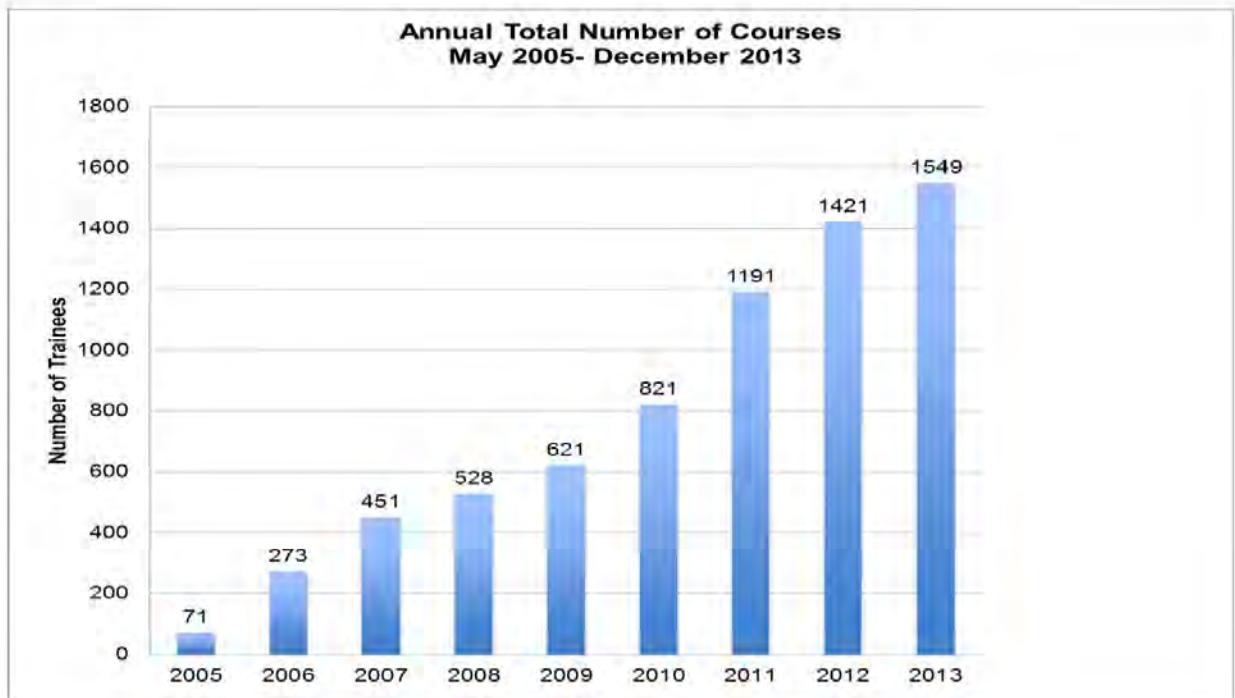
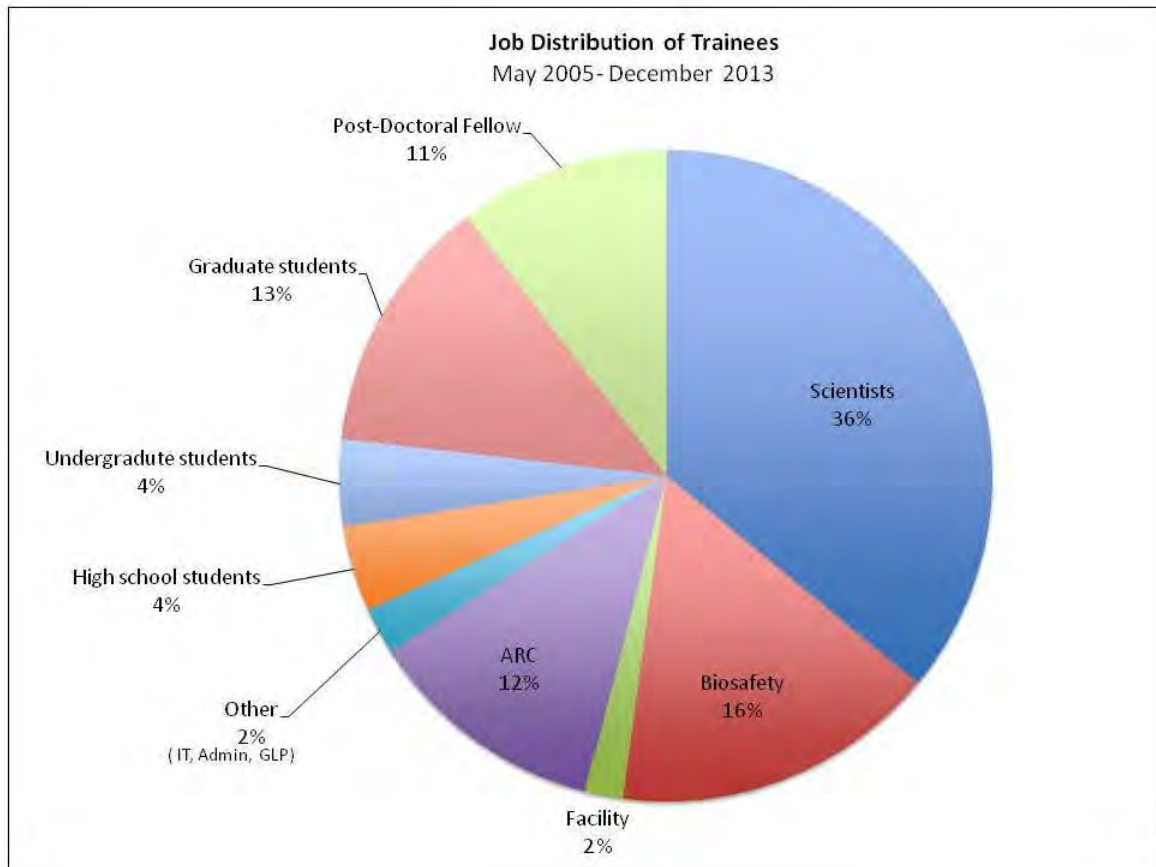


Figure 8. Job distribution of trainees, May 2005 to December, 2013.



KEY RESEARCH ACCOMPLISHMENTS 2013-2014:

- Our comprehensive, standards-based training program was continued and expanded to prepare individuals for work at all levels of biocontainment.
- Advanced, mentored training was provided to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL4 level.
- Our unique fellowship was continued to provide training to the next generation of containment laboratory facility operations professionals to prepare them to oversee the safe operations of these complex facilities.
- As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we continued to offer our unique seminar series, *Topics in Biosecurity*. Sessions offered continue to be attended by large crowds and draw positive attention and feedback. Planning is underway to continue the series with 2014-2015 sessions.

REPORTABLE OUTCOMES 2013-2014:

- Since the inception of UTMB's Laboratory Biosafety Training Program, prior to the TATRC funding award in 2009, nearly 7,400 individuals – both internal to UTMB and external, both nationally and internationally – have been instructed in the safe research and operation in biocontainment laboratories. The vast majority of these trainees have taken part in the program since 2009 when TATRC funding allowed for significant growth of the program.
- Requests for external biosafety training continue to be received in increasing numbers providing clear evidence of the strong demand for high quality training in biosafety and biosecurity.

CONCLUSIONS:

The National Biocontainment Training Center offers a robust and intensive training program devoted to all aspects of biological safety, biocontainment, and biosecurity. This program offers unique, hands-on training to trainees, staff and external partners at all levels of biocontainment, including focused, mentored training in the BSL4 laboratory.

Nearly 7,400 persons have benefited from one or more of these training courses, many of whom are now pursuing graduate education and using these specialized skills in the GNL containment facilities and in other biocontainment facilities around the world. Our intensive, mentored fellowship programs offer opportunities for in-depth training in research under all levels of biocontainment to include BSL4 conditions. We also offer unique training opportunities in containment laboratory operations and maintenance. These fellowships are proving quite successful and are helping address the critical national shortage of well-trained containment laboratory scientists and facility operations specialists.

2013 Table of Contents	1
Introduction	2
Body	
Staffing Report	3-4
Teaching Laboratory Facilities	4-5
Overview of NBTC training	5-7
BSL2 and BSL3 training	7
Animal BSL2/3 training	7
BSL4 training	7
Specific Aims 1-6	8-23
Table 1. Summary of Courses/Participants	24
Figure 3. Total number of courses administered	25
Annually – May 2005-December 2012.	
Figure 4. Distribution of courses administered during	26
the 2012 calendar year.	
Key Research Accomplishments	27
Reportable Outcomes	27-28
Conclusions	29
References	29

INTRODUCTION

The **National Biocontainment Training Center (NBTC)** provides standards-based theoretical and practical training to students and professionals preparing for work in biocontainment laboratories where infectious agents, possibly including especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL2), BSL3 and BSL4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee. Advanced coursework includes hands-on mentored training in the containment laboratories, including consecutive training at BSL3 and BSL4 levels of containment should that be required by the researcher's needs. Specialized training in the handling of laboratory animals is also offered. Sponsored mentored training is available to scientists embarking on a career focused on high hazard pathogens at the BSL4 level through a dedicated fellowship. Fellows in this program work under the close supervision of an established mentor while addressing a research topic of their own choosing. Mentored scientists and fellows progress to full independent access to the BSL4 laboratory only when their mentor and laboratory director are fully confident of the individual's skills and abilities to work independently in this environment.

The NBTC also offers a unique training opportunity for facility operations specialists interested in pursuing a career as a biocontainment operations manager. To the best of our knowledge, this is the only such training program in the world. This program is designed as a series of modules which address specific aspects of the construction, maintenance and safe operation of a biocontainment laboratory. The coursework is tailored to the specific needs of the individual trainee and involves both didactic training and mentored hands-on work using the Galveston National Laboratory (GNL) as its classroom. Over the course of the training period, which is anticipated to require up to two years for completion, the fellow(s) will be directly involved in the maintenance of the laboratory, decontamination of specific laboratories, monitoring and replacement of filters, fans and control units, understanding the Building Automation System (BAS), and a wealth of other duties routinely seen in the operations of typical biocontainment facilities.

BODY

TATRC's financial support for the NBTC formally began on May 22, 2009 and this submission comprises our annual report for the period May 2012 to May 2013 for this initiative. The Laboratory Biosafety Training Center at The University of Texas Medical Branch was established and operational prior to receiving TATRC funding; consequently, the course structure and procedures were already in place and allowed the NBTC to implement enhanced training operations almost immediately. From inception to date, the NBTC has provided training to nearly 5,000 participants through the various courses offered. Below is a summary of the significant progress made over the preceding year (2012-2013) under TATRC support. Funding and accomplishments are organized by each specific aim as they were presented in our original proposal.

Staffing Report.

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. Below is a summary of the individuals supported in part by the TATRC award over the past reporting year and their roles in the operation and management of the NBTC.

Dr. Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr. Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr. Ksiazek also oversees the BSL4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL4 environment.

Dr. Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr. Anne-Sophie Brocard, an accomplished virologist and experienced biosafety trainer who has directed the training center courses since their inception. Dr. Brocard provides both theoretical and practical training to trainees and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms. Je T'aime Newton. Dr. Brocard is ably assisted by Ms. Je T'aime Newton, a highly experienced instructor with extensive expertise in biocontainment. Ms. Newton provides specialized training at all levels of containment, but is specifically responsible for preparing trainees for BSL4 investigations, focusing her efforts on the proper care, use and maintenance of the protective "space suits" used in the BSL4 laboratory and other aspects of work in this highly specialized environment.

Ms. Vicki Jones. Ms. Jones is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera. Ms. Rivera is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical animal training modules.

Mr. Jason Hardcastle. Mr. Hardcastle is a trainer and assists Ms. Jones and Rivera with the training of students, specializing in *in-vitro* techniques.

Ms. Dee Zimmerman. Ms. Zimmerman is the director of the University's biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Mr. Rodrigo Marques dos Santos. Dr. Santos works with ticks and tick borne pathogens, mainly tick-borne encephalitis virus. He will work with ticks and BSL4 agents within the maximum containment laboratories. He is currently undergoing mentored BSL4 training to gain independent access.

Ms. Sharon Walters. Ms. Walters serves as the business coordinator for the NBTC and is involved in the outreach program as well as registration process for all external trainees, nationally and internationally.

Dr. Janice Endsley. Dr. Endsley is an assistant professor on the UTMB faculty. She entered the BSL4 fellowship program in 2010. Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. Dr. Endsley will continue in the fellowship for much of the current year as she gains critical experience and masters skills needed to work in this environment.

Dr. Dennis Bente. Dr. Bente is a BSL4 research scientist with the GNL at UTMB. He is an assistant professor in the Department of Microbiology & Immunology and he serves as a BSL4 scientific mentor for the NBTC. Dr. Bente's research concentrates on understanding how viruses cause disease with special focus on the pathogenesis of Crimean-Congo hemorrhagic fever virus and its transmission by tick vectors.

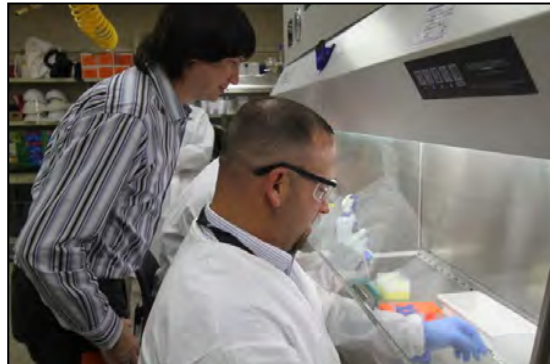
Dr. James LeDuc. Dr. LeDuc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr. LeDuc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions and he has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

Teaching Laboratory Facilities.

The teaching laboratory is a critical asset of the NBTC and it is designed to offer trainees realistic exposure to the conditions and equipment they will typically encounter at each level of biocontainment as they conduct their studies.

At the **BSL2** level, this typically includes a biological safety cabinet where infectious pathogens are handled. *(pictured)*. Biological safety cabinets are used at all levels of biocontainment. The teaching laboratory also includes limited specialized equipment, as well as facilities to manage laboratory waste and storage of pathogens. Training for individuals preparing for work in the **BSL3** laboratory includes a dedicated area where individuals master the donning and doffing of protective gear and its proper disposal.

Those trainees going on to prepare for work in the **BSL4** laboratory have specialized instruction in the care and use of the positive pressure encapsulating ensemble or "space suit" that is worn in the most common type of **BSL4** laboratory in use today *(pictured)*. This includes inspection of the suit for any evidence of leaks prior to use, gaining experience and familiarity in the wearing of the suit, use of compressed air



hoses, and training in emergency procedures. In order to provide this training under realistic conditions, the training facility has been outfitted with a breathing air compressor and a mock laboratory where trainees can experience wearing the suit and become familiar with working in this unique environment. Some people discover that they experience claustrophobic reactions when wearing a suit; this practical, realistic suit training environment allows them to overcome any such reactions under well-controlled conditions, or decide that this work is not a good fit for them.

A key benefit of the support provided to the NBTC is the availability of resources that allowed for the renovation of our existing teaching laboratory facilities. We completely refurbished the training facility to significantly expand the mock laboratory space available to us, and to enhance the breathing air compressor and suit training area.

Laboratory training is conducted in the mock training laboratory with authentic laboratory equipment utilizing non-infectious materials. Entry into the lab is through a double door anteroom with directional airflow and mock pressure monitors. The laboratory has four class II biological safety cabinets, three of which are constructed with see-through panels which allow the trainer to introduce smoke into the BSC to visualize air movement within the BSC. One BSC



class II cabinet also has see-through panels and **BSL4** air connections ports. Two of the BSC cabinets are equipped with cameras inside that allow for remote demonstrations. The laboratory itself also has two cameras installed for remote demonstrations. The laboratory has two class III biosafety cabinets, incubators, centrifuges, bench top autoclave, refrigerator, -80° freezer, dunk tank, and general laboratory equipment to allow for mock BSL2 to BSL3 and -4 laboratory work. The laboratory is equipped with a compressor and air lines for practice in the suit check examination and use of BSL4 suits within that facility prior to the trainee entering the active BSL4 laboratories. The laboratory also has multiple airline drops allowing the trainee to work throughout the laboratory with the ability to connect and disconnect airlines as needed.

Overview of NBTC Training.

The NBTC provides a series of training modules involving a mixture of didactic instruction and hands-on training to be carried out within an existing mock BSL3/4 training laboratory that is located within the Environmental Health and Safety Office space in the Materials Management Building on the UTMB campus. The intent of the NBTC is to promote good laboratory techniques and safe procedures to be used at all biosafety levels, and to provide consistency in research practices. The program is designed to ensure that all training attendees have the same general biosafety training at BLS2 and -3, and if necessary BSL4, prior to entering an active biocontainment laboratory, thus ensuring that high safety standards are observed and good practice is consistently pursued.

BSL2 and BSL3 Training.

The BSL2 and -3 training provide a multi-phased approach:

- the assessment phase
- the training phase
 - theory
 - hands- on practicum
- final assessment



Each trainee begins with an **assessment phase** that includes a written test focusing on safety related topics, hands-on skills related to protocols based on their research using appropriate biosafety practices and procedures. During the assessment the trainer does not intervene as he/she notes both safety and scientific techniques employed by the trainee. This allows for the determination of experience and level of training that will be required for each trainee. Once the initial assessment is completed the results are reviewed with the trainee, the specific areas of training focus are identified. A written report is then sent to the trainee and their principal investigator or supervisor.

The **training phase** includes a theoretical class which covers the following topics:

- BSL1 through -4 standard microbiological practices, special practices, safety equipment and laboratory facilities.
- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of laminar flow biological safety cabinets (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work, and spill response in the BSC.
- Procedures with the potential for creating infectious aerosols, recognizing aerosol producing devices and learning how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory, BSC, centrifuge, incident response, cleanup, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- Introduction to select agent rules and NIH-Office of Biotechnology Activities guidelines.

The hands-on practicum during the training phase compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a non-hazardous environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as scientific issues (e.g. contamination of cultures). The practicum is specific to biosafety and agents to be used (e.g. bacteria, parasites, viruses) by the trainee. This approach also allows the use of specific protocols or facility specific practices that the trainee brings with them. Emergency response and spill mitigation training allows the trainee to visualize and respond to spills and contamination with the use of florescent dye and breakable training lab ware.

The **final assessment** is identical to the initial assessment, with a written exam and hands-on skills assessment. Once the trainee has completed and passed the final assessment, the trainee is provided with a certificate of training for the biosafety level they completed. A report is sent to the principal investigator, the trainee and the laboratory director.

Animal BSL2 (ABSL2) and Animal BSL3 (ABSL3) Training.

An animal biosafety training program was developed and instituted based on the same concepts as the BSL3 training program. Trainees must have completed BSL3 training before commencing ABSL3 training. All animal use is approved by our institutional animal care and use committee, and our animal holding facilities and procedures have been approved by AAALAC. All aspects of our ABSL2 and ABSL3 training program have been reviewed and approved by the USAMRMC Animal Care and Use Review Office (ACURO).

The ABSL training phase includes a theoretical class which covers the following topics:

- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the BSC, how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work and spill response in the BSC.
- Procedures with the potential to create infectious aerosols, recognizing an aerosol producing devices and learning procedures to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory or in the BSC, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a safe working environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as animal handling. The practicum is specific to biosafety and animal species to be handled. This approach to training also allows the use of specific protocols or facility specific practices the trainee brings with them.

In the third phase, the final assessment includes a written exam and a hands-on skills assessment. Once the trainee has completed and passed the final assessment the trainee is provided with a certificate of training for the biosafety level they completed.

BSL4 Training.

BSL4 training rests upon a firm adherence to the principles and specific practices of safe BSL-3 research. This practice prevents an over-reliance on the BSL4 suit as a primary means of personal protection, and makes the suit an operationally redundant means of personal protection, significantly enhancing overall containment. Accordingly, individuals who are selected for BSL4 training will have completed training at BSL3 and have been approved for independent access to the BSL3 laboratories. These individuals would then complete the BSL4 modular training.

Specific Aims.

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the year. The number of individuals trained at each level is summarized in **Table 1** below and the associated figures. As summarized above, the topics typically covered in this introductory training include the principles of basic safety precautions in the laboratory, routine rules and regulations designed to protect the individual and environment from accidental contamination by an infectious microbe, and the care and use of the biological safety cabinet. Also covered are the appropriate procedures of clean-up following a spill, decontamination procedures, principles of the care and use of autoclaves and other essential equipment.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, real-world training in the laboratory setting. Course content is tailored to include those procedures and the use of specific equipment likely to be encountered by the trainee in their routine work. Thus, those destined to work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL-2 laboratory and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals, allowing for intense interaction between the instructor and trainees. By actually doing the procedures essential to their day-to-day laboratory work under the close supervision an instructor (with the use of indicator dyes that allow clear recognition of contamination), the trainee quickly grasps the key teaching points and rapidly masters safe laboratory practices. Training is offered in the state-of-the-art training laboratory described above.

The numbers of individuals trained under Aim 2 for the NBTC is summarized in **Table 1**.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in containment laboratories is the need to be able to properly operate autoclaves. A dedicated training session is offered to all individuals as a separate element of their orientation to the GNL, and this training is offered to individuals working in other laboratories using the same or similar equipment.

Aerobiology. The GNL contains aerobiology laboratories at both the BSL3 and BSL4 levels of containment. The BSL3 facilities were fully commissioned and approved for use by the CDC and USDA in early 2010, and the GNL BSL4 facilities were approved for full operations in May 2010 with operations beginning in September 2010. These facilities are highly complex and require specialized



training not only in the operation of this sophisticated equipment, but also in the proper care and handling of the laboratory animals that will be experimentally infected.

Over the course of the past reporting year, aerobiology trainees have completed training on the BSL4 aerobiology equipment and have successfully performed BSL4 aerosol runs using Nipah virus and Ebola virus in the GNL. Training has also taken place on the EMKA plethysmography equipment. Aerobiology personnel continue to receive instruction and specialized training about how aerosols are generated, the safety precautions in place in aerobiology laboratories and how to quantitate virus in aerosol samples.

Gamma Irradiator Training. BSL4 laboratories utilize a number of techniques to inactivate biological materials prior to removal from the containment laboratory. One of the most frequently utilized means of removing materials from the BSL4 laboratory is inactivation by gamma irradiation. In an effort to provide training of individuals that use gamma irradiation at UTMB, a module providing background on radiation biology, radiological and biological safety training, select agent and radiological security training, introductory training on dosage determination and method validation, and practical instruction on the use of the devices used for gamma bombardment was assembled and is offered to staff on an as needed basis.

High Through-Put Screening. We are working to develop a systematic training program focused on the safety concerns associated with high through-put screening. We will continue to develop this capability in future years as it represents the cutting-edge interface between technology and biological sciences and as such potentially creates new challenges for biological safety.

Aim 4: To provide a mentorship program for scientists working in BSL3/ABLS3 or BSL4/ABSL4 facilities.

Mentored training typically extends beyond a given reporting quarter. The BSL4 mentorship program provides a hands-on training experience under the tutelage of a senior staff scientist (mentor) with guidance from other experienced laboratorians in the real-world environment of a functioning BSL4 laboratory. The experience includes an orientation to the laboratory environment by a senior BSL4 scientist and then working experience with tasks germane to the proposed tasking of the person being mentored.

As the GNL laboratory was brought online and the Shope laboratory continues to operate, our cadre of experienced BSL4 scientists and scientific staff continues to expand (Figures 1 & 2). This is actually decreasing the individual burden of training as it is now spread across a larger number of scientists and staff. The numbers of staff that have passed into and out of the mentorship program is presented in **Table 1**.

An extensive listing of the number of individuals trained during the reporting year can be found in **Table 1**.

Figure 1. Cumulative Number of Independent BSL4 Users – January 2005-January 2013

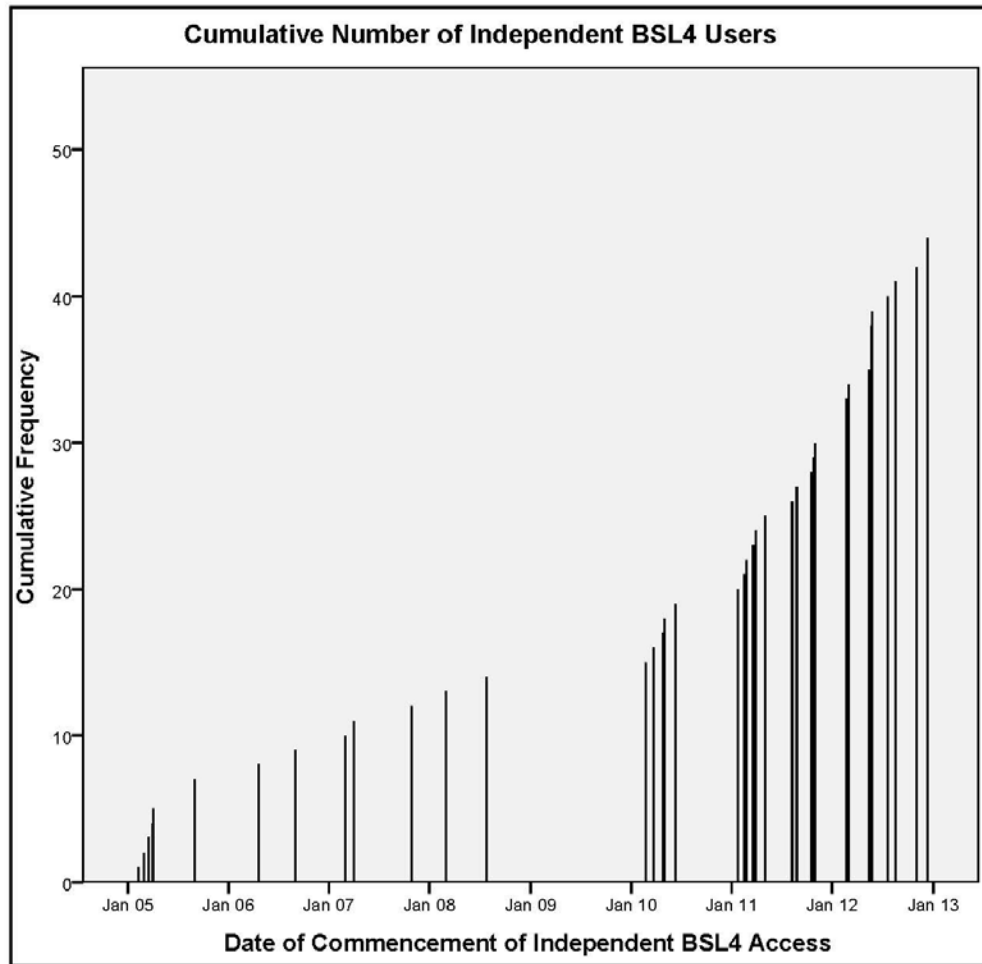
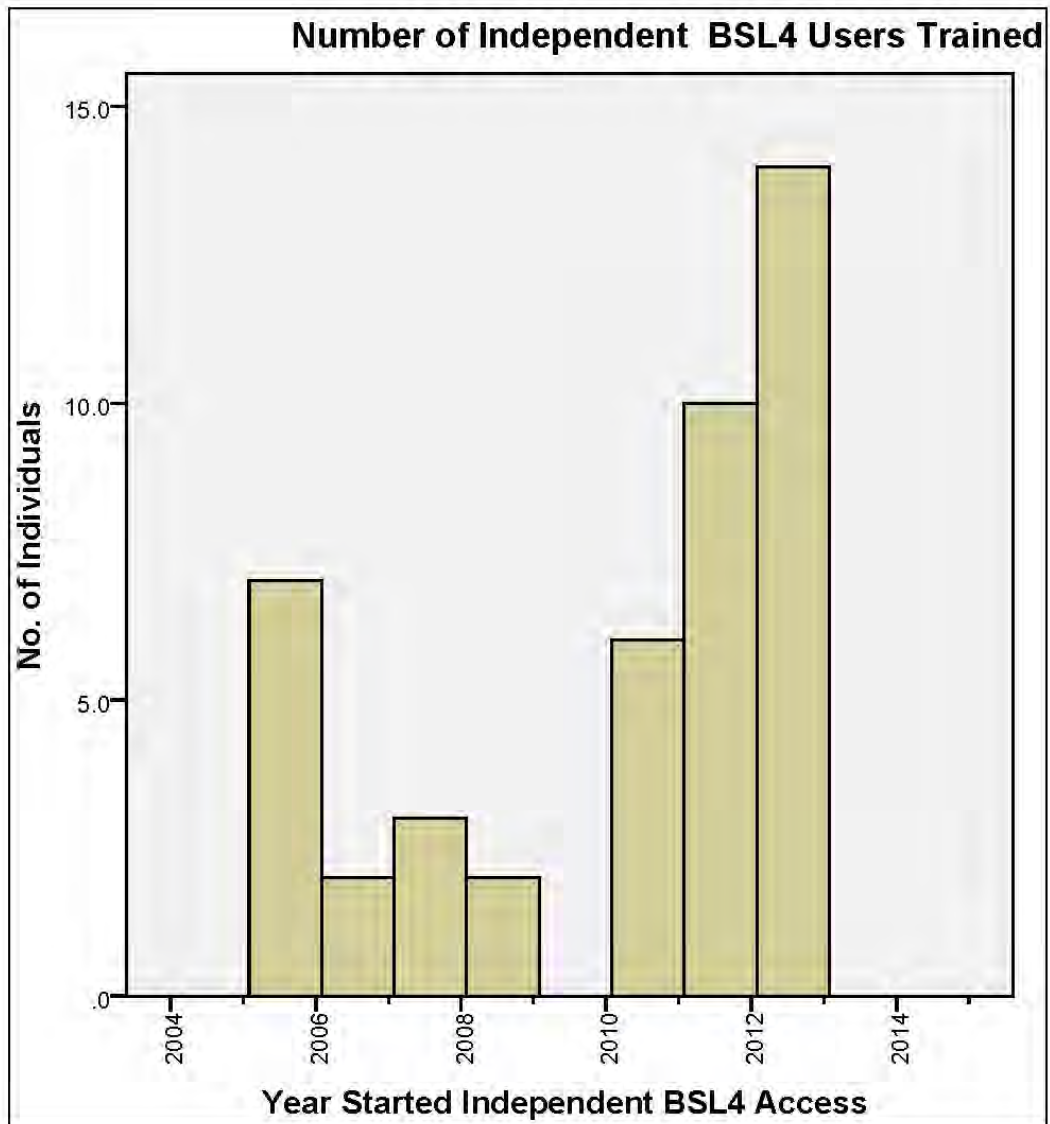


Figure 2. Number of Independent BSL4 Users Trained – 2004-2013



Aim 5: To establish a fellowship program for scientists and facility operations professionals working in BSL3/ABSL3 or BSL4/ABSL4 facilities.

The high and maximum containment fellowship program for scientists is in place. We have two fellows now in training, and one fellow who has transitioned from the program to a permanent UTMB faculty position involving BSL4 pathogen research.

Dr. Gavin Bowick is the first NBTC fellow who had transitioned from the NBTC fellowship to a permanent UTMB faculty position. Unfortunately, Dr. Bowick left UTMB following his training. Dr. Janice Endsley is the second fellow sponsored by the program. As indicated previously, Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr. Endsley will continue in the fellowship as she gains critical experience and masters skills needed to work in this environment.

Dr. Endsley's updates from quarterly reports over the past year detail her progress:

August 2012 Report: Dr. Janice Endsley is a fellow in training in the high and maximum containment fellowship program for scientists. To date she has gained two years of BSL3 laboratory experience performing independent in vitro and animal research in BSL3. In the ABLS3, she has optimized in vivo imaging using the Caliper Life Sciences IVIS system (equipment scheduled for use in the ABSL4 facilities) to track infection in the lung over the time course of disease in a mouse model. She has completed theoretical training for BSL4 work, successfully passed the BSL4 health screening process, and completed BSL4 facilities and suit training. Her mentored training in the BSL4 is continuing under the guidance of Dr. Alex Freiberg. During the mentored training component she will be contributing immunological expertise towards investigations by Dr. Freiberg and Dr. Nadya Yun specific to innate immunity and vaccine development for Rift Valley fever virus and Lassa virus (LV).

October 2012 Report: She has completed all the training and health screening to move forward with lab BSL4 training. Her mentored training in the BSL4 is under the guidance of Dr. Alex Freiberg and she further contributes immunology expertise for Dr. Slobodan Paessler's BSL4 virus (Junin) work at UTMB. This year she is additionally providing hands on training for Environmental Health and Safety specialist Vickie Jones specific to work with *Mycobacterium tuberculosis* (*M.tb*). This training allows Ms. Jones to make biosafety recommendations and provide pathogen-specific training for laboratory personnel that will be working with *M.tb*. She additionally consults with the faculty at the Universidad de Monterrey in Monterrey, MX regarding SOP for working with *M.tb* and handling of MDR-TB isolates that will be shared with UTMB and other U.S. investigators through collaborative arrangements.

January 2013 Report: Dr. Janice Endsley has been the principle investigator for the tuberculosis laboratory in the GNL since 2010 and supervises a research team working with TB in the BSL3 and ABSL3. Her research with *M.tb* is focused on discovery of mechanisms of protective immunity to *M.tb* and gaining an understanding of the microbial synergy between *M.tb* and HIV. Additionally she has developed standard operating procedures (SOP) for measuring immune status parameters in high containment, including T cell memory recall and inflammatory cell (e.g. neutrophils, monocytes) recruitment to sites of infection using animal models of *M.tb*, *Burkholderia mallei*, and *B. pseudomallei*. These procedures include application of magnetic bead-based cell sorting, fluorescent microscopy, and multivariate (11 color) flow cytometry

within high containment. Her lab has recently been approved for work with MDR-TB and the use of an *in vitro* assay that employs human macrophages to screen activity of novel anti-mycobacterial drug compounds. Currently she is providing mentored training to two new scientists for work with *M.tb* in the BSL3 and ABSL3, bringing the total number of scientist trained for work in the TB laboratory to six. Specific to BSL4, this year she has been collaborating with Dr. Slobodan Paessler on a Junin virus project that is focused on investigation of the anti-viral immune response of human dendritic cells to bridge innate and adaptive immunity.

Current quarterly report (through March 2013): Dr. Janice Endsley continues to build and maintains a collection of *M.tb* reference isolates and clinical isolates obtained from patients with drug resistant and drug susceptible TB. This past year she provided mentored training for UTMB EH&S personnel for work with *M.tb*. This allows the EH&S staff to develop TB protocols and training programs as part of their educational mission through the Laboratory Bio-containment Training Program including training workshops held in South America and Africa, where TB is a high priority area for labs beginning to work in BSL3 environments. In addition she has provided TB lab training for a senior GNL laboratory scientist, three research associates, and two graduate students. She also mentored a graduate student and a postdoctoral fellow for BSL3 work with *Burkholderia pseudomallei*. Dr. Endsley has developed several animal models in ABSL3 including a humanized mouse model of TB, a TB/HIV co-infection model, and is currently working to develop an latent TB model. She additionally works in collaboration with Dr. Alfredo Torres to develop mouse models of aerosol-acquired Mellioidosis due to *Burkholderia pseudomallei* (Tier 1 select agent) infection. She has developed, optimized, and/or adapted several new techniques for study of *M.tb* or *B. pseudomallei* in the BSL3/ABSL3 including confocal microscopy-based bacterial viability detection, in vivo imaging of bacterial infection in live animals., multi-color flow cytometry, multi-plex ELISA, and in vitro HIV/TB co-infection assays. Her lab is now approved for work with MDR-TB and the use of an in vitro assay that employs human macrophages to screen activity of novel anti-mycobacterial drug compounds.

Dr. Aysen Gargili is the program's third fellow. Dr. Gargili a veterinarian and internationally recognized tick expert from Turkey who is also participating in the maximum containment fellowship program for scientists. She has spent a year onsite at UTMB and has recently gained full independent access to our BSL4 laboratories. (She began her fellowship in January 2012 and will be departing in summer 2013).

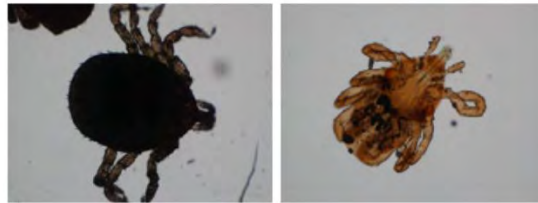
Dr. Gargili's updates from quarterly reports over the past year detail her progress:

August 2012 Report: Dr. Gargili has been working with Dr. Dennis Bente and a team of researchers to establish colonies of vector ticks from Turkey and elsewhere and will be studying how the virus is maintained and transmitted in nature. This is the first step in what we hope will grow into sustained field and laboratory collaborations with Turkish students and scientists. Dr. Gargili has also been studying the various methods and mechanics of biocontainment as a part of her fellowship.

October 2012 Report: Dr. Aysen Gargili, also a fellow in training in the high and maximum containment fellowship program for scientists, completed mentored training this quarter as well as individual hours in BSL3 and is now certified to work individually in BSL3. Dr. Gargili also completed her checklist training, suit tests and started to her mentored hours in the BSL4. Thus far she has made ten entrances and amassed thirty hours of mentored hours in the BSL4. She

has added more vector tick species to our colonies and has been successful in establishing a self-sustaining colony establishment. She has also developed and improved the infestation techniques that her team will use for animal infestations in BSL4. They presented some of these data in FP-7Arbozoonet's final meeting poster presentation. She and her team have also collaborated with researchers working on real-time live imaging, and currently are working on the development of imaging techniques in live ticks/animals which will be employed in BSL4 for the visualization of the virus in the vector and the host. Dr. Gargili's plan for the next quarter is to complete her mentored entrances and hours in the BSL4 and begin planned studies.

January 2013 Report: During this reporting quarter Dr. Gargili has made 33 entrances and amassed 80 hours in the BSL4 laboratory as a part of her training toward full, independent access to the laboratory. She has started infectious disease studies and has undertaken



the establishment of an infected tick colony in BSL4. She and her research team have also made progress on further infectious studies for the visualization of virus either in the tick or in infected animals with real-time imaging techniques. They have accumulated critical data on the imaging techniques in live ticks/animals and started to use this data in BSL4 for the visualization of the virus in the vector and the host. Collaborations with Dr. Gustavo Valbuena – a GNL researcher – and his team have begun with humanized mice and infected ticks in BSL4 to see the preliminary results of the infection on human skin.

Current quarterly report (through March 2013): Upon her return to Turkey later this year, Dr. Gargili will direct a national biocontainment facility outside Istanbul. During this reporting quarter we are enthusiastic that Dr. Gargili accumulated necessary entries and hours in the BSL4 and qualified for independent access. She and her team of researchers began infectious studies with the establishment of an infected tick colony in BSL4. To our knowledge, this is the only such work being conducted at BSL4 in the country and potentially the world. Dr. Gargili and her colleagues also designed further infectious studies for the visualization of the virus either in the tick or in infected animals with real-time imaging techniques. They accumulated critical data on the imaging techniques in live ticks/animals and started to use them in BSL4 for the visualization of the virus in the vector and the host. Her team also continued to collaborate with UTMB researcher Dr. Gustavo Valbuena's team and began to infest humanized mice with infected ticks in BSL4 to see the preliminary results of the infection on human skin. We are proud to have the opportunity to mentor the next generation of scientists that will undertake this groundbreaking research.

The laboratory containment operations fellowship is unique and is, to the best of our knowledge the only one of its kind. The program promises to set a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists, where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, most entering facility operators will require a more structured course of study. Consequently, we have identified fourteen distinct modules to be covered over the course of the fellowship. These structured modules cover basic microbiology, provide an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, select agent regulations, formal Good Laboratory Practices, annual certification of laboratories, testing of HEPA filter

housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping.

During the course of their training, fellows will directly participate in each of these activities, as well as be personally involved in the planned shut down and decontamination of containment suites, validate decontamination, and conduct and oversee maintenance activities. Plans are being developed to allow fellows to visit other high and maximum containment laboratories across the nation during the second year of their fellowship to better understand the diversity of facilities and variations in containment practices.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over this past year of support we have actively participated in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology and other organizations at the fore of these discussions. We have also participated in ongoing discussions on these topics hosted by the National Science Advisory Board for Biosecurity (NSABB) and the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.

Biosurety and biosecurity are currently covered in our theoretical training sessions, and we are in the process of developing a structured course to more specifically address biosurety and biosecurity in depth. We anticipate posting this course on our internal website as an educational tool to augment our more formal training opportunities and to complement lectures already offered. Depending upon the success of this internal posting, we will then consider posting the course on our website where it would be available to the general public.

As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established a distinguished speaker series. Our *Topics in Biosecurity Symposia Series* has been offered since 2010. Sessions in the series continue to be of great interest to students, faculty and community members and are consistently attended by large crowds drawing positive attention and feedback.

Summary of Biosurety and Biosecurity training activities this past year:

Topics in Biosecurity Symposia Series.

- **October 4, 2012 – Dr. Jeanne Guillemin.** Dr. Guillemin (pictured right with Dr. James W. Le Duc) was the guest speaker for the eighth session in this distinguished speaker series. She was a guest of the NBTC on Thursday, October 4, 2012. She delivered a seminar



entitled *The 2001 Anthrax Letter Attacks: Bioterrorism and the American Response*. Dr. Guillemin is a senior fellow with the Massachusetts Institute of Technology's Center for International Studies. She is also an acclaimed author of *Anthrax* (1999), *Biological Weapons* (2005) and *American Anthrax* (2012).



Dr. Guillemin delivered her seminar to a capacity crowd of students, staff and local community members to great reviews. She also spent time with our aerobiology service division students and staff (*pictured right*) discussing the intricate aspects of her research.

- **December 7, 2012 – Dr. Philip K. Russell (US Army MG, ret.) and Dr. Gigi Kwik Gronvall** (*pictured right*) jointly presented the session “Biological Weapons: Does U.S. biodefense meet the threat?” Dr. Russell is a former senior advisor to the Assistant Secretary for Public Health and Emergency Preparedness, U.S. Department of Health and Human Services – and the former Commanding General of the U.S.



Army Medical Research and Material Command. Dr. Gronvall is a senior associate at the University of Pittsburgh Medical Center's Center for Biosecurity.

- **January 7, 2013 –** The NBTC was proud to host **Dr. James P. Burans** and his team (*pictured right*) from the National Biodefense Analysis and Countermeasures Center's (NBACC) genomics program. Dr. Burans, along with **Dr. Nicholas Bergman**, **Dr. Adam Phillipy** and **Dr. M.J. Rosovitz** presented a program of the work underway at NBACC and the use of advanced genomics in their research entitled “*The National Bioforensic Analysis Center and the Use of Genomics in Bioforensic Analysis.*”



- **February 12, 2013 – Dr. Malcolm Dando** was the featured guest for this eleventh session in the speaker series. Dr. Dando (*pictured right*) is a professor of international security at the University of Bradford in the United Kingdom. A biologist by training, his main research interest is in the preservation of the prohibitions embodied in the Chemical and the Biological Weapons Conventions at a time of rapid scientific and technological change in the life sciences. His presentation topic was entitled, *“Biosecurity Education for Practicing Life Scientists: The Missing Past, Unsatisfactory Present and Uncertain Future.”*



- **April 18, 2013 – Dr. Patricia Nuttall** was the honored guest for the most recent session in the speaker series. Dr. Nuttall (*pictured right alongside UTMB faculty and NBTC scientists Drs. Dennis Bente, Aysen Gargili and Jim LeDuc*) is a professor of arbovirology in the Zoology Department at Oxford University in the United Kingdom. Dr. Nuttall is formerly with the Natural Environment Research Council where she served as director of the Centre for Ecology & Hydrology. Her research interests focus on viruses transmitted by ticks and how tick saliva promoted virus transmission. Her presentation was entitled, *“The Role of the Health Protection Agency in Homeland Defense for the United Kingdom.”*



Each of these sessions was widely attended by UTMB faculty, staff, students and Galveston community members. This popular speaker series will continue through 2013 with several sessions already in the planning stages.

NBTC Website.

Over the past reporting year, the new NBTC website has continued to develop - www.utmb.edu/nbtc and it has become a home base for the program. Course training schedules and staff listings are continuously added to the website. We also updated our staff listing with new members of the training team. Per its intent, this site serves as a hub of information regarding the Center, our goals, and the resources that the NBTC makes available to the biosafety and research communities.



Onsite/Offsite training and related updates from the past reporting year.

- **NBTC Informational Booth.** The NBTC informational booth was present at an impressive number of professional meetings during this reporting year. In each location, NBTC trainers detail the program for prospective participants and are on hand to answer specific questions from interested individuals. :
 - The American Society for Microbiology Biodefense Meeting, February 26-29, 2012 in Washington, DC
 - The American Society for Microbiology 112th General Meeting, June 16-19, 2012 in San Francisco, CA
 - The African Biological Safety Association Conference, June 24-27, 2012 in Johannesburg, South Africa
 - The American Society of Virology Annual Meeting, July 21-25, 2012 in Madison, WI
 - The 55th Annual American Biological Safety Association Conference/Meeting, October 18-24, 2012 in Orlando, FL
 - 63rd American Association for Laboratory Animal Science National Meeting, November 4-8, 2012 in Minneapolis, MN
 - The American Society of Tropical Medicine and Hygiene Annual Meeting/Conference, November 11-15, 2012 in Atlanta, GA
 - USDA/ARS/ABSA, February 4-7, 2013 in Alexandria, VA
 - The American Society for Microbiology Biodefense Meeting, February 25-27, 2013 in Washington, DC
- **Biocontainment engineering.**
 - Throughout the past reporting year, resident biocontainment engineer Mr. Miguel Grimaldo, actively participated as a member of the ANSI Z9.14 Committee to development of an **American National Standards Institute (ANSI)** standard for "Testing and Performance Verification Methodologies for Ventilation Systems for Biological Safety Level 3 (BSL3) and Animal Biological Safety Level 3 (ABSL3) Facilities." This work has included the writing and/or revision of sections of the standards and participations in conference calls. The third draft of the standard was presented to the full committee on March 31, 2013 and it is currently going through the final comments and edits. It is expected that the standard should be ready for public review by the fall of 2013.
 - From June 2012 to May 2013, Mr. Grimaldo responded to requests for information/guidance on biocontainment related issues from the following:
 - **NIH Integrated Research Facility** in Ft. Detrick, MD regarding autoclave cycles and APR door operations for BSL4 Laboratories.
 - **University of Monterey, Mexico** regarding BSL3 Facility Commissioning and Testing.
 - **Centers for Disease Control and Prevention's Office of Health and Safety** regarding the decontamination and certification of Membrane (PTFE) filters used on vent lines of BSL4 and BSL3 Enhance Laboratories.
 - **National Institute for Human Viral Diseases "Dr. Julio I. Maiztegui". Pergamino, Argentina** regarding BSL3 Commissioning and Operations.
 - **University of Hawaii** on BSL3 facility re-verification.

- **Victorian Infectious Disease Reference Laboratory, Melbourne, Australia** regarding BSL4 operations.
- **National Institute of Health, Office of Research Facilities** on BSL4 Facility Operations.
- **Public Health Agency of Canada. Biocontainment Engineering and Facility Operations. Pathogen Regulation Directorate** on BSL4 breathing air suit airflow setup and verification.
- **Centers for Disease Control and Prevention (CDC)**, BSL4 Facility Training of a select Agent Inspector.
- **U.S. Army Corps of Engineers, Fort Detrick Integrated Program Office** on Certification of membrane (PTFE) filters used on Effluent Decontamination Systems.
- **Boston University, National Emerging Infectious Diseases Laboratories** regarding BSL4 Operations.

- **NIAID NBL/RBL Facilities Network.** As part of the ongoing collaboration with other institutions who are home to biocontainment research facilities, Mr. Grimaldo actively participates on the conference calls for the Facility Operations Group of the **NIH/NIAID National Biocontainment Laboratory/Regional**



Biocontainment Laboratory Network. He also coordinated training activities for visiting biocontainment facility engineers and maintenance staff from the NBL/RBL Network during the annual meeting of the group in April 2013 (*pictured top*). The GNL was pleased to host this 5th Annual Meeting in April 2013. This was the third time that UTMB has hosted this meeting. Biocontainment researchers and practitioners (*pictured bottom*) from the 15



academically-based BSL3 and BSL4 laboratories supported by NIAID travelled to UTMB for two days of collaborative meetings. The topic of biosecurity always plays a prominent role in this meeting and the staff of the National Biocontainment Training Center, like Mr. Grimaldo, played a key role in biosafety instruction and presentations.

- **Guests and Outside Groups/Visitors.**

- *August 2012 quarterly report* - the NBTC was honored to be among the UTMB infectious disease groups to host summer interns from West Point. West Point cadets Nicholas Tubbs and Whitney Strong spent part of their summers as interns through UTMB's Institute for Human Infections and Immunity while participating in the Academy's Academic Individual Advanced Development program. The purpose of the AIAD program is to provide a venue for educational experiences that would not be possible within the usual framework of academic, military, and physical programs. Cadet Tubbs completed a biocontainment engineering internship with the NBTC's Miguel Grimaldo in the GNL and Cadet Strong joined the lab of Dr. Alex Freiberg in Keiller for a scientific research internship. Cadet Tubbs shadowed GNL biomechanical engineers during his stay, learning the basics of building engineering from air flow and filtration to electronic monitoring systems and routine maintenance. 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. These types of internships provide an excellent "on the job" training opportunity to students with an interest in biocontainment research and engineering.
- *August 2012 quarterly report* - One of our newest biocontainment trainee/researchers who has an active interest in biosecurity and biocontainment has decided to pursue a nontraditional path outside of the bench research arena. Dr. Ashley Grant has been selected as a fellow in the 2012 class of the *Emerging Leaders in Biosecurity Initiative* by the Center for Biosecurity at the University of Pittsburgh. Over 150 talented individuals from across the country applied for the prestigious fellowship and Dr. Grant was among the 25 awardees. Fellows participate in a series of events in Washington, D.C., designed to facilitate candid discussions about current and anticipated biosecurity challenges and to afford them the opportunity to contribute ideas to the U.S. scientific and policy communities. Dr. Grant's participation in the program places her in elite company alongside participants from federal agencies, national laboratories and academia. Dr. Grant has also been awarded the National Academies Christine Mirzayan Science and Technology Policy Graduate Fellowship Program sponsored by the National Academy of Sciences and its constituent organizations (collectively known as the National Academies). She will be a policy fellow with the Committee on International Security and Arms Control (CISAC) within the Policy and Global Affairs (PGA) Division focusing on the India-U.S. Workshop on Biosafety and Biosecurity and development activities associated with CISAC's Chinese and Russian biosecurity dialogues. *As an update to this entry, another member of the GNL team was selected to participate in the second class (2013) of the Emerging Leaders in Biosecurity Initiative by the Center for Biosecurity at the University of Pittsburgh. Michael Patterson, a virology student soon due to complete his course of study at UTMB, will participate in the program beginning later this fall. We will make note of his progress in future quarterly reports.*

- *Current reporting quarter* - A pilot course entitled *Achieving Data Quality and Integrity in Maximum Containment Laboratories* was held April 1-5, 2013 in the GNL. Developed as a collaborative project between UTMB and the United States Food and Drug Administration (FDA), the training program included four days of instruction plus a half day of interactive mock-BSL4 laboratory exercises in the NBTC training laboratory (*pictured is NIAID program officer Dr. Kimberly L. Taylor in a BSL4 training suit in the mock training laboratory*). The primary course objective was to cross educate sponsors, scientists, veterinarians, quality assurance personnel, regulators, Agency reviewers, and Agency policy-makers to enable the conduct of regulated studies in support of product approval via FDA's Animal Rule. For many Agency reviewers and Sponsor Contracting Officers, the laboratory exercise was a rare opportunity to experience physical restrictions due to biosafety requirements. Sixty-nine attendees participated in the course, including FDA representatives from the Centers for Drugs, Biologics, and Veterinary Medicine, the Office of Regulatory Affairs, and the Office of Counterterrorism and Emerging Threats. Faculty and attendees included members from the Centers for Disease Control and Prevention (CDC), Department of Army Inspector General (DAIG), Battelle, US Army Medical Research Institute of Infectious Diseases (USAMRIID), National Institute of Allergy and Infectious Diseases (NIAID), National Biodefense Analysis and Countermeasures Center and the Health Protection Agency (HPA) from Public Health England, United Kingdom.



Additional training opportunities of note over the past reporting year.

- *October 2012 quarterly report* – On October 1, 2012 Belinda Rivera and Dr. Curtis Klages travelled to Baylor College of Medicine Houston to provide hands-on ferret training to four individuals involved in influenza research. Training was requested by and provided to a principal investigator and his research staff in anticipation of the start of an influenza study utilizing ferrets. They specifically asked the NBTC staff to provide training for them on ferret handling techniques in BSL2 biocontainment.
- *October 2012 quarterly report* – NBTC trainers and staffers Vickie Jones, Belinda Rivera, Je T'Aime Newton, Dee Zimmerman, Miguel Grimaldo and Sophie Brocard attended the 54th American Biological Safety Association (ABSA) annual meeting October 18-24, 2012 in Orlando, Florida to promote the training program, maintain continuing education credits and augment national and international networking groups. The ABSA conference is the nationally and internationally recognized biological safety conference for biosafety professionals. The conference is the focal point for current biosafety professional development, accreditation, national and international recognition and resources. Pre-conference courses are designed to provide training for

those entering the field as well as allowing for maintenance accreditation for the Registered Biosafety Professional and the Certified Biosafety Professionals.

- Ms. Rivera taught a pre-conference course at ABSA entitled *“Introduction to a Nonhuman Primate Training Program.”*
 - Ms. Zimmerman co-taught a pre-conference course entitled *“BSL3 Operation and Maintenance”* at the conference.
 - Dr. Brocard co-taught a pre-conference course entitled *“Introduction to Biological Risk Assessment”* at the conference.
 - Ms. Jones facilitated the pre-conference courses *“Concepts of Virology and Virus-based Gene Vectors”* and *“Fundamentals of Biosafety”*.
 - Ms. Zimmerman facilitated the pre-conference courses *“Biosafety Management Techniques for Improving Organization Program Understanding and Support.”*
 - Ms. Newton facilitated the pre-conference course *“Fundamentals of the Class III Biosafety Cabinet.”* This course was held at the Germfree company facilities in Ormond Beach, Florida. As the Chair of the Pre-Conference Course Committee Ms. Newton was responsible for all the pre-course meetings with the facilitators and ensuring that all the courses at the pre-conference had the needed material and ran smoothly. A total of 27 courses over a 3 day period were offered this year.
 - Dr. Brocard facilitated the pre-conference course *“Aerobiology in Infectious Disease Research: Fundamental and Applied Concepts.”*
 - Mr. Grimaldo participated in the daylong session *“Sharing Biorisk Management Success Stories.”* As a part of this session, he provided information regarding the training program to many potential international training fellows.
- *January 2013 quarterly report* - During this reporting quarter, senior biocontainment veterinarian Dr. Curtis Klages traveled to the Oregon Health & Science University and the Oregon National Primate Research Center to discuss and evaluate the operation of their ABSL3 non-human primate facility. This trip also determined the scope of training that the NBTC could potentially offer the university/center in the operation of their ABSL3 laboratories. Follow-up discussions and a training proposal will be provided to the group during the next reporting quarter.
 - *Current reporting quarter* – In April 2013, and NBTC trainer was invited to The University of Texas at Austin to provide BSL3 theoretical and practical training for 15 staff (10 participated in the theoretical course only and 5 took the full course – *four of whom are pictured*) who will work in the containment laboratory. The principal investigator, biosafety officer, safety manager, graduate student 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 scenarios. Evidence of achievement by the trainees was demonstrated in successful completion of theoretical and practical assessments. All participants were awarded certificates.

Table 1. Summary of training courses offered and number of participants in each course, May 2009 through April 2013.

Training Course/Module	May-Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-Dec 2012	Jan-April 2013	Total
BSL4	9	28	59	47	12	155
BSL3 Theoretical	45	119	100	135	34	433
BSL3 hands-on	45	101	94	76	29	345
BSL2 Theoretical	107	144	251	160	24	686
BSL2 hands-on	64	76	92	117	16	365
ABSL3 Theoretical	29	55	47	73	17	221
ABSL3 hands-on	29	50	46	37	19	181
ABSL2 Theoretical	N/A	1	79	149	94	323
ABSL2 hands-on	N/A	1	40	76	81	198
Graduate Program	39	36	32	13	0	120
Aerobiology	19	5	2	8	0	34
Autoclave	195	27	46	30	9	307
High Throughput Safety training	8	11	3	2	2	26
Non-human primate theoretical	16	15	60	41	4	136
Non-human primate hands-on	N/A	N/A	90	41	8	139
Non-human primate annual refresher	N/A	N/A	37	114	0	151
BSL3 mentorship	36	41	24	18	4	123
ABSL3 mentorship	N/A	N/A	38	19	9	66
PAPR	N/A	10	49	52	31	142
Intro to Micro	18	0	6	4	0	28
Animal handling certificates	N/A	N/A	22	75	3	100
ABSA/AfBSA courses	84	175	87	207	40	593
Total trained	743	895	1304	1494	436	4872

Figure 3. Total number of courses administered annually over the history of the biosafety training program – May 2005-December 2012. The creation of the NBTC in 2009 has contributed significantly to the exponential growth of the biosafety training program.

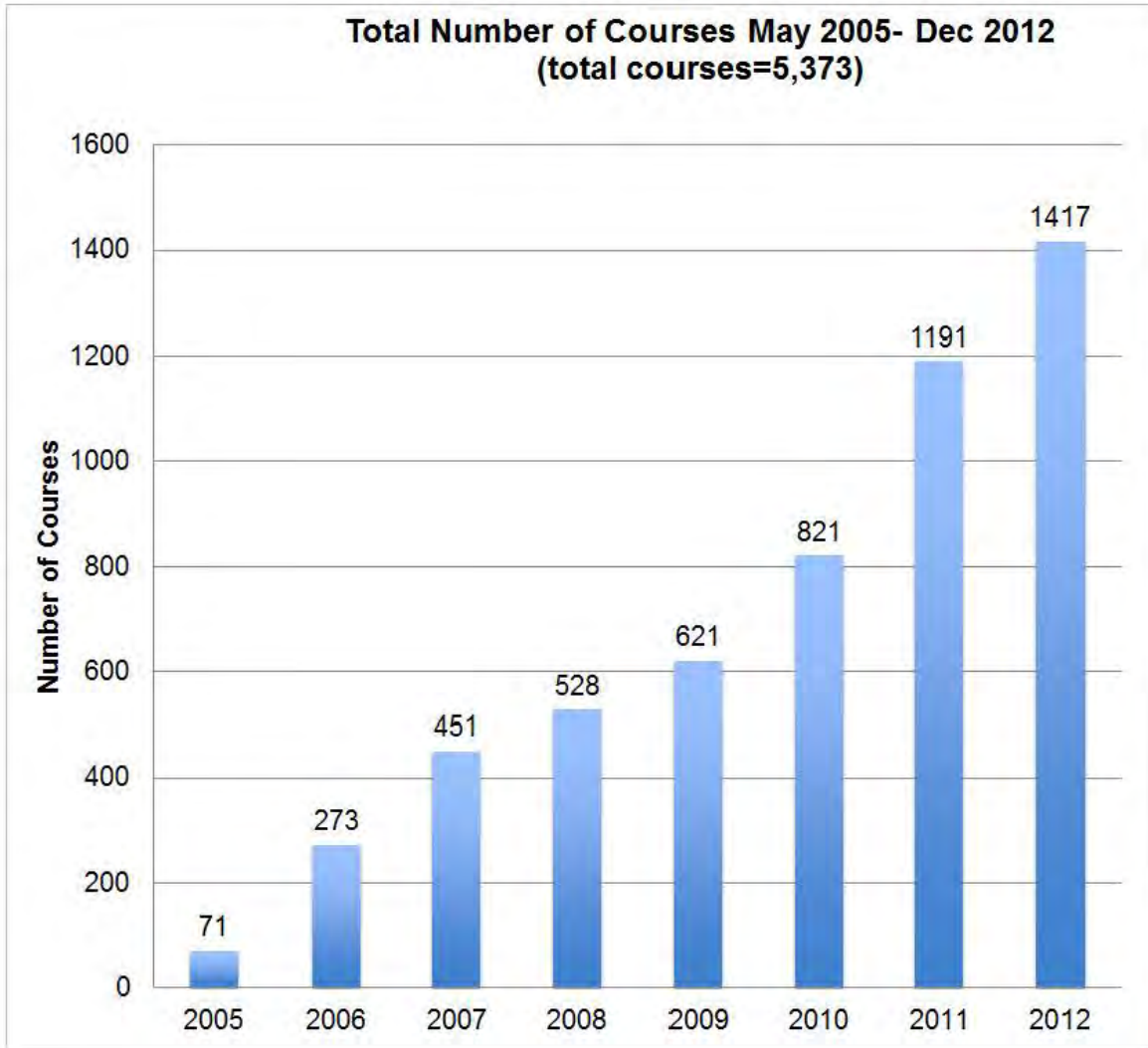
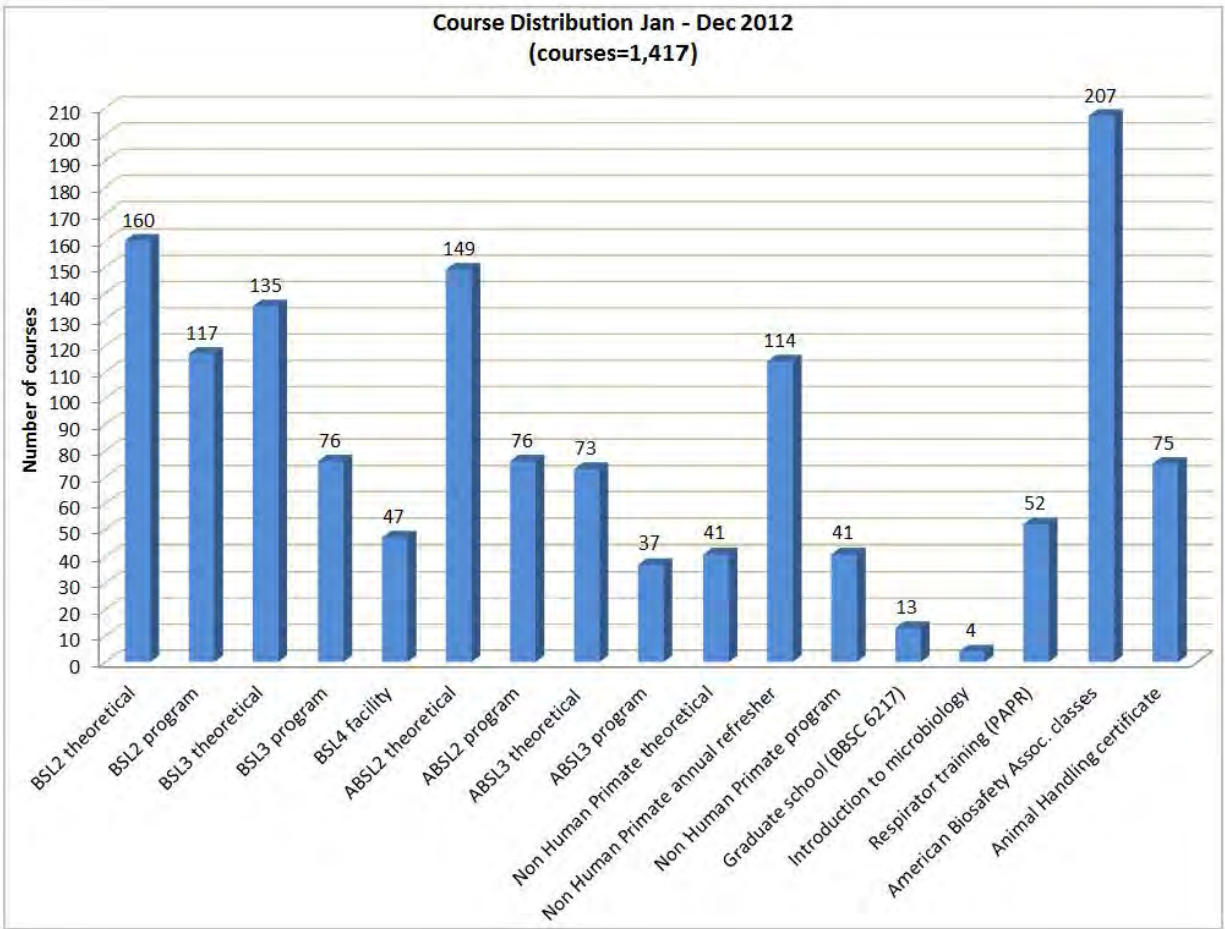


Figure 4. Distribution of courses administered during the 2012 calendar year. This chart provides a glimpse into the demand for courses over a twelve month period.



KEY RESEARCH ACCOMPLISHMENTS 2012-2013:

- A comprehensive, standards-based training program has been established and implemented to prepare individuals for work at all levels of biocontainment.
- Advanced, mentored training is available to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL4 level.
- A unique fellowship has been created to train the next generation of containment laboratory facility operations professionals prepared to oversee the safe operations of these complex facilities.
- A novel training opportunity addresses the safety considerations emerging at the interface of high through-put screening of potentially infectious material.
- As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established the *Topics in Biosecurity Symposia Series*. Sessions offered thus far continue to be attended by large crowds and draw positive attention and feedback. Planning is underway to continue the series with 2013-2014 sessions.

REPORTABLE OUTCOMES 2012-2013:

- Since the inception of UTMB's Laboratory Biosafety Training Program, prior to the TATRC funding award in 2009, nearly 5,000 individuals – both internal to UTMB and external, both nationally and internationally – have been instructed in the safe research and operation in biocontainment laboratories. The vast majority of these trainees have taken part in the program since 2009 when TATRC funding allowed for significant growth of the program.
- Requests for external biosafety training are being continuously received. As evidenced by the list below, this past reporting year has been an active one. Several events have already been scheduled for the next reporting year.

2012 External Training at UTMB:	
January	BSL3 - one individual from University of Monterrey in Monterrey, Mexico
March	BSL3 - two individuals from City of Houston Department of Health & Human Services ABSL3 - one individual from UT-San Antonio ABSL3 - one individual from Baylor University in Waco, TX
July	BSL2 - one individual from University of Houston in Houston, TX BSL3 - two individuals from City of Houston Department of Health & Human Services
August	BSL2 - one individual from UT-Austin BSL3 - one individual from KOC University in Istanbul, Turkey BSL3 - three individuals from UT Southwestern ABSL3 - one individual from KOC University in Istanbul, Turkey
September	BSL2 - two individuals from Lynntech, Inc. in College Station, TX BSL3 - two individuals from City of Houston Department of Health & Human Services

November	BSL2 - one individual from Lynntech, Inc. in College Station, TX BSL2 - one individual from Milwaukee School of Engineering in Milwaukee, WI BSL3 - one individual from Milwaukee School of Engineering in Milwaukee, WI BSL3 - one individual from City of Houston Department of Health & Human Services
2013 External Training at UTMB:	
January	BSL2 - one individual from Texas Southern University (TSU) in Houston, TX BSL3 - one individual from the Brooke Army Medical Center in San Antonio, TX
February	ABSL3 - one individual from Arizona State University in Tempe, Arizona
March	BSL2 - one individual from ABC Actini in Lewis Run, PA ABSL3 - two individuals from UT El Paso
April	BSL3 - two individuals from University of New Mexico in Albuquerque, NM ABSL3 - one individual from University of Houston ABSL3 - one individual from Research Animal Resource Center in New York, NY
May	BSL2 - two individuals from University of Houston BSL3 - one individual from Oklahoma State in Stillwater, OK BSL3 - one individual from Fred Hutchinson Cancer Research Center in Seattle, WA
July – (confirmed)	BSL2 - one individual from NuAire in Phoenix, AZ BSL3 - one individual from Booz Allen Hamilton, Inc. (DTRA contractor) in Lorton, VA BSL3 - one individual from Arizona State University in Tempe, AZ
August	BSL3 - one individual from University of New Mexico in Albuquerque, NM
December	BSL3 - one individual from Texas A&M University in College Station, TX
Offsite Training 2012-2013	
January 2012	BSL3 - four individuals at Battelle Facility in Columbus, OH ABSL3 - four individuals at Battelle Facility in Columbus, OH
May	BSL2 & BSL3 in Pergamino, Argentina (35 trained)
June	BSL3 - six individuals at City of Laredo Health Department in Laredo, TX
August	BSL3 - 44 individuals at AFRIMS Facility in Bangkok, Thailand ABSL3 - 14 individuals at AFRIMS Facility in Bangkok, Thailand NHP - 22 individuals at AFRIMS Facility in Bangkok, Thailand BSL2 - 11 individuals at Caliber Biotherapeutics in College Station, TX BSL3 - 23 individuals at CENETROP facility in Santa Cruz, Bolivia
April 2013	BSL3 - 16 individuals at UT Austin facility in Austin, TX
Pending for 2013	
	BSL2 - 6 individuals training at UTMB from Methodist Hospital in Houston, TX
	BSL3 - 6 individuals at the Florida Department of Agriculture in Kissimmee, FL
	BSL3 - 6 individuals either at UTMB or at Tulane University in New Orleans, LA

CONCLUSIONS:

The National Biocontainment Training Center offers a robust and intensive training program devoted to all aspects of biological safety, biocontainment, and biosecurity. This program offers unique, hands-on training to trainees, staff and external partners at all levels of biocontainment, including focused, mentored training in the BSL4 laboratory.

Nearly 5,000 persons have benefited from one or more of these training courses, many of whom are now pursuing graduate education and using these specialized skills in the recently constructed GNL containment facilities. Intensive, mentored fellowship programs have been established to offer opportunities for in-depth training in research under BSL4 conditions and also in containment laboratory operations and maintenance. These fellowships are proving quite successful and are helping address the critical national shortage of well-trained containment laboratory scientists and facility operations specialists.

2012 Table of Contents	1
Introduction	2
Body	
Staffing Report	3
Teaching Laboratory Facilities	5
Overview of NBTC training	6
BSL-2 and BSL-3 training	6-7
Animal BSL-3 training	7-8
BSL-4 training	8
Specific Aims 1-6	8-18
Table 1. Summary of Courses/Participants	19
Figure 1. Trainees 2005-2012	20
Figure 2. Course distribution.	20
Figure 3. Geographic distribution.	21
Key Research Accomplishments	21
Reportable Outcomes	22
Conclusions	22
References	23

INTRODUCTION

The **National Biocontainment Training Center (NBTC)** provides standards-based theoretical and practical training to students and professionals preparing for work in biocontainment laboratories where especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL-2), BSL-3 and BSL-4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee. Advanced coursework includes hands-on mentored training in the containment laboratories, including consecutive training at BSL-3 and BSL-4 levels of containment should that meet the researcher's needs. Specialized training in the handling of laboratory animals is also offered. Sponsored mentored training is available to scientists embarking on a career focused on high hazard pathogens at the BSL-4 level through a dedicated fellowship. Fellows in this program work under the close supervision of an established mentor while addressing a research topic of their own choosing. Mentored scientists and fellows progress to full independent access to the BSL-4 laboratory only when their mentor and laboratory director are fully confident of the individual's skills and ability to work independently in this environment.

The NBTC also offers a unique training opportunity for facility operations specialists interested in pursuing a career as a biocontainment operations manager. To the best of our knowledge, this is the only such training program in the world. This program is designed as a series of modules which address specific aspects of the construction, maintenance and safe operation of a biocontainment laboratory. The coursework is tailored to the specific needs of the individual trainee and involves both didactic training and mentored hands-on work using the Galveston National Laboratory (GNL) as its classroom. Over the course of the training period, which is anticipated to require up to two years for completion, the fellow(s) will be directly involved in the maintenance of the laboratory, decontamination of specific laboratories, monitoring and replacement of filters, fans and control units, understanding the Building Automation System (BAS), and a wealth of other duties routinely seen in the operations of typical biocontainment facilities.

BODY

TATRC's financial support for the NBTC formally began on May 22, 2009 and this submission comprises our second annual report for this initiative. The Laboratory Biosafety Training Center at The University of Texas Medical Branch was established and operational prior to receiving TATRC funding; consequently, the course structure and procedures were already in place and allowed the NBTC to implement enhanced training operations almost immediately. From inception to date, the NBTC has provided training to more than 3,000 participants through the various courses offered. Below is a summary of the significant progress made over the preceding year (2011-2012) under TATRC support. Funding and accomplishments are organized by each specific aim as they were presented in our original proposal.

Staffing Report.

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. Below is a summary of the individuals supported by the TATRC award over the past reporting year and their roles in the operation and management of the NBTC.

Dr. Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr. Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr. Ksiazek also oversees the BSL-4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL-4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL-4 environment.

Dr. Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr. Anne-Sophie Brocard, an accomplished virologist and experienced biosafety trainer who has directed the training center courses since their inception. Dr. Brocard provides both theoretical and practical training to trainees and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms. Je T'aime Newton. Dr. Brocard is ably assisted by Ms. Je T'aime Newton, a highly experienced instructor with extensive expertise in biocontainment. Ms. Newton provides specialized training at all levels of containment, but is specifically responsible for preparing trainees for BSL-4 investigations, focusing her efforts on the proper care, use and maintenance of the protective "space suits" used in the BSL-4 laboratory and other aspects of work in this highly specialized environment.

Ms. Vicki Jones. Ms. Jones is a critical member of the teaching faculty who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera. Ms. Rivera is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical animal training modules.

Mr. Jason Hardcastle. Mr. Hardcastle is a trainer and assists Ms. Jones and Rivera with the training of students, specializing in *in-vitro* techniques.

Ms. Dee Zimmerman. Ms. Zimmerman is the director of the University's biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Dr. Sarah Ziegler. Dr. Ziegler is a trainer and assists Ms. Jones and Mr. Hardcastle with the training of students, specializing in *in-vitro* techniques.

Mr. Lee Thompson and Mr. Miguel Grimaldo. The containment operations fellowship is currently coordinated through the efforts of Mr. Grimaldo (funded by other GNL and UTMB

resources). Mr. Thompson aided in this effort until his retirement at the end of the second quarter during the past reporting year. Mr. Grimaldo is responsible for the content development of each module of the containment engineering and operations fellowship and also provides the dedicated instruction associated with each module. He also serves as the primary mentor for the containment operations fellows.

Ms. Sharon Walters. Ms. Walters serves as the business coordinator for the NBTC and is involved in the outreach program as well as registration process for all external trainees, nationally and internationally.

Dr. Janice Endsley. Dr. Endsley is an assistant professor on the UTMB faculty. She entered the BSL-4 fellowship program in 2010. Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. Dr. Endsley will continue in the fellowship for much of the current year as she gains critical experience and masters skills needed to work in this environment.

Dr. Aysen Gargili. Dr. Gargili is a visiting scientist in the Department of Microbiology & Immunology. Dr. Gargili an internationally recognized veterinarian and tick expert from Turkey. She is a participant in the NBTC's high and maximum containment fellowship program for scientists. She began her yearlong fellowship in January 2012.

Ms. Joan Geisbert. Ms. Geisbert joined the NBTC in 2010 to assist in training at the BSL-4 level. Ms. Geisbert has over 30 years of experience in BSL-4 laboratories and has worked extensively with experimentally infected animals, including non-human primates, under containment conditions. As our animal handling in containment training module is developed, Ms. Geisbert plays a key role in leading this effort and is lending her practical skills to mentor users in the BSL-4 laboratory.

Dr. Dennis Bente. Dr. Bente is a BSL-4 researcher with the GNL at UTMB. He is an assistant professor in the Department of Microbiology & Immunology. He serves as a BSL-4 scientific mentor for the NBTC. Dr. Bente's own research concentrates on understanding how viruses cause disease with special focus on the pathogenesis of Crimean-Congo hemorrhagic fever virus.

Additional Mentors. We anticipate expanding our cadre of skilled mentors to provide oversight and supervision of trainees as they complete their hands-on training under BSL-3 or BSL-4 laboratory conditions. Mentors will be existing faculty members who have earned independent access to the containment laboratories and who have extensive and proven experience working in the laboratory. They will incorporate this added duty into their existing activities.

Dr. James LeDuc. Dr. LeDuc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr. LeDuc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions and he has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

Teaching Laboratory Facilities.

The teaching laboratory is a critical asset of the NBTC and it is designed to offer trainees realistic exposure to the conditions and equipment they will typically encounter as they conduct their studies in the containment laboratory.



At the **BSL-2** level, this typically includes a biological safety cabinet where handling of pathogens at all levels of containment takes place (*pictured*). It also includes limited specialized equipment, as well as facilities to manage laboratory waste and storage of pathogens. Training for individuals preparing for work in the **BSL-3** laboratory includes a dedicated area where individuals master the donning and doffing of protective gear and its proper disposal.

Those trainees going on to prepare for work in the **BSL-4** laboratory have specialized instruction in the care and use of the positive pressure encapsulating ensemble or “space suit” that is worn in the most common type of **BSL-4** laboratory in use today (*pictured*). This includes inspection of the suit for any evidence of leaks prior to use, gaining experience and familiarity in the wearing of the suit, use of compressed air hoses, and training in emergency procedures. In order to provide this training under realistic conditions, the training facility has been outfitted with a breathing air compressor and a mock laboratory where trainees can experience wearing the suit and become familiar with working in this unique environment. Some people discover that they experience claustrophobic reactions when wearing a suit; and this practical, realistic suit training environment allows them to overcome any such reactions under well-controlled conditions, or decide that this work is not a good fit for them.



A key benefit of the support provided to the NBTC is the availability of resources that allowed for the renovation of our existing teaching laboratory facilities. We completely refurbished the training facility to significantly expand the mock laboratory space available to us, and to enhance the breathing air compressor and suit training area.

Laboratory training is conducted in the mock training laboratory with authentic laboratory equipment utilizing non-infectious materials. Entry into the lab is through a double door anteroom with directional airflow and mock pressure monitors. The laboratory has four class II biological safety cabinets, three of which are constructed with see-through panels which allow the trainer to introduce smoke into the BSC to visualize air movement within the BSC. One BSC class II cabinet also has see-through panels and **BSL-4** air connections ports. Two of the BSC cabinets are equipped with cameras inside that allow for remote demonstrations. The laboratory itself also has two cameras installed for remote demonstrations. The laboratory has two class III biosafety cabinets, incubators, centrifuges, bench top autoclave, refrigerator, -80° freezer, dunk tank, and general laboratory equipment to allow for mock BSL-2 to BSL-3 and -4

laboratory work. The laboratory is equipped with a compressor and air lines for practice in the suit check examination and use of BSL-4 suits within that facility prior to the trainee entering the active BSL-4 laboratories. The laboratory also has multiple airline drops allowing the trainee to work throughout the laboratory with the ability to connect and disconnect airlines as needed.



Overview of NBTC Training.

The NBTC provides a series of training modules involving a mixture of didactic instruction and hands-on training to be carried out within an existing mock BSL-3/-4 training laboratory located within the Environmental Health and Safety Office space in the Materials Management Building on the UTMB campus. The intent of the NBTC is to promote good techniques and safe procedures to be used at all biosafety levels, and to provide consistency in research practices. The program is designed to ensure that all training attendees have the same general biosafety training at BLS-2 and -3, and if necessary BSL-4, prior to entering an active biocontainment laboratory, thus ensuring that safety standards are observed and good practice is pursued.

BSL-2 and BSL-3 Training.

The BSL-2 and -3 training provide a multi-phased approach:

- the assessment phase
- the training phase
 - theory
 - hands- on practicum
- final assessment

Each trainee begins with an **assessment phase** that includes a written test focusing on safety related topics, hands-on skills related to protocols based on their research using appropriate biosafety practices and procedures. During the assessment the trainer does not intervene as he/she notes both safety and scientific techniques employed by the trainee. This allows for the determination of experience and level of training that will be required for each trainee. Once the initial assessment is completed the results are reviewed with the trainee, the specific areas of training focus are identified. A written report is then sent to the trainee and their principal investigator or supervisor.



The **training phase** includes a theoretical class which covers the following topics:

- BSL-1 through 4 standard microbiological practices, special practices, safety equipment and laboratory facilities.
- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work, and spill response in the BSC.
- Procedures with the potential for creating infectious aerosols, recognizing aerosol producing devices and learning how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory, BSC, centrifuge, incident response, cleanup, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- Introduction to select agent rules and NIH-OBA guidelines.

The hands-on practicum during the training phase compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a non-hazardous environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as scientific issues (e.g. contamination of cultures). The practicum is specific to biosafety and agents to be used (e.g. bacteria, parasites, viruses) by the trainee. This approach also allows the use of specific protocols or facility specific practices that the trainee brings with them. Emergency response and spill mitigation training allows the trainee to visualize and respond to spills and contamination with the use of florescent dye and breakable training lab ware.

The **final assessment** is identical to the initial assessment, with a written exam and hands-on skills assessment. Once the trainee has completed and passed the final assessment, the trainee is provided with a certificate of training for the biosafety level they completed. A report is sent to the principal investigator, trainee and laboratory director.

Animal BSL-2 and Animal BSL-3 Training.

An animal biosafety training program was developed and instituted based on the same concepts as the BSL-3 training program. Trainees must have completed BSL-3 training before commencing ABSL-3 training. All animal use is approved by our institutional animal care and use committee, and our animal holding facilities and procedures have been approved by AAALAC. All aspects of our ABSL-2 and ABSL-3 training program have been reviewed and approved by the USAMRMC Animal Care and Use Review Office (ACURO).

The ABSL training phase includes a theoretical class which covers the following topics:

- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.

- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work and spill response in the BSC.
- Procedures with the potential to create infectious aerosols, recognizing an aerosol producing devices and learning procedures to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory or in the BSC, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a safe working environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as animal handling. The practicum is specific to biosafety and animal species to be handled. This approach to training also allows the use of specific protocols or facility specific practices the trainee brings with them.

In the third phase, the final assessment includes a written exam and a hands-on skills assessment. Once the trainee has completed and passed the final assessment the trainee is provided with a certificate of training for the biosafety level they completed.

BSL-4 Training.

BSL-4 training rests upon a firm adherence to the principles and specific practices of safe BSL-3 research. This practice prevents an over-reliance on the BSL-4 suit as a primary means of personal protection, and makes the suit an operationally redundant means of personal protection, significantly enhancing overall containment. Accordingly, individuals who are selected for BSL-4 training will have completed training at BSL-3 and have been approved for independent access to the BSL-3 laboratories. These individuals would then complete the BSL-4 modular training.

Specific Aims.

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the year. The number of individuals trained at each level is summarized in **Table 1** below and the associated figures. As summarized above, the topics typically covered in this introductory training include the principles of basic safety precautions in the laboratory, routine rules and regulations designed to protect the individual and environment from accidental contamination by an infectious microbe, and the care and use of the biological safety cabinet. Also covered are the appropriate procedures of clean-up following a spill, decontamination procedures, principles of the care and use of autoclaves and other essential equipment.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, real-world training in the laboratory setting. Course content is tailored to include those procedures and the use of specific equipment likely to be encountered by the trainee in their routine work. Thus, those destined to work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL-2 laboratory and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals, allowing for intense interaction between the instructor and trainees. By actually doing the procedures essential to their day-to-day laboratory work under the close supervision an instructor (with the use of indicator dyes that allow clear recognition of contamination), the trainee quickly grasps the key teaching points and rapidly masters safe laboratory practices. Training is offered in the state-of-the-art training laboratory described above.

The numbers of individuals trained under Aim 2 for the NBTC is summarized in **Table 1**.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in containment laboratories is the need to be able to properly operate autoclaves. A dedicated training session is offered to all individuals as a separate element of their orientation to the GNL, and this training is offered to individuals working in other laboratories using the same or similar equipment. We trained more than 50 individuals this reporting year in the proper care, use and operations of autoclaves. As new hiring actions within the GNL occur routinely, we anticipate ongoing demand for this training through coming years.

Aerobiology. The GNL contains aerobiology laboratories at both the BSL-3 and BSL-4 levels of containment. The BSL-3 facilities were fully commissioned and approved for use by the CDC and USDA in early 2010, and the GNL BSL-4 facilities were approved for full operations in May 2010 with operations beginning in September 2010. These facilities are highly complex and require specialized training not only in the operation of this sophisticated equipment, but also in the proper care and handling of the laboratory animals that will be experimentally infected.

Over the course of the past reporting year, aerobiology trainees have completed training on the BSL-4 aerobiology equipment and have successfully performed BSL-4 aerosol runs using Nipah virus and Ebola virus in the GNL. Training has also taken place on the EMKA plethysmography equipment. Aerobiology personnel continue to receive instruction and specialized training about how aerosols are generated, the safety precautions in place in aerobiology laboratories and how to quantitate virus in aerosol samples.



Gamma Irradiator Training. BSL-4 laboratories utilize a number of techniques to inactivate biological materials prior to removal from the containment laboratory. One of the most frequently utilized means of removing materials from the BSL-4 laboratory is inactivation by gamma irradiation. In an effort to provide training of individuals that use gamma irradiation at UTMB, a module providing background on radiation biology, radiological and biological safety training, select agent and radiological security training, introductory training on dosage determination and method validation, and practical instruction on the use of the devices used for gamma bombardment was assembled and offered to staff. Instructors included members of the Radiation Safety Office and Biological Safety Office of UTMB's Environmental Health and Safety Office and faculty and staff from the GNL.

High Through-Put Screening. We are working to develop a systematic training program focused on the safety concerns associated with high through-put screening. We will continue to develop this capability in future years as it represents the cutting-edge interface between technology and biological sciences and as such potentially creates new challenges for biological safety.

Aim 4: To provide a mentorship program for scientists working in BSL-3/ABLS-3 or BSL4/ABSL4 facilities.

Mentored training typically extends beyond a given reporting quarter. The BSL4 mentorship program provides a hands-on training experience under the tutelage of a senior staff scientist (mentor) with guidance from other experienced laboratorians in the real-world environment of a functioning BSL4 laboratory. The experience includes an orientation to the laboratory environment by a senior BSL4 scientist and then working experience with tasks germane to the proposed tasking of the person being mentored.

As the GNL laboratory has been brought online additional modules and the Shope laboratory continues to operate, our cadre of experienced scientists and scientific staff continues to expand (see figure on pg. 11). This is actually decreasing the individual burden of training as it is spread across a larger number of scientists and staff. The numbers of staff that have passed into and out of the mentorship program is presented in **Table 1**. Though the figure on pg. 11 captures data only through January 2012, it is interesting to note that between May 2011 and May 2012, 23 individuals began their initial BSL-4 training and proceeded on to mentored training in the BSL4 laboratory. Of those 23 individuals, 13 have successfully completed their mentorships and progressed to independent access. The remaining 10 individuals are in various stages of completing their mentored training requirements.

In the BSL-3 mentorship category, we signed off on more than 15 individuals for independent BSL-3 access over the past reporting year. Furthermore, we currently have at least 3 trainees in the pipeline who lack less than one hour of additional required mentor training to achieve full access.

A more extensive listing of the number of individuals trained during the year can be found in **Table 1**.

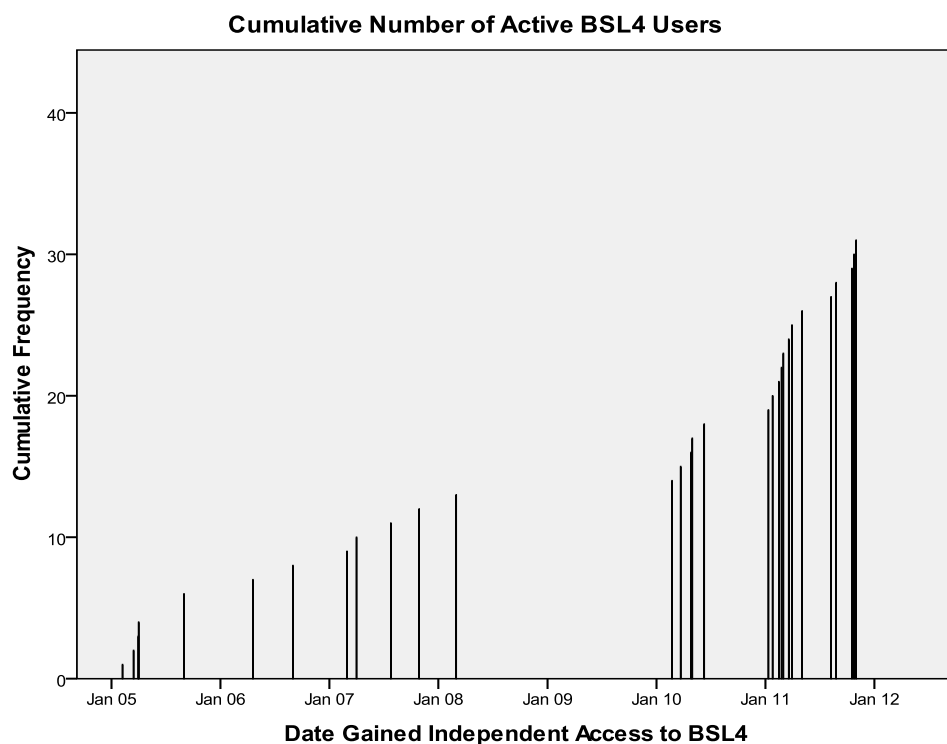


Figure: Cumulative number of active BSL4 Users approved for independent access.

Aim 5: To establish a fellowship program for scientists and facility operations professionals working in BSL-3/ABSL-3 or BSL-4/ABSL-4 facilities.

The high and maximum containment fellowship program for scientists is in place. We have two fellows now in training, and one fellow who has transitioned from the program to a permanent UTMB faculty position involving BSL-4 pathogen research.

Dr. Gavin Bowick is the first NBTC fellow who has transitioned from the NBTC fellowship to a permanent UTMB faculty position. Dr. Janice Endsley is the second fellow sponsored by the program. As indicated previously, Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr. Endsley will continue in the fellowship for much of the coming year as she gains critical experience and masters skills needed to work in this environment.

Dr. Aysen Gargili is the program's third fellow. Dr. Gargili an internationally recognized veterinarian and tick expert from Turkey who is also participating in the maximum containment fellowship program for scientists and will be spending a year onsite at UTMB (she began her fellowship in January 2012). She is working with Dr. Dennis Bente and a team of researchers to establish colonies of vector ticks from Turkey and elsewhere and will be studying how the virus is maintained and transmitted in nature. This is the first step in what we hope will grow into sustained field and laboratory collaborations with Turkish students and scientists. Dr. Gargili will also study the various methods and mechanics of biocontainment as a part of her fellowship.

The laboratory containment operations fellowship is unique and is, to the best of our knowledge the only one of its kind. The program promises to set a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists, where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, most entering facility operators will require a more structured course of study. Consequently, we have identified fourteen distinct modules to be covered over the course of the fellowship. These structured modules cover basic microbiology, provide an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, select agent regulations, formal Good Laboratory Practices, annual certification of laboratories, testing of HEPA filter housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping.

During the course of their training, fellows will directly participate in each of these activities, as well as be personally involved in the planned shut down and decontamination of containment suites, validate decontamination, and conduct and oversee maintenance activities. Plans are being developed to allow fellows to visit other high and maximum containment laboratories across the nation during the second year of their fellowship to better understand the diversity of facilities and variations in containment practices.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over this past year of support we have actively participated in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology and other organizations at the fore of these discussions. We have also participated in ongoing discussions on these topics hosted by the National Science Advisory Board for Biosecurity (NSABB) and the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.

Biosurety and biosecurity are currently covered in our theoretical training sessions, and we are in the process of developing a structured course to more specifically address biosurety and biosecurity in depth. We anticipate posting this course on our internal website as an educational tool to augment our more formal training opportunities and to complement lectures already offered. Depending upon the success of this internal posting, we will then consider posting the course on our general website where it would be available to the general public.

As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established a distinguished speaker series. Our *Topics in Biosecurity Symposia Series* has been offered since 2010. Sessions in the series continue to be of

great interest to students, faculty and community members and are consistently attended by large crowds drawing positive attention and feedback.

Summary of Biosurety and Biosecurity training activities this past year:

Topics in Biosecurity Symposia Series.

- **September 29, 2011.** The NBTC hosted the third session of this symposia series which featured a discussion with special guest **Mr. Edward H. You, a Supervisory Special Agent in the Federal Bureau of Investigation's Weapons of Mass Destruction Directorate, Biological Countermeasures Unit.** Mr. You is responsible for creating programs and activities to coordinate and improve FBI and interagency efforts to identify, assess, and respond to potential intentional biological threats or incidents. These efforts include expanding FBI outreach to the biological sciences community to address biosecurity. Before being promoted to the Weapons of Mass Destruction Directorate, Mr. You was a member of the FBI Los Angeles Field Office Joint Terrorism Task Force and served on the FBI Hazardous Materials Response Team. Mr. You has also been directly involved in policy-making efforts with a focus on biosecurity. He holds *ex officio* positions on the NIH National Science Advisory Board for Biosecurity and the Synthetic Biology and Engineering Research Center Scientific Advisory Board. He is also an active Working Group member of the National Security Council Interagency Policy Committee on Countering Biological Threats; is the FBI representative on the Executive Order 13546 Select Agent Program Federal Experts Security Advisory Panel; and presented, on behalf of the FBI, to the Presidential Commission for the Study of Bioethical Issues regarding biosecurity and synthetic biology. A capacity crowd attended Mr. You's presentation.



Pictured left: The Honorable Susan Ehrlich, UTMB Adjunct Faculty Member; GNL Director Dr. Jim Le Duc, and Mr. You. Pictured right: A capacity crowd attended the session, including students, faculty and special guests from UTMB Police, the local FBI office and members of the community.

- **November 7, 2011.** The fourth session of the series featured a lively conversation on the origins of the biodefense enterprise as well as on combating weapons of mass destruction. Special guests for this session were **Dale Klein, PhD** and **Stewart Simonson, JD.** Dr. Klein is **Associate Vice Chancellor for Research in the Office of Academic Affairs for The University of Texas System.** Before joining UT System, he had a distinguished career overseeing nuclear, chemical and biological matters for the federal government including service as **Chairman of the U.S. Nuclear Regulatory Commission** and as **U.S. Assistant Secretary of Defense for Nuclear, Chemical and Biological Defense** programs. Mr. Simonson has more

than 20 years of experience serving in leadership roles in the public and private sectors, including nearly five years with the **U.S. Department of Health and Human Services (HHS)** where he served in several senior positions including deputy general counsel and the first appointee to the role of **Assistant Secretary for Preparedness and Response**. He is currently general counsel for the Washington, DC based **Futures Group**. Dr. Klein is an expert in nuclear energy and during his presentation we were fortunate to learn details of his recent trip to Japan to assist in the US response following the Fukushima disaster and his observations on the current status of the recovery efforts and looming challenges.

- December 2, 2011.** The fifth and final 2011 session of the series featured a review of current federal science policy with specific emphasis on how to foster stronger medical countermeasures programs. **George W. Korch, Jr., PhD** led this informative discussion that featured a review of the findings of the **Federal Experts Security Advisory Panel** which he **co-chairs**. Included was a review of the process currently underway to establish a tiered ranking of select agents and how those pathogens currently proposed as Tier 1 agents were selected. **Dr. Korch is a senior science advisor to the Assistant Secretary for Preparedness and Response at the U.S. Department of Health and Human Services.** He also retired from a distinguished career in the U.S. Army where he served as **commander of the USAMRIID** and as the **director of the Department of Defense Medical Chemical and Biological Defense Research Program**.



Session 4: (l to r) Dr. Dale Klein, UT System; GNL Director Dr. Jim Le Duc, and Mr. Stewart Simonson, Futures Group.



Session 5: (l to r) Dr. George Korch, Jr., HHS; and GNL Director Dr. Jim Le Duc.

- March 15, 2012.** The sixth session of the series featured **Dr. Robert Swanepol** as the guest speaker. Dr. Swanepol, a member of the **Zoonoses Research Unit and the Faculty of Health Sciences at the University of Pretoria in South Africa** provided an international perspective on biosecurity research in his talk “Biosafety and biosecurity challenges of investigating hazardous endemic diseases in South Africa.” Dr. Swanepol is the former director of the Special Pathogens Unit at the National Institute for Communicable Diseases in South Africa, home to one the only true BSL4 facility in sub-Saharan Africa. Dr. Swanepol recently joined the University of Pretoria where he heads the Zoonoses Research Unit and is about to commission their own BSL3 laboratory. He described the trials and tribulations of building and operating a maximum containment facility in Africa, while sharing stories of his adventures investigating outbreaks of Ebola, Marburg, Rift Valley fever and many other emerging diseases. We are excited about the possibility of exchanges of students and faculty as his new unit comes on line. During his visit to campus, Dr. Swanepol also had the

opportunity to meet with many of our infectious disease researchers and tour the research facilities.

- March 21, 2012.** The seventh session of the series featured **Dr. Onder Ergonul** as the guest speaker. Dr. Ergonul is a **professor at Koc University School of Medicine in Istanbul, Turkey**. He also serves as general secretary of Turkish Society of Clinical Microbiology and Infectious Diseases. His symposium talk entitled, “Crimean-Congo Hemorrhagic Fever and Biosecurity” detailed much of the history of his international research on the disease. He discussed the discovery of Crimean-Congo hemorrhagic fever (CCHF) in Turkey where over the past decade he has led efforts to recognize this often fatal disease previously unknown in the country, but that today causes more than 1,000 cases annually. CCHF is a tick-borne virus and a researcher here at UTMB’s GNL, **Dr. Dennis Bente**, is spearheading a research program to study this deadly disease in partnership with the team in the GNL insectary, and an internationally recognized tick expert from Turkey, **Dr. Aysen Gargili**. As mentioned previously in this report, Dr. Gargili is participating in a yearlong fellowship here at UTMB as part of the NBTC’s maximum containment fellowship program for scientists. The team is establishing colonies of vector ticks from Turkey and elsewhere and will be studying how the virus is maintained and transmitted in nature. This is the first step in what we hope will grow into sustained field and laboratory collaborations between UTMB and Turkish students and scientists.



Session 6: (l to r) Dr. Jim LeDuc, GNL director; Dr. Tom Ksiazek, NBTC director, Dee Zimmerman, Biosafety Director and Dr. Swanepol.



Session 7: Dr. Ergonul during his presentation.

NBTC Website.

Over the past reporting year, the new NBTC website has continued to develop - www.utmb.edu/nbtc. The new course training schedule for 2012 was added to the website. We also updated our staff listing with new members of the training team. Per its intent, this site serves as a hub of information regarding the Center, our goals, and the resources



that the NBTC makes available to the biosafety and research communities. We continue to develop a dedicated section focused on biosecurity which will offer a comprehensive review of the topic and practical guidance.

Onsite training and related updates.

- During this reporting year, the NBTC also provided facility engineering and maintenance consultation to the **National Aeronautics and Space Agency's Johnson Space Center** team responsible for constructing laboratory space in Houston, Texas for the future processing of planetary and space samples received from expeditions to Mars. Representatives from the lunar sample curation team visited our laboratories and consulted with both scientific and engineering staff.
- This past year the NBTC ABSL2 and ABSL3 courses were accepted by AALAS for continuing education credit. Credits will be given out based on contact time with each trainee.
- The NBTC informational booth was present at the following professional meetings during this reporting year:
 - The **American Society for Microbiology General Meeting** , May 20 – 25, 2011 in New Orleans, LA
 - The **American Society for Virology Annual Meeting**, July 15 – 21, 2011 in Minneapolis, MN
 - **63rd American Association for Laboratory Animal Science National Meeting**, October 1-7, 2011 in San Diego, CA
 - **54th Annual American Biological Safety Association Biosafety Conference/Meeting**, October 26 -November 3, 2011 in Anaheim, CA
 - **60th Annual Meeting of the American Society of Tropical Medicine and Hygiene**, December 3-9, 2011 in Philadelphia, PA
 - **The American Society for Microbiology Biodefense Meeting**, February 25 – 30, 2012 in Washington, DC
- Dr. Brocard co-taught a course “Basic Risk Assessment” (an ABSA owned course) at the 54th annual ABSA meeting October 26-Nov 3, 2011 in Anaheim, CA.
- Biosafety training program personnel traveled to **Baylor University** in Waco, TX in 2011 to provide BSL3 training to new users.
- Dr. Brocard successfully completed and passed the National Registry of Certified Microbiologists (NRCM) examination in Biological Safety Microbiology and is now a Certified Specialist Microbiologist. This is the first step towards the Certificate for Biosafety professionals (CBSP).

- The ABSL3 course became a certificate (1 credit hour) with the graduate course. Below are all of the biosafety training courses registered with the graduate school:
 - Basic BSL2, BBSC 6217
 - BSL2 programs, CTPS 6112
 - BSL3 programs, CTPS 6203
 - ABSL2 programs, CTPS 6114
 - ABSL3 programs, CTPS 6118
- Throughout the past year, resident biocontainment engineer Mr. Miguel Grimaldo, actively participated as a member of the ANSI Z9.14 Committee to development of an **American National Standards Institute (ANSI)** standard for "Testing and Performance Verification Methodologies for Ventilation Systems for Biological Safety Level 3 (BSL-3) and Animal Biological Safety Level 3 (ABSL-3) Facilities." This work has included the writing and/or revision of sections of the standards, conference calls and participation of an "All-Hands" Meeting held on the Emory University campus in Atlanta, Georgia. It is expected that the standard should be ready for public review by the end of 2012.
- Mr. Grimaldo co-taught an eight-hour course on "Waste Water Management for Unique Laboratory Operations" at the 54th Annual American Biological Safety Association (ABSA) meeting October 28-Nov 3, 2011 in Anaheim, CA.
- Mr. Grimaldo was invited to present his work on "Development of Autoclave Decontamination Cycles: Animal Carcasses and Laboratory Waste" at the at the 54th Annual American Biological Safety Association (ABSA) meeting October 28-November 3, 2011 in Anaheim, CA.
- From June 2011 to May 2012, Mr. Grimaldo responded to requests for information/guidance on biocontainment related issues from the following:
 - **Lovelace Respiratory Research Institute** regarding membrane filter testing.
 - **University of Massachusetts Medical School** regarding BSL3 lab construction.
 - **University of North Dakota Research Foundation** regarding BSL3 air balance.
 - **Montana State University** on autoclave cycle development.
 - **University of Monterey, Mexico** regarding BSL3 Facility Commissioning and Testing.
 - **NIH Integrated Research Facility** in Ft. Detrick, MD regarding autoclave cycles and APR door operations for BSL4 Laboratories.
 - **The Animal Health Research Center (CISA)** Valdeolmos in Madrid, Spain, regarding autoclave cycle development.
 - The **National Biodefense Analysis and Countermeasures Center (NBACC)** at Ft. Detrick, MD regarding membrane filter types used on the effluent decontamination systems.
 - **University of Montana** regarding autoclave cycles.
 - **Centers for Disease Control and Prevention's Office of Health and Safety** regarding the decontamination and certification of Membrane (PTFE) filters used on vent lines of BSL4 and BSL3 Enhance Laboratories.

- As part of the ongoing collaboration with other institutions who are home to biocontainment research facilities, Mr. Grimaldo actively participates on the conference calls for the Facility Operations Group of the **NIH/NIAID National Biocontainment Laboratory/Regional Biocontainment Laboratory Network**.
- This past reporting year, Mr. Grimaldo continued to provide BSL4 Facility Operations training to one of **Centers for Disease Control and Prevention's Select Agent Program** Inspectors at UTMB and via conference calls.
- Mr. Grimaldo was invited to present "Biocontainment Challenges for Handling and Life Detection of Extraterrestrial Samples" at the **Life Detection in Extraterrestrial Samples Conference** in La Jolla, California at the Samuel H. Scripps Auditorium in February, 2012.

Table 1.

Summary of training courses offered and number of participants in each course, May 2009 through May 2012.

Training Course/Module	May-Dec 2009	Jan-Dec 2010	Jan-Dec 2011	Jan-March 2012	Apr-May 2012	Total
BSL4	9	34	43	8	8	102
BSL3	45	87	95	10	20	257
BSL2 Theoretical	107	156	254	17	38	572
BSL2 hands-on	64	73	99	12	13	261
ABSL3 Theoretical	29	55	52	15	6	157
ABSL3 hands-on	29	36	50	11	4	130
ABSL2 Theoretical	N/A	N/A	81	9	11	101
ABSL2 hands-on	N/A	N/A	44	10	10	64
Graduate Program	48	35	32	0	0	115
Aerobiology	19	5	2	8	0	34
Autoclave	195	27	46	27	5	300
High Throughput Safety training	8	11	3	2	0	24
Non-human primate theoretical	16	15	99	2	7	139
Non-human primate hands-on	N/A	N/A	91	11	7	109
BSL3 mentorship	36	41	24	7	5	113
ABSL3 mentorship	N/A	N/A	38	5	11	54
Specialized training (PAPR; intro - to Micro-Animal handling certificates)	18	0	29	33	13	93
Total trained	623	575	1082	187	158	2625

Figure 1. Total number of trainees from 2005-2012. As expected the number of trainees has continuously been increasing as indicated by the percentage noted atop each year.

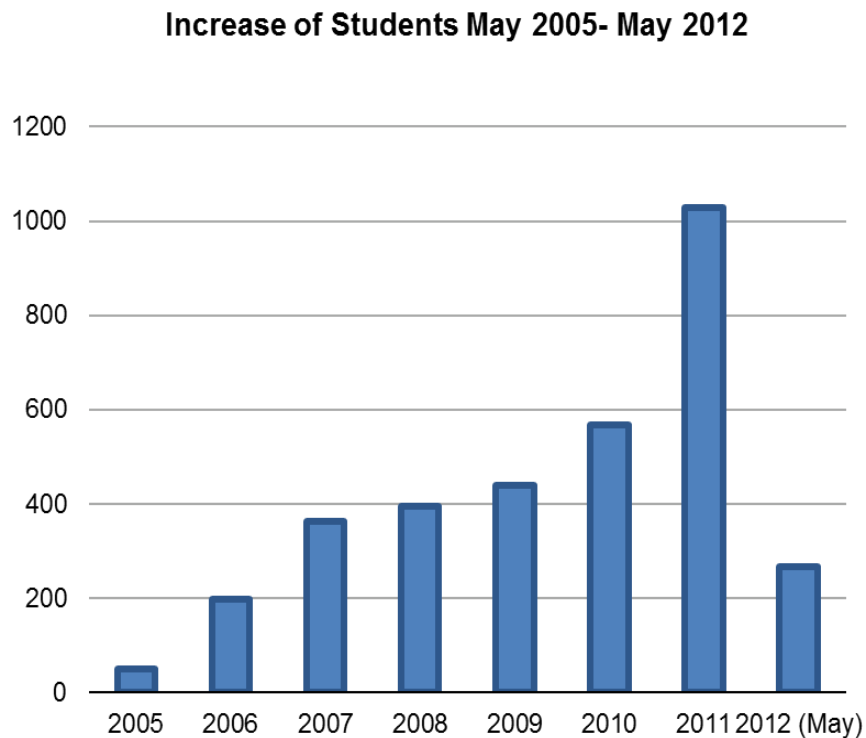


Figure 2. Distribution of trainees based on the courses taken. As expected the number of trainees follows the normal biosafety level pyramid with a large amount of BSL-2 trainees and then fewer as the biosafety level increases.

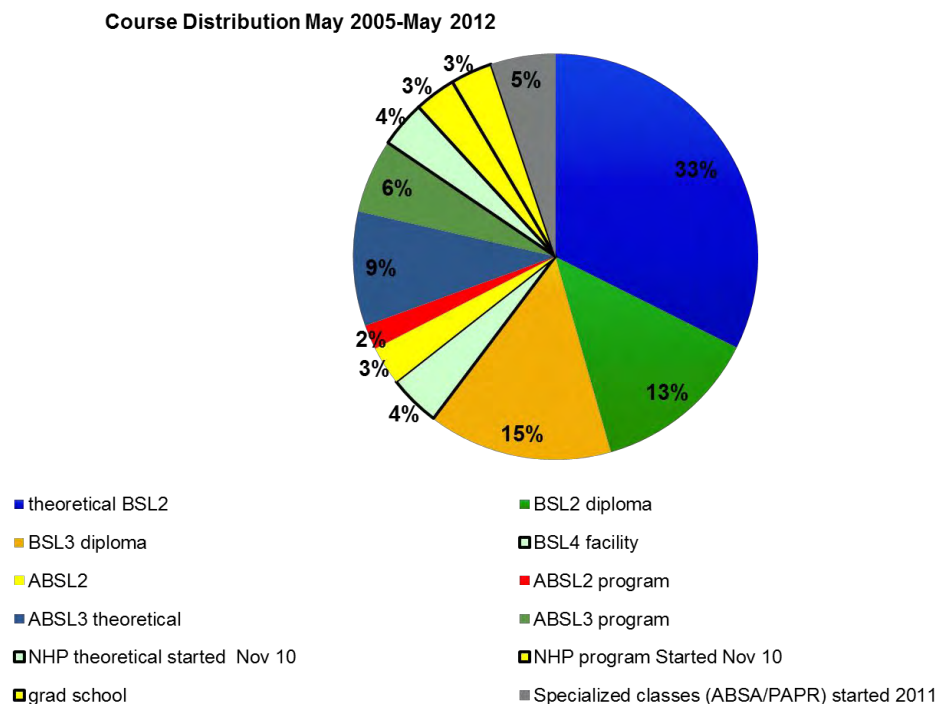
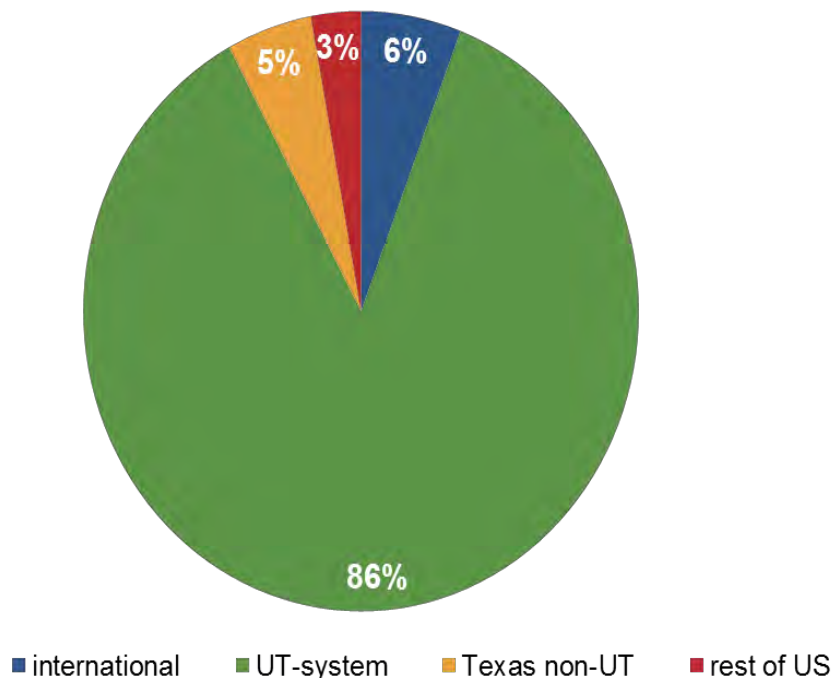


Figure 3. Distribution of the trainees based on their geographic location. UT-System includes all university members of the University of Texas group, of which UTMB is a member.

Geographic Distribution of Trainees May 2005- May 2012



KEY RESEARCH ACCOMPLISHMENTS 2011-2012:

- A comprehensive, standards-based training program has been established and implemented to prepare individuals for work at all levels of biocontainment.
- Advanced, mentored training is available to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL-4 level.
- A unique fellowship has been created to train the next generation of containment laboratory containment facility operations professionals prepared to oversee the safe operations of these complex facilities.
- A novel training opportunity addresses the safety considerations emerging at the interface of high through-put screening of potentially infectious material.
- As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established the *Topics in Biosecurity Symposia Series*. Sessions offered thus far continue to be attended by large crowds and draw positive attention and feedback. Planning is underway to continue the series with 2012-2013 sessions.

REPORTABLE OUTCOMES 2011-2012:

- Since the inception of UTMB's Laboratory Biosafety Training Program, prior to the TATRC funding award in 2009, more than 3,000 individuals have been instructed in the safe research and operation in biocontainment laboratories. The vast majority of these trainees have taken part in the program since 2009 when TATRC funding allowed for significant growth of the program.
- Requests for external biosafety training are being continuously received. Some examples include:
 - Members of our team of biosafety trainers were requested by the Baylor University Institute of Medicine in Waco, Texas to provide BSL3 training for their staff in December 2011. Eleven individuals received BSL3 theoretical and practicum training.
 - Battelle Corporation also requested BSL3 and ABSL3 training for their staff in January 2012. Four individuals received BSL3 theoretical and practicum training and four individuals received ABSL3 theoretical and practicum training on rabbits and guinea pigs.
 - The year ahead looks to be equally busy. Immediately upcoming will be a training session requested by the City of Laredo, Texas. The City's health department has requested that the NBTC provide BSL-3 training to six of their personnel in June of 2012.
- Dr. James W. LeDuc, the principle investigator in the NBTC award, published two nationally recognized commentaries regarding training during the reporting year. Dr. LeDuc and colleague Dr. David R. Franz, the Vice President and Chief Biological Scientist at the Midwest Research Institute and Senior Advisor to the Office of the Assistant to the Secretary of Defense for Nuclear, Chemical and Biological Defense Programs jointly published the following:
 - *Balancing Our Approach to the Insider Threat*. Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science. Volume 9, Number 3, 2011.
 - *Genetically Engineered Transmissible H5N1: A Call for Laboratory Safety and Security*. Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science. Volume 10, Number 1, 2012.

CONCLUSIONS:

The National Biocontainment Training Center offers a robust and intensive training program devoted to all aspects of biological safety, biocontainment, and biosecurity. This program offers unique, hands-on training to trainees, staff and external partners at all levels of biocontainment, including focused, mentored training in the BSL-4 laboratory.

Over 3,000 persons have benefited from one or more of these training courses, many of whom are now pursuing graduate education and using these specialized skills in the newly constructed GNL containment facilities. Intensive, mentored fellowship programs have been established to offer opportunities for in-depth training in research under BSL-4 conditions and also in containment laboratory operations and maintenance. These fellowships are proving quite successful and are helping address the critical national shortage of well-trained containment laboratory scientists and facility operations specialists.

2011 Table of Contents	1
Introduction	2
Body	2
Staffing Report	3
Renovation of Teaching Laboratory	5
Overview of NBTC training	6
BSL-2 and BSL-3 training	6
Animal BSL-3 training	8
BSL-4 training	8
Specific Aims 1-6	9
Table 1. Summary of Courses	16
Figure 1. Trainees 2005-2011	17
Figure 2. Course distribution.	17
Figure 3. Trainees by job description.	18
Figure 4. Geographic distribution.	19
Figure 5. International distribution.	20
Key Research Accomplishments	21
Reportable Outcomes	21
Conclusions	22
References	22

INTRODUCTION

The **National Biocontainment Training Center (NBTC)** provides standards-based theoretical and practical training to students and professionals preparing for work in biocontainment laboratories where especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL-2), BSL-3 and BSL-4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee. Advanced coursework includes hands-on mentored training in the containment laboratories, including consecutive training at BSL-3 and BSL-4 levels of containment. Specialized training in the handling of laboratory animals is also offered. Sponsored mentored training is available to scientists embarking on a career focused on high hazard pathogens at the BSL-4 level through a dedicated fellowship. Fellows in this program work under the close supervision of an established mentor while addressing a research topic of their own choosing. Mentored scientists and fellows progress to full independent access to the BSL-4 laboratory only when the mentor and laboratory director are fully confident of the individual's skills and ability to work independently in this environment.

The NBTC also offers a unique training opportunity for facility operations specialists interested in pursuing a career as a biocontainment operations manager. To the best of our knowledge, this is the only such training program in the world. This program is designed as a series of modules which address specific aspects of the construction, maintenance and safe operation of a biocontainment laboratory. The coursework is tailored to the specific needs of the individual trainee and involves both didactic training and mentored hands-on work using the Galveston National Laboratory (GNL) as its classroom. Over the course of the training period, which is anticipated to require up to two years for completion, the fellow will be directly involved in the maintenance of the laboratory, decontamination of specific laboratories, monitoring and replacement of filters, and a wealth of other duties routinely seen in the operations of typical biocontainment facilities.

BODY

TATRC's financial support for the NBTC formally began on 22 May 2009 and this submission comprises our second annual report for this initiative. The Laboratory Biosafety Training Center was established and operational prior to receiving TATRC funding; consequently, the course structure and procedures were already in place and allowed the NBTC to implement enhanced training operations almost immediately. From inception to date, the NBTC has provided training to approximately 2,500 participants through the various courses offered. Below is a summary of the significant progress made over the preceding year (2010-2011) under TATRC support. Funding and accomplishments are organized by each specific aim as they were presented in our original proposal.

Staffing Report.

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. Below is a summary of these individuals and their roles in the operation and management of the NBTC.

Dr. Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr. Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr. Ksiazek also oversees the BSL-4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL-4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL-4 environment.

Dr. Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr. Anne-Sophie Brocard, an accomplished virologist and experienced trainer who has directed the training center courses since their inception. Dr. Brocard provides both theoretical and practical training to trainees and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms. Je T'aime Newton. Dr. Brocard is ably assisted by Ms. Je T'aime Newton, a highly experienced instructor with extensive expertise in biocontainment. Ms. Newton provides specialized training at all levels of containment, but is specifically responsible for preparing trainees for BSL-4 investigations, focusing her efforts on the proper care, use and maintenance of the protective “space suits” used in the BSL-4 laboratory and other aspects of work in this highly specialized environment.

Ms. Vicki Jones. Ms. Jones is a critical member of the teaching faculty who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera. Ms. Rivera is a critical member of the teaching staff who assists as a trainer in both the theoretical and practical animal training modules.

Mr. Jason Hardcastle. Mr. Hardcastle is a trainer and assists Ms. Jones and Rivera with the training of students, specializing in *in-vitro* techniques.

Ms. Dee Zimmerman. Ms. Zimmerman is the director of the University’s biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Mr. Lee Thompson and Mr. Miguel Grimaldo. The containment operations fellowship is coordinated through the efforts of Mr. Thompson and Mr. Grimaldo (currently funded

by other GNL and UTMB resources). They are responsible for the content development of each module of the containment operations fellowship and they also provide the dedicated instruction associated with each module. They serve as the primary mentors for the containment operations fellows.

Ms. Sharon Walters. Ms. Walters serves as the business coordinator for the NBTC and is involved in the outreach program as well as registration process for all external trainees, nationally and internationally.

Dr. Gavin Bowick. Dr. Bowick was a senior biocontainment fellow preparing for work in the BSL-4 laboratory during the first year of the TATRC contract. Dr. Bowick's training, which focused on preparing him to work on BSL-4 arenaviruses, was interrupted due to visa issues and he had to depart UTMB. His visa issues were subsequently resolved and he has now returned to UTMB as a faculty member with sponsorship from other funding sources. He has not received support from the NBTC fellowship during the current reporting period. However, involvement in the fellowship did allow him to transition into a permanent faculty position with sponsored funding directed at BSL-4 pathogens.

Dr. Janice Endsley. Dr. Endsley is an assistant professor on the UTMB faculty. She entered the BSL-4 fellowship program in 2010. Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr. Endsley will continue in the fellowship for much of the coming year as she gains critical experience and masters skills needed to work in this environment.

Ms. Joan Geisbert. Ms. Geisbert joined the NBTC in 2010 to assist in training at the BSL-4 level. Ms. Geisbert has over 30 years of experience in BSL-4 laboratories and has worked extensively with experimentally infected animals, including non-human primates, under containment conditions. As our animal handling in containment training module is developed, Ms. Geisbert plays a key role in leading this effort and is lending her practical skills to mentor users in the BSL-4 laboratory.

Additional Mentors. We anticipate expanding our cadre of skilled mentors to provide oversight and supervision of trainees as they complete their hands-on training under BSL-3 or BSL-4 laboratory conditions. Mentors will be existing faculty members who have earned independent access to the containment laboratories and they will incorporate this added duty into their existing activities.

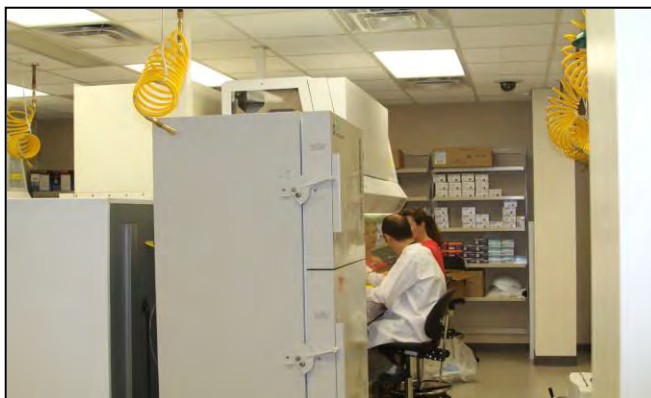
Dr. James LeDuc. Dr. LeDuc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr. LeDuc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions and he has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

To meet the growing demand for training opportunities offered through the NBTC, we are in the process of recruiting additional trainers and mentors. We are also in the

process of developing skilled trainers to assist in the education of trainees and fellows in the safe and appropriate handling of laboratory animals in the context of research under biocontainment conditions.

Teaching Laboratory Facilities.

The teaching laboratory is a critical asset of the NBTC and it is designed to offer trainees realistic exposure to the conditions and equipment they will typically encounter as they conduct their studies in the containment laboratory.



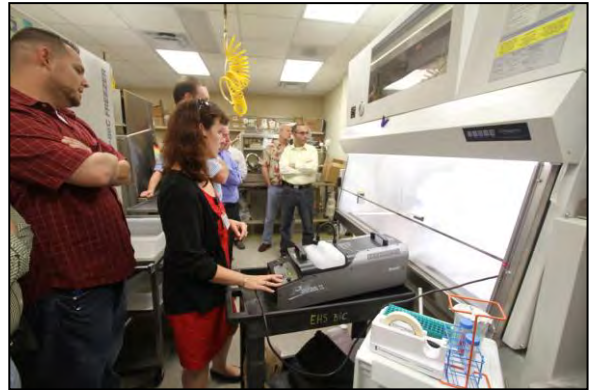
At the BSL-2 level, this typically includes a biological safety cabinet where handling of pathogens at all levels of containment takes place (*pictured*). It also includes limited specialized equipment, as well as facilities to manage laboratory waste and storage of pathogens. Training for individuals preparing for work in the BSL-3 laboratory includes a dedicated area where individuals master the donning and doffing of protective gear and its proper disposal.

Those trainees going on to prepare for work in the BSL-4 laboratory have specialized instruction in the care and use of the positive pressure encapsulating ensemble or “space suit” that is worn in the most common type of BSL-4 laboratory in use today (*pictured*). This includes inspection of the suit for any evidence of leaks prior to use, gaining experience and familiarity in the wearing of the suit, use of compressed air hoses, and training in emergency procedures. In order to provide this training under realistic conditions, the training facility has been outfitted with a breathing air compressor and a mock laboratory where trainees can experience wearing the suit and become familiar with working in this unique environment. Some people discover that they experience claustrophobic reactions when wearing a suit; and this practical, realistic suit training environment allows them to overcome any such reactions under well-controlled conditions, or decide that this work is not a good fit for them.



A key benefit of the support provided to the NBTC is the availability of resources that allowed for the renovation of our existing teaching laboratory facilities. We have completely refurbished the training facility to significantly expand the mock laboratory space available to us, and to enhance the breathing air compressor and suit training area.

Laboratory training is conducted in the mock training laboratory with authentic laboratory equipment utilizing non-infectious materials. Entry into the lab is through a double door anteroom with directional airflow and mock pressure monitors. The laboratory has three class II biological safety cabinets, two of which are constructed with see-through panels which allow the trainer to introduce smoke into the BSC to visualize air movement within the BSC (*pictured*). There is a third BSC class II cabinet on order which has see-through panels and BSL-4 air connections ports. Two of the BSC cabinets are equipped with cameras inside that allow us to perform remote demonstrations. The laboratory itself also has two cameras installed for remote demonstrations. The laboratory has two class III glove boxes, incubators, centrifuges, bench top autoclave, refrigerator, -80° freezer, dunk tank, and general laboratory equipment to allow for mock BSL-2 to BSL-3 and -4 laboratory work. The laboratory is equipped with a compressor and air lines for practice in the suit check examination and use of BSL-4 suits within that facility prior to the trainee entering the active BSL-4 laboratories. The laboratory also has multiple airline drops allowing the trainee to work throughout the laboratory with the ability to connect and disconnect airlines as needed.



Overview of NBTC Training.

The NBTC provides a series of training modules involving a mixture of didactic instruction and hands-on training to be carried out within an existing mock BSL-3/-4 training laboratory located within the Environmental Health and Safety Office space in the Materials Management Building on the UTMB campus. The intent of the NBTC is to promote good techniques and safe procedures to be used at all biosafety levels, and to provide consistency in research practices. The program is designed to ensure that all training attendees have the same general biosafety training at BLS-2 and -3, and if necessary BSL-4, prior to entering an active biocontainment laboratory, thus ensuring that safety standards are observed and good practice is pursued.

BSL-2 and BSL-3 Training.

The BSL-2 and -3 training provide a multi-phased approach:

- the assessment phase
- the training phase
 - theory
 - hands- on practicum
- final assessment

Each trainee begins with an **assessment phase** that includes a written test focusing on safety related topics, hands-on skills related to protocols based on their research using appropriate biosafety practices and procedures. During the assessment the trainer does not intervene as he/she notes both safety and scientific techniques employed by the trainee. This allows for the determination of experience and level of training that will be required for each trainee. Once the initial assessment is completed the results are reviewed with the trainee, the specific areas of training focus are identified. A written report is then sent to the trainee and their principal investigator or supervisor.

The **training phase** includes a theoretical class which covers the following topics:

- BSL-1 through 4 standard microbiological practices, special practices, safety equipment and laboratory facilities.
- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work, and spill response in the BSC.
- Procedures with the potential for creating infectious aerosols, recognizing aerosol producing devices and learning how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory, BSC, centrifuge, incident response, cleanup, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- Introduction to select agent rules and NIH-OBA guidelines.

The hands-on practicum during the training phase compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a non-hazardous environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as scientific issues (e.g. contamination of cultures). The practicum is specific to biosafety and agents to be used (e.g. bacteria, parasites, viruses) by the trainee. This approach also allows the use of specific protocols or facility specific practices that the trainee brings with them. Emergency response and spill training allows the trainee to visualize and respond to spills and contamination with the use of florescent dye and breakable training lab ware.

The **final assessment** is identical to the initial assessment, with a written exam and hands-on skills assessment. Once the trainee has completed and passed the final assessment, the trainee is provided with a certificate of training for the biosafety level they completed. A report is sent to the principal investigator, trainee and laboratory director.

Animal BSL-2 and Animal BSL-3 Training.

An animal biosafety training program was developed and instituted based on the same concepts as the BSL-3 training program. Trainees must have completed BSL-3 training before commencing ABSL-3 training. All animal use is approved by our institutional animal care and use committee, and our animal holding facilities and procedures have been approved by AAALAC. All aspects of our ABSL-2 and ABSL-3 training program have been reviewed and approved by the USAMRMC Animal Care and Use Review Office (ACURO).

The ABSL training phase includes a theoretical class which covers the following topics:

- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work and spill response in the BSC.
- Procedures with the potential to create infectious aerosols, recognizing an aerosol producing devices and learning procedures to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory or in the BSC, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a safe working environment. It also allows the trainer to observe, advise and correct the trainee's techniques in the laboratory relative to safety as well as animal handling. The practicum is specific to biosafety and animal species to be handled. This approach to training also allows the use of specific protocols or facility specific practices the trainee brings with them.

In the third phase, the final assessment includes a written exam and a hands-on skills assessment. Once the trainee has completed and passed the final assessment the trainee is provided with a certificate of training for the biosafety level they completed.

BSL-4 Training.

BSL-4 training rests upon a firm adherence to the principles and specific practices of safe BSL-3 research. This practice prevents an over-reliance on the BSL-4 suit as a primary means of personal protection, and makes the suit an operationally redundant means of personal protection, significantly enhancing overall containment. Accordingly, individuals who are selected for BSL-4 training will have completed training at BSL-3 and have been approved for independent access to the BSL-3 laboratories. These individuals would then complete the BSL-4 modular training.

Specific Aims.

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the year. The number of individuals trained at each level is summarized in Table 1 below and the associated figures. As summarized above, the topics typically covered in this introductory training include the principles of basic safety precautions in the laboratory, routine rules and regulations designed to protect the individual and environment from accidental contamination by an infectious microbe, and the care and use of the biological safety cabinet. Also covered are the appropriate procedures of clean-up following a spill, decontamination procedures, principles of the care and use of autoclaves and other essential equipment.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this aim is directed at providing trainees with practical, real-world training in the laboratory setting. Course content is tailored to include those procedures and the use of specific equipment likely to be encountered by the trainee in their routine work. Thus, those destined to work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL-2 laboratory and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals, allowing for intense interaction between the instructor and trainees. By actually doing the procedures essential to their day-to-day laboratory work under the close supervision an instructor (with the use of indicator dyes that allow clear recognition of contamination), the trainee quickly grasps the key teaching points and rapidly masters safe laboratory practices. Training is offered in the newly renovated training laboratory described above.

The numbers of individuals trained under Aim 2 for the NBTC is summarized in **Table 1**.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in containment laboratories is the need to be able to properly operate autoclaves. A dedicated training session is offered to all individuals as a separate element of their orientation to the GNL, and this training is offered to individuals working in other laboratories using the same or similar equipment. During the first year of support we trained 26 individuals in the proper care, use and operations of autoclaves. As new hiring actions within the GNL occur routinely, we anticipate ongoing demand for this training through coming years.

Aerobiology. The GNL contains aerobiology laboratories at both the BSL-3 and BSL-4 levels of containment. The BSL-3 facilities were fully commissioned and approved for use by the CDC and USDA during the year just completed; however, the GNL BSL-4

facilities were approved for full operations in May 2010 and operations began in September of 2010. These facilities are highly complex and require specialized training not only in the operation of this sophisticated equipment, but also in the proper care and handling of the laboratory animals that will be experimentally infected. During the course of the year we have trained 42 individuals for work in the BSL-3 facility, and during the coming year we anticipate that many of these same persons will acquire training in the BSL-4 facility as well.

External Training: As highlighted later in this report, the Kenya Medical Research Institute (KEMRI) in Nairobi, Kenya requested that we provide BSL-3 training for their staff prior to opening their new BSL-3 facility. Subsequently 19 trainees received external theoretical BSL-3 training of which 10 trainees also received hands-on training. Trainers also travelled to the University of Texas El Paso (UTEP) to provide BSL-3 and ABSL-3 training in laboratory operations prior to the opening of their research facilities. The topics discussed included biocontainment operations, BSL-3 facility maintenance, the Select Agent registration process, record keeping, the benefits for annual biocontainment maintenance validations, and an extensive tour of BSL-3 laboratories and support spaces. Additionally, the World Health Organization (WHO) sent 18 of their worldwide BSL3 facilities staff to the NBTC for training.

Gamma Irradiator Training. BSL-4 laboratories utilize a number of techniques to inactivate biological materials prior to removal from the containment laboratory. One of the most frequently utilized means of removing materials from the BSL-4 laboratory is inactivation by gamma irradiation. In an effort to provide training of individuals that use gamma irradiation at UTMB, a module providing background on radiation biology, radiological and biological safety training, select agent and radiological security training, introductory training on dosage determination and method validation, and practical instruction on the use of the devices used for gamma bombardment was assembled and offered to staff. Instructors included members of the Radiation Safety Office and Biological Safety Office of UTMB's Environmental Health and Safety Office and Faculty and Staff from the Galveston National Lab.

High Through-Put Screening. We continue to work to develop a systematic training program focused on the safety concerns associated with high through-put screening. Four of the original 8 trainees introduced to the program are continuing personalized training on this unique equipment, and we anticipate an additional 2 trainees to start during the next quarter. In addition, we purchased a major piece of equipment, a pyrosequencer, to augment the existing robotics and PCR equipment already in use in the laboratory. All of this equipment was used to assist the Texas Department of State Health Services and other collaborating laboratories in response to the emergence of Influenza A H1N1 that recently occurred. We will continue to develop this capability in future years as it represents the cutting-edge interface between technology and biological sciences and as such potentially creates new challenges for biological safety.

Aim 4: To provide a mentorship program for scientists working in BSL-3/ABLS-3 or BSL4/ABSL4 facilities.

A total of 93 trainees and staff were enrolled in ongoing mentored guidance in the BSL-3 laboratory suites during the year just completed, while 16 participated in supervised training at the BSL-4 level. Mentored training typically extends beyond a given reporting quarter. A more extensive listing of the number of individuals trained during the year can be found in **Table 1**.

Aim 5: To establish a fellowship program for scientists and facility operations professionals working in BSL-3/ABSL-3 or BSL-4/ABSL-4 facilities.

The high and maximum containment fellowship program for scientists is in place and we have two fellows now in training. Dr Gavin Bowick, the first NBTC fellow, has transitioned from the NBTC fellowship to a permanent UTMB faculty position involving BSL4 pathogen research. Dr. Janice Endsley is the second fellow sponsored by the program. As indicated above, Dr. Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr. Endsley will continue in the fellowship for much of the coming year as she gains critical experience and masters skills needed to work in this environment. As the GNL BSL-4 laboratories have become operational and expand to a full scope of operations, we anticipate the possibility of expanding the number of fellows.

The laboratory containment operations fellowship is unique and is, to the best of our knowledge the only one of its kind. The program promises to set a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists, where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, most entering facility operators will require a more structured course of study. Consequently, we have identified fourteen distinct modules to be covered over the course of the fellowship. These structured modules will cover basic microbiology, provide an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, select agent regulations, formal Good Laboratory Practices, annual certification of laboratories, testing of HEPA filter housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping. During the course of their training, fellows will directly participate in each of these activities, as well as be personally involved in the planned shut down and decontamination of containment suites, validate decontamination, and conduct and oversee maintenance activities. Plans are being developed to allow fellows to visit other high and maximum containment laboratories across the nation during the second year of their fellowship to better understand the diversity of facilities and variations in containment practices.

At the current time, our first biocontainment operations fellow is in-processing and we anticipate that he will begin formal training within the next 60 days. This individual comes from the construction industry and was directly involved in the construction of the GNL, so he is especially well qualified to participate in the fellowship. We are designing his course of study to be flexible to allow him to participate in the fellowship while retaining some of his duties with his current employer.

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over this past year of support we have actively participated in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology and other organizations at the fore of these discussions. We have also participated in ongoing discussions on these topics hosted by the National Science Advisory Board for Biosecurity (NSABB) and the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight.

Biosurety and biosecurity are currently covered in our theoretical training sessions, and we are in the process of developing a structured course to more specifically address biosurety and biosecurity in depth. We anticipate posting this course on our internal website as an educational tool to augment our more formal training opportunities and to complement lectures already offered. Depending upon the success of this internal posting, we will then consider posting the course on our general website where it would be available to the general public.

As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established a distinguished speaker series. Our *Topics in Biosecurity Symposia Series* has been offered twice thus far – in November 2010 and February 2011. Both sessions were attended by large crowds and drew positive attention and feedback.

Summary of Biosurety and Biosecurity training activities this past year:

Topics in Biosecurity Symposia Series – Session I.

A symposium on biosecurity policy was held at the Galveston National Laboratory on November 9, 2010. This was the inaugural symposium in the Topics in Biosecurity Symposia Series included as speakers the Honorable Judge Susan A. Ehrlich, a current member of the National Science Advisory



Board on Biosecurity, and Dr. Victoria Sutton, a Professor of Law and Director of the Center for Biodefense, Law and Public Policy at Texas Tech University School of Law. The symposium was open to the public and to students and faculty from across the UTMB campus.

We enjoyed excellent attendance with standing room only for the presentations and following discussions. Members of the greater Galveston County participated in the symposium, and included in the audience was at least one member of the UTMB Community Advisory Board and the Galveston National Laboratory Community Liaison Committee. Also present was the editor of the local newspaper, the Galveston County Daily News, and a reporter from the Houston affiliate of National Public Radio (NPR). The presentations and subsequent discussion focused on the yet to be released report from the Federal Experts Security Advisory Panel and their draft recommendations concerning the Select Agent Program. One of the topics of most interest to symposium participants was the issue of personnel reliability and how organizations handling Select Agents might best reduce the risk of insider misuse of Select Agents.



Following the symposium, the Galveston County Daily News published an editorial based on the presentations and discussions made during the symposium, “Unique Opportunities at Galveston National Laboratory, 14 November 2010 (www.galvestondailynews.com)”.

Topics in Biosecurity Symposia Series – Session II.

On February 28, 2011, the NBTC and the GNL hosted the second symposium in our series. Our guest speakers for this second session were: 1) RADM Kenneth Bernard, MD, USPHS (Ret.), a noted expert on biodefense who has influenced national and international biosecurity policy during stints, among others, as Special Assistant to the President for Biodefense, Assistant Surgeon General, Senior Advisor for Security and Health on President Clinton’s National Security Council staff, and with former U.S. Senator Bill Frist on assignment by the U.S. Surgeon General; and 2) Robert Kadlec, MD, a homeland security veteran with more than three decades of experience shaping, executing and championing public health and bioterrorism policies and preparedness. Dr. Kadlec



served as a career officer and physician in the United States Air Force with placements in several senior positions in the White House, the U.S. Senate and the Department of Defense. He served as the Special Assistant to the President and Senior Director for Biodefense Policy on the Homeland Security Council and as staff director for the congressional Subcommittee on Bioterrorism and Public Health under its chairman Senator Richard Burr. He was responsible for conducting the biodefense end-to-end assessment, which culminated in drafting the National Biodefense Policy for the 21st Century and is currently with global management consulting firm PRTM as a vice president in its Global Public Sector business, based in Washington, DC.

These distinguished speakers provided symposium attendees an “insiders” understanding on the current state of policy and legislation concerning biosecurity and biodefense issues. During their presentations they provided key insight as to the legislative process, the thinking behind some of the policy decisions made, and future challenges yet to be addressed.

The symposia series is open to the public and to students and faculty from across the UTMB campus.



At both Session I and Session II we enjoyed excellent attendance with standing room only for the presentations and following discussions. Community members from greater Galveston County participated in the symposium, and included in the audience were also members of the UTMB Community Advisory Board and the Galveston National Laboratory Community Liaison Committee. The presentations and subsequent discussion focused on the mechanisms of federal policy regarding biosecurity and biodefense, particularly from the international perspective

Session III in the series is planned for Fall 2011.

NBTC Website.

Over the past reporting year, the new NBTC website was created and published - www.utmb.edu/nbtc. We will continue to add content to the site over the course of the coming year. The site serves as a hub of information regarding the Center, our goals, and the resources that the NBTC makes available to the biosafety and research communities. We are currently developing a dedicated section focused on biosecurity which will offer a comprehensive review of the topic and practical guidance.



External Onsite Training - KEMRI, Nairobi, Kenya.

The NBTC was invited to provide BSL3 training for a new facility in the process of opening at the Kenya Medical Research Institute (KEMRI) in Nairobi, Kenya. In this capacity two NBTC trainers travelled to the institution in February 2011 and provided biosafety training onsite to ten individuals (*pictured*). This trip was sponsored by a UTMB principal investigator who is in the process of establishing a formal collaboration with the institution.



2nd Annual African Biosafety Association meeting.

In February 2011, the NBTC was invited to attend the 2nd Annual African Biosafety Association meeting held in Accra, Ghana. At this meeting a number of different African countries were represented and each highlighted their biosafety efforts. Meeting attendees agreed to work together in an effort to improve training and biosafety knowledge of all laboratorians working in biosafety level laboratories in the different countries. The training program also received significant attention during the conference as an exhibitor and during a formal presentation on biosafety training provided to attendees by Dr. Brocard (*pictured*). The NBTC has already been invited to return to next year's conference.



NASA's Johnson Space Center.

The trainers from the NBTC were invited to NASA's Johnson Space Center in Houston to provide BSL2 training to ten of their laboratory workers. The training was very well received and members of our team were invited back to the center to present on biosafety topics at a meeting of environmental health and safety professionals in May 2011 (*pictured*).



Table 1.

Summary of training courses offered and number of participants in each course, May 2009 through May 2011.

Module	May-Dec 2009	Jan-March 2010	April-June 2010	July-Sept 2010	Oct-Dec 2010	Jan-March 2011	April-June 2011	Total
BSL-4	9	2	6	2	24	5	26	74
BSL-3	45	14	28	27	18	31	11	174
BSL-2 Theoretical	107	30	62	38	26	44	56	363
BSL-2	64	11	18	28	16	33	26	196
ABSL-3 Theoretical	29	8	16	13	18	12	11	107
ABSL-3 hands-on	29	7	9	12	8	14	10	89
ABSL-2 Theoretical	N/A	N/A	N/A	N/A	N/A	20	32	52
ABSL-2 hands on	N/A	N/A	N/A	N/A	N/A	3	13	16
Comprehensive Facility Training for External Trainees <i>(new 2011)</i>	N/A	N/A	N/A	N/A	N/A	N/A	1	1
Graduate Program	48	N/A	N/A	N/A	35	N/A	N/A	83
Aerobiology	19	0	3	0	2	0		24
Autoclave	195	0	0	21	6	9	5	236
Annual Autoclave Retraining of ARC staff	N/A	N/A	N/A	N/A	N/A	N/A	15	15
High Through-put Safety training	8	0	9	0	3	0		20
Theoretical non human primate	16	0	0	0	15	20	62	123
Non-human primate hands-on						6	44	50
BSL-3 mentorship	36	26	7	5	3	4	2	93
ABSL-4 sign-off						6		6
ABSL-3 mentorship						9	8	15
Specialized training (Assay Development)	18	0	0	0	0	0		18
Total trained	623	98	158	146	174	216	322	1755

Figure 1: Total number of trainee from 2005-2011. As expected the number of trainees has continuously been increasing as indicated by the percentage noted atop each year.

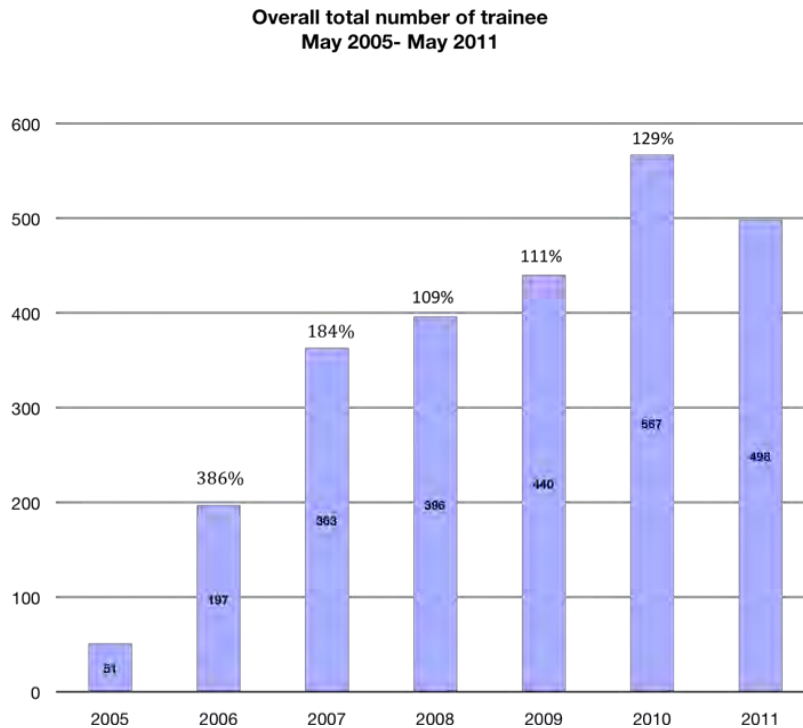


Figure 2: Distribution of trainees based on the courses taken. As expected the number of trainees follows the normal biosafety level pyramid with a large amount of BSL-2 trainees and then fewer as the biosafety level increases.

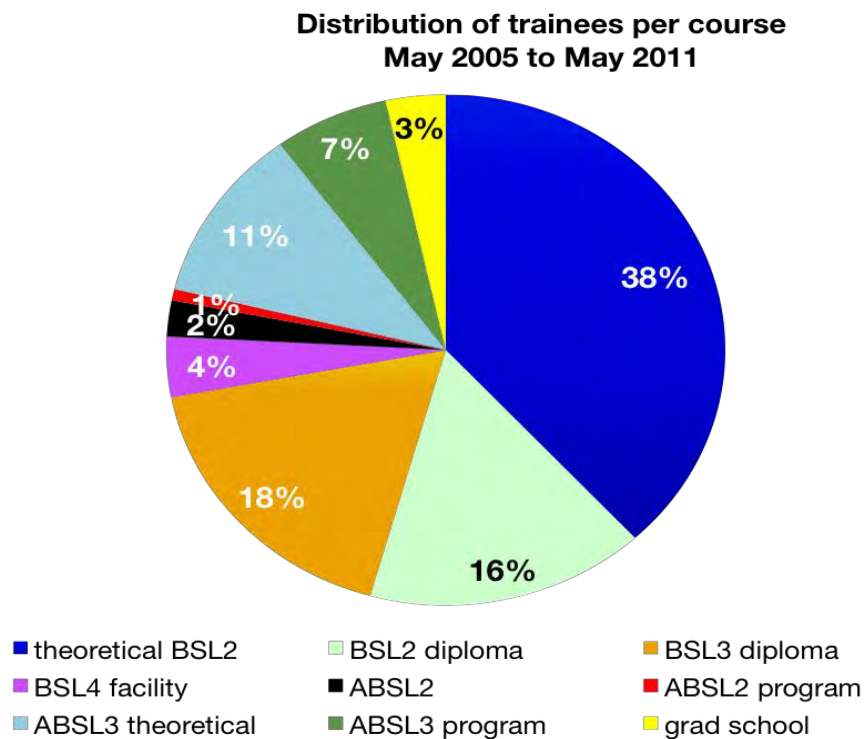


Figure 3: Distribution of trainees based on their main job occupation. Others include information services personnel, animal care staff, public relations personnel, and lawyers. In this graph we can see that as expected the scientific community is the major beneficiary of the training program, as this was designed specifically for them.

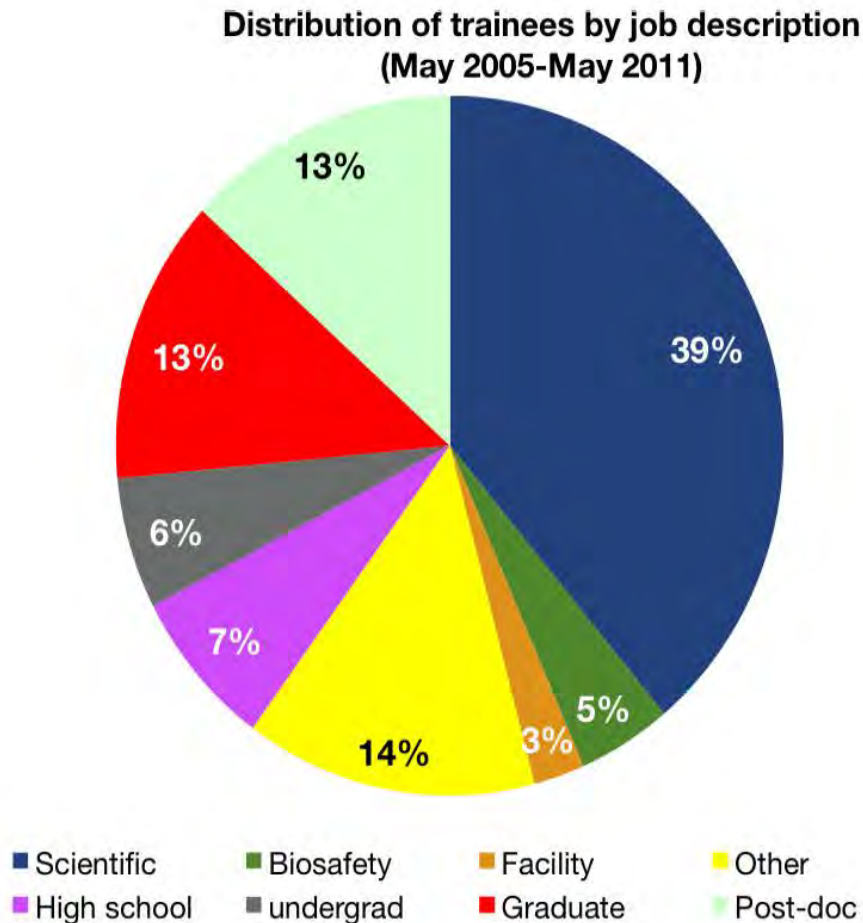


Figure 4: Distribution of the trainees based on their geographic location. UT-System includes all university members of the University of Texas group, of which UTMB is a member.

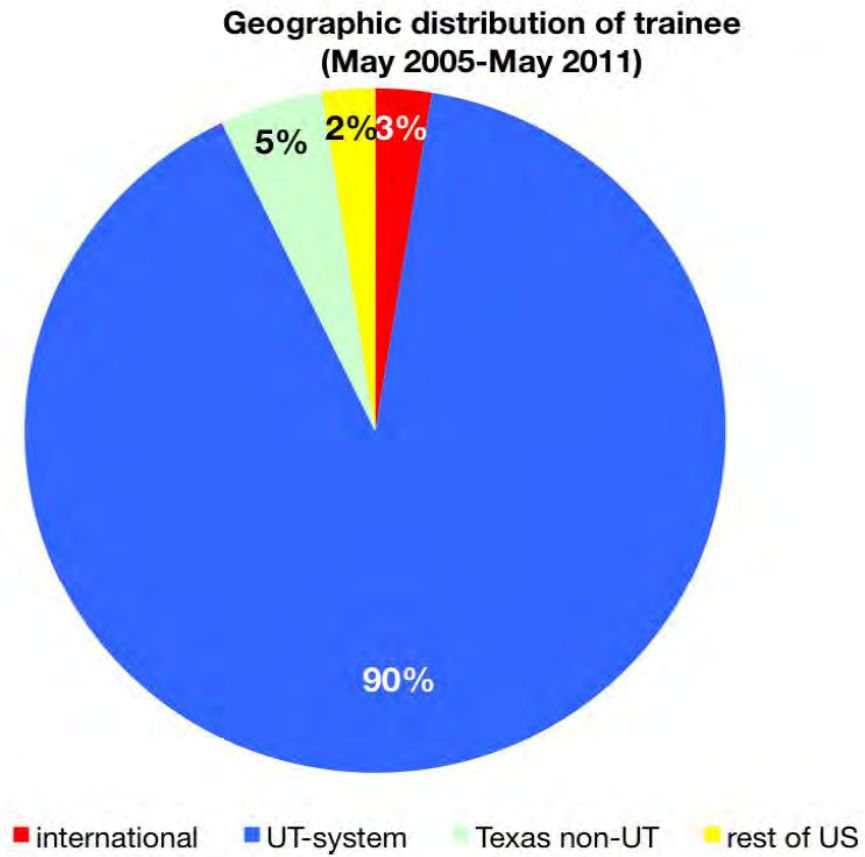
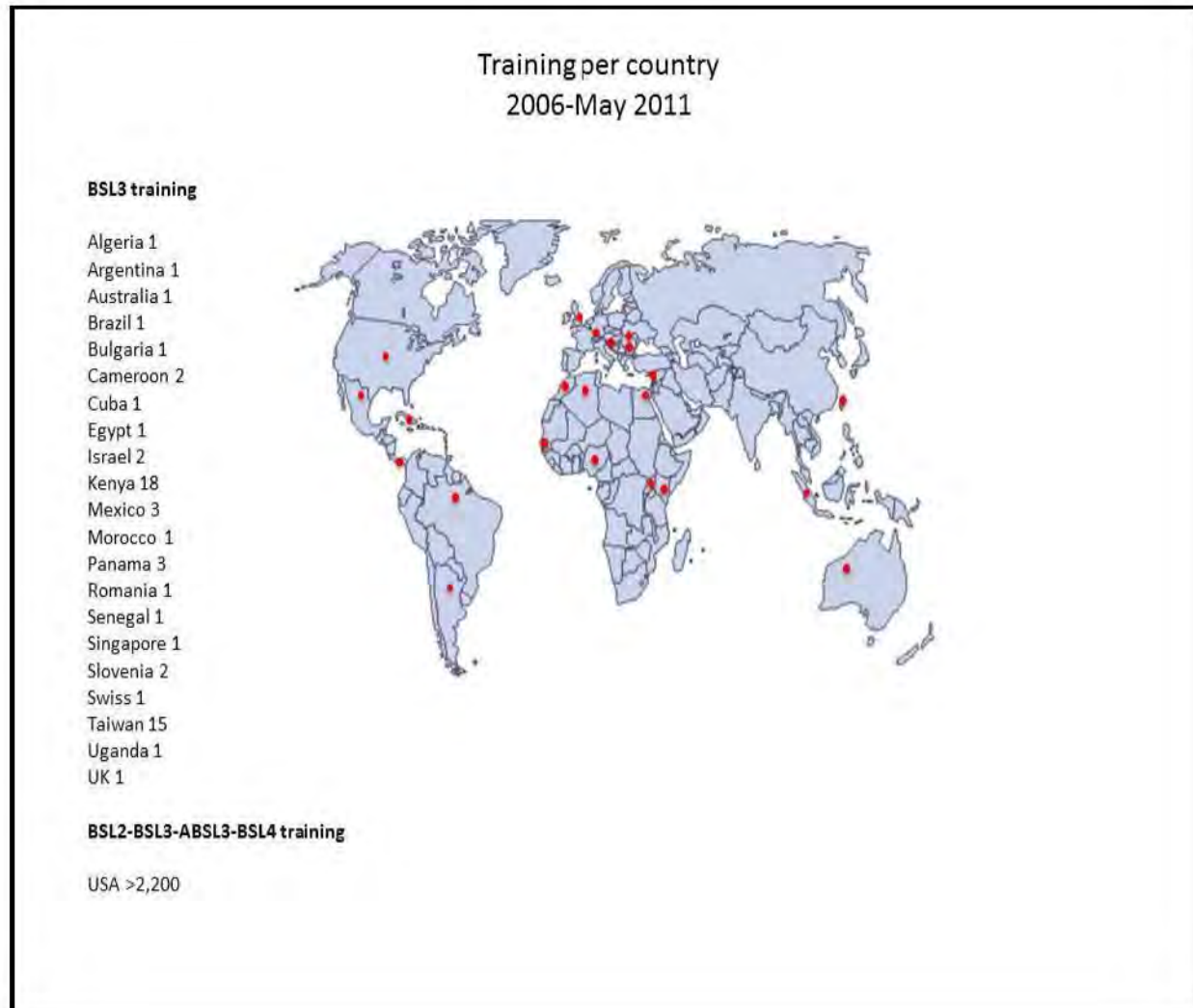


Figure 5: The world map below indicates the diversity of national and international trainees coming to the NBTC for containment training over the course of the program.



KEY RESEARCH ACCOMPLISHMENTS:

- A comprehensive, standards-based training program has been established and implemented to prepare individuals for work at all levels of biocontainment.
- Advanced, mentored training is available to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL-4 level.
- A unique fellowship has been created to train the next generation of containment laboratory containment facility operations professionals prepared to oversee the safe operations of these complex facilities.
- A novel training opportunity addresses the safety considerations emerging at the interface of high through-put screening of potentially infectious material.
- As part of our participation in the national dialogue on biosecurity – and as a service to the research community – we also established the *Topics in Biosecurity Symposia Series*. Both sessions offered thus far – in November 2010 and February 2011 – were attended by large crowds and drew positive attention and feedback.

REPORTABLE OUTCOMES:

- A total of 855 training experiences were provided to trainees, staff and external participants. These courses ranged from basic introduction to biocontainment to mentored hands-on research under BSL-4 containment conditions.
- Two doctoral level fellows are participating in advanced mentored training to become independent investigators able to conduct their research under BSL-4 containment.
- One individual was selected for the facility operations fellowship and has begun training in the operation and maintenance of a major biocontainment facility.
- Specialized training and dedicated courses (Pre-conference course: "BSL-3 Operations and Management" and "BSL3 for biosafety professionals: what they need to know") was provided to participants at an important national scientific meeting relevant to scientists working in biocontainment, the American Biological Safety Association annual meeting (October 2010).
- Literature describing the NBTC program was made available at a manned booth hosted at the following meetings: American Biological Safety Association annual meeting, the American Society of Tropical Medicine and Hygiene annual meeting (November 2010), the ARS/ABSA meeting (Feb 2010), the American Society of Microbiology Biodefense meeting (Feb 2010) and the 2nd African Biosafety Association annual meeting.
- Round table discussions led on the topic of "Training and Mentorship" in biosafety, and two formal presentations, "Creating a culture of Biosafety" and "BSL4 Graduate Student Training Process" were offered at the NBL-RBL facilities network meeting, Boston, 2-5 May 2010.
- Guidelines for Biosafety, Laboratory Competency were published in the MMWR April 15, 2011 / 60(02); 1-6, Dr. Brocard was a member of the expert panel.

- A formal report relevant to the safe operations of containment laboratories was published in the peer reviewed journal, *Emerging Infectious Diseases*: LeDuc, J.W., Anderson, K., Bloom, M.E., Carrion Jr., R., Feldmann, H., Fitch, J.P., Geisbert, T.W., Geisbert, J.B., Holbrook, M.R., Jahrling, P.B., Ksiazek, T.G., Patterson, J., Rollin, P.E. 2009. Potential Impact of a Two-Person Security Rule on Biological Safety Level-4. *Emerging Infectious Diseases* 15 (7), July 2009 online only. ISSN: 1080-6059.

CONCLUSIONS:

The National Biocontainment Training Center offers a robust and intensive training program devoted to all aspects of biological safety, biocontainment, and biosecurity. This program offers unique, hands-on training to trainees, staff and external partners at all levels of biocontainment, including focused, mentored training in the BSL-4 laboratory.

Over 850 persons benefited from one or more of these training courses, many of whom are now pursuing graduate education and using these specialized skills in the newly constructed GNL containment facilities. Intensive, mentored fellowship programs were established to offer opportunities for in-depth training in research under BSL-4 conditions and also in containment laboratory operations and maintenance. These fellowships help address the critical national shortage of well-trained containment laboratory scientists and facility operations specialists.

REFERENCES:

None.

2010 Table of Contents

Introduction	2
Body	2
Staffing Report	3
Renovation of teaching laboratory	4
Overview of NBTC training	5
BSL-2 and BSL-3 training	6
Animal BSL-3 training	7
BSL-4 training	7
Specific Aims 1-6	8
Key Research Accomplishments	16
Reportable Outcomes	16
Conclusions	17
References	17
Appendices	18

INTRODUCTION

The National Biocontainment Training Center (NBTC) provides standards-based theoretical and practical training to trainees and professionals preparing for work in biocontainment laboratories where especially dangerous pathogens will be handled. Training is staged and appropriately targeted to requirements for biological safety level 2 (BSL-2), BSL-3 and BSL-4. Structured coursework is designed to prepare trainees to safely manipulate pathogens, including growth, genetic and antigenic characterization, and molecular studies of pathogenesis. Coursework includes both theoretical training and supervised hands-on procedures tailored to meet the specific needs and requirements of the individual trainee. Advanced coursework includes hands-on mentored training in the containment laboratories, including consecutively at BSL-3 and BSL-4 levels of containment. Specialized training in the handling of laboratory animals is under development and will be offered during year 2 of activities. Extensive mentored training is offered for scientists at the BSL-4 level through a dedicated fellowship. Fellows work under the close supervision of an established mentor while addressing a research topic of their own choosing. Fellowships are open-ended and fellows progress to full independent access to the BSL-4 laboratory only when the mentor and laboratory director are fully confident of the individual's skills and ability to work independently in this environment. The NBTC also offers a unique training opportunity for building engineers interested in pursuing a career as a biocontainment building engineer. To the best of our knowledge, this is the only such training program in the world. This program is designed as a series of modules which address specific aspects of the construction, maintenance and safe operations of a biocontainment laboratory. The course is tailored to the specific needs of the individual trainee and involves both didactic training and mentored hands-on work using the Galveston National Laboratory (GNL) as its classroom. Over the course of the training period, which is anticipated to require up to two years for completion, the fellow will be directly involved in the maintenance of the laboratory, decontamination of specific laboratories, monitoring and replacement of filters, and a wealth of other duties routinely seen in the operations of typical biocontainment facilities.

BODY

TATRC support for the NBTC formally began on 22 May 2009 and we are now submitting our first annual report for this initiative. The Training Center had been established and operational prior to receiving TATRC funding; consequently, the course structure and procedures were already in place and allowed the Center to implement enhanced training operations almost immediately. From inception to date, the Center has provided training to approximately 1640 participants through the various courses offered. Below we have summarized progress made since receiving TATRC support; funding and accomplishments are organized by each specific aim as they were presented in our original proposal.

Staffing Report

The NBTC relies on a cadre of highly skilled scientists, engineers and technicians to offer a robust portfolio of training opportunities to trainees and professionals working in the field of biocontainment. A summary of these individuals and their roles in the operation and management of the NBTC is below.

Dr Tom Ksiazek. Leadership of the overall NBTC program is provided by Dr Tom Ksiazek, a veteran of nearly four decades of research and development addressing some of the most dangerous pathogens known to humankind, including the filoviruses, Ebola and Marburg, as well as other causes of viral hemorrhagic fevers such as Crimean-Congo hemorrhagic fever, yellow fever and dengue. Dr Ksiazek also oversees the BSL-4 mentored fellowship program and is responsible for the selection of fellows and for monitoring their progress. As the director of the GNL BSL-4 laboratories, he has ultimate responsibility for the individuals working in this space and as such has final approval in determining when an individual has successfully mastered the essential skills needed to safely work independently in the BSL-4 environment.

Dr Anne-Sophie Brocard. Classroom and laboratory training is directed by Dr Anne-Sophie Brocard, an accomplished virologist and experienced trainer who has directed the training center since its inception. Dr Brocard provides both theoretical and practical training to trainees, and monitors their progress as they develop appropriate skills for work at each level of biocontainment.

Ms Je T'aime Newton. Dr Brocard is ably assisted by Ms Je T'aime Newton, a highly experienced instructor with extensive expertise. Ms Newton provides specialized training at all levels of containment, but is responsible for preparing trainees for BSL-4 investigations, focusing her efforts on the proper care, use and maintenance of the protective "space suits" used in the BSL-4 laboratory, and other aspects of work in this highly specialized environment.

Ms Vicki Jones. Ms Jones is a critical member of the teaching faculty who assists as a trainer in both the theoretical and practical training modules.

Ms. Belinda Rivera and Mr. Jason Hardcastle recently joined our team as animal and in-vitro trainers.

Ms Dee Zimmerman is the director of the University biosafety program and offers guidance in the regulatory requirements for operation of any biocontainment facility.

Ms Paige Carness. A dedicated module on biosecurity is included in the portfolio of training opportunities and the content of this course is the responsibility of Ms Carness.

Mr Lee Thompson and Mr Miguel Grimaldo. The building engineering fellowship is coordinated through the efforts of Mr Lee Thompson and Mr Miguel Grimaldo (not currently funded by this award). They are responsible for the content development of each module of the building engineering fellowship and they also provide the dedicated instruction associated with each module. They serve as the primary mentors for the building engineering fellows.

Ms Bonnie Walters was employed as a business manager for the NBTC during a portion of the year just completed, but she resigned for personal reasons. Recruitment of a replacement is underway and we anticipate filling this vacancy in the next 60 days.

Dr Gavin Bowick was a senior biocontainment fellow preparing for work in the BSL-4 laboratory for much of the year just completed. Dr Bowick is a virologist working on

arenaviruses, the cause of viral hemorrhagic fevers. Dr Bowick's training was interrupted due to visa issues and he has returned to his home in the UK while this is being resolved. We anticipate that he will return in the coming months and will complete his fellowship training. He is also a candidate for a permanent position on the UTMB faculty.

Dr Janice Endsley is an assistant professor on the faculty of UTMB and entered the BSL-4 fellowship program in 2010. Dr Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr Endsley will continue in the fellowship for much of the coming year as she gains critical experience and masters skills needed to work in this environment.

Ms Joan Geisbert will join the NBTC in July 2010 to assist in training at the BSL-4 level. Ms Geisbert has over 30 years experience in BSL-4 laboratories and has worked extensively with experimentally infected animals, including non-human primates, under containment conditions. As our animal handling in containment training module is developed, Ms Geisbert will play a key role in leading this effort.

Additional Mentors. We anticipate expanding our cadre of skilled mentors to provide oversight and supervision of trainees as they complete their hands-on training under BSL-3 or BSL-4 laboratory conditions. Mentors will be existing faculty members who have earned independent access to the containment laboratories, and they will incorporate this added duty into their existing activities.

Dr James Le Duc. Dr Le Duc serves as the principal investigator for the NBTC award and is responsible for programmatic oversight, budgetary issues and reporting requirements. Dr Le Duc has nearly four decades of experience in the conduct and supervision of research and development activities under biocontainment conditions, and has been intimately involved in the development of national policy in the fields of emerging infectious diseases, bioterrorism preparedness and biocontainment.

To meet the growing demand for training opportunities offered through the NBTC, we are in the process of recruiting additional trainers and mentors. We are also in the process of developing skilled trainers to assist in the education of trainees and fellows in the safe and appropriate handling of laboratory animals in the context of research under biocontainment conditions.

Renovation of Teaching Laboratory facilities.

The teaching laboratory is a critical asset of the NBTC designed to offer trainees a realistic exposure to the conditions and equipment they will typically encounter as they conduct their studies in the containment laboratory. At the BSL-2 level, this typically includes a biological safety cabinet where most handling of pathogens takes place. It also includes limited specialized equipment, as well as facilities to manage laboratory waste and storage of pathogens. Training for individuals preparing for work in the BSL-3 laboratory includes a dedicated area where individuals master the donning and doffing of protective gear and its proper disposal. Those going on to prepare for work in the BSL-4 laboratory have specialized training in the care and use of the "space suit" that is routinely worn there. This includes inspection of the suit for any evidence of leaks prior to use, gaining experience and familiarity in the wearing of the suit, use of compressed air hoses, and training in emergency procedures. In order to provide this training under

realistic conditions, the training facility has been outfitted with a breathing air compressor and a mock laboratory where trainees can experience wearing the suit and become familiar with working in this unique environment. Some people discover that they experience claustrophobic reactions when wearing a suit, and this practical, realistic suit training environment allows them to overcome any such reactions under well-controlled conditions, or decide that this work is not a good fit for them.

A key benefit of the support provided to the NBTC is the availability of resources that allowed for the renovation of our existing teaching laboratory facilities. This work has been in progress throughout this funding period and is now complete. We have completely refurbished the training facility to significantly expand the mock laboratory space available to us, and to enhance the breathing air compressor and suit training area. There have been several complications as this work has progressed, but the work is now completed and the mock training laboratory is now in full use. We have used existing/interim BSL-2 laboratory space in the GNL for training throughout the year, so there has been no significant delay in the advancement of our trainees as these renovations were being made. Similarly, we used the west end BSL-4 laboratory in the GNL for training at this level of containment.

Laboratory training is conducted in a mock training laboratory with authentic laboratory equipment utilizing non-infectious materials. Entry into the lab is through a double door anteroom with directional airflow and mock pressure monitors. The laboratory has three class II biological safety cabinets, two of which are constructed with see through panels which allow the trainer to introduce smoke into the BSC to visualize air movement within BSC. There is a third BSC class II cabinet on order which will have see through panels and BSL-4 air connections ports. Two of the BSC will be equipped with a camera inside that will allow us to perform remote demonstrations. The laboratory will also have two cameras installed for remote demonstrations. The laboratory will have two class III glove boxes, incubators, centrifuges, bench top autoclave, refrigerator, -80 freezer, dunk tank, general laboratory equipment to allow for BSL-2 to mock BSL-3 and -4 laboratory work. The laboratory is equipped with a compressor and air lines for practice in the suit check examination and use of BSL-4 suits within that facility prior to the trainee entering the active BSL-4 laboratories. The laboratory has airline drops allowing the trainee to work throughout the laboratory with the ability to connect and disconnect airlines as needed.

Overview of NBTC Training

The NBTC provides a series of training modules involving a mixture of didactic instruction and hands-on training to be carried out within an existing mock BSL-3/-4 training laboratory located within the Environmental Health and Safety Office space in the Materials Management Building on the UTMB campus. The intent of the NBTC is to promote good techniques and safe procedures to be used at all biosafety levels, and to provide consistency in research practices. The program ensures that all training attendees have the same general biosafety training at BSL-2 and -3, and if necessary BSL-4, prior to entering a biocontainment laboratory, thus ensuring that safety standards are observed and good practice is pursued.

BSL-2 and BSL-3 Training

The BSL-2 and -3 training provide a multi-phased approach:

- the assessment phase
- the training phase
 - theory
 - hands- on practicum
- final assessment

Each person begins with an assessment that includes a written test focusing on safety related topics, hands-on skills related to protocols based on their research using appropriate biosafety practices and procedures. During the assessment the trainer does not intervene and notes both safety and scientific techniques employed. This allows the determination of experience and level of training that will be required for each trainee. Once the assessment is completed the results are reviewed with the trainee and the specific areas of training focus are identified. A written report is sent to the trainee and their principal investigator or supervisor.

The training phase includes a theoretical class which covers the following topics:

- Biological safety levels 1 through 4, standard microbiological practices, special practices, safety equipment and laboratory facilities.
- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work, and spill response in the BSC.
- Procedures with the potential for creating infectious aerosols, how to recognize aerosol producing devices and how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory, BSC, centrifuge, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- Introduction to select agent rules and NIH-OBA guidelines.

The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a non-hazardous environment. It allows the trainer to observe, advise, and correct the trainee's techniques in the laboratory relative to safety as well as scientific issues (e.g. contamination of cultures). The practicum is specific to biosafety and agents to be used (e.g. bacteria, parasites, viruses). This approach also allows the use of specific protocols or facility specific practices the trainee brings with them. Emergency response and spill training allows the trainee to visualize and respond to spills and contamination with the use of florescent dye and breakable training lab ware.

The final assessment is identical to the initial assessment, with a written exam and hands on skills assessment. Once the trainee has completed and passed the final

assessment the trainee is provided with a certificate of training for the biosafety level they completed. A report is sent to the principal investigator, trainee and laboratory director.

Animal BSL-3 Training

An animal biosafety training program was developed on the same concepts as the BSL-3 program. Trainees must have completed the BSL-3 training before commencing ABSL-3 training.

The training phase includes a theoretical class which covers the following topics:

- Personal protective equipment, types of respiratory protection, gloves, gowns, use and disposal.
- Proper use of the biological safety cabinet (BSC), how the cabinet functions, monitoring the BSC functions, setting up the work field, decontamination prior to and after work and spill response in the BSC.
- Procedures with the potential to create infectious aerosols, how to recognize aerosol producing devices and procedures and how to mitigate and control aerosol production.
- Emergency procedures, spills in the laboratory or in the BSC, incident response, first aid, reporting procedures, and medical emergencies in the lab.
- Waste management, types of disinfectants, types of waste generated, the differences in disinfection, decontamination and sterilization.
- The hands-on practicum compliments and reinforces the theoretical class and allows the trainee to experience different scenarios in a safe environment. It allows the trainer to observe, advise, and correct the trainee's techniques in the laboratory relative to safety as well as animal handling. The practicum is specific to biosafety and animal species to be handled. This approach to training also allows the use of specific protocols or facility specific practices the trainee brings with them.

In the third phase, the final assessment includes a written exam and a hands-on skills assessment. Once the trainee has completed and passed the final assessment the trainee is provided with a certificate of training for the biosafety level they completed.

BSL-4 Training

BSL-4 training rests upon a firm adherence to the principles and specific practices of safe BSL-3 research. This prevents an over-reliance on the BSL-4 suit as a primary means of containment, and makes the suit environment an operationally redundant means of protection, significantly enhancing protection. Accordingly, individuals who are selected for BSL-4 training will have completed training at BSL-3 and have been approved for independent access to the BSL-3 laboratories. These individuals would then complete the BSL-4 modular training.

Specific Aims

Aim 1: To provide standards-based, high containment laboratory safety knowledge.

Standard training activities for UTMB staff, trainees and investigators from outside the University have been in place throughout the year. The number of individuals trained at each level is summarized in Table 1 below and the associated figures. As summarized above, the topics typically covered in this introductory training include the principles of basic safety precautions in the laboratory, routine rules and regulations designed to protect the individual and environment from accidental contamination by an infectious microbe, and the care and use of the biological safety cabinet. Also covered are the appropriate procedures of clean-up following a spill, decontamination procedures, principles of the care and use of autoclaves and other essential equipment. A summary of the modules covered in this course is included in Appendix 1.

Aim 2: To provide standards-based, high containment laboratory hands-on training.

Training offered under this Aim is directed at providing trainees with practical, real-world training in the laboratory setting. Course content is tailored to include those procedures and the use of specific equipment likely to be encountered by the trainee in their routine work. Thus, those destined to work in a virology laboratory may focus on those protocols most appropriate for use in a virology laboratory as opposed to those typically used when working with bacteria. There are, of course, common practices used in any BSL-2 laboratory and training on the safe conduct of these procedures is the foundation of this course. Training typically is undertaken in small groups of only one or two individuals, allowing for intense interaction between the instructor and trainees. By actually doing the procedures essential to their day-to-day laboratory work under the close supervision an instructor (with the use of indicator dyes that allow clear recognition of contamination), the trainee quickly grasps the key teaching points and rapidly masters safe laboratory practices. Training is offered in the newly renovated training laboratory described above.

The numbers of individuals trained under Aim 2 for the NBTC are summarized in Table 1 below and include a total of 91 individuals who have complimented their theoretical training at the BSL-2 level with practical hands-on BSL-2 training in the laboratory setting. A total of 80 were trained at the high containment BSL-3 level with practical hands-on experiences. Animal BSL-3 (ABSL-3) theoretical training was provided to 53 individuals, and 36 completed their hands-on training. Sixteen individuals participated in maximum containment BSL-4 training.

Aim 3: To provide topic-specific training.

Autoclave Operations. A routine requirement for all persons working in the containment laboratories is the need to be able to properly operate the autoclaves. A dedicated training session is offered to all individuals as a separate element of their orientation to the GNL, and this training is offered to individuals working in other laboratories using the same or similar equipment. During the first year of support we trained 195 individuals in the proper care, use and operations of autoclaves. As several new hiring actions within the GNL occur routinely, we anticipate ongoing demand for this training through coming years.

Aerobiology. The GNL contains aerobiology laboratories at both the BSL-3 and BSL-4 levels of containment. The BSL-3 facilities were fully commissioned and approved for use by the CDC and USDA during the year just completed; however, the BSL-4 facilities were only finally approved for full operations very recently. These facilities are highly complex and require specialized training not only in the operation of this sophisticated equipment, but also in the proper care and handling of the laboratory animals that will be experimentally exposed. During the course of the year we have trained 19 individuals for work in the BSL-3 facility, and during the coming year we anticipate that many of these same persons will acquire training in the BSL-4 facility as well.

External Training: A local institution requested that we provide BSL-3 training for their staff prior to opening their new BSL-3 facility. Therefore 26 trainees received theoretical BSL-3 training of which 9 trainees also received hands-on training. As part of their training process we will be also providing ABSL-3 training to their scientist and support staff.

Gamma Irradiator Training. BSL-4 laboratories utilize a number of techniques to inactivate biological materials prior to removal from the containment laboratory. One of the most frequently utilized means of removing materials from the BSL-4 laboratory is inactivation by gamma irradiation. In an effort to update training of individuals that use gamma irradiation at UTMB, a new training module was formulated to provide background radiation biology information, radiological and biological safety training, select agent and radiological security training, introductory training on dosage determination and method validation, and practical instruction on the use of the devices used for gamma bombardment. Instructors included members of the Radiation Safety Office and Biological Safety Office of UTMB's Environmental Health and Safety Office and Faculty and Staff from the Galveston National Lab/Keiller Complex. Nineteen individuals were trained in the session offered on 25 May 2010. Materials developed for the course have been organized and will form the basis for future training and refresher courses at UTMB and for others interested in the subject matter.

High Through-put Screening. We continue to work to develop a systematic training program focused on the safety concerns associated with high through-put screening. Four of the original 8 trainees introduced to the program are continuing personalized training on this unique equipment, and we anticipate an additional 2 trainees to start during the next quarter. In addition, we purchased a major piece of equipment, a pyrosequencer, to augment the existing robotics and PCR equipment already in use in the laboratory. All this equipment was used to assist the Texas Department of State Health Services and other collaborating laboratories in response to the emergence of Influenza A H1N1 that recently occurred. We will continue to develop this capability in future years as it represents the cutting-edge interface between technology and biological sciences and as such potentially creates new challenges for biological safety.

Aim 4: To provide a mentorship program for scientists working in BSL-3/ABLS-3 or BSL4/ABSL4 facilities.

A total of 53 trainees and staff were enrolled in ongoing mentored guidance in the BSL-3 laboratory suites during the year just completed, while 16 participated in supervised training at the BSL-4 level. Mentored training typically extends beyond a

given reporting quarter. A more extensive listing of the number of individuals trained during the year can be found in Table 1 below.

Aim 5: To establish a fellowship program for scientists and building engineers working in BSL-3/ABSL-3 or BSL-4/ABSL-4 facilities.

The high and maximum containment fellowship program for scientists is in place and we have two fellows now in training. Gavin Bowick, PhD, is currently enrolled in the mentored training phase of BSL-3, and will soon begin his mentorship in the BSL-4 laboratory. Dr Bowick is a junior faculty member at UTMB and is studying the pathogenesis of Junin virus, an arenavirus endemic in Argentina and a Category A recognized bioterrorism threat agent. Junin virus is a Select Agent. As indicated above, Dr Bowick's training was interrupted due to visa issues and he has returned to his home in the UK while this is being resolved. We anticipate that he will return in the coming months and will complete his fellowship training. He is also a candidate for a permanent position on the UTMB faculty. Dr Janice J Endsley, has now begun as the second fellow sponsored by the program. As indicated above, Dr Endsley is an expert in tuberculosis and is preparing for work with XDR-TB. We anticipate that Dr Endsley will continue in the fellowship for much of the coming year as she gains critical experience and masters skills needed to work in this environment. As the GNL BSL-4 laboratories become operational in the next few months, we anticipate the possibility of expanding the number of fellows.

The containment laboratory building engineer fellowship is unique and is, to the best of our knowledge the only one of its kind. It promises to set a new standard for preparation of individuals working in this highly specialized environment. Unlike the fellowship for scientists, where the candidate is likely to already have solid technical skills and will be applying them in the containment environment, we anticipate that entering building engineers will require a more structured course of study. Consequently, we have identified 14 distinct modules to be covered during the course of the 2 year fellowship (see Appendix 1). These modules will cover basic microbiology, provide an overview of biosafety and biocontainment principles, construction methodologies specific for each level of containment, risk assessments, select agent regulations, formal Good Laboratory Practices, annual certification of laboratories, testing of HEPA filter housing and filters, air balancing procedures, building automated systems and engineering controls, effluent treatment systems, autoclaves care and use, decontamination procedures, biosafety cabinet certification, and laboratory operations SOP development and record keeping. During the course of their training, we anticipate that fellows will directly participate in each of these activities, as well as be personally involved in the planned shut down and decontamination of containment suites, validate decontamination, and conduct and oversee maintenance activities. Plans are being developed to allow fellows to visit other high and maximum containment laboratories across the nation during the second year of their fellowship to better understand the diversity of facilities and variations in containment practices.

At the current time, our first biocontainment engineering fellow is in-processing and we anticipate that he will begin formal training within the next 60 days. This individual comes from the construction industry and was directly involved in the construction of the GNL, so he is especially well qualified to participate in the

fellowship. We are designing his course of study to be flexible to allow him to participate in the fellowship while retaining some of his duties with his current employer.

This past year we also assisted the University of Texas El Paso (UTEP) safety and facilities staff by hosting a visit to the GNL to provide them a better understanding of issues related to BSL-3 laboratory facilities operations. The topics discussed included Biocontainment Operations, BSL-3 facility maintenance, the Select Agent registration process, record keeping, the benefits for annual biocontainment maintenance shutdowns, and an extensive tour of BSL-3 laboratories and support spaces.

UTEP participants:

Greg McNicol – Associate Vice President for Business Affairs

Robert Moss – Assistant Vice President for Environmental Health & Safety

Emilio Rodriguez – Environmental Health & Safety

Danny Cisneros – Facility Services

Aim 6: To provide training in Biosurety and Biosecurity for both leaders of biocontainment laboratories and for staff working in such facilities.

Over the first year of support we have actively participated in the national dialogue over the critical elements necessary for an effective program in biosurety and biosecurity of biocontainment laboratories. This remains an evolving field, with guidelines still being developed and a legal foundation yet to be established. As these issues are being debated nationally, we have continued to provide our expert opinion through the American Society of Microbiology and other organizations at the fore of these discussions. We have also participated in ongoing discussions on these topics hosted by the National Science Advisory Board for Biosecurity (NSABB) and the Trans-Federal Task Force on Optimizing Biosafety and Biocontainment Oversight. Biosurety and biosecurity are currently covered in our theoretical training sessions, and we are in the process of developing a structured course to more specifically address biosurety and biosecurity in depth. We anticipate posting this course on our internal website as an educational tool to augment our more formal training opportunities and to complement lectures already offered. Depending upon the success of this internal posting, we will then consider posting the course on our general website where it would be available to the general public.

Table 1. Summary of training courses offered and number of participants in each course, May 2009 through March 2010.

Module	May- Sept 2009	Oct-Dec 2009	Jan-March 2010	April- June 2010	Total
BSL-4	4	5	2	5	16
BSL3	26	19	14	21	80
BSL2 Theoretical	71	36	30	62	199
BSL2	42	22	11	16	91
ABSL3	19	10	8	16	53
Theoretical					
ABSL3 hands on	24	5	7	6	42
Graduate Program	14	34	0	0	48
Aerobiology	19	0	0	0	19
Autoclave	135	13+(47 refresher)	0	0	195
High Through-put Safety training	NA	8	0	0	8
Theoretical non human primate	16	0	0	0	16
BSL3 mentorship	26	10	0	17	53
Specialized training (Assay Development division) BSL3 theoretical	0	18	0	17	35
Total trained	396	227	72	160	855

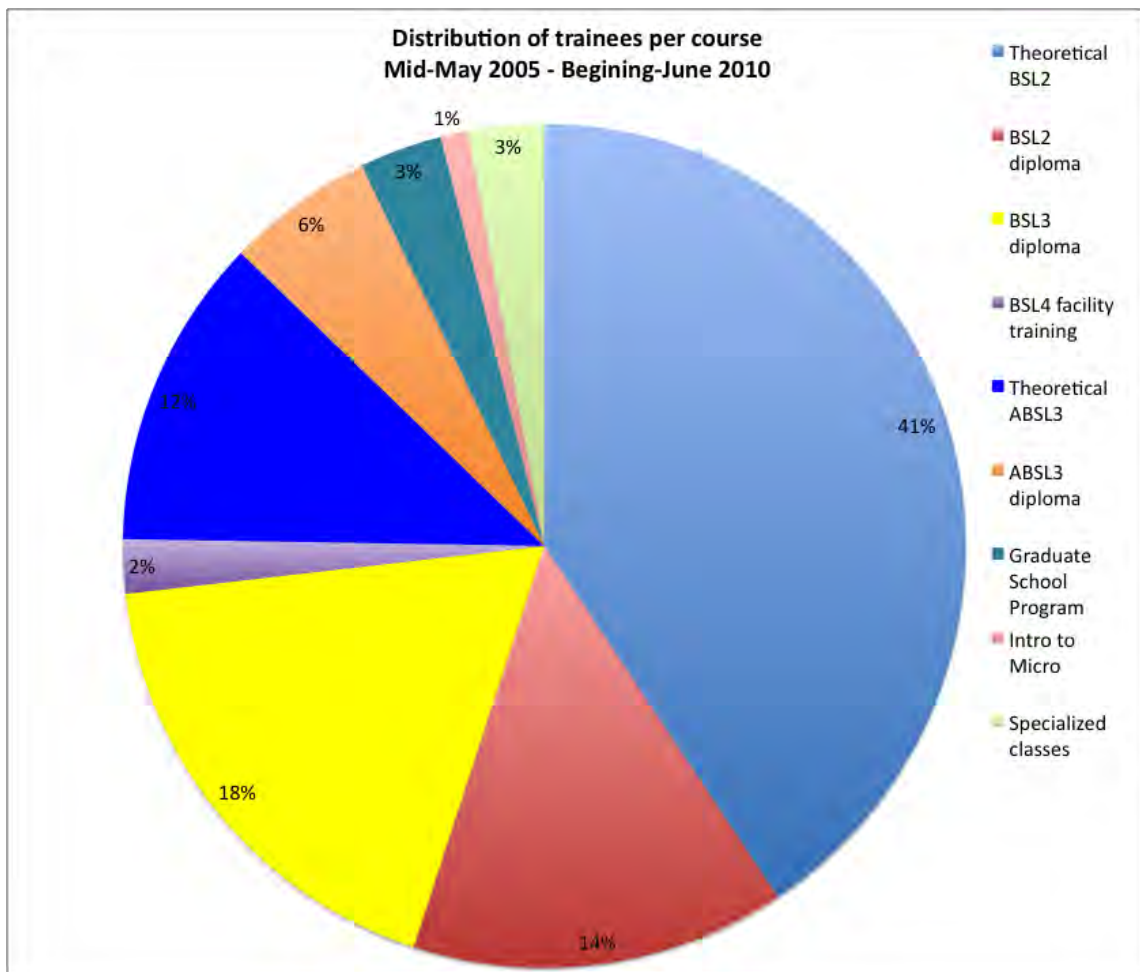


Figure 1: Distribution of trainees based on the courses taken over the past five years. Specialized classes include number of trainees that have only taken theoretical training on BSC and BSL-3 theoretical. As expected the number of trainees follows the normal biosafety level pyramid with a large amount of BSL-2 trainees and then fewer as the biosafety level increases.

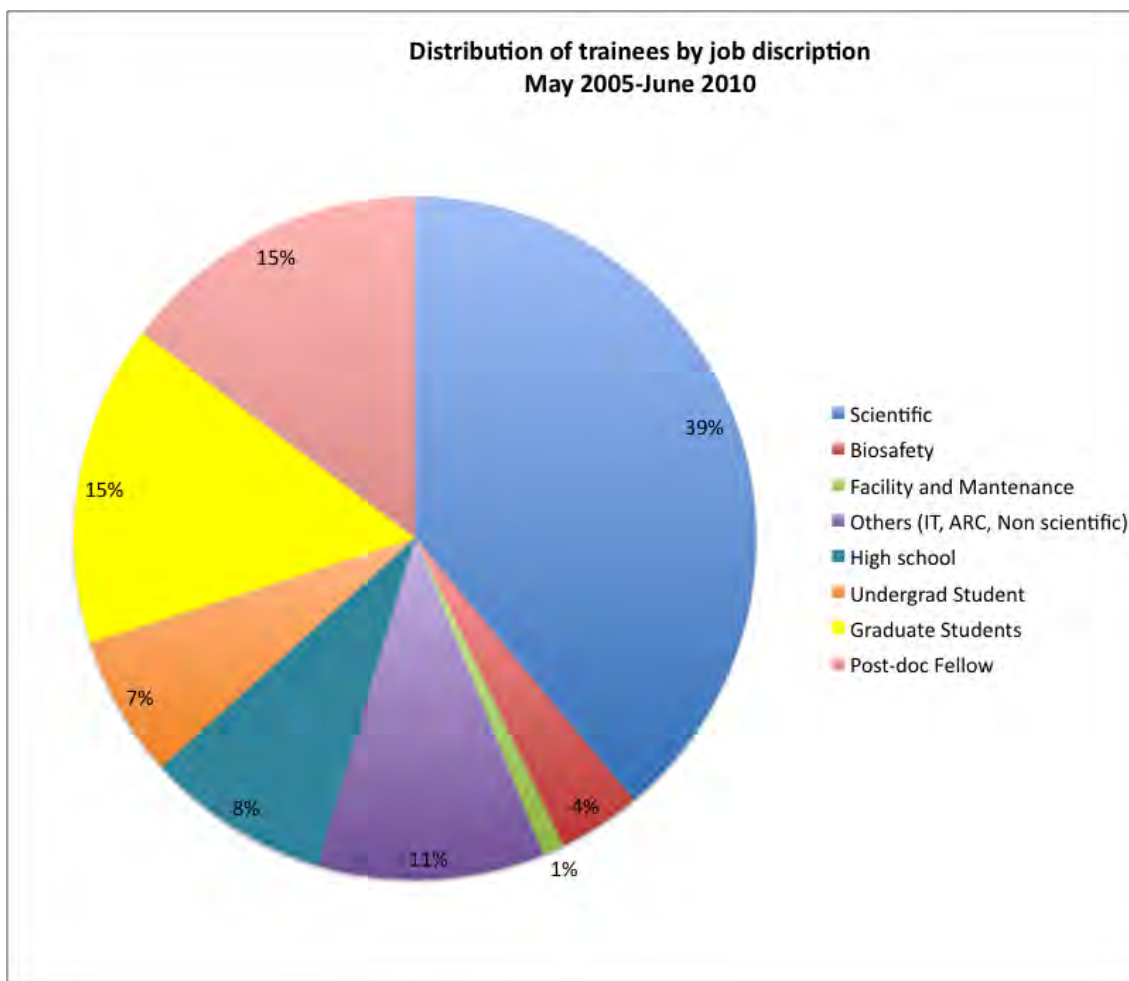


Figure 2: Distribution of trainees based on their main job occupation. Others include information services personnel, animal care staff, public relations personnel, and lawyers. In this graph we can see that as expected the scientific community is the major beneficiary of the training program, as this was designed specifically for them.

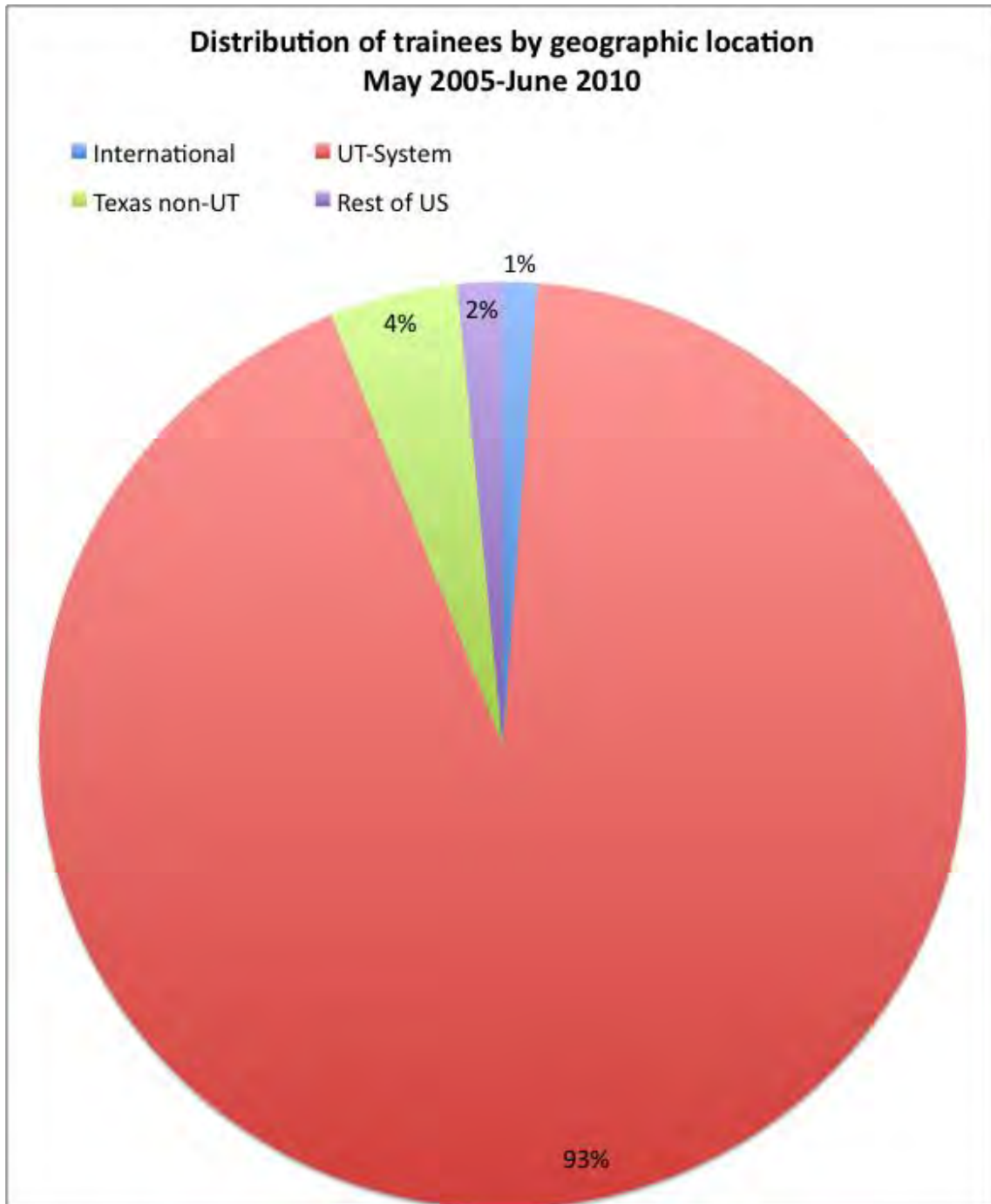


Figure 3: Distribution of the trainees based on their geographic location. UT-System includes all university members of the University of Texas group, of which UTMB is a member.

KEY RESEARCH ACCOMPLISHMENTS

- A comprehensive, standards-based training program has been established and implemented to prepare individuals for work at all levels of biocontainment.
- A fully renovated teaching laboratory allows for full hands-on training under close supervision under realistic containment conditions.
- Advanced, mentored training is available to select fellows with exceptional skill who desire to expand their research activities to include studies at the BSL-4 level.
- A unique fellowship has been created to train the next generation of containment laboratory building engineers prepared to oversee the safe operations of these complex facilities.
- A novel training opportunity addresses the safety considerations emerging at the interface of high through-put screening of potentially infectious material.

REPORTABLE OUTCOMES

- A total of 855 training experiences were provided to trainees, staff and external participants. These courses ranged from basic introduction to biocontainment to mentored hands-on research under BSL-4 containment conditions.
- Two doctoral level fellows are participating in advanced mentored training to become independent investigators able conduct their research under BSL-4 containment.
- One building engineer has been selected and will begin training very soon in the operation and maintenance of a major biocontainment facility.
- Specialized training and a dedicated course (Pre-conference course: "BSL-3 Operations and Management") was provided to participants at an important national scientific meeting relevant to scientists working in biocontainment, the American Biological Safety Association annual meeting (18-21 October 2009). This training was augmented by the availability of literature describing the NBTC program at a manned booth hosted during the meeting as well as at the American Society of Tropical Medicine and Hygiene annual meeting (18-22 November 2009).
- Round table discussions led on the topic of "Training and Mentorship" in biosafety, and two formal presentations, "Creating a culture of Biosafety" and "BSL4 Graduate Student Training Process" were offered at the NBL-RBL facilities network meeting, Boston, 2-5 May 2010.
- Assistance was provided to the University of Texas El Paso in the operation and maintenance of BSL-3 containment laboratories.
- A formal report relevant to the safe operations of containment laboratories was published in the peer reviewed journal, *Emerging Infectious Diseases*: **Le Duc, J.W.**, Anderson, K., Bloom, M.E., Carrion Jr., R., Feldmann, H., Fitch, J.P., Geisbert, T.W., Geisbert, J.B., Holbrook, M.R., Jahrling, P.B., Ksiazek, T.G., Patterson, J., Rollin, P.E. 2009. Potential Impact of a Two-Person Security Rule on Biological Safety Level-4. *Emerging Infectious Diseases* 15 (7), July 2009 online only. ISSN: 1080-6059.

CONCLUSIONS

The National Biocontainment Training Center offers a robust and intensive training program devoted to all aspects of biological safety, biocontainment, and biosecurity. This program offers unique, hands-on training to trainees, staff and external partners at all levels of biocontainment, including focused, mentored training in the BSL-4 laboratory. Over 850 persons benefited from one or more of these training courses, many of whom are trainees now pursuing graduate education and using these specialized skills in the newly constructed GNL containment facilities. Intensive, mentored fellowship programs were established to offer opportunities for in-depth training in research under BSL-4 conditions and also in containment laboratory operations and maintenance. These fellowships help address the critical national shortage of well-trained containment laboratory scientists and building engineers.

REFERENCES

none

APPENDICES

1. Biocontainment Operations Fellowship Training Modules. Modules vary in length of time and are informally schedule throughout the fellowship to meet the needs of the fellows and staff.

1. Basic Microbiology
2. Overview of Biosafety and Biocontainment Principals
 - a. Microbiological Practices
 - b. Primary containment devices
 - c. Biosafety cabinets
3. Construction Methodologies for BSL3, BSL3E and BSL4 Laboratories
 - a. Architectural details
 - b. Mechanical
 - c. Electrical
 - d. Plumbing
4. Risk Assessments
5. Select Agent Regulations and GLP
6. Annual Certification of Laboratories
 - a. Aerobiology Labs
 - b. BSL3
 - c. BSL4
7. Testing of HEPA Filter Housing and Filters for ventilation Systems
8. Air Balancing Procedures
9. Engineering Controls - BAS
10. Effluent Treatment Systems
 - a. Types
 - b. Validation and Testing
11. Autoclaves
 - a. Cycles
 - b. Validation
 - c. Testing
12. Decontamination
 - a. Types
 - b. Methods
 - c. Validation
13. Biosafety Cabinet Certification
14. Laboratory Operations SOP Developments and Record Keeping.

2. Modules covered under BSL4 training.

- Confirmation that trainee has completed required BSL-3 training requirements and started FBI clearance
- Practical suit training; have trainee put on suit and practice connecting to breathing air
- Confirmation that the trainee has read Biosafety Manual and SOP manual (sign off)
- Explanation of criteria for independent access to the BSL-4 laboratory, including the number of hours of training and approval of mentor and laboratory director
- Walk-thru of outside corridor and familiarization with the 3 levels
- Introduction to and performance of exterior check-off
- Familiarization with chain of command and reporting issues
- General laboratory walk-thru with questions and problem solving session
- Oral explanation of entrance/exit procedures
- Introduction to the suit room with explanation and performance of a suit inspection
- Trainee independently conducts suit inspection
- Explanation of chemical shower procedures and how to properly remove the suit
- Enter laboratory, practice maneuvering and chemical shower exit
- Explanation of shower out and change room policies and procedures
- Explanation of breathing air and back-up breathing air systems
- Overview of chemical disinfectant shower
- Explanation of alarms and response procedures
- Explanation of emergency procedures