

The Midwest Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MRCE) Biosafety Training Program: An Integrated Approach to Biosafety Education

Joseph Kanabrocki¹ and Samuel Stanley, Jr.²

¹The University of Chicago, Chicago, Illinois and ²Washington University, St. Louis, Missouri

Introduction

The events of September 11, the intentional release of anthrax and the emergence of novel pathogens have resulted in a remarkable change in the biomedical research agenda of the United States, with a new focus on biodefense and emerging infectious diseases. The immediate result has been an extraordinary expansion of the resources devoted to research on the National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIH-NIAID) Category A agents. By definition, most of these agents are dangerous and pose hazards to those who work with them. Safe use of these agents requires an enormous infrastructure, beginning with providing and maintaining the appropriate facilities, providing the necessary education and training, performing the appropriate monitoring, ensuring protective medical measures are taken (e.g., vaccination when appropriate), securing the dangerous agents, and complying with regulatory agencies. There is a critical need to provide training to scientists and other professionals wanting to work with pathogens, including select agents, and an even more pressing need for the individuals that can provide training as well as supervise and establish biosafety programs throughout the United States. The MRCE Biosafety Training Program is designed to meet these needs. We have established an integrated biosafety education program with a curriculum that will provide didactic and hands-on training in all areas of the safe use of infectious agents, with an emphasis on the management of select agents. In addition, we have created an MRCE Biosafety Fellowship Program intended to train two scientists annually to become biosafety officers, capable of establishing and supervising biosafety programs in government, industry and academics. In addition, MRCE Biosafety Fellows play an important role in the development and delivery of the MRCE Biosafety Education Program. This integrated biosafety program, which includes as its two primary elements the MRCE *Biosafety Education for the Research Scientist* course and the MRCE Biosafety Fellowship Program, is a key component of the MRCE plan to serve the biodefense needs of Region VII and the nation.

Biosafety Education for the Research Scientist

The increase in the demand for training opportunities is being met, in part, by organizations such as the American Biological Safety Association, which has spon-

sored short courses designed to introduce safety professionals and others involved with related aspects of biosafety to the science of biosafety. Several undergraduate level programs for the development of specialists in environmental health and safety have been very successful in turning out graduates with well-rounded training in aspects of safety. Only recently have other RCE-based training programs, such as those offered at Colorado State University and at Emory University, been developed to address training needs for bench scientists. There is a serious deficit in programs designed for graduate and post-graduate basic scientists with a focus on risk assessment, laboratory practices and engineering controls.

This 40-hour education program seeks to increase awareness of biological hazards encountered in biodefense and emerging disease research laboratories, to provide a scientific basis for assessing risks associated with this research, to provide guidance on recommended practices and to promote the development of required skills to work safely with human pathogens. The object of safety awareness and practice is to assure laboratory and support personnel that—with proper precautions, equipment and facilities—biohazardous materials can be handled without undue risk to themselves, their associates, their families, and the environment. This program is intended not only for trained microbiologists, but also for clinicians, scientists trained in other disciplines and other individuals involved, either directly or indirectly, with biodefense or emerging disease research.

The safety principles promoted are based on scientific risk assessment, sound safety practices, common sense, good housekeeping, thorough personal hygiene, and a plan for responding to accidents. It is likely that laboratories that are well organized and procedurally disciplined are not only effective scientifically, but safe as well.

To date, we have conducted this education program once annually for each of the past five years at Washington University School of Medicine. We have enrolled 15 to 25 scientists as students for each rendition of the program. The MRCE has subsidized the costs of tuition and has also subsidized the costs of room and board for those individuals in Region VII coming from outside the St. Louis area. The MRCE Administrative Core has aided with the registration process, and has been responsible for verifying the credentials of all applicants (social security number, citizenship status, employment/student status, current research effort, and good standing) with

their parent institution. The course is advertised through electronic mailings to all Region VII academic institutions, and is posted on the MRCE and the St. Louis University Center for Bioterrorism and Emerging Infectious Diseases web sites.

The course plays a critical role in the overall MRCE Biosafety Training Program. It provides a platform for integrating not only the Biosafety Fellows as faculty for the course, but also for integrating MRCE-funded principal investigators as faculty for this course. Faculty is asked to share the discoveries of their research endeavors with an emphasis on the practical aspects and operational challenges of working at BSL-3. This approach of coordinating and integrating training and education efforts across the spectrum of those involved with this research, basic scientists, support staff and safety professionals, is a fundamental strategy of the MRCE. We believe providing this type of education is a primary mission of the MRCE and that this training is essential for the region's scientists to insure they can safely work with biohazardous and select agents. Course offering topics included are listed in Table 1.

A summary of a demographic analysis of the *Biosafety Education for the Research Scientist* course participants is

presented in Appendix I.

Biosafety Fellowship Program

Career development is a strategic goal of the of the MRCE mission. A primary objective of the MRCE is to develop the region's biodefense infrastructure by enabling more scientists to work safely with infectious agents, including select agents, as well as to manage the biosafety programs required to support these research endeavors. We have established a career development program for a biosafety professional, a "train-the-trainer" program that is designed to meet the growing need for individuals capable of leading biosafety programs in government, industry, and academics. The MRCE Biosafety Fellowship Program is the first of its kind in the world. A similar program, the National Biosafety and Biocontainment Training Program (NBBTP) has also been established by the NIH-NIAID.

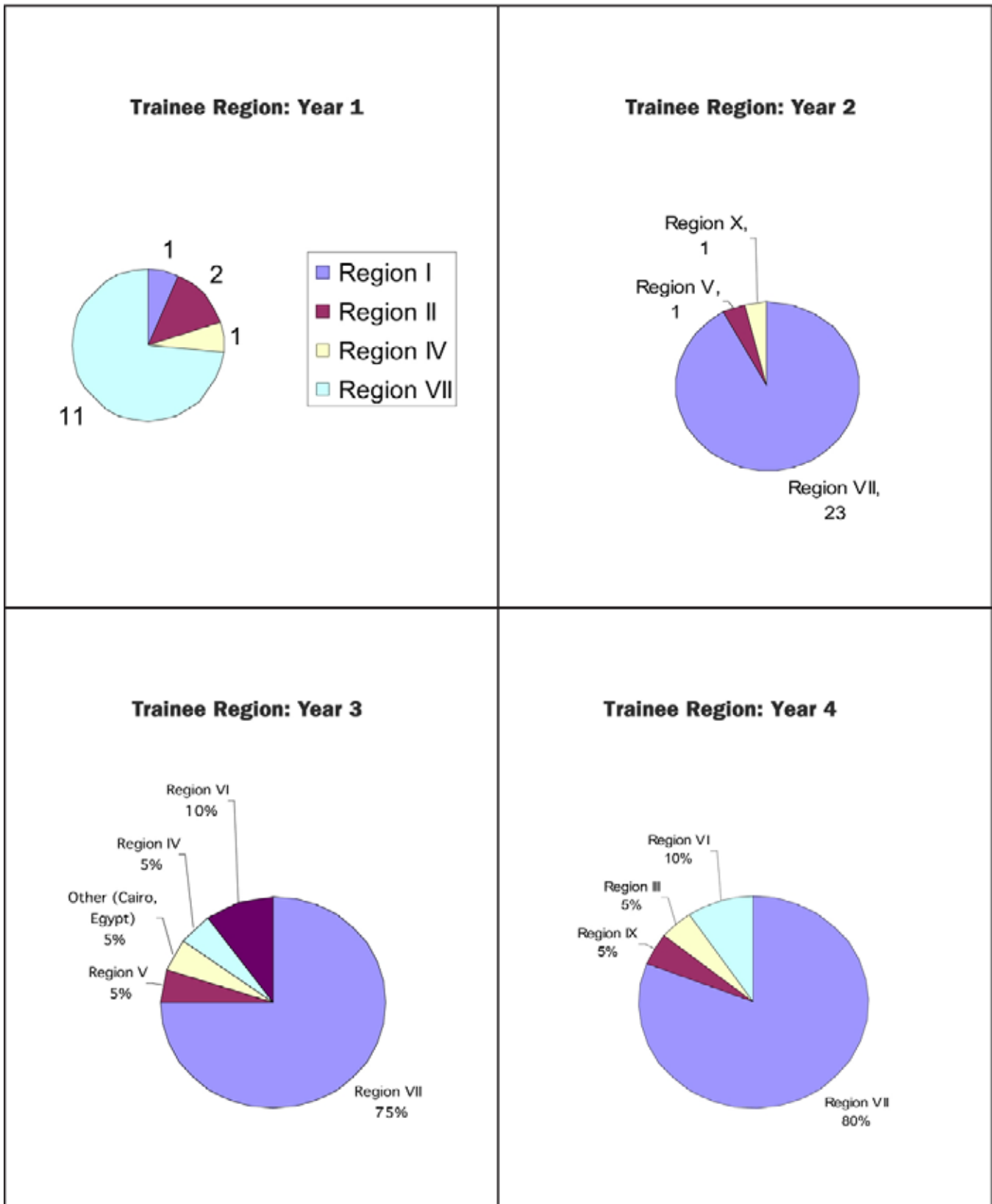
As a profession, biosafety has its roots in the mid-1950s in the biowarfare programs of the U.S. military. This program involved principally three U.S. Army labs, the Biological Research Laboratories at Camp Detrick, the Biological Production and Development Laboratories of the Pine Bluff Arsenal, Arkansas and the Biological

Table 1
Lecture Titles

| | |
|--|---|
| U.S. Biodefense Efforts | Flow Cytometry |
| Introduction to Biocontainment | Aerosol Control—Open Discussion |
| Laboratory Safety Operations/Primary and Secondary Containment | BSL-3 Virology |
| Properties of Biological Agents/Exposure Sources/Routes of Infection | BSL-3 Bacteriology |
| Risk Assessment of Biological Agents | Select Agent Program Management |
| Epidemiology and Case Studies of Laboratory-Acquired Infections | BSL-3 Design Considerations |
| Host Defenses | Shipping (Infectious, Recombinant) |
| Viral Vectors/rDNA Risk Assessment | ABSL-3 Operations |
| Biological Toxins | Zoonoses |
| Institutional Biosafety Committee Case Scenarios | Lab Animal Allergies |
| Lab Ergonomics | Inspection Programs & Lab Safety Manuals |
| Respiratory Protection & Fit-testing | Research Protocols/Institutional Biosafety Committee |
| Decontamination/Disinfection Strategies | Database Management |
| Clinical Infection Control | Good Manufacturing Practices: Facility Design and Operation |
| Engineering Controls—Fume Hoods | BSL-3 Exercises |
| Engineering Controls—BSC Selection, Operation and Maintenance | ABSL-3 Facility Tour |
| Aerosol Biology | GMP Laboratory Tour |

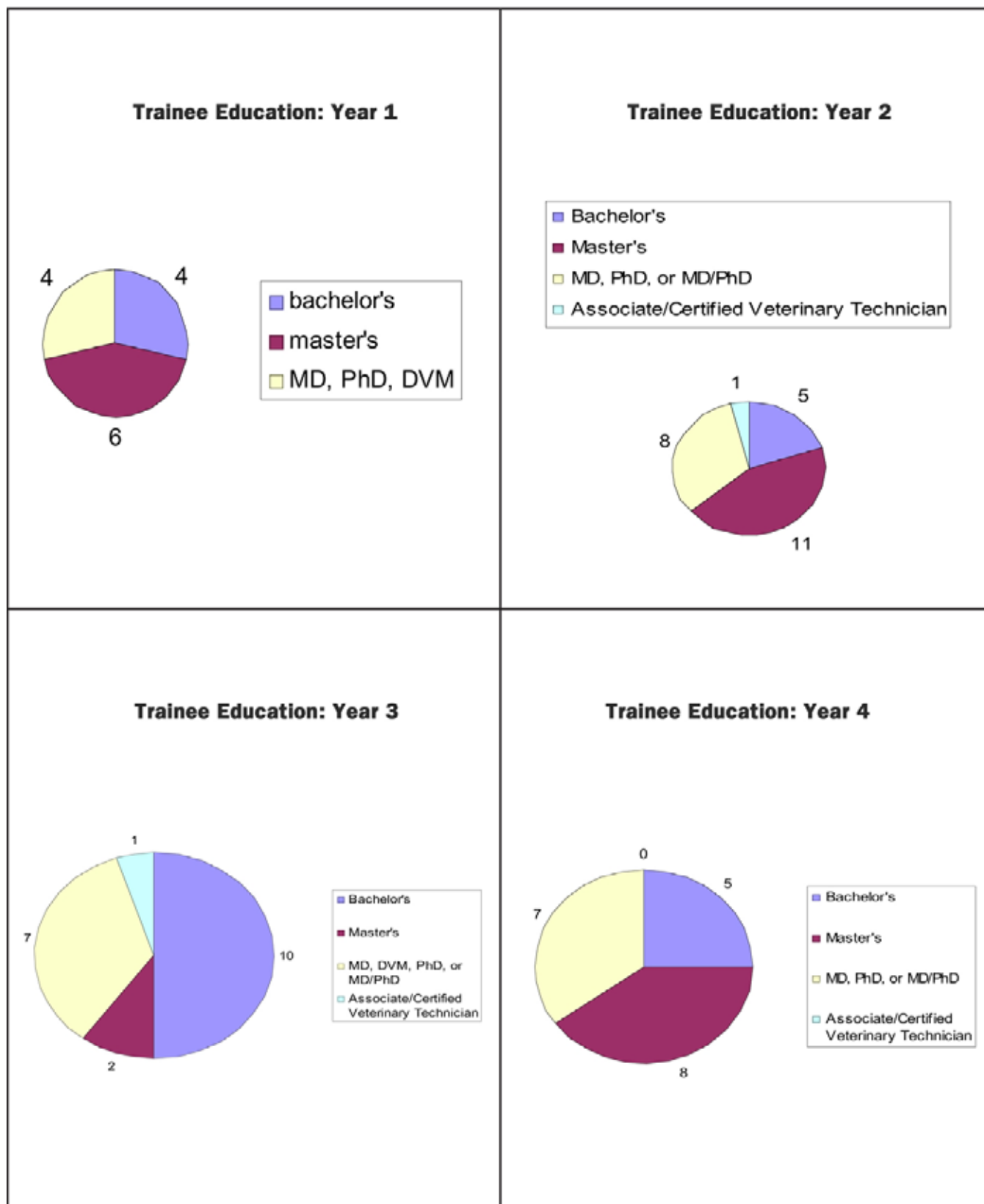
APPENDIX I: Trainee Profiles

Trainee Region: The majority of *Biosafety Education for the Research Scientist* course participants were from Region VII, although many U.S. regions were represented.



APPENDIX I: Trainee Profiles (con't.)

Trainee Education: The majority of *Biosafety Education for the Research Scientist* course held advanced degrees.



Assessment Laboratories at Dugway Proving Grounds, Utah. The clear need for safety programs was recognized early in the U.S. offensive bioweapons program. At this time, biosafety began to emerge as a unique discipline, requiring expertise in basic microbiology, aerobiology and engineering. As the U.S. abandoned its offensive bioweapons program in the late 1960s and early 1970s, it turned its focus to the development of biodefense programs.

The early 1970s also marked the advent of recombinant DNA technology. To address the growing concern regarding the safety of this technology, the National Science Foundation, the National Cancer Institute and the American Cancer Society held a conference in Asilomar, California in 1973. The outcome of this conference was the development of guidelines for working safely with recombinant organisms; these guidelines served as the framework of the first *Guidelines for Research Involving Recombinant DNA Molecules* published by the NIH in 1976.

Over the past several decades, the science of biosafety has evolved with the philosophy of facilitating the safe conduct of basic science research and it has applications in many disciplines of biomedical sciences, including, but certainly not limited to, infectious diseases research. Scientists from diverse disciplines, many with little or no expertise in microbiology and/or biocontainment engineering, have embarked on research involving recombinant DNA technologies, including the use of infectious viruses as molecular vectors for gene transfer.

This evolution is evident with the growth of biosafety organizations such as the American Biological Safety Association (ABSA). As mentioned above, ABSA has sponsored short courses designed to introduce safety professionals to the science of biosafety. Several undergraduate level programs for the development of specialists in environmental health and safety have been very successful in turning out graduates with well-rounded training in aspects of safety. However, many of these programs have as their focus industrial hygiene and related aspects of safety. There is a serious deficit in programs designed for graduate and post-graduate basic scientists with a focus on risk assessment, laboratory practices and engineering controls.

In short, biosafety, as a profession, is under-represented by basic life science PhDs and MD/DVM level clinical scientists. Clearly, understanding scientific process is central to accurate risk assessment and establishment of protocols which incorporate features of safety while also taking into consideration the nuances of the art of science. As exhibited by the NIAID RCE initiative, the need for professional biosafety scientists is critical and growing more critical. For these reasons, we have established two postdoctoral fellowship positions in biosafety. A primary role of these post graduate trainees is to assist in the development and delivery of biosafety training and education for the MRCE. While funded by this fellow-

ship, the post graduate scientists are also tutored in, and assist in, all aspects of biosafety program development and management at one of the nation's premier biomedical research institutions. Elements of the Biosafety Program Management aspect of this training program are described in detail below.

Biosafety Fellowship Program Focus Areas

Fellows receive training in the following areas:

Administrative Organization and Responsibilities

A. Role and Management of Institutional Biosafety Committee

B. Facility Design and Facility Operations

C. Policy and Procedures Manuals

D. Operations

1. Laboratory Audits

2. Agent Inventories, Tracking (e.g., Database Development)

3. Employee Health and Medical Surveillance

4. Injury/Illness Reporting and Recordkeeping

5. Waste Management

E. Training Programs and Training Records

F. Compliance Coordination (involves interaction with Principal Investigators, Institutional Review Board, Institutional Animal Care and Use Committee, Research Administration and external regulatory agencies).

This is a hands-on program with Dr. Kanabrocki providing the primary educational experience over the one-to two-year training period. The fellows accepted into this program participate in all of the day-to-day operations of the biosafety officer. In addition, they participate in the biosafety course taught as part of the MRCE Biodefense Clinician/Translational Research Training Program, and participate in the monthly MRCE Research Seminars, and well as the yearly MRCE Research Symposium. They interact with Dr. Boschert in comparative medicine to learn about biosafety issues in animal research, and attend meetings of the Barnes Hospital Infection Control committee, to learn about the conduct of biosafety management within the hospital environment. They play a key role in the *Biosafety Education for the Research Scientist* course, aiding Dr. Kanabrocki in the day-to-day management of the course and participating as instructors in lectures and the hands-on component. The involvement of MRCE Biosafety Fellows and MRCE Principal Investigators in the MRCE *Biosafety Education for the Research Scientist Program* is indicative of the integrated approach to biosafety education promoted by the MRCE.

Fellowship Eligibility: PhD, MD, DVM, Postdoctoral fellows (preferably in the life sciences).

Trainees: The Biosafety Fellows prepare for and take the certification exam for biosafety professionals offered by the American Society of Microbiologists (National Registry of Microbiologists-Specialist Microbiologist in Biosafety) during the tenure of their fellowship. The MRCE supports the exam cost.

To date, the MRCE has graduated two Biosafety Fellows. Dr. Stone Cao joined the MRCE Biosafety Fellowship Program in January 2005. Dr. Susan Cook joined the MRCE Biosafety Fellowship Program in March 2006. After less than one year in the MRCE Biosafety Program, Drs. Cook and Cao successfully passed the ASM NRM-SM(BS) exam offered in October 2005. Recently, Dr. Stone Cao has accepted a position with the Midwest Research Institute while Dr. Susan Cook has accepted a position at Washington University in St. Louis. (An account of the MRCE Biosafety Fellowship experiences of Dr. Cook and Dr. Cao are included in Appendices II and III.) Marcia Espinola, DVM, MS, has recently joined the MRCE as a Biosafety Fellow. Dr. Espinola formerly worked in the laboratory of an MRCE-funded investigator, Professor Mark Buller, St. Louis University. The MRCE currently has one Fellowship available for this year and is currently seeking applicants.

Conclusion

In August, 2002, the NIH NIAID published a request for applications (RFA) for the establishment of Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Research. In this RFA, the NIAID cited as one of six strategic goals "to train researchers and other personnel for biodefense activities;" further stating that the "RCE must include a consistent and significant commitment to career development with the goal of increasing the availability of researchers for biodefense... must be an integral part of the strategic plan, and complement the research activities. The long-range goal of the training component is development of an expanded cadre of new researchers, clinicians, and technical personnel who can help lead the national biodefense mission into the future."

The MRCE has attempted to meet this NIAID challenge through the establishment of biosafety education and training programs that take advantage of the expertise and integrate the activities of MRCE Principal Investigators, MRCE basic scientists, MRCE safety professionals, and MRCE Fellows. We believe that this integrated educational strategy is critical to the safe conduct of biodefense and emerging infectious diseases research. We believe further that the most effective biosafety training and education programs empower those at the "front line," namely the scientists working within containment laboratories, with knowledge about scientific risk assessment and safe laboratory operations. We believe that efforts of this type are critical, but represent only a first step. Our thesis is that true laboratory safety can only be accomplished by directly educating the scientists performing the research activities. To this end, we recommend that formal biosafety education be incorporated into the curricula of our medical and graduate schools, as well as into the curricula of basic life sciences undergraduate education. To accomplish this goal, we believe that pro-

fessional educators well versed in the science of biosafety risk assessment and biocontainment operations must be a product of the national commitment to biodefense and emerging infectious diseases research and that the RCE network is exceptionally well suited to meet this demand.

This work was supported by National Institutes of Health grant U54 AI057160 to the Midwest Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MRCE).

Appendix II

Post-Doctoral Experience of Dr. Susan Cook, MRCE Fellow

Biological safety, as the name implies, encompasses two fields of study; biology and safety. Both aspects are equally important, but the field of biosafety currently is staffed by many more professionals from the safety field than from the biology field. In an attempt to even out this balance, Dr. Joseph Kanabrocki has established a training program for post-doctoral fellows from the fields of basic science and medicine to recruit these individuals into biological safety. The program is run under the auspices of the Midwest Regional Center of Excellence in Biodefense and Emerging Infectious Disease Research (MRCE) at the Washington University in St. Louis School of Medicine and is designed to accommodate two Fellows with advanced degrees (MD, PhD, DVM).

The MRCE Biosafety Fellowship Program is more similar to an internship than a traditional post-doctoral position. Some of the Fellows' time is spent shadowing Dr. Kanabrocki in his day-to-day activities as Biological Safety Officer. This includes meeting with principle investigators to discuss current and planned research, attending planning and progress meetings about the renovation of a BSL-3 suite, and observing inspections from federal agencies. They also spend time with other members of the biological safety division to learn about all aspects of the program, including laboratory inspections, research and clinical lab safety training, and research protocol registration.

The first "class" of Fellows started in January of 2004 and consisted of one MD and one PhD. Initially, the Fellows participated in all aspects of the biosafety program. Once they became familiar with the research protocol registration process, the bulk of their time was spent reviewing all protocols as they were submitted, deciding what additional information was necessary for a thorough risk assessment, and contacting the principle investigator for that information. The Fellows also participated in the monthly meetings of the Washington University Institutional Biological and Chemical Safety Committee (IBC), where they learned about the practical risk assessment of research protocols involving the use of rDNA and micro-biological agents.

While the Fellowship is based at Washington University, the Fellows were able to take advantage of expertise available at other locations during their training. They

attended an OBA training session that covered the NIH *Guidelines for Research Involving Recombinant DNA Molecules*, the role of IBCs in a university setting, and the tricky question of IBC meeting minutes availability. They traveled to Madison, Wisconsin to learn about biological safety cabinet certification and the advantages of having an in-house certification program as part of the biological safety program. Finally, they attended the Annual American Biological Safety Association (ABSA) Conference in October to participate in the Review Course for Biosafety Exam in Biological Safety, take the National Registry of Microbiologists (NRM) Specialist Microbiologist in Biological Safety exam, and learn more about the biological safety profession as a whole.

A large part of biosafety involves training, and the Fellowship reflects that. The Fellows assisted in the development of a training course designed for researchers preparing to work at BSL-3. They also helped deliver the annual refresher training for laboratory and clinic workers, as well as the new employee orientation for faculty and post-doctoral fellows. Both Fellows returned to the MRCE to deliver lectures at the MRCE Biosafety for the Research Scientist course.

The first year of the MRCE Biosafety Fellowship was a great success from an institutional point of view. Both Fellows successfully passed the NRM exam and earned the CBSP certification from ABSA. One of the Fellows went on to be a Senior Scientist at a prominent not-for-profit research institute and the other recently was hired as the Associate Biological Safety Officer at a private university. During their tenure, the Fellows also contributed greatly to the Washington University biosafety program through the creation of an IBC web page, development of summary reports to aid in the risk assessment of research protocols, and assistance with various training programs.

Personally, I am very grateful for the opportunity to participate in the Biosafety Fellowship Program. After completing my PhD and one traditional post-doctoral fellowship, I was looking for a way to utilize my scientific training in a non-laboratory setting. Since I was already at Washington University, I was aware of the MRCE and learned of the Fellowship through the MRCE webpage. I greatly enjoyed my time as a Fellow and felt that I learned a lot in a relatively short period of time. I also feel that my training as a scientist has been valuable to the biosafety program. Understanding the science behind a research protocol is advantageous when performing a thorough risk assessment; understanding the techniques involved is important when considering the practical implications of the safety precautions we request of the investigators. The researchers also seem to more readily accept requests for increased safety precautions from someone who has worked in a lab than they would from someone they see as an outsider trying to impose limitations on their work. For me, the direct outcome of the Fellowship was being offered a position as Washington University's Associate Biosafety Officer, which I gladly accepted. On a final per-

sonal note, I would like to encourage any scientists looking for something other than the traditional academic career path to consider the Biosafety Fellowship Program.

Appendix III

Post-Doctoral Experience of Dr. Stone Cao, MRCE Fellow

Since September 11 and bio-terrorists attack with anthrax, biosafety has become more and more vital to the public health and laboratory safety. Consequently, there is an urgency to have medical and basic biomedical scientists properly trained in biosafety. I have taken this opportunity to participate in the NIH-NIAID-funded, Midwest Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MRCE) Biosafety Fellowship Program at Washington University in St. Louis.

My area of focus related to reviewing rDNA and gene therapy research protocols, including providing assistance to and participating in meetings of the Washington University in St. Louis Institutional Biological and Chemical Safety Committee (IBC). As part of the biosafety team, I worked daily with safety and security issues related with infectious agents and selected agents as well as development of rDNA research and biosafety databases. I contributed to the development of MRCE *Biosafety Education for the Research Scientist* course and participated as an instructor. In my pursuit to generate an objective overview of biosafety policies in the nation, I have studied and evaluated biosafety plans, rDNA and gene therapy protocols from many other institutes as well as public opinions (including the sunshine project) relevant to bio-science research and biosafety. Through these experiences, I have not only learned and developed fundamental knowledge in biosafety, but also practiced as a biosafety officer. My research and comments have been presented at the American Biological Safety Association Annual Conference, Vancouver 2005 and the First Meeting of the National Science Advisory Board for Biosecurity 2005. Currently, I am employed by one of MRCE consortium members as a senior scientist in biosafety.

This fellowship program has provided an excellent learning opportunity for bio-medical scientists to develop their knowledge and skills in biosafety. I highly recommend scientists who are interested in biosafety to join this program.

Authors' Note

Dr. Kanabrocki has recently accepted a position at the University of Chicago (GLRCE) where he intends to establish a Biosafety Program based upon this MRCE model. Please direct all inquiries regarding the MRCE Biosafety Program to Dr. Susan Cook, who has assumed the role of MRCE Biosafety Program Director, or to Dr. Scott Handley, MRCE Projects Manager, Washington University in St. Louis.