Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories

ISBN
978-0-309-22575-5

216 pages
8 1/2 x 11
PAPERBACK (2012)

Alison K. Hottes, Benjamin Rusek, and Fran Sharples, Rapporteurs; Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories; National Academy of Sciences and National Research Council

Biosecurity Challenges of the Global Expansion of High-Containment Biological Laboratories

Summary of a Workshop

Alison K. Hottes, Benjamin Rusek, and Fran Sharples, Rapporteurs

Committee on Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories

Committee on International Security and Arms Control
Policy and Global Affairs
Board on Life Sciences
Division on Earth and Life Studies

NATIONAL ACADEMY OF SCIENCES *AND*
NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

THE NATIONAL ACADEMIES PRESS
Washington, D.C.
www.nap.edu

THE NATIONAL ACADEMIES PRESS 500 Fifth Street, N.W. Washington, DC 20001

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This study was supported by Contract/Grant No. STAT-8740 / S-L-MAQM-08-CA-140 and STAT-6253 / S-LMAQM-09-GR-056 between the National Academy of Sciences and the United States Department of State's Biosecurity Engagement Program. Any opinions, findings, conclusions, or recommendations expressed in this publication are those of the authors and do not necessarily reflect the views of the organizations or agencies that provided support for the project.

International Standard Book Number 13: 978-0-309-22575-5
International Standard Book Number 10: -0-309-22575-2

Additional copies of this report are available from the National Academies Press, 500 Fifth Street, N.W., Lockbox 285, Washington, DC 20055; (800) 624-6242 or (202) 334-3313 (in the Washington metropolitan area); Internet, http://www.nap.edu.

Printed in the United States of America.

THE NATIONAL ACADEMIES
Advisers to the Nation on Science, Engineering, and Medicine

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Ralph J. Cicerone is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. Charles M. Vest is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Harvey V. Fineberg is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Ralph J. Cicerone and Dr. Charles M. Vest are chair and vice chair, respectively, of the National Research Council.

www.national-academies.org

COMMITTEE ON ANTICIPATING BIOSECURITY CHALLENGES OF THE GLOBAL EXPANSION OF HIGH-CONTAINMENT BIOLOGICAL LABORATORIES

ADEL A. F. MAHMOUD *(Chair*), Princeton University
MICHAEL V. CALLAHAN, DARPA
TECK-MEAN CHUA, Asia-Pacific Biosafety Association
DAVID R. FRANZ, MRIGlobal
KATSUHISA FURUKAWA, Rebuild Japan Initiative
JENNIFER GAUDIOSO, Sandia National Laboratories, International Biological Threat Reduction
BARBARA JOHNSON, Barbara Johnson & Associates, LLC
INGEGERD KALLINGS, Swedish Institute for Infectious Disease Control
SERHIY KOMISARENKO, Palladin Institute of Biochemistry
JAMES W. LE DUC, The University of Texas Medical Branch at Galveston
ANWAR NASIM, Ministerial Standing Committee on Scientific and Technological Cooperation (COMSTECH)
PETER PALESE, Mount Sinai School of Medicine
J. CRAIG REED, Inspirion Biosciences
WILLY TONUI, Kenya Medical Research Institute

STAFF

ALISON HOTTES, Consultant, CISAC
BENJAMIN RUSEK, Program Officer, CISAC
FRAN SHARPLES, Director, Board on Life Sciences
HEATHER CHIARELLO, Senior Program Assistant, CISAC
JO HUSBANDS, Scholar/Senior Project Director, Board on Life Sciences

COMMITTEE ON INTERNATIONAL SECURITY AND ARMS CONTROL

RAYMOND JEANLOZ (*Chair*), University of California, Berkeley
JOHN F. AHEARNE, Sigma Xi, The Scientific Research Society
CHRISTOPHER CHYBA, Princeton University
STEPHEN COHEN, The Brookings Institution
DAVID FRANZ, MRIGlobal
RICHARD L. GARWIN, IBM Corporation
ALASTAIR IAIN JOHNSTON, Harvard University
JAMES W. LE DUC, Galveston National Laboratory and The University of Texas Medical Branch at Galveston
RICHARD MIES, Independent Consultant
NORMAN NEUREITER, American Association for the Advancement of Science
PETER PALESE, Mount Sinai School of Medicine

CISAC STAFF

MICAH LOWENTHAL, Director
RITA GUENTHER, Program Officer
BENJAMIN RUSEK, Program Officer
LA'FAYE LEWIS-OLIVER, Administrative Coordinator
HEATHER CHIARELLO, Senior Program Assistant
ALISON HOTTES, Christine Mirzayan Policy Fellow

BOARD ON LIFE SCIENCES

BLS STAFF

Preface and Acknowledgments

The project, *Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories,* culminated in a workshop that took place in Istanbul, Turkey from July 10-13, 2011. The workshop would not have been possible without the contributions of many individuals. The members of the United States National Research Council (NRC) committee, which was chaired by Adel Mahmoud of Princeton University, offered numerous suggestions and guided the selection of the agenda, participants, and speakers. The country study writers, many of whom attended the workshop and presented their work (see Appendix E), provided invaluable assistance in advance of the workshop as the project was developed.

The committee and the National Research Council staff were fortunate to have the Turkish Academy of Sciences (TÜBA) as a partner in this endeavor. TÜBA Vice President Tarik Çelik, TÜBA member and Dean of Koç University's School of Medicine Sevket Ruacan, and Professor Onder Ergonul of Koç University's School of Medicine provided invaluable assistance in organizing and arranging for the participation of Turkish experts in the workshop.

We are grateful to Ayşe Selma İyisan of the Turkish Ministry of Agriculture and Rural Affairs (MARA) who along with Ayşen Gargili of Marmara University, Sevil Erdenlig of MARA, and Naci Sivri of Gebze Plastic Manufacturer Organization (HTL) organized and led an informative tour of Pendik Veterinary Control and Research Institute's new biosafety level 3 laboratory immediately following the conclusion of the workshop.

We would also like to acknowledge the contributions of those who gave presentations, chaired sessions, served as rapporteurs, and participated in discussions during the workshop as their reflections, deliberations, and insights form the foundation for this document.

This report has been prepared by the workshop rapporteurs as a factual summary of what occurred at the workshop. The planning committee's role was limited to planning and convening the workshop. The views contained in the report are those of individual workshop participants and do not necessarily represent the views of all workshop participants, the planning committee, or the National Research Council.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the National Academies' Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making its published report as sound as possible and to ensure that the report meets institutional standards for quality and objectivity. The review comments and draft manuscript remain confidential to protect the integrity of the process.

We wish to thank the following individuals for their review of this report: Stuart Blacksell, Mahidol University, Thailand; Mohammed Hassar, Institut Pasteur du Maroc, Morocco; Alemka Markotic, University Hospital for Infectious Disease, Croatia; Piers Millett, United Nations Office at Geneva; Uwe Mueller-Doblies, Institute for Animal Health, UK; Alfred Sommer, Johns Hopkins University; Mark Smolinski, Skoll Global Threats Foundation; and Victoria Sutton, Texas Tech University.

Although the reviewers listed above have provided many constructive comments and suggestions, they were not asked to endorse the content of the report, nor did they see the final draft before its release. Responsibility for the final content of this report rests entirely with the rapporteurs and the institution.

CONTENTS

OVERVIEW

During July 10-13, 2011, 68 participants from 32 countries gathered in Istanbul, Turkey for a workshop organized by the United States National Research Council on Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories. The United States Department of State's Biosecurity Engagement Program sponsored the workshop, which was held in partnership with the Turkish Academy of Sciences. The attendees included laboratory directors, scientists, engineers, and members of governmental and non-governmental organizations. The participants were active in the fields of biosafety, biosecurity, scientific research, disease surveillance, and public health. Some came from countries with a long history of operating multiple laboratories while others were from countries that had only recently opened their first biological containment (biocontainment) lab. Many were affiliated with groups contemplating the construction of new laboratories or interested in improving their existing facilities.

The international workshop examined biosafety and biosecurity issues related to the design, construction, maintenance, and operation of high-containment biological laboratories—equivalent to United States Centers for Disease Control and Prevention biological safety level 3 or 4 labs. Although these laboratories are needed to characterize highly dangerous human and animal pathogens, assist in disease surveillance, and produce vaccines, they are complex systems with inherent risks.

During the course of the meeting, participants discussed many aspects of the topic including:

- Technological options to meet diagnostic, research, and other goals;
- Laboratory construction and commissioning;
- Operational maintenance to provide sustainable capabilities, safety, and security; and
- Measures for encouraging a culture of responsible conduct.

To develop a sense of the current norms in the world, workshop attendees described the history and current challenges they face in their individual laboratories. Speakers recounted steps they were taking to improve safety and security, from running training programs to implementing a variety of personnel reliability measures. Many also spoke about physical security, access controls, and monitoring pathogen inventories. Workshop participants also identified tensions in the field and suggested possible areas for action.

DETERMINING AND ADOPTING APPROPIRATE SAFEGUARDS

Participants described many examples where, in their opinion, biosafety and biosecurity precautions were not proportional to the risks. In some labs, poorly trained workers perform aerosol-generating procedures without the benefit of personal protective equipment and functional, certified biosafety cabinets. In contrast, other labs invest in cutting-edge air-handling engineering and adhere to all recommendations of a standard biosafety level, regardless of the particulars of their mission or setting (e.g., disease endemicity, local population immunity, and local risk tolerance). One participant argued that given the high costs of an accidental or deliberate pathogen release, not using all possible safeguards could be considered irresponsible and was likely to upset communities in which laboratories reside. Others argued that regulations have not kept pace with evolving practices and engineering options and that the ensemble of options used today is both unnecessarily expensive and does not provide the

maximum risk reduction. Accordingly, some workshop attendees urged that more applied biosafety research be funded. Yet others suggested that in view of limited resources and competing funding priorities, labs and the communities in which they reside should define an acceptable level of risk and select their precautions accordingly using a qualitative and/or quantitative risk analysis.

SAMPLE AND STRAIN TRANSPORT

Participants also discussed the need to balance the risks and intellectual property concerns of transporting strains and diagnostic samples with the costs of maintaining additional biocontainment labs and pathogen collections. Numerous participants expressed frustration with what they perceived as unnecessarily restrictive transport, import, and export regulations. Individuals also complained about burdensome paperwork, precautions perceived as out of proportion to the risk, long delays to obtain permission, and multiple levels of officials who could block a transfer. To ameliorate some of these problems, several participants suggested continuing to engage the International Air Transport Association, the United Nations Committee on Dangerous Goods Transport, and national governments in dialogs to better define the requirements for safe transport and to accurately characterize the associated risks.

NATIONAL REGULATIONS

Many workshop attendees expressed the need for regulatory frameworks that support safe and secure research without adding undue burdens. Currently, some laboratories work under a limited or poorly enforced national regulatory framework, while others must comply with multiple sets of regulations to satisfy donor and national requirements. Similarly, a lack of national and international guidance and accreditation standards frustrates some laboratories seeking formal accreditation or certification. While most felt that implementing national regulatory frameworks and certification procedures was largely a responsibility of individual countries, many suggested that international assistance could facilitate the process. Others urged donors to simplify their regulatory requirements.

LABORATORY PLANNING

Numerous discussions emphasized the importance of the planning (needs assessment) phase that precedes facility construction and upgrades. Many workshop attendees stressed the benefits of involving everyone (e.g., the community, architects, the lab director, scientists, regulators, designers, contractors, and certifiers) from the very beginning and keeping them involved throughout the process. Some participants suggested that the planning phase might consider provisions for surge capacity (temporary increases in capacity of a needed containment level) in response to disease outbreaks; ways a new laboratory might expand and complement existing national and regional capabilities; and how emerging technologies, such as molecular diagnostics, affect containment requirements. Preparations for long-term sustainability including planning for maintenance and operational funds, obtaining equipment and reagents, and recruiting or training people with the needed expertise (e.g., engineers, technicians, biosafety professionals, craftspeople, and lab workers) can also start during the planning phase.

Many participants identified the Biological and Toxin Weapons Convention review conference in December of 2011 and the subsequent annual "experts meetings," the International Health Regulations update in 2014, and the next revision of the World Health Organization's Laboratory Biosafety Manual as places the biosafety, biosecurity, and public health communities might try to make changes. Biosafety associations could assist by providing

neutral, national and regional platforms for discussions among stakeholders from multiple agencies and encouraging the adoption of a biosafety culture. Additionally, individual "champions" could take up the cause and spread the message in their countries and regions.

1

INTRODUCTION

BACKGROUND

During July 10-13, 2011, 68 participants from 32 countries gathered in Istanbul, Turkey for a workshop organized by the United States National Research Council (NRC) on Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories. The United States Department of State's Biosecurity Engagement Program (BEP) sponsored the workshop, which was held in partnership with the Turkish Academy of Sciences. The attendees included laboratory directors, scientists, engineers, and members of governmental and non-governmental organizations. The participants were active in the fields of biosafety, biosecurity, scientific research, disease surveillance, and public health. Some came from countries with a long history of operating multiple laboratories, while others were from countries that had only recently opened their first biological containment (biocontainment) lab. Many were affiliated with groups contemplating the construction of new laboratories or interested in improving their existing facilities. The workshop agenda and biographies of participants and the NRC organizing committee are included as appendixes A-C at the end of this summary.

The workshop was multi-national in recognition of the international nature of the issue. Containment labs are no longer solely the province of "high resource" or developed countries. Low resource countries are also investing in labs to produce livestock vaccines matched to local strains, perform research on endemic diseases, and combat local human and animal disease outbreaks. Many nations are enhancing their laboratory and surveillance capabilities to comply with the World Health Organization's (WHO) International Health Regulations (IHR) (2005), which require States Parties to have the capacity to detect unusual levels of disease or death in all parts of their territory and to be able to analyze samples either domestically or through a collaborative agreement (WHO, 2008). Furthermore, infectious diseases do not respect national borders (NRC, 2010a), and biocontainment labs often play an integral part in global disease surveillance efforts. The full statement of task is in Box 1-1.

This chapter provides an overview of the topics discussed in the workshop and assembles background information that was presented throughout the workshop in one place as an introduction and guide to the reader. This information is included at the beginning of the workshop summary to give the reader an appropriate level of context to understand the more detailed talks and discussion summarized in the later chapters.

Box 1-1
Statement of Task

This international workshop will examine issues related to the design, construction, and operation of high-containment biological laboratories—equivalent to United States Centers for Disease Control and Prevention Biological Safety 3 or 4 level labs. Although these laboratories are needed to isolate some highly dangerous pathogens, they are complex systems with inherent risks. The workshop will aim to engage scientific experts and policy makers both from countries experienced in operating laboratories and from countries that are contemplating or undertaking the construction of new facilities. Possible areas for discussion include:

- Technological options to meet diagnostic, research, and other goals;
- Laboratory construction and commissioning;
- Operational maintenance to provide sustainable capabilities, safety, and security;
- Measures for encouraging a culture of responsible conduct.

Additionally, some workshop participants will develop and present case studies. Case studies may describe a country's facilities, capabilities, and regulations as well as past accidents, safety and security issues, and lessons learned.

Workshop participants will explore possible strategies for enhancing biological safety and security worldwide and will offer practical suggestions to countries considering constructing or expanding their high biocontainment facilities. An individually authored workshop summary will be issued.

WORKSHOP STRUCTURE

A number of international organizations have encouraged countries to improve their laboratory biosafety and biosecurity,[1] and workshop participants were asked to examine the growing number of high biocontainment labs in the context of the full biosafety and biosecurity spectrum (see Box 1-2).

Box 1-2
Biosafety and Biosecurity: Historical Context

In general, this report uses the term 'biosecurity' to refer to measures intended to reduce the deliberate misuse of biological materials or biotechnology[a] while 'biosafety' refers to protecting laboratory workers, community members, and the environment from accidental exposure to pathogens (NRC, 2009d; see pages 8-9). Nonetheless, the topics are interrelated. Proper maintenance and operations increase the ability to secure a facility, and a well-trained staff that takes pride in their work is less likely to cause an accidental breach and more likely to detect an insider threat and successfully guard against deliberate breaches (Franz and Le Duc, 2011).

[1] In 2005, the World Health Assembly adopted Resolution WHA58.29, which encourages the use of national and international resources to improve laboratory biosafety (WHO, 2005). In 2004, the United Nations Security Council passed Resolution 1540, which requires States to take measures to stop the proliferation of weapons of mass destruction, including biological weapons, by State and non-State actors (U.N. Security Council, 2004).

As a source of pathogens, equipment, and expertise, all of which could be misused, many aspects of biocontainment labs have dual-use potential (NRC, 2009a).[b] Although the Biological and Toxin Weapons Convention (BWC), which entered into force in 1975, bans the development, production, and stockpiling of biological agents and toxins for all but "prophylactic, protective, or other peaceful" purposes,[c] concerns remain. Examples of recent threats include an attempted theft of a lab's pathogen collection by an external group[d] and a purported biological attack by a rogue biocontainment lab employee.[e]

Concerns about the possibility of events of this nature following the breakup of the Soviet Union led to the creation of the United States Department of Defense's Biological Threat Reduction Program (BTRP), as part of the Defense Threat Reduction Agency's (DTRA) Cooperative Threat Reduction (CTR) Program[f] (NRC, 2009b; 2009c). Initially, the BTRP worked with states of the former Soviet Union to redirect to peaceful projects facilities, research, and people that had been engaged in the USSR's bioweapons program. The redirection work included facility upgrades to improve safety and security, cooperative research, and consolidation and protection of pathogen collections. Since the program's inception, U.S. concerns have broadened, and in 2006, the United States Department of State's Biosecurity Engagement Program (BEP) began funding cooperative efforts to promote responsible biological practices and use of biological materials in regions outside the former Soviet Union (NRC, 2009c; see page 147). The G-8 Global Partnership Against the Spread of Weapons and Materials of Mass Destruction also finances activities to support biological non-proliferation, biological safety (biosafety), and biological security (biosecurity).

Not all threats emanating from containment labs, however, are deliberate in nature. Accidental pathogen releases can also occur and have serious consequences. Accidents could, for example, include a worker developing a laboratory-acquired infection and then inadvertently exposing the community[g] or improper maintenance leading to environmental contamination.[h] Regardless of the accidental or intentional nature of a release, the result can be expensive both in terms of loss of life, economic losses, and erosion of public confidence in those conducting important research for the purpose of protecting humans, animals, and plants from infectious diseases.

[a] The meaning of the term "biosecurity" can vary widely. "The term does not exist in some languages, or is identical to 'biosafety' in others. In addition 'the term is already used to refer to several other major international issues. For example, to many 'biosecurity' refers to the obligations undertaken by states adhering to the Convention on Biodiversity and particularly the Cartagena Protocol on Biosafety, which is intended to protect biological diversity from the potential risks posed by living modified organisms resulting from modern biotechnology. 'Biosecurity' has also been applied to efforts to increase the security of dangerous pathogens, either in the laboratory or in dedicated collections" (NRC, 2009d; see pages 8-9).

[b] See reference for more information on the dual use dilemma and attitudes towards the dual use issue among life scientists.

[c] The complete text of the BWC is available at: http://www.opbw.org/. Accessed September 8, 2011.

[d] A pathogen collection at an animal laboratory in Indonesia was the target of a theft attempt in 2007 (NRC, 2007a).

[e] A chronicle of the events surrounding the mailing of anthrax-containing letters in the United States in 2001 that the United States Federal Bureau of Investigation concluded was the work of Bruce Ivins, an employee of the United States Army Medical Research Institute of Infectious Diseases, may be found in (NRC 2011a).

[f] The CTR program also worked to reduce nuclear and chemical threats.

[g] In Beijing, China in 2004, two lab workers acquired severe acute respiratory syndrome (SARS). Ultimately, seven additional people contracted the disease, one of whom one died. Available at: http://www.who.int/csr/don/2004_04_30/en/. Accessed September 9, 2011.

[h] The foot and mouth disease (FMD) outbreak in the U.K. in August 2007 was likely caused by FMD virus from one of the laboratories at the Pirbright site and escaped through poorly maintained pipes. See: http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf. Accessed September 19, 2011.

Introductory Plenary Sessions

The workshop's first day featured several plenary sessions that discussed the scope of the current worldwide laboratory expansion as well as many of the current issues facing labs throughout the world. The full agenda is in Appendix A.

While the number of containment laboratories is clearly increasing, exact numbers are difficult to obtain. For example, the number of U.S. BSL-3 labs registered with the United States Centers for Disease Control and Preventions' Select Agent Program increased from 415 in 2004 to 1495 in 2010 (Kaiser, 2011). However, BSL-3 labs that do not work with pathogens or toxins classified as "Select Agents"[2] need not register with the United States government, and no federal agency is required to track the number of biocontainment labs (United States GAO, 2009). Growth is also taking place worldwide. BSL-3 labs have recently been built or are being built in Bangladesh, India, Indonesia, China, Brazil, and Mexico and other countries are expanding existing labs. India and China are interested in increasing their BSL-4 capacity (see Gaudioso, p. 26).

Internationally, funding for new biological laboratories of all types and laboratory upgrades is coming from national governments as well as donors such as the World Bank, the Asian Development Bank, Fondation Mérieux, the Global Partnership, the Australian Government Overseas Aid Program (AusAID), CDC, the United States Defense Threat Reduction Agency (DTRA), BEP, the Japan International Cooperation Agency (JICA), and others. When contributing to a new laboratory, donor groups and national governments do not, however, always ascertain how the new facility will complement other existing and planned infrastructure. In the United States, for example, no single government agency is responsible for coordinating the on-going expansion in the number of biocontainment labs or determining the needed capacity (United States GAO, 2009).

The workshop also examined the assessment process whereby a planned lab's needs and available resources are characterized and the challenges likely to be encountered identified. The assessment process can help determine scientific, budgetary, and security requirements and provides an opportunity to build community support. Fully characterizing risks, which come not just from the design, standard operating procedures, and organisms to be studied, but also from the lab's location, which includes factors such as endemicity of diseases, presence of immunity in the local population, population density, and reliability of utilities, can provide a valuable early warning for possible utility, security, or operational problems and suggest alternatives for consideration. The NRC has provided input on a number of risk assessments for planned containment labs in the United States including facilities at Fort Detrick, Maryland (NRC, 2010b), Boston, Massachusetts (NRC, 2007b), and Manhattan, Kansas (NRC, 2010c).

Depending on their location and funding sources, containment labs may operate in drastically different regulatory environments. To illustrate the current variation, some participants wrote and presented papers that described their country's high-containment biological facilities, capabilities, and regulations as well as past accidents and safety and security issues (see Appendix E). While many countries have few or no regulations and little enforcement, others have elaborate and quite extensive requirements. Participants also discussed the need for national regulatory frameworks whose enforcement increases safety and security without imposing undue burdens on scientists.

Guidance regarding these matters is increasingly available, not just from national and international legal frameworks, but also from national and regional biosafety associations (BSA).

[2] National Select Agent Registry. Available at: *http://www.selectagents.gov/select%20agents%20and%20Toxins%20list.html*. Accessed September 14, 2011.

These professional associations bring together members from a variety of backgrounds including scientists, administrators, engineers, architects, and technicians as well as stakeholders from multiple agencies including those responsible for human health, animal health, and domestic security. By providing a neutral, national platform, BSAs can educate workers as well as key officials and politicians and help encourage the adoption of a culture supportive of biosafety and biosecurity in the labs in their networks.

In 2001, national and regional BSAs and non-governmental and governmental organizations banded together to form the International Federation of Biosafety Associations (IFBA).[3] Table 1-1 contains a list of BSAs that are IFBA members or observers. IFBA's goals include serving as an international biosafety advisory body, compiling and disseminating information about best practices, and supporting applied biosafety research. On 15-17 February 2011 in Bangkok, Thailand, IFBA held its first international conference, which sought to identify gaps in global biosafety and biosecurity practices, engage senior governmental officials, and attract funding to the field. During IFBA's conference, participants developed an agenda for advancing global biosafety and biosecurity that emphasizes raising awareness, education, and development and implementation of regulatory frameworks.[4]

Table 1-1 Biosafety Associations That Are Members or Observers of IFBA as of September 2011.

Association	**Date Founded**
Afghan Biorisk Association (ABA)	
African Biosafety Association (AfBSA)	2007
American Biological Safety Association (ABSA)	1984[b]
Asia-Pacific Biosafety Association (A-PBA)	2005
Associacao Nacional de Biossegurance, Brasil (ANBio)	1999
Association of Biosafety for Australia and New Zealand (ABSANZ)	2011
Azerbaijan Biological Safety Association (ABTA)	2009
Belgian Biosafety Professionals (BBP)[a]	2006
Biological Safety Association of Pakistan (BSAP)[a]	2007
Biosafety and Biosurity Network, Thailand (BSNT)	2009
Biosafety Association for the Central Asia and Caucasus (BACAC)	2008
Canadian Association of Biological Safety (CABS)	1990
Egyptian Biosafety Association (EGBSA)	2009
European Biological Safety Association (EBSA)	1996
Georgian Biosafety Association (GeBSA)	2009
Japanese Biosafety Association (JBSA)	2001
Korean Biosafety Association (KOBSA)	2008
Mexican Biosafety Association (AMEXBIO)	2009
Moroccan Association of Biosafety (AMBS)	2009
Moroccan Biosafety Association (AMABIOS)	2009
Pakistan Biological Safety Association (PBSA)	2008
Philippine Biosafety and Biosecurity Association (PHBBA)	2006

SOURCE: *http://www.internationalbiosafety.org/*. Accessed September 30, 2011.
[a] Denotes observer; all others are IFBA members.
[b] ABSA was formally incorporated as a professional organization in 1984; United States biosafety professionals started holding informal, annual conferences in 1955.

[3] IFBA was originally called the International Biosafety Working Group. The present name was adopted in 2009.
[4] The full declaration is available at: *http://2011.absa.org/pdf/IFBABangkokDeclaration.pdf*. Accessed September 9, 2011.

Breakout Sessions

At the end of the first day of the present workshop and during much of the second day, participants divided into groups for a series of breakout sessions. These small sessions allowed more participants to share their experiences and develop a sense of the current norms in the world.

During the first set of breakout sessions (Chapter 5), participants described the history and current challenges they face in their individual laboratories. Speakers described steps they were taking to improve safety and security, from running training programs to implementing a variety of personnel reliability measures. Many also spoke about physical security, access controls, and creating pathogen inventories.

The second set of breakout sessions (Chapter 6) examined the present and future role of containment labs in human and animal disease diagnostics. Presenters described their current protocols and precautions and discussed the potential for the use of molecular diagnostics, which unlike traditional culture-based assays do not use viable pathogens or require containment labs.

The third and final set of breakout sessions (Chapter 7) asked the attendees to identify high-priority areas for taking action to improve biosafety and biosecurity. Some groups discussed the need for more applied biosafety data, the benefits of laboratories tracking and reporting accidents, and approaches to improving organizational culture and practices. Another group defined the key events in each stage of a laboratory's life cycle from the planning phase through on-going maintenance.

Concluding Plenary Sessions

After the final breakout session, all attendees participated in a plenary session on the unique challenges associated with BSL-4 labs. While there are many fewer BSL-4 labs than BSL-3 labs, the approximately two dozen operational BSL-4 labs located throughout the world pose a unique challenge (see Table 8-1 in Chapter 8) and several additional facilities are planned or under construction (Kaiser, 2011). Participants discussed BSL-4 laboratories that community opposition has prevented from operating at their originally intended biosafety level (see Table 8-2 in Chapter 8). In addition to examining the impact of a community's perceptions on laboratory operations, workshop attendees also commented on gaps in the world's BSL-4 capacity and the usefulness and ethics of personnel reliability measures.

On the final morning, Adel Mahmoud, the chair of the NRC committee that guided workshop preparations, led a discussion to draw attention to the main themes of the workshop, and discuss possible next steps. Many participants sought ways that the present workshop could extend progress made during previous, related meetings and activities (see Box 1-3).

Immediately following the workshop, many participants visited the nearby Pendik Veterinary Control and Research Institute and toured their new BSL-3 facility, which was in the final stages of construction (see Appendix D).

Box 1-3
Contributions of International Scientific Organizations to Biosafety and Biosecurity

Many national academies of science have contributed to discussions on biosafety and biosecurity. The InterAcademy Panel on International Issues (IAP), a global network of science academies, released a statement on biosecurity in 2005.[a] The statement, which was endorsed

by 70 member academies, advocates education and "awareness raising" by creating scientific codes of conduct and presents five principles for consideration when formulating codes:

1. Scientists should be aware of the possible consequences of their work.
2. Scientists have the responsibility to use safe and secure practices.
3. Scientists should educate others to prevent the misuse of research.
4. Scientists have an obligation to report activities that violate the BWC or international norms.
5. Scientists should keep these principles in mind when acting in supervisory roles.

Soon after the statement was released, the IAP formed the IAP Biosecurity Working Group (IAP BWG) to take up and coordinate similar biosecurity related work on behalf of IAP.[b] Recently the IAP, in conjunction with the Polish and United States Academies of Sciences, the International Union of Biochemistry and Molecular Biology, and the International Union of Microbiological Societies, organized a November 2009 workshop on ways to educate life scientists about dual use issues associated with biological research (NRC, 2010d).

Working with the same two professional societies and in close cooperation with the Biological and Toxin Weapons Convention (BWC), the Chinese and United States Academies of Sciences and the IAP organized an international meeting to inform governmental and non-governmental organizations about current trends in science and technology in preparation for the 7th Review Conference of the BWC in December of 2011 (NRC, 2011b). This meeting followed a similar meeting at the U.K. Royal Society in 2006 in advance of the 6th Review Conference. Additionally, the Uganda National Academy of Science (UNAS) organized workshops on promoting biosafety and biosecurity in East Africa (UNAS, 2008) and promoting good laboratory practices in Sub-Saharan Africa (UNAS, 2009). UNAS also wrote a report analyzing biosafety and biosecurity in Uganda (UNAS, 2010).

[a] The full IAP Statement on Biosecurity is available at: www.interacademies.net/File.aspx?id=5401. Accessed September 9, 2011.

[b] As of September 2011, the IAP BWG includes Poland (chair), the United States, the U.K., China, Cuba, Nigeria and recently added countries Australia, Egypt and India. Russia will join soon.

Development of the Issue

In many of the workshop presentations, speakers reflected on the evolution of the techniques used to handle dangerous pathogens, current practices, and desirable future directions. They presented information on the historical prevalence of laboratory-acquired infections, the range of precautions available, and the basis of commonly used approaches to biosafety and biosecurity. In order to increase the coherence of the following chapters, this section assembles information that was presented as part of the workshop plenary, working group sessions, discussions or appended country study background papers in a single location to inform the reader.

THE FUNCTION AND EVOLUTION OF BIOCONTAINMENT LABS

In the late 1800s, soon after scientists began isolating and studying microorganisms that cause infectious diseases, reports of workers suffering from laboratory-acquired infections (LAIs) started to appear (Table 1-2). Since that time, understanding of the risks associated with working with pathogens and options for protecting laboratory workers and the communities in which laboratories reside have greatly improved.

Improvements, however, have been gradual, and LAIs continue to occur, albeit at a much lower frequency than in the past. Over 4,000 LAIs (168 fatal) were documented between 1930 and 1978 (Pike, 1979), and over 1,200 LAIs (22 fatal) occurred between 1978 and 1999 (Harding and Byers, 2000). As LAIs may go unreported, those numbers are likely to be underestimates. LAIs continue to occur today with notable instances including fatalities from Ebola[5] and severe acute respiratory syndrome (SARS) in 2004.[6]

Table 1-2 Dates of First LAIs Caused by Selected Bacterial Species.

Organism	Date Isolated, Cultured, or Described	First Reported LAI
Corynebacterium diphtheriae	1881-1884	1898
Vibrio cholerae	1883	1894
Salmonella typhi	1884	1885
Brucella melitensis	1887	1887
Clostridium tetani	1889	1893
Sporothrix schenkii	1896	1904

SOURCE: NRC Staff; Adapted from Kruse et al., 1991.

Laboratory practices and primary barriers have been developed to reduce occupational exposures through the four main routes of infection: ingestion; inhalation; parenteral inoculation; and direct eye, skin, or mucosal membrane contact (United States HHS, 2009). Good microbiological practices minimize aerosol generation and lessen the chances of ingestion and sharps injuries (e.g., needle sticks). A range of personal protective equipment (e.g., gloves, lab coats, eye protection, and respirators) can be used to protect against direct pathogen contact and inhalation. Class I and Class II biological safety cabinets (BSC) reduce aerosol exposure, and Class III BSCs and full-body, positive pressure suit technologies can fully-isolate workers from pathogens. In some cases, immunizations against specific pathogens are available, which provide a measurable decrease in LAIs compared to the use of personal protective equipment and BSCs alone, particularly for agents with low infective doses (NRC, 2011c, Rusnak et al., 2004).

The laboratory itself functions as a secondary barrier that protects the community from the potential release of the pathogens contained within. Laboratories are typically constructed using materials that allow for easy decontamination and include equipment for this purpose (e.g., autoclaves, incinerators, liquid effluent decontamination systems, and chemical disinfectants). When deemed necessary, laboratories also include sophisticated air handling mechanisms such as inward airflow, negative pressure, filtering of exhaust air, or airtight construction, to reduce the chance of pathogen escape and enable gaseous decontamination.

STANDARDIZING BIOSAFETY

To help workers select the appropriate precautions, a number of organizations have assigned pathogens to risk groups based on the severity of disease they cause, the route of infection, the risk to the community, and the availability of effective prophylactic or therapeutic measures. As an example, the risk group definitions used by the United States National Institutes of Health (NIH) and the World Health Organization (WHO) are shown in Table 1-3.[7]

[5] Ebola, Lab Accident Death: Russia (Siberia). Available at: *http://www.promedmail.org/pls/apex/f?p=2400:1001:::NO::F2400_P1001_BACK_PAGE,F2400_P1001_PUB_MAIL_ID:1000,25465*. Accessed September 19, 2011.

[6] Available at: *http://www.who.int/csr/don/2004_04_30/en/*. Accessed September 9, 2011.

[7] Some countries use alternative approaches. As an example, a description of Russian hazard groups may be found in Stavskiy et al., 2003.

For a number of common pathogens, the Biosafety in Microbiological and Biomedical Laboratories (BMBL) manual recommends suitable combinations of precautions for typical procedures based on risk assessments (United States HHS, 2009).

Table 1-3 United States NIH and WHO Risk Group Definitions.

Risk Group	NIH Guidelines	WHO Laboratory Biosafety Manual	Example Organisms (NIH)
1	Agents not associated with disease in healthy adult humans.	(No or low individual and community risk) A microorganism unlikely to cause human or animal disease.	*Bacillus subtilis*
2	Agents associated with human disease that is rarely serious and for which preventive or therapeutic interventions are *often* available.	(Moderate individual risk; low community risk) A pathogen that can cause human or animal disease but is unlikely to be a serious hazard to laboratory workers, the community, livestock or the environment. Laboratory exposures may cause serious infection, but effective treatment and preventive measures are available and the risk of spread of infection is limited.	Rabies virus; *Bacillus anthracis;*
3	Agents associated with serious or lethal human disease for which preventive or therapeutic interventions may be available (high individual risk but low community risk).	(High individual risk; low community risk) A pathogen that usually causes serious human or animal disease but does not ordinarily spread from one infected individual to another. Effective treatment and preventive measures are available.	Human immunodeficiency virus; *Mycobacterium tuberculosis*
4	Agents likely to cause serious or lethal human disease for which preventive or therapeutic interventions are not usually available (high individual risk and high community risk).	(High individual and community risk) A pathogen that usually causes serious human or animal disease and can be readily transmitted from one individual to another, directly or indirectly. Effective treatment and preventive measures are not usually available.	Ebola virus; Marburg virus

SOURCE: Adapted from United States HHS, 2009.
NOTES: The United States uses the Risk Group definitions of NIH Guidelines for Research Involving Recombinant DNA Molecules. Appendix B, Available at: *http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm*. Accessed September 19, 2011. WHO risk group definitions are in WHO's Laboratory Biosafety Manual (WHO 2004).

More generally, the BMBL describes four standard biological safety levels (BSL), each of which includes a combination of practices, safety equipment, and laboratory features that are summarized in .[8] BSL levels roughly correlate with, but do not directly correspond to, risk group assignments. The workshop focused on laboratories that operate at the two most stringent BSL levels, BSL-3 and BSL-4, which are referred to as high and maximum containment, respectively.[9] According to the BMBL, BSL-3 and BSL-4 are intended for:

[8] WHO also describes four standard biosafety levels (WHO, 2004). Some countries use alternative approaches. Russia, for example, describes labs as being Zone I, Zone II, or Zone III, where Zone I labs are containment labs (Stavskiy et al., 2003).
[9] Due to the variety of classification systems in use in the world, laboratories that provide roughly equivalent levels of containment were also discussed.

BSL-3: Indigenous or exotic agents that may cause serious or potentially lethal disease through the inhalation route of exposure.

BSL-4: Dangerous/exotic agents, which pose high individual risk of aerosol-transmitted laboratory infections that are frequently fatal, for which there are no vaccines or treatments; agents with a close or identical antigenic relationship to an agent requiring BSL-4 until data are available to redesignate the level; and related agents with unknown risk of transmission (United States HHS, 2009; see page 59).

Table 1-4 Summary of BMBL Biosafety Levels for Infectious Agents.

BSL Level	Practices	Primary Barriers and Safety Equipment	Facilities (Secondary Barriers)[a]
1	Standard microbiological practices	No primary barriers required. PPE: laboratory coats and gloves; eye, face protection, as needed	Laboratory bench and sink required
2	BSL-1 practice plus: Limited access, biohazard warning signs, "sharps" precautions, biosafety manual defining any needed waste decontamination or medical surveillance policies	Primary barriers: BSCs or other physical containment devices used for all manipulations of agents that cause splashes or aerosols of infectious materials PPE: Laboratory coats, gloves, face and eye protection, as needed	BSL-1 plus: Autoclave available
3	BSL-2 practice plus: Controlled access, decontamination of all waste, decontamination of laboratory clothing before laundering	Primary barriers: BSCs or other physical containment devices used for all open manipulations of agents PPE: Protective laboratory clothing, gloves, face, eye and respiratory protection, as needed	BSL-2 plus: Physical separation from access corridors; self-closing, double-door access; exhausted air not recirculated; negative airflow into laboratory; entry through airlock or anteroom; hand washing sink near laboratory exit
4	BSL-3 practices plus: Clothing change before entering, shower on exit, all material decontaminated on exit from facility	Primary barriers: all procedures conducted in Class III BSCs or Class I or II BSCs in combination with full-body, air-supplied, positive pressure suit	BSL-3 plus: Separate building or isolated zone, dedicated supply and exhaust, vacuum, decontamination systems, and other requirements outlined in BMBL

SOURCE: United States HHS, 2009; see page 59. (PPE: personal protective equipment)

[a] Detailed design requirements may be found in the United States NIH Design Requirements Manual Version 1.7. Available at: *http://orf.od.nih.gov/PoliciesAndGuidelines/BiomedicalandAnimalResearchFacilitiesDesignPoliciesandGuidelines/DesignRequirementsManualPDF.htm*. Accessed September 19, 2011.

While similar, the particulars of the recommendations for each BSL level differ among sources. BMBL recommendations are generally considered stricter than those in WHO's Laboratory Biosafety Manual (LBM) (WHO, 2004). Furthermore, recommendations from a single source change over time, usually becoming more rigorous. For example, the 5th edition of the BMBL added the BSL-3 criterion that the inward flow of air into a laboratory will not be reversed even under failure conditions (United States HHS, 2009, see page 43). Similarly, the BMBL currently urges groups building new BSL-2 facilities to consider including systems that create an inward flow of air, a feature that is a traditional hallmark of BSL-3 laboratories (United States HHS, 2009, see page 38). Additionally, for many laboratories, such as those that are described as BSL-2 enhanced or BSL-3+, protections from a higher level have been incorporated with the result that such labs do not fit into the standard classification scheme.

FUTURE TRENDS

While following the recommendations of a pre-defined BSL level is comparatively convenient and simple, laboratory authorities are increasingly seeking the flexibility to tailor precautions to their particular risks. Additionally, awareness of the importance of a laboratory's management system to safety and security is increasing (Gaudioso et al., 2009). Options such as the European Committee for Standardization's (CEN) voluntary Laboratory Biorisk Management standard CWA (CEN workshop agreement) 15793:2008,[10] which describes a system management approach to laboratory risk reduction centered on the principle of continual improvement, are growing in popularity. More detailed discussions of these and many related developments appear in the ensuing chapters.

[10] Available at: *ftp://ftp.cenorm.be/PUBLIC/CWAs/wokrshop31/CWA15793.pdf*. Accessed September 19, 2011.

2

FRAMING THE ISSUE (PLENARY SESSIONS)

OPENING REMARKS

The organizers and sponsor opened the workshop on Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories by welcoming the participants and describing the motivations for and objectives of the meeting.

Adel Mahmoud (Princeton University, United States), Chair of the United States National Research Council (NRC) organizing committee for the workshop, reminded the group of the high prevalence of infectious diseases throughout the world. Infectious diseases place great health and economic burdens on society, and the relationship between humans, animals, and microbes is ancient and continually evolving. During the last 30 years, 20-30 new diseases emerged, including AIDS, and dealing with an opponent that greatly outnumbers us will require humankind's collective intelligence. To that end, he argued that society needs to find new ways to deal with microbes, which necessitates doing research in high-containment labs.

In conducting research to combat infection, Dr. Mahmoud acknowledged that lack of strict adherence to laboratory practices can also result in the spread of disease. Nonetheless, he stressed that in discussing the need for safe and secure labs, the group should not forget that society does need labs. He also recognized that in some cases the results of an experiment, such as the often-cited work where the introduction of a cytokine into a virus caused mice to lose resistance to mousepox (Jackson et al., 2001), are unpredictable. With that in mind, Dr. Mahmoud argued that we must choose between either stopping science or doing science responsibly, and he strongly advocated for the latter. He also cautioned that while we may need improved or new standards to protect scientists, the community, and the environment, we should avoid being unnecessarily restrictive and keep in mind that humanity is served by the new tools and discoveries produced by science.

Then, **Şevket Ruacan** (Koç University and Turkish Academy of Sciences) welcomed the group to Turkey; explained that biosafety, biosecurity, and responsible science are a priority for both Turkey and world; and provided some background information about the Turkish Academy of Sciences (TÜBA).[1] He noted that TÜBA, which was founded in 1993 and currently includes about 130 members, was a founding member of both the InterAcademy Panel and the InterAcademy Medical Panel. As a reflection of Turkey's geography, TÜBA is also a member of both the Association of Academies of Sciences in Asia and the All European Academies.

Next, **Sumi Paranjape** (United States Department of State Biosecurity Engagement Program) thanked the attendees for traveling to the meeting and thanked the United States National Research Council for their efforts in organizing the workshop. She observed that it was an important and timely meeting and an opportunity to synthesize lessons learned from prior experience and to suggest strategies for moving forward. She then introduced the three main priorities of the United States State Department's Biosecurity Engagement Program (BEP): (1) improving biosafety and biosecurity, (2) enhancing disease surveillance, and (3) supporting research and development in these areas.[2]

After reiterating the importance of international high-containment lab capacity, she mentioned that the United States government is discussing ways to help satisfy that need. The report of this workshop will inform that discussion. While the United States government has put

[1] *http://www.tuba.gov.tr/en.html*
[2] *http://www.bepstate.net/*

effort and resources into building facilities, she contended that creative solutions are also needed to help meet health and veterinary needs and to improve lab sustainability. As an example, she cited the growing interest in using molecular diagnostics instead of culture-based assays for some tests.

PART 1: THE FUNCTION OF HIGH-CONTAINMENT LABS AND FACTORS ENCOURAGING AND CONSTRAINING THE CREATION OF NEW LABS
Chair: Katsuhisa Furukawa

Katsuhisa Furukawa (Rebuild Japan Initiative, Japan) opened the session by relating that the March 11, 2011 earthquake off the Pacific coast of Tohoku and the resulting tsunami is the worst natural disaster his country has experienced in the last 1,000 years, and that even though the resulting nuclear power crisis at the Fukushima nuclear plant was caused by an exceedingly rare combination of events, the public blamed the government and the power companies for their lack of preparation. He cautioned the audience that if a similar incident were to occur at a biological laboratory, they should not expect their failure to be met with public forgiveness.

Dr. Furukawa continued that in view of the number of labs being built or expanding, it is particularly important to think about the responsibility of the scientific community, the potential for both accidental and malicious breaches, and what is required to be safe. He explained that the first two talks in the session would provide examples of some of the many ways different countries may choose to approach biosafety and biosecurity using regulations, improved training, and investments in technology. He expressed his hope that in the course of the discussions participants would report on the options their countries were using.

To end the introduction, he explained that the third talk would provide some background on the scale of containment laboratory capacity expansion as well as some of the factors underlying this growth. He then reiterated his hope that in the discussions participants would add additional information about their countries and regions.

PLENARY PRESENTATIONS

United States Biosafety Experiences During the Last Two Decades: Lessons and Achievements

The first speaker in this session was **Peter Palese** (Mount Sinai School of Medicine, United States), who described the United States requirements for biosafety and biosecurity from the point of view of a working scientist.

Dr. Palese works with negative strand RNA viruses, including influenza, measles, Newcastle disease, and Ebola. His lab relies on the 5th edition of the manual "Biosafety in Microbiological and Biomedical Laboratories" (BMBL) (United States HHS, 2009), which is considered the "biosafety bible," as well as the Centers for Disease Control and Prevention (CDC) website[3] for biosafety guidance. To decide on the risk level of an experiment and what precautions are appropriate, he consults the United States National Institutes of Health (NIH) guidelines on risk groups[4] and proposed biosafety levels, evaluates proposed lab procedures, including the quantity of the organism to be used in the work, and considers the staff involved.

[3] Centers for Disease Control and Prevention. Available at: *http://www.cdc.gov/biosafety/index.htm*. Accessed August 29, 2011.
[4] NIH Guidelines for Research Involving Recombinant DNA Molecules (Appendix B). Available at: *http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm*. Accessed September 14, 2011.

He also seeks permission from his local Institutional Biosafety Committee (IBC) to conduct the experiment.

About five years ago, the 1918 influenza virus, which he helped reconstruct (Tumpey et al., 2005), was added to the United States Select Agents list, which controls the possession, use, and transfer of the hazardous pathogens classified as Select Agents in the United States. To accommodate the new requirements imposed by Select Agent classification of the 1918 flu virus, he asked the NIH to pay for a BSL 3+ facility that would allow him to continue his work. The NIH agreed and built the lab on the 17th floor of a building in New York City next to Central Park. He indicated that there have been no incidents and no objections voiced in either the community or facility, demonstrating that it is possible to put containment labs in urban settings.

Working in the new facility, his research group used animal tests to show that the 2009 H1N1 influenza vaccine is 100 percent effective against the 1918 virus, the most virulent influenza strain known. Given that research has recently shown that the current H1N1 vaccine provides some cross protection against the 1918 flu, the 1918 strain should no longer be as effective as a bioterrorism agent (Medina et al., 2010).

To emphasize the real dangers inherent in biological laboratories, Dr. Palese reminded the audience that over 5,000 people have suffered from laboratory-acquired infections (LAIs) since 1930, and nearly 200 have died (Pike, 1979; Harding and Byers, 2000). While the numbers of LAIs have decreased in recent years and the organisms responsible for the bulk of these infections have changed, laboratory work has not become risk-free.

Dr. Palese finished his presentation by sharing a quote[5] that argues that unnecessary regulation is in itself a threat to good science and stated that he agrees with a recent United States National Research Council report that argues for a healthy balance in regulations (NRC, 2009e).

Russian Biosafety Experiences During the Last Two Decades: Lessons and Achievements

Sergey Netesov (Novosibirsk State University, Russia) described Russian successes in disease control, current health threats, and steps Russia is taking to improve biosafety and biosecurity.

Dr. Netesov relayed to the group that over the years, Russia has successfully controlled a number of diseases within its borders. The country virtually eradicated plague in the 1930s through the creation of an approach that combined research with surveillance and the eradication of large rodents. Russia had also eradicated smallpox nationally by the end of the 1930s. Later, Russia manufactured polio vaccine and implemented a successful polio vaccination strategy. The country has also controlled measles, mumps, and tick-borne encephalitis.

Dr. Netesov then acknowledged that some new diseases including respiratory diseases, tuberculosis, AIDS, hepatitis C, Crimean-Congo hemorrhagic fever (CCHF), Lyme disease, Yersiniosis, hemorrhagic fever with renal syndrome (HFRS), and West Nile virus fever currently require more attention from the Russian public health system. Additionally, a number of cases of dengue fever, malaria, and other diseases are imported into Russia annually.

He noted that Russia's successes in disease control have not been without cost. Some researchers working on Venezuelan equine encephalitis, HFRS, CCHF, Machupo, Dhori, vesicular stomatitis virus, and Kyasanur Forest disease in Russia between 1950 and 1990

[5] "Biological science provides our primary, continuing defense against diseases, natural or man-made, with knowledge that can be translated into effective countermeasures such as vaccines and new therapies. Any regulation that unnecessarily hinders this research is a real and unnecessary threat to our health, our economy, and our national security" (Franz et al., 2009).

(Gaidamovich et al., 2000) suffered LAIs. More recently, in May 2004, an experienced technician who worked at the State Research Center of Virology and Biotechnology (Vector Institute) pricked herself with a syringe needle containing blood from a guinea pig infected with Ebola virus (Akinfeeva et al., 2005) and, in spite of extensive treatment, she died. This incident, he said, illustrates the need for even experienced workers to receive regular refresher training.

Dr. Netesov argued that biosafety and biosecurity should be enhanced not only due to the large number of non-intentional laboratory accidents in the world (>5,400 during the last 70 years), but also because of the larger consequences from the much smaller number (<50) of unintentional release accidents at industrial biotech plants and the even smaller number of instances of bioterrorism in the world (<5). To that end, he reported that Russia's leading universities are developing and offering new courses in biosafety, biosecurity, and bioethics, many of which are described in the country overview for Russia (Appendix E4). He feels that these subjects should be taught according to modern international recommendations, should include the history of bioethics, and should cover the Biological and Toxin Weapons Convention (BWC). In particular, he would like bioethics courses to educate students about the social responsibility of researchers working in dual-use research fields.

Containment Labs: Who Wants Them, Who Funds Them, and Why

Jennifer Gaudioso (Sandia National Laboratories, United States) described the recent expansion in the number of high biological containment labs worldwide as well as some of the factors motivating lab construction.

Dr. Gaudioso explained that her talk was based on public information that Sandia National Laboratories (SNL) gathered and acknowledged that workshop participants might find omissions. She elaborated that international information is always difficult to obtain; the United States picture is also incomplete, in part because labs that do not work with Select Agents are not required to register or report their activities to any central authority. She also explained that many labs do not describe themselves with a particular World Health Organization (WHO) biosafety level, and the terms BSL-3 and BSL-4 encompass a range of capabilities.

Caveats notwithstanding, she reported that the United States has experienced tremendous growth in the number of containment labs. According to the United States Government Accountability Office, the number of BSL-3 labs increased from 415 in 2004 to 1362 in 2008, and the number of entities with BSL-3 labs increased from 150 to 242 during the same time period[6] (United States GAO, 2009 and Appendix E9). In 1998, which was prior to the creation of the Laboratory Response Network (LRN), only 12 states had public health labs with BSL-3 space; by 2007, 46 had BSL-3 labs.[7] Overall, the LRN contained 120 labs with BSL-3 capabilities in 2005 and that number had grown to 150 by 2011[3] including federal, state, and local public health laboratories; military labs; food testing labs; veterinary labs; and even some international labs (e.g., Canada, U.K., and Australia).

She then described similar growth worldwide, citing as examples BSL-3 labs that have recently been built or are being built in Bangladesh, India, Indonesia, China, Brazil, and Mexico. She also noted India's and China's interest in increasing their BSL-4 capacity. The World Bank is currently funding 43 labs.

Dr. Gaudioso then provided a number of reasons for building a lab:

- Management of an existing lab may want to improve safety.

[6] Numbers are for BSL-3 labs registered with the United States CDC Division of Select Agents and Toxins.

[7] Facts about the Laboratory Response Network. Available at: *http://www.bt.cdc.gov/lrn/factsheet.asp*. Accessed August 29, 2011.

- A university may want to attract external funding.
- A country may want to increase national prestige, promote growth in the biotechnology sector, or support the government's desire to combat effectively endemic or emerging infectious diseases.
- A region may decide that existing labs are farther away than samples can realistically be transported.

On the most fundamental level, she indicated that scientific or diagnostic needs typically motivate lab construction. For example, the Stop TB Partnership recommended one BSL-3 lab for every 500,000-1 million people,[8] which would necessitate 6,800-13,000 labs worldwide for tuberculosis (TB) diagnostics alone. More recently, however, the Stop TB Partnership and WHO are promoting molecular diagnostics that require fewer safety precautions as an alternative to culture-based tests.[9] The advantage of molecular diagnostics is that these methods generally do not necessitate working in a BSL-3 facility. However, the disadvantage is that they may require difficult-to-obtain reagents and offer less flexibility than traditional, culture-based tests.

She also noted that political competition or a lack of trust between countries can motivate lab construction. She recounted how during the 2009 H1N1 influenza outbreak wealthy, vaccine-producing countries did not deliver on their promises to share vaccines with low-income countries until scientists reduced the recommended number of doses for adults from two to one and the pandemic strain proved less virulent than initially feared. Such experiences reinforce lack of trust.

In spite of the attractiveness and utility of containment labs, she pointed out that some countries and institutions are choosing not to build their own. For example, while SNL and its sister lab, Los Alamos National Lab (LANL), both consider biology a priority, LANL decided to build a BSL-3 lab and SNL did not because SNL did not consider Select Agent work a priority and thought a BSL-3 lab was too expensive. Although the LANL lab was built seven years ago, it is still not functional. Without a BSL-3, SNL found strategic partners, invested in molecular techniques including sequencing, and was able to play a role in the Amerithrax investigation.[10]

DISCUSSIONS

During the discussion, several participants shared stories of how containment labs had helped their country characterize and control disease outbreaks. A few indicated that when diagnostics are needed during a crisis and an appropriate laboratory is not available, the work is by necessity done using the facilities that are available. These participants argued that this risk should be weighed against the risk of having an additional facility housing pathogens. Others offered additional reasons for building labs or elaborated on those that had been presented:

- Due to intellectual property concerns, some countries do not want to share biological materials, such as those that could be used to make vaccines, and hence prefer to build their own lab and do the research and development work within their own borders.

[8]TB Diagnostics and Laboratory Services: Information Note. Available at: *http://www.stoptb.org/assets/documents/global/tbfriends/laboratory%20info%20note%20GF%20R%2011.pdf*. Accessed August 29, 2011.
[9]World Health Organization. Tuberculosis Diagnostics Xpert MTB/RIF Test: WHO Endorsement and Recommendations. Available at: *http://www.who.int/tb/features_archive/factsheet_xpert_may2011update.pdf*. Accessed August 29, 2011.
[10] LANL also participated in the Amerithrax investigation. NRC, 2011a; pp. 100-102.

- Private companies may build BSL-3 labs to help them win government contracts, even if the labs themselves lose money.
- In addition to promoting human health, labs can also contribute to animal and plant health.

An opinion frequently expressed was that all countries should have access to containment labs, and it was pointed out that the WHO International Health Regulations (IHR) (2005) require States Parties to have the capacity to analyze samples either domestically or through a collaborative agreement (WHO, 2008). One person noted that some countries may not want their own BSL-4 lab, but would like to be able to use one if the need arose. Many argued, however, that the difficulty of transporting samples, both from regulatory and logistical points-of-view, effectively requires most countries that want laboratory access to build their own lab (the numerous conversations about transportation issues that occurred during the workshop are summarized in Chapter 6). Another individual acknowledged the merits of a regional approach, but felt that the rights of countries to act autonomously and take whatever actions they deemed necessary to protect their citizens from disease took precedence.

PART 2: THE CURRENT STATUS AND OPPORTUNITIES FOR THE FUTURE
Chair: Anwar Nasim

Anwar Nasim (Ministerial Standing Committee on Scientific and Technological Cooperation [COMSTECH], Pakistan) chaired this session, which was intended to describe the challenges that currently operating labs are encountering, summarize the current discussions on this topic, and conjecture about future trends. The first talk described the current situation in Africa as an example of the types of difficulties being encountered worldwide and examined the increasing role of biosafety organizations in bringing attention to laboratories and catalyzing change. The second talk described challenges commonly encountered in Southeast Asia and questioned whether the current trend of developing countries adopting energy and technology intensive laboratory design standards from the West will continue.

PLENARY PRESENTATIONS

Laboratory Capacity, Biosafety, and Biosecurity in Africa: Gaps, Goals, Needs, and Progress

Willy Tonui (African Biological Safety Association [AfBSA], Kenya) described the current status of African labs, common challenges in the region, and the roles of AfBSA and the International Federation of Biosafety Associations (IFBA) in promoting change.

Dr. Tonui opened by explaining that the concepts of biosafety and especially biosecurity are still in their formative stages in most institutions in Africa. However, biotechnology, particularly work on genetically modified organisms, has raised public awareness about biosafety in the context of GMOs. Many African countries are signatories of the Cartagena Protocol on Biosafety and have created biosafety laws to ensure compliance. African countries are also building biosecurity awareness through their membership in the Biological and Toxin Weapons Convention (BWC) and implementation of United Nations Security Council Resolution 1540.

Many labs in the region are BSL-1 facilities, although research institutions often have BSL-2 labs and some have BSL-3 facilities. The Kenya Medical Research Institute, for example, has five BSL-3 labs. Enhanced BSL-3 facilities exist at the Naval Medical Research Unit No. 3 in Cairo, Egypt and the University of Nairobi. Africa has two BSL-4 facilities: the International

Center for Medical Research of Franceville in Gabon and the National Institute for Communicable Diseases in South Africa.

Dr. Tonui reported that many laboratories in African countries suffer from a number of common problems: poor spill management, inappropriate waste disposal, poor post-exposure management, minimal recording mechanisms for tracking safety errors and laboratory-acquired infections (LAIs), inadequate availability or use of personal protective equipment, poor use and maintenance of biosafety equipment, and no mandatory immunizations for lab workers (e.g., tuberculosis, hepatitis B, and typhoid fever). Additionally, there are few high-quality biosafety training programs, and the region lacks technical expertise and the budgetary resources to maintain containment labs. Most institutions do not designate a safety officer, safety guidelines are frequently not available, and policies and standard operating procedures (SOPs) are often not available or not followed. Most countries have little regulation due to a lack of both resources and awareness among top-level officials.

Dr. Tonui explained that AfBSA,[11] which he helped found in 2007, is a professional association that promotes biosafety and biosecurity in the African region and is working to address a number of issues. AfBSA currently sees opportunities to promote international partnerships, to work with governments to develop biosafety and biosecurity standards, to enhance collaboration and networking among laboratories, to help African laboratories implement risk assessment principles, and to design and implement biosafety training programs. Several African countries have formed or are forming their own national biosafety organizations to pursue similar goals within their borders.

AfBSA is one of many national and regional biosafety associations that belong to IFBA,[12] a not-for-profit, non-governmental organization (NGO) that works with national and international public and animal health authorities and international agencies (e.g., the World Health Organization [WHO], the World Organisation for Animal Health [OIE], the Food and Agriculture Organization of the United Nations [FAO]) to enhance biosafety, biosecurity, and biocontainment laboratory capacity within the greater framework of strengthening health systems. In addition to member organizations, IFBA also has observer organizations such as the Griffin Foundation, the United States Biosecurity Engagement Program (BEP), and the International Council for the Life Sciences (ICLS). IFBA programs include helping members to develop national biosafety guidelines and policies; adapt international best practices (i.e., the WHO Laboratory Biosafety Manual) to local needs and conditions; design, equip, and operate diagnostic laboratories to safely handle and contain infectious diseases; and establish and support regional biosafety training centers, train-the-trainer programs, and twinning and mentoring programs.

Dr. Tonui, who is a co-chair of IFBA, concluded by noting that IFBA and the Elizabeth R. Griffin Foundation designated 2011 as the "Year of Building International Biosafety Communities."

Current Thinking and Trends Ahead

Teck-Mean Chua (Asia-Pacific Biosafety Association [A-PBA], Malaysia) described the technology-intensive nature of today's high-containment laboratory facilities. He hypothesized that in the future, scientists, engineers, and regulators will work together more closely to assess accurately their needs and options to create more sustainable, less energy-intensive labs that provide the desired containment.

[11] African Biological Safety Association. Available at: *www.afbsa.org*. Accessed August 29, 2011.
[12] International Federation of Biosafety Associations. Available at: *http://www.internationalbiosafety.org/english/index.asp*. Accessed August 29, 2011.

Dr. Chua reminded the participants that disease outbreaks, whether from bioterrorism or naturally occurring emerging or re-emerging diseases, do not respect national boundaries and are a global problem. Thus, even though people work in different environments and cultures, everyone faces many of the same issues and threats and no one is safe unless their neighbors are.

He pointed out that developed countries had a head start on biosafety and biosecurity and have led with regulations, standards, and guidelines that call for complex, technology-intensive facilities. Hallmarks of high-containment facility designs in developed countries include double door entries, directional airflow, negative pressure gradients, single pass air, many air changes per hour, autoclaves, 24/7 operation, and multiple safety redundancies.

Dr. Chua then explained that countries that do not have their own guidelines often adopt the guidelines of another country. For example, the United States guidelines described in "Biosafety in Microbiological and Biomedical Laboratories" (BMBL) (United States HHS, 2009) are commonly used world-wide both to allow labs to apply for United States research funding and because biosafety professionals helping with a foreign project often import their own practices. WHO's Laboratory Biosafety Manual (LBM) (WHO, 2004), whose guidelines are less comprehensive than the BMBL, is another popular choice for countries without their own guidelines.

For many developing countries, however, Dr. Chua called for a greater focus on the fundamentals of biosafety because many of their facilities for handling infectious agents were built more than 10 or 20 years ago and incorporate limited biosafety measures. A recent survey[13] by FAO and A-PBA of BSL-2 and BSL-3 labs in seven countries in the Asia-Pacific region, for example, indicated that many labs are below an acceptable level of functionality for their BSL level. The survey noted that often HEPA filters lack the dampers necessary for maintenance, biological safety cabinets (BSCs) are uncertified and usually powered off, and unreliable electrical power is not backed up with generators. Overall, about 30% of the Class II BSCs tested were poorly designed or dysfunctional and failed, and many BSL-3 facilities were either designed incorrectly or being operated incorrectly.

Dr. Chua argued that future goals should not simply be about closing gaps between developed and developing countries but about providing practical, sustainable solutions for effective biocontainment in countries with limited resources. Additionally, he speculated that the effects of global warming and higher energy costs will create a demand for a "green technology approach" towards the design and operation of high-containment facilities and that threats of bioterrorism and emerging and re-emerging diseases will continue to drive the integration of national communities into a global biosafety community.

Dr. Chua pointed to the BSL-3 airflow requirements described in the LBM as an area where greener approaches might be useful. For example, as HEPA-filtered air that is already conditioned can be recirculated into a lab, perhaps it could also be used in other areas of the building. Furthermore, he urged people to consider whether it might be possible to create a 'sleep mode' for a lab with reduced airflow. Given the expense involved in high numbers of air changes per hour, he also proposed examining the issue to determine conditions when a lower number of air changes would be acceptable. Also, as not all BSL-3 labs house the same scientific activities and face the same biorisks, he suggested that creating a spectrum of BSL-3 types, rather than the current one-size-fits all solution, might provide the required containment with simpler, less-expensive, easier-to-maintain facilities.

Rather than simply taking the developed world approach of focusing on engineering and equipment, Dr. Chua advised balancing engineering controls with scientific and management controls. Scientific controls include risk assessments of the work to be undertaken, proper

[13] Dr. Pawin Padungtod (FAO Regional Office for Asia and the Pacific) and Dr. Robert A. Heckert (Robert Heckert Consulting, LLC) were co-authors on the study.

SOPs, and the employment of well-trained scientists and technicians. Management controls include policies, administrative support, and funding availability. He made the analogy that a BSL-3 lab is like a car— while engineering and maintenance are critical, safe operation also requires a trained driver and prudent traffic laws.

Dr. Chua concluded by noting that developing countries may be the weakest link in the chain of control in biosecurity against the misuse of biological agents to inflict harm.

DISCUSSION

During the discussion, a number of participants commented on common laboratory usage and funding patterns. Several mentioned that BSL-3 and BSL-4 labs, particularly diagnostic labs, are (1) typically used at that level only a small fraction of the time and (2) often do not have sufficient capacity to handle the required workload during an outbreak. A few individuals gave examples of BSL-2 labs adopting BSL-3 procedures to provide needed surge capacity during times of high demand. One mentioned that research labs can supplement the local public health system during outbreaks and indicated this is most effective when an institution's director regularly makes and communicates an inventory of available resources and capabilities. Others observed that funding is often tied to demand and that labs often lose resources during periods without a disease outbreak. A few indicated that labs could perform research during times of low diagnostic demand in order to maintain readiness, but noted that research funds are not always available. Several suggested that guidelines from developed country or international organizations should offer more guidance on creating scalable capacity.

A number of individuals speculated on whether the number of containment labs will continue growing at its current pace. A few hypothesized that the increasing availability of molecular diagnostic methods, which have the potential to replace culture-based tests, will reduce the demand for new BSL-3 and BSL-4 labs, while others felt that the pace would continue or increase with every country or institute wanting their own lab. One conjectured that the factors driving capacity have changed; where previously labs were desired simply to diagnose dangerous pathogens, increasing travel and difficulty in containing diseases within national borders has increased the demand for cures, which requires research.

3

ASSESSMENTS OF NEEDS, CHALLENGES, AND RESOURCES (PLENARY SESSION)

Chair: Seval Korkmaz

In view of the complexity of both containment labs and the human and agricultural health challenges containment labs aim to ameliorate, a detailed examination of specific situations often helps in optimizing allocation of resources. This session was intended to provide an overview of local assessments including what they are, what purpose they serve, who should be involved in a local assessment, and what information might be included in an assessment.

Session chair **Seval Korkmaz** (Abdi Ibrahim, Turkey) opened by explaining that she has established many types of pharmaceutical laboratories that comply with Good Manufacturing Practices (GMP) and that each required a unique assessment. She then introduced the speakers and their topics indicating that the first talk would present many of the common needs and resources that might be considered while doing an assessment and that the second would give an example of a regional assessment.

PLENARY PRESENTATIONS

Global Biosafety and Biosecurity Challenges: Options for Nations with Limited Resources

J. Craig Reed (Inspirion Biosciences, United States) described biosafety and biosecurity needs that are common in low-resource countries and the challenges associated with using the available resources to address those needs. He based his talk on a co-authored paper that has been submitted for publication (Heckert et al., 2011).

Dr. Reed first observed that all resources, including those of both donors and recipients, are limited and stressed the need for capacity building efforts that lead to self-sufficiency. He defined low resource countries as those with a United Nations Human Development Index less than 0.85, which roughly corresponds to a gross national income less than $10,000 per capita.

Low resource countries typically share a common set of needs. These include safe containment lab capacity, biosafety and disease surveillance equipment, diagnostic reagents that are handled and stored properly, trained staff, training opportunities, reliable utility service, and a regulatory framework for biosafety.

Dr. Reed explained that while a number of resources are available to address these needs each presents challenges:

- International engagement programs, such as those funded by the United States, can address many needs, but the process, which often is managed by large defense contractors with high personnel turnover and complicated contracts, may overwhelm recipients. Additionally, this money may come with regulations created by the donor without input from the recipient.
- Donors sometimes introduce over-engineered and energy-intensive equipment, protocols that require large amounts of consumables, and solutions that emphasize technology over technique. He argued that this is due to the mistaken notion that approaches that work in western countries can simply be applied without modification in other countries.

- He recommended that donors and recipients agree on both financial and managerial transition plans so that the recipient is ultimately able to run the facility without further aid.
- Elected officials, Ministers, and senior laboratory management can help formulate a national plan, allocate budgets for maintenance and improvements, and establish regulatory frameworks. Typically, however, educational and awareness-raising activities are required to engage the desired leaders.
- The local economy, ideally, should provide services, reagents, and equipment, but development and investment are typically required before this can become a reality.
- Technical information is commonly available from a variety of sources including regional biosafety associations, the International Federation of Biosafety Associations (IFBA), and government ministries, but the information often requires translation and distribution.
- Similarly, online resources, such as the IFBA[1] and American Biological Safety Association[2] (ABSA) websites, offer a wealth of training materials and examples of guidelines and standards, but most need translation into the local language. Furthermore, many training programs do not use adult education techniques, making them less effective than they could be.

Dr. Reed said that regional biosafety associations can help communicate with the government, establish local credentialing systems, offer twinning and mentoring services, and distribute training materials, but the capacity of many is still developing. Ideally, donors would work with regional and national biosafety organizations to avoid duplicating training and other efforts.

Dr. Reed also addressed the benefits of recipients developing a national implementation plan that balances human and animal disease efforts, creates a national regulatory framework, focuses on laboratory consolidation rather than expansion, emphasizes international collaborative relationships, and identifies funding for creating a professional biosafety society and national biosafety training centers.

Biosafety and Biosecurity Challenges in the Caribbean Region

Valerie Wilson (Caribbean Med Labs Foundation [CMLF], Trinidad and Tobago) shared the results of a recent regional biosafety assessment by CMLF.[3]

Ms. Wilson started by introducing CMLF and the 23 countries in the Caribbean region that it serves. The member countries speak different languages and vary widely in population and per capita income. She noted that the Caribbean is the most tourism dependant region in the world with visitors from North America, Europe, China, and India, and that the large number of tourists makes the region vulnerable to a number of communicable diseases, which could have a major impact on the economy and the local population.

She explained that CMLF's objectives include developing a supportive environment for high quality regional laboratory services; advocating at the highest levels for laws, regulations, and laboratory accreditation; mobilizing resources to strengthen laboratories; and creating a regional sustainability strategy.

To best determine how to achieve its goals, CMLF undertook a regional assessment. CMLF asked medical labs, public health labs, veterinary labs, agriculture labs, labs that test for zoonotic diseases, and food and water labs a total of 204 questions in 20 categories addressing

[1] Available at: *http://www.internationalbiosafety.org/english/index.asp*. Accessed August 29, 2011.
[2] Available at: *http://www.absa.org/index.html*. Accessed August 29, 2011.
[3] Caribbean Med Labs Foundation. Available at: *http://cmedlabsfoundation.net*. Accessed August 29, 2011.

national infrastructure, the World Health Organization (WHO) International Health Regulations (IHR), and laboratory safety standards.

In her presentation, Ms. Wilson focused on the responses of the major medical and public health laboratories in 13 countries, two of which have BSL-3 labs that are used mainly for tuberculosis testing.

Overall, the assessment indicated that major gaps in biosafety implementation exist in the Caribbean region. She noted a lack of national policies and regulatory mechanisms for biosafety; a lack of systems for biorisk assessment at both the national and laboratory level; challenges in finding time for staff, including biosafety officers, to devote to safety functions; limited adoption and monitoring of safety standards; and limited access to BSL-3 facilities. Furthermore, while approximately half the respondents indicated that their country had a formal laboratory network, rarely did the networks include animal testing labs, and formal collaborations between Ministries of Health and Agriculture on zoonotic diseases were uncommon. Respondents all reported that lab coats and gloves were available. Respiratory protection was usually available when needed, but only about half the respondents indicated that respirators were used correctly. Just over half reported that biological safety cabinets (BSCs) are certified annually.

After noting that capacity building for the implementation of safety systems is urgently needed, Ms. Wilson ended by describing two developments that promise to improve regional and national systems. First, development of national reference laboratories has progressed significantly in the past 5-10 years, with Haiti, the Dominican Republic, Guyana, Suriname, and Jamaica establishing labs. Second, the Caribbean Epidemiology Centre (CAREC), which was founded in 1985 and is administered by the Pan-American Health Organization and WHO, is transitioning into the Caribbean Public Health Agency, which will serve as a regional reference laboratory for communicable diseases. CAREC previously served as a regional network hub, but recently the regional network fragmented into smaller, geographically based networks. She mentioned that the small size of the countries and a sense of regional identity support and facilitate regional solutions and that the CAREC network had a strong tradition of sharing information to allow creation of a regional picture. Nonetheless, she indicated that a regional network of laboratories will require development of systems for allowing efficient transport, navigating of customs procedures, ensuring quality results, and obtaining financing.

DISCUSSION

While most of the discussion focused on assessments of individual countries considering containment labs, one individual felt that decisions about where to place labs would be handled better on the regional or international, rather than the national, level. In addition to the considerations identified by the speakers, some participants also suggested looking at a location's ability to absorb donor resources, considering alternatives to containment labs, and involving people who will be working in the lab.

Some indicated that the assessment process itself is an area in which some countries are interested in receiving assistance. One person mentioned that external parties might have greater capabilities to compile figures and statistics and noted that the Defense Threats Reduction Agency (DTRA) recently created a bio-risk management program to build international capacity in this area. Several people noted that while donors can provide useful information, countries should seek information from other sources as well and suggested that donors should be careful not to rush the process. Many indicated that while obtaining broad participation is beneficial, countries need to ensure that they are full participants in the process.

Participants also commented on both the importance of realistically estimating the cost of a new facility as well as determining whether the expected benefits justify those costs. Given the high cost of imports, one person stressed that generating an accurate budget requires

ascertaining which materials and expertise can and cannot be obtained locally. Another wondered about the cost of preventing one infection and speculated that in some cases improving the safety and facilities of BSL-2 diagnostic labs or spending the money on other aspects of public health altogether might be a better investment. Several encouraged countries to examine how containment labs fit in with their national public health priorities.

4

AVAILABLE RESOURCES, REGULATIONS, AND GUIDELINES (PLENARY SESSION)

Chair: Serhiy Komisarenko

This session described and evaluated many of the international, regional, and national resources available to countries looking for guidance on how to build, operate, and improve containment labs. The first talk provided an overview of the regulatory landscape and an orientation to the wide variety of guidance available. The second presentation then highlighted an international network of biocontainment expertise, while the third examined elements involved in creating a successful regional or national biosafety organization. Finally, a number of people gave short presentations detailing their countries' national regulatory frameworks. During the subsequent discussion, Session Chair **Serhiy Komisarenko** (Palladin Institute of Biochemistry, Ukraine) encouraged the group to think about how they could spread their knowledge to their intended audience.

PLENARY PRESENTATIONS

International Regulatory Frameworks, Standards and Guidelines

Ingegerd Kallings (Swedish Institute for Communicable Disease Control, Sweden) presented examples of various international standards and guidelines and detailed the documents' contribution to biosafety.

Dr. Kallings explained that regulations (and biosafety itself) are an attempt to address the very real problem of laboratory-associated infections (LAIs), which started soon after microorganisms were first cultured in labs. While the incidence of LAIs has decreased in recent years, they still occur and cause fatal infections in lab workers.[1] While human failures are typically blamed for LAIs, Dr. Kallings feels it would be more productive to think of LAIs as indicators of systemic failure stemming from a lack of training, understanding, and validation resulting in non-compliance.

Dr. Kallings then discussed some of the international frameworks developed to contribute to biosafety and biosecurity (Box 4-1). In an attempt to increase the availability of biosafety information, the International Federation of Biosafety Associations (IFBA) created a compendium of regulations and guidelines from around the world.[2]

[1] Examples of recent fatal LAIs include cases of herpes B encephalitis in 1997, meningitis in 2000, severe acute respiratory syndrome in 2003, and Ebola in 2004.

[2] International Federation of Biosafety Associations. Available at: *http://www.internationalbiosafety.org/Organizations/fde5681c-ca94-4a20-827a-0716f524babc/Resources/pdf/Compendium/Compendium_Update_Feb_10_2010.pdf*. Accessed September 10, 2011.

Box 4-1
Some Key International Biosafety and Biosecurity Documents and Organizations

The Protocol for the Prohibition of the Use in War of Asphyxiating, Poisonous or Other Gases, and of Bacteriological Methods of Warfare (Geneva Protocol), which was signed in 1925 and entered into force in 1928, prohibits the use of chemical and biological weapons.[a]

The Biological and Toxin Weapons Convention (BWC), which was signed in 1972 and entered into force in 1975**,** prohibits States Parties from producing, developing, or retaining biological or toxin weapons or their means of delivery.[b] States Parties retain the right to use biological agents and toxins for peaceful purposes.

United Nations Security Council Resolution 1540, which was adopted in 2004, requires States to ensure that their domestic resources are not misused to support the proliferation of biological, chemical, or nuclear weapons.[c]

The Cartagena Protocol on Biosafety to the Convention on Biological Diversity, which was adopted in 2000 and entered into force in 2003, governs the transfer of genetically modified organisms (GMOs) between countries.[d]

The Global Partnership Program Against the Spread of Weapons and Materials of Mass Destruction, which Canada as chair of the G8 started in 2002, is an international cooperative threat reduction program.[e] The program initially focused on non-proliferation and disarmament activities in the former Soviet Union but has since expanded to address threats in other locations. Over a ten-year period, more than $20 billion U.S. have been pledged to the program.

Australia Group's Export Control Lists specify dual-use biological equipment, toxins, pathogens, and chemical weapons precursors that participating countries agree to exercise vigilance when exporting.[f]

The United Nations Educational, Scientific and Cultural Organization (UNESCO) Universal Declaration on Bioethics and Human Rights, which was adopted in 2005, provides a framework for guiding ethical decision-making in medicine and the life sciences.[g]

Organisation for Economic Co-operation and Development (OECD) Best Practice Guidelines on Biosecurity for Biological Research Centers, which were published in 2007, are guidelines for securing repositories of biological information and materials.[h]

The World Health Organization (WHO) has put out widely used biosafety[l] and biosecurity[j] guidelines.

Biosafety in Microbiological and Biomedical Laboratories (BMBL) (United States HHS, 2009) is a national document that is widely used internationally.

The World Organisation for Animal Health (OIE) publishes standards for testing for terrestrial and acquatic animal diseases of global importance and standards for vaccine banks. The recommendations are widely used in international trade for screening animals and animal products.[k]

The Food and Agriculture Organization of the United Nations (FAO) has produced a number of publications on biosecurity for food and agriculture.[l]

The International Plant Protection Convention produces standards that may be incorporated into national legislation to reduce the spread of plant pests and pathogens.[m]

The International Criminal Police Organization works to stop criminal and terrorist use of biological agents and toxins and publishes bioterrorism incident pre-planning and response guides.[n]

[a] The text of the Geneva Protocols is available at: http://www.un.org/disarmament/WMD/Bio/pdf/Status_Protocol.pdf. Accessed October 13, 2011.

[b] The Biological Weapons Convention. Available at: www.unog.ch/bwc. Accessed August 29, 2011.

[c] http://daccess-ods.un.org/TMP/5389472.24617004.html. Accessed September 10, 2011

[d] The Cartagena Protocol on Biosafety. Available at: www.cbd.int/biosafety. Accessed August 29, 2011.

[e] Global Partnership Program. Available at: http://www.international.gc.ca/gpp-ppm/global_partnership-partenariat_mondial.aspx?menu_id=1&view=d. Accessed August 29, 2011.

[f] The Australia Group. Available at: http://australiagroup.net. Accessed August 29, 2011.

[g] Universal Declaration on Bioethics and Human Rights. Available at: http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/bioethics-and-human-rights/. Accessed August 29, 2011.

[h] OECD. Available at: http://www.oecd.org. Accessed August 29, 2011.

[I] Laboratory Biosafety Manual. Available at: http://www.who.int/csr/resources/publications/biosafety/en/Biosafety7.pdf. Accessed August 29, 2011.

[j] Biorisk Management: Laboratory Biosecurity Guidance. Available at: http://www.who.int/ihr/biosafety/publications_WHO_CDS_EPR_2006_6/en/index.html. Accessed August 29, 2011.

[k] World Organisation for Animal Health. Available at: www.oie.int. Accessed August 29, 2011.

[l] Food and Agriculture Organization of the United Nations. Available at: www.fao.org. Accessed August 29, 2011.

[m] International Plant Protection Convention. Available at: www.ippc.int. Accessed August 29, 2011.

[n] INTERPOL. Available at: www.interpol.int. Accessed August 29, 2011.

She also described internationally binding transport regulations (see Box 4-2), and Dr. Kallings indicated she generally considers transport regulations to be unnecessarily strict and lacking the solid foundation that a risk-analysis could provide.

Box 4-2
Transport Regulations and Guidance in International Law

The United Nations Economic Commission for Europe's Recommendations on the Transport of Dangerous Goods (U.N. Model Regulations), which were last updated in June 2011, form the foundation for most international shipping regulations.[a]

The International Civil Aviation Organization (ICAO) issues internationally binding transport regulations based on the U.N. Model Regulations[b]

The International Air Transport Association (IATA) adds some additional transport requirements.[c]

The World Health Organization (WHO) compiles and regularly updates a guidance document that serves as a comparatively-user friendly source on transport requirements.[d]

[a]http://live.unece.org/fileadmin/DAM/trans/danger/publi/unrec/English/Recommend.pdf. Accessed September 10, 2011. U.N. Model Regulations Available at: http://www.unece.org/trans/danger/publi/unrec/rev16/16fword_e.html. Accessed September 30, 2011.

[b] International Civil Aviation Organization. Available at: www.icao.int. Accessed August 29, 2011.

[c] International Air Transport Association. Available at: http://www.iata.org/whatwedo/cargo/dangerous_goods/Pages/index.aspx. Accessed September 10, 2011.

[d] Guidance on regulations for the Transport of Infectious Substances 2011-2012. Available at: http://www.who.int/ihr/publications/who_hse_ihr_20100801/en/index.html. Accessed August 29, 2011.

She then provided information about the multiple International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) European Committee for Standardization (CEN) standards related to biosafety and biosecurity, including the CEN Workshop Agreement (CWA) 15793:2008 Laboratory Biorisk Management Standard.[3] A diverse international group of 76 participants from 26 countries developed CWA 15793 using the CEN procedures, which facilitated the rapid development of the standard. While CWA 15793 is a generic document that defines a voluntary standard for a risk-based, performance-oriented approach to biosafety and management of biological risks, she indicated that its voluntary rules may be adopted nationally. In the CWA 15793 approach, all components of a laboratory (e.g., workers, pathogens, standard operating procedures, equipment, buildings, the community, etc.) are considered as parts of a unified system. The standard describes a system management approach centered on the principle of continual improvement for reducing risks below a target level. While CWA 15793 is compatible with a framework based on pre-defined BSL levels, the method frees its users to design and implement precautions completely tailored to their particular situation and goals.[4] She also noted that another CEN workshop is currently working on a new document describing the roles, responsibilities, and competencies necessary to be a biosafety professional.

Dr. Kallings concluded by observing that in the current system, national regulations take precedence over international guidelines but many countries still lack a national regulatory framework. She feels there are currently a sufficient number of regulations to support biosafety and biosecurity but recommends that gaps be identified and filled and compliance with existing regulations encouraged before new regulations are added.

IFBA's Biocontainment Engineering Network

Ken Ugwu (Foreign Affairs and International Trade Canada and IFBA Biocontainment Engineering Working Group, Canada) described IFBA's Biocontainment Engineering Network (BEN) and the main challenges the group is working to address.

Mr. Ugwu introduced IFBA as an international, nonprofit non-governmental organization (NGO) that has been working in advocacy and operational roles since 2001 to address biological threats and to advance biosafety and biosecurity worldwide. He explained that IFBA's member biosafety professionals, scientists, lab technicians, academics, architects, engineers, managers, and policymakers form a network of containment expertise. The IFBA BEN then leverages that expertise to identify practical solutions for containment facilities; advocates to include those approaches in international guidelines and best practices; mentors individuals new to the field; builds global capacity; creates consensus on controversial issues; and finds simple, safe, and workable solutions for low-resource establishments. To achieve those goals, the IFBA BEN works to find sustainable, practical, and local solutions that create safe and secure facilities that can be successfully certified and sustained in the long-term.

In Mr. Ugwu's opinion, the best solutions typically understand and account for cost pressures, the lack of local technical equipment and replacement parts, unreliable utilities, and local inexperience in constructing and operating complex BSL-3 facilities. Rather than using a "one size fits all" approach to BSL-3 facilities, the IFBA BEN advocates tailoring solutions to the

[3] CEN 15793:2008 Laboratory Biorisk Management Standard. Available at: *ftp://ftp.cenorm.be/PUBLIC/CWAs/wokrshop31/CWA15793.pdf*. Accessed September 10, 2011.

[4] The Global Laboratory Initiative (GLI), for example, used the CWA 15793 method to determine minimal, risk-based recommendations for tuberculosis work without using the traditional BSL nomenclature. See TB Laboratory Biosafety Guidance. Available at: *http://www.stoptb.org/wg/gli/assets/documents/TB%20Lab%20Biosafety%20Guidance%20factsheet.pdf*. Accessed September 30, 2011.

situation. As BSL-3 containment space is very expensive to build, operate, and maintain, and working at the BSL-3 level is less efficient (e.g., protective clothing, entry/exit procedures, and medical surveillance) than working at lower containment levels, he argued that overdesign and unnecessary use of BSL-3 labs should be avoided.

To ensure that all needs are met without resorting to overdesign, the IFBA BEN recommends that a laboratory planning and programming phase precede the design phase of lab construction. This programming phase should involve architects, engineers, and scientists, and answer the questions that will drive the design including defining the pathogens and standard operating procedures to be used, the diagnostic tests to be performed, and the number of samples to be processed. He suggests the discussion produce a risk assessment that defines the containment requirements and the facility's architectural and mechanical concepts. In particular, IFBA BEN recommends not over-designing BSL-2 and support spaces and balancing electronic and operational solutions (e.g., considering visual signage instead of electronic door interlocks). Simple architectural solutions such as epoxy-based paint on gypsum board for interior BSL-3 walls and simple mechanical solutions such as limiting the number of Class II, Type B2 BSCs, which are difficult to install and maintain, should also be considered.

Mr. Ugwu concluded by mentioning that the IFBA BEN is also exploring options for recognizing qualified certifiers. He explained that while several national authorities including Singapore and Canada have accredited certifiers, there is no accredited international certification program for biocontainment facilities. Nor is there a detailed set of criteria for international certification as the WHO Laboratory Biosafety Manual contains only general certification guidelines.

Sustaining Regional and National Biosafety Associations: Challenges and Considerations

Teck-Mean Chua (Asia-Pacific Biosafety Organization [A-PBSA], Malaysia) discussed the need for biosafety associations (BSAs) and the factors that contribute to the success and sustainability of professional organizations.

Dr. Chua argued that as we are all exposed to collective risks (e.g., emerging and re-emerging diseases and bioterrorism) that do not respect national boundaries, we also share a collective responsibility and should take collective action. He believes that BSAs can help focus and direct that action at the national, regional, and international levels and observed that in recent years, many national and regional biosafety organizations have been created as has IFBA.

He has found no set rule as to whether national or regional BSAs should come first. As an example, he noted that the A-PBA formed at the regional level in 2005 and then proceeded to assist members in forming national associations. He feels that starting at the regional level was logical given that the Asia-Pacific region is a hotbed for emerging and re-emerging disease outbreaks and that severe acute respiratory syndrome (SARS) and other outbreaks had created a sense of regionalization among the generally small countries. However, he indicated that it is also possible for existing national organizations to band together into a regional organization.

Dr. Chua emphasized that new associations should ensure that they have a multi-disciplinary membership from the beginning. Members should include scientists, administrators, engineers, architects, and technicians and a variety of agencies including those responsible for human health, animal health, and domestic security. All desired countries should be represented, and an association should welcome members from outside its borders.

He also suggested that an association's organizational structure facilitate collective leadership and be flexible enough to respond to future challenges. He reminded the group that BSAs, like all nonprofits with expenses, need realistic business plans and should (1) identify

activities, such as conferences, that will produce income; (2) produce transparent financial statements that are audited annually; and (3) use membership resources to formulate programs that serve the collective interests of their members and promote the organization's mission and vision.

NATIONAL RESOURCES, REGULATIONS, AND GUIDELINES: SUMMARIES OF COUNTRY OVERVIEWS

To compare and contrast the approaches different countries use to manage and regulate high-containment biological labs, some workshop participants developed country overviews that described a country's facilities, capabilities, and regulations as well as past accidents, safety and security issues, and lessons learned. All of the country overviews are included in Appendix E. Additionally, five of the overview writers presented brief summaries to the group:

- Hüseyin Avni Öktem (Middle East Technical University, Turkey overview),
- Olena Kysil (Taras Shevchenko National University of Kyiv, Ukraine overview),
- Leila dos Santos Macedo (Brazilian Biosafety Association [ANBio], Brazil overview),
- Anwar Nasim (Ministerial Standing Committee on Scientific and Technological Cooperation, Pakistan overview), and
- Ingegerd Kallings (Swedish Institute for Communicable Disease Control, EU overview).

The countries have chosen a variety of approaches for regulating the biosafety and biosecurity of their containment labs. Exact numbers of containment labs are typically difficult to obtain—except for Ukraine where all microbiology labs are required to register with the government. Only the overview for Sweden indicated the presence of a comprehensive system for reporting accidents and LAIs; in some cases, no accidents had ever been reported. In many cases, legislation relevant to containment labs was created to comply with international agreements such as the BWC, United Nations Security Council Resolution 1540, and the Cartagena Protocol on Biosafety. Many writers reported comprehensive legislation to regulate GMOs and recombinant DNA usage. A number of countries have recently developed biosafety courses for their universities, and many of those courses contain a biosecurity component. Biosafety training seminars and workshops appear to be becoming more common, and some countries are starting to translate biosafety documents into their native languages. In general, high variance exists in the number of laws relevant to and government agencies responsible for containment labs.

DISCUSSION

Much of the discussion focused on national regulations, which aside from requirements imposed by donors, are the only rules labs are required to follow. Many speakers stressed that aside from implementing the International Health Regulations (IHR) and complying with transport rules, countries have the right to create whatever laws they deem appropriate. (Discussion of transport regulations is presented in Chapter 6.) While supporting countries' sovereign rights, many participants still felt that the lack of national regulations or lax enforcement of those regulations constituted the biggest gaps in the regulatory framework. One person wondered if a process could be developed to help countries that want to create regulations, and another warned that reducing the intensity of existing regulations is extremely difficult. Someone else encouraged countries to adopt risk-based regulations rather than rules that simply require ticking boxes.

Perceptions of the impact of biosafety and biosecurity regulations on work varied. One person indicated that regulations are felt but that they are generally helpful and necessary. Another pointed to an elevated awareness on the subject increasing international cooperation and the amount of available equipment. A third commented on a high paperwork burden.

5

PATHS FROM ASSESSMENTS TO FUNCTIONAL LABS (BREAKOUT SESSIONS)

While the Chapter 3 examined assessments broadly, this session provided specific examples of the process by which countries and corporations decide where and when to build labs, the degree to which their original objectives have been achieved, and the lessons they have learned from their experiences.

In order to inform discussions, each breakout session started with several short talks highlighting containment lab facilities in one geographic region. Each speaker focused mainly on a single lab and described that lab's strengths, ongoing efforts to sustain and improve capabilities, and key obstacles that had been successfully overcome. Topics discussed included how well each lab is fulfilling its original research and public health goals; where each lab is situated within country and regional networks; whether initial and on-going costs and funding have been as expected; and ongoing laboratory biosafety, biosecurity, and maintenance efforts.

During the discussions, participants in each breakout session were asked to consider a number of questions about the accuracy and completeness of the original needs assessment:

1. How well are labs fulfilling their original research and public health goals?
2. Did design, construction, and commissioning proceed as expected? Did the initial assessments consider all the relevant issues? How were difficulties overcome? With the benefit of hindsight, what could have been done differently?
3. Are costs as expected? Was initial and on-going funding as expected? How involved are donors? How are labs affecting the local economy?
4. How well are labs recruiting and retaining qualified scientific and engineering staff?
5. What steps are labs taking to provide the desired levels of biosafety and biosecurity?
6. How are local communities receiving labs?

BREAKOUT SESSION 1: EASTERN ASIA
Chair: Leila dos Santos Macedo
Rapporteur: Fran Sharples

Leila dos Santos Macedo (Brazilian Biosafety Association [ANBio], Brazil) opened the session by reiterating the observation from earlier sessions that East Asia is a hotbed of emerging and re-emerging infectious diseases. Participants then heard talks describing labs in South Korea and Thailand.

BREAKOUT SESSION PRESENTATIONS

Meeting International Biosafety and Biocontainment Standards in Low-resource Settings: The Southeast Asian Experience

Stuart Blacksell (Mahidol Oxford Tropical Medicine Research Unit [MORU]) described challenges MORU has experienced in Southeast Asia.

Dr. Blacksell started by noting that the world's population is concentrated in Southeast Asia and that newly emerging diseases (e.g., severe acute respiratory syndrome [SARS] and Nipah), agents of increased virulence (e.g., avian influenza and tuberculosis), and endemic diseases caused by risk group 3 agents drive the region's diagnostic and research needs.

While Southeast Asia has at least 45 BSL-3 labs, Dr. Blacksell explained that running a facility responsibly requires a huge investment of time, people, facilities, and money, and questions exist about standards, management, training, and security for most labs in the region.

As an example of the challenges, Dr. Blacksell described his experiences with MORU, which maintains a regional network of field sites and BSL-2 and BSL-3 labs. MORU recently built new labs in Bangkok, Thailand and Vientane, Laos and has three additional labs in Thailand as well as labs in Cambodia and Bangladesh.

Historically, the area has lacked a safety culture, so MORU requires a robust induction procedure and documents all training and the resulting competencies of its employees. For its training, MORU utilizes consultants, the United States Department of State Biosecurity Engagement Program (BEP), Sandia National Laboratories, the World Health Organization (WHO), and the Australian Government Overseas Aid Program (AusAID). Training includes dual-use awareness, and labs hold regular refresher training.

MORU employs a full time Biosafety Administrator, a 50 percent time Registered Biosafety Professional, and seven biosafety site representatives. To help address the severe regional lack of biosafety experience and fill the required positions, MORU formed a regional twinning partnership with the Australian Animal Health Laboratory.

Dr. Blacksell stated that security is a concern and that each lab has a site-specific security plan. Because the lab's funding includes U.S. money, to obtain access, staff must pass a United States Federal Bureau of Investigation security risk assessment and be a United States Department of Justice "registered entity." Where possible (i.e., Thailand), local police also check all staff using national and international databases.

In additional to personnel checks, the labs have also invested in physical security. BSL-3 freezers require fingerprint access, and access is restricted to three people; incubators with BSL-3 organisms use coded locks. Additionally, MORU has catalogued 20,000 freezer samples, documenting agent, source, intended use, and quantity using software that creates an audit trail. Audits are conducted every three months.

While South Korea and Singapore and to a lesser extent Thailand have well-developed laws governing the safe and secure operation of biocontainment facilities, he observed that most countries in the region either lack national biosafety legislation or have laws that are poorly enforced and understood. MORU is required to follow the host country's local laws, United Kingdom rules because of their Oxford University affiliation, and Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines and United States Select Agent rules to obtain access to U.S. funds. He elaborated that earning Select Agent qualification turned out to be a bigger task than initially expected but that it was ultimately worthwhile both because of the resulting access to funds and because it gave them added confidence in their operation. The application process, which made them examine everything they did, ultimately resulted in good databases, emergency response procedures, and standard operating procedures (SOP) in both English and Thai.

Other challenges include mismanagement, finding local services and resources, and limited budgets, particularly for maintenance and training. Additionally, the tropical climate makes it very wasteful to cool and dry air only to ultimately pump it back outside; he suggested that regulators consider allowing recirculation of 85 percent of the air with additional high-efficiency particulate air (HEPA) filtration.

Given the complexity of running BSL-3 labs in the area, Dr. Blacksell encouraged people considering new labs to accurately assess their initial expenses, anticipated operational and

maintenance costs, and the associated biosafety and biosecurity risks to determine if a BSL-3 is truly needed or if a BSL-2 with BSL-3 practices might be sufficient to meet their needs.

Operating a BSL-3 Facility in Korea: The IVI Experience

Soh Jin Lee (International Vaccine Institute [IVI], South Korea) discussed the history and operations of IVI's BSL-3 facility. IVI is a non-profit, international organization, headquartered in Seoul, South Korea that was created under the auspices of the United Nations Development Program. IVI's mission is to improve the health of people in developing countries by the development, introduction, and use of new and improved vaccines.

Ms. Lee explained that IVI's BSL-3+ project, which consists of 350 m^2 of animal biosafety level (ABSL) -3 and BSL-3 areas, was funded by the South Korean government and was initiated in 2005 before most of the current Korean regulations were passed. Construction started in 2007, and the facility was certified using international standards in 2008. The facility was recertified by the Korean Center for Disease Control and Prevention (KCDC) in 2009. Like the other 19 certified BSL-3 facilities in Korea, IVI requires an annual inspection that includes a shutdown, general decontamination, and new training. IVI also requires reaccreditation every three years by the KCDC.

IVI operates in compliance with all relevant Korean laws including the Act on the Prevention and Control of Infectious Diseases, which includes a pathogen tracking system and a list of pathogens under the control of the KCDC; the Act on the Prohibition of Biological or Chemical Weapons and the Control of the Production, Export, and Import of Special Biological or Chemical Agents; the Living Modified Organism Regulations; and the Act on Transnational Transportation of Living Modified Organisms.

IVI also has its own internal BSL-3 management system, manuals, SOPs, and training practices. For example, approval of the Institutional Biosafety Committee is required before changing experimental protocols or using new animals or infectious materials, and the General Manager must authorize all new facility users. BSL-3 training is provided to scientists, research assistants, maintenance engineers, and institutional safety committee members. The goal of the training is to give people the confidence and skills to create a safe work environment. The training includes biosafety lectures and general information on biosecurity. It also includes theoretical and practical training on BSL-3 operations, cleaning and decontamination, animal handling, equipment usage, and emergency procedures. The facility is monitored using closed circuit television and an automatic central monitoring system that notifies the appropriate people by text message in the event of an emergency.

Biocontainment for Clinical and Research Activities

Sunee Sirivichayakul (Chulalongkorn University, Thailand) presented the goals and policies of the Central Biocontainment Lab, which is located in Bangkok, Thailand and is part of Chulalongkorn University and the Thai Red Cross Society.

The BSL-3 facility, which has operated since Thailand's 2008 bird flu epidemic, strives to provide a safe environment for working with biological agents. The facility is particularly interested in agents that threaten national security due to the ease of their transmission or dissemination, high mortality rates, potential for a major public health impact, potential for public panic and social disruption, or requirements for special action for public health preparedness.

Dr. Sirivichayakul noted that the lab widely solicits proposals for work and has a number of attractive features including a review group of at least five knowledgeable committee members, one full-time staffer who cares for the facility and its equipment, regular maintenance, and training for new users. Facility rules dictate that no more than three people may work in the

lab simultaneously, and if only one person is working in the BSL-3, then a second person must be available outside in case of emergency.

She observed that one key challenge for the laboratory has been its high operational and maintenance costs, which exist even during those times when the facilities are not heavily used. So far, the Faculty of Medicine has provided funding, and individual users help by bearing the cost of disposable items such as N95 respirators and gowns.

BREAKOUT SESSION 2: AFRICA
Chair: Michael Ugrumov
Rapporteur: Benjamin Rusek

This session comprised presentations from three labs in African countries. Two are located in North Africa and one Central Africa, a hotbed for emerging infectious diseases. Although all three are in developing countries, all are well funded through a combination of federal sponsorships, international partnerships, and corporate support. While all engage in research and disease surveillance, the primary function of two of the labs is vaccine production. Following the talks, **Michael Ugrumov** (Institute of Developmental Biology, Russian Academy of Sciences, Russia) led a discussion between the speakers and the audience on issues introduced during the talks.

BREAKOUT SESSION SPRESENTATIONS

Biopharma's Vaccine and Diagnostics Production in Morocco: Current Situation and Future Changes

Mehdi El Harrak (Biopharma) described Biopharma's facilities and capabilities and the role of vaccine production in security.

Dr. El Harrak started by explaining that North Africa is a homogeneous epidemiological area and is constantly at risk for the introduction of exotic diseases. The state laboratory Biopharma was created in 1984 to serve as a national center of biotechnology. In that capacity, the facility develops diagnostics for local diseases, performs active surveillance that plays a strategic role in providing early warnings and controlling epidemics, and produces 90% of the vaccines for national veterinary prophylactic campaigns as well as for the private sector and for export. Production techniques include bacterial fermentation, production on specific pathogen-free eggs, conventional cell culture, and suspension cell culture. Biopharma maintains BSL-3 labs that serve a variety of functions: bacterial fermentation, viral vaccine production, quality control, research and development, and animal housing. Dr. El Harrak noted several examples of his facility's work:

- Biopharma developed a live attenuated vaccine for African horse sickness that successfully eliminated the disease locally.
- In addition to supplying national prophylactic campaigns against sheep and goat pox, Biopharma has also supplied vaccine campaigns in Libya and Tunisia. Many of the 15 - 25 million vaccine doses produced annually are exported to other African and Middle Eastern countries.
- An inactivated camel pox vaccine developed by Biopharma from a local strain has been used in Morocco, Western Sahara, Algeria, Tunisia, Libya, Mauritania, and the Middle East.

- In collaboration with WHO and the Institut Pasteur, Biopharma is developing an inactivated rabies vaccine for a national rabies eradication program. The program aims to vaccinate 70 percent of the dog population, which acts as the vector and reservoir for rabies in North Africa.
- Biopharma stockpiles the equivalent of 2 million bovine doses of foot and mouth disease (FMD) vaccine as a concentrated, inactivated antigen that could be manufactured within 48 hours. While Morocco has been free from FMD without vaccination since 2006, Biopharma performs large serological surveys and looks for evidence of FMD virus circulation using enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR) tests.
- Biopharma stores a national collection of cells, bacteria, and viruses and conducts active surveillance of circulating strains for many diseases to ensure correct vaccine formulations.

Dr. El Harrak then described some of Biopharma's constraints. Many laboratories are in old buildings that require structural improvement. For example, many use centralized rather than terminal HEPA filters, and fluid distribution and waste treatment systems are in poor condition. Also, the facility itself is currently located in a residential area inconsistent with the risk associated with its activities and biosecurity requirements.

Biopharma plans to move and build a new laboratory according to international good manufacturing practice (GMP) standards. The new facility will have 1,850 m^2; 1,330 m^2; and 400 m^2 of BSL-3, BSL-2, and clean room space, respectively. Biopharma is also trying to become a World Organisation for Animal Health (OIE) Reference Laboratory for bluetongue disease, sheep pox, African horse sickness, and peste des petits ruminants.

Veterinary Serum and Vaccine Research Institute in Egypt: Present and Future Prospects

Seham El-Zeedy (Veterinary Serum and Vaccine Research Institute [VSVRI], Egypt) described the past, current, and future efforts of VSVRI to improve animal health in Egypt.

Dr. El-Zeedy started her presentation by explaining that VSVRI was established in the Abbassia district of east Cairo in 1903 to produce vaccines and antisera to protect cattle against rinderpest. Since its founding, VSVRI's mission and facilities have expanded, and the institute now has multiple goals: producing highly effective veterinary vaccines, sera, and diagnostic reagents using both reference and local isolates; producing cost-effective combination vaccines; and conducting research for improved veterinary vaccines, sera, and diagnostic reagents.

VSVRI currently produces both live and inactivated vaccines for large animals and poultry as well as a number of antigens and sera. Overall, the facility has over 600 workers including a research team of more than 200 that studies both viral and bacterial pathogens. VSVRI cooperates with the United States Naval Medical Research Unit 3, the United States Biosecurity Engagement Program (BEP), the Food and Agriculture Organization of the United Nations (FAO), OIE, and WHO.

She also said that VSVRI uses standard design principles for safety and security. The facilities include primary containment barriers that protect workers from the agents (e.g., gloves, gowns, masks, biological safety cabinets [BSCs], and vaccines), secondary containment barriers that separate the agents and the outside environment (e.g., air tight rooms, showers, sewage treatment, and proper waste disposal), and tertiary containment barriers (e.g., walls, fences, security, and quarantine rules).

In the future, Dr. El-Zeedy would like to see increased use of molecular biology for improving vaccines and diagnostic reagents; more innovative veterinary vaccines, sera, and diagnostic reagents; and expanded training on current technologies. Her plans call for the production facilities to be certified according to GMP requirements for veterinary vaccine

production, and she also expects on-going upgrades to convert an existing laboratory to BSL-3 standards to be completed soon.

The new BSL-3 facility is being built in response to Egypt's avian influenza (AI) outbreaks. Egypt's first highly pathogenic avian influenza (HPAI) outbreak was announced in February 2007, and the country began vaccination in March 2007 using imported inactivated H5N1 and H5N2 vaccines. As the disease is now endemic and controlling poultry outbreaks is the key to preventing human AI infections, she explained that Egypt needs a national laboratory that can produce vaccines effective against the local AI strains. To meet this need, VSVRI is upgrading an existing laboratory to BSL-3 standards to create the appropriate protection for working with HPAI. The new laboratory will also manufacture FMD vaccine.

In preparation for the new BSL-3 facility, VSVRI is developing a training program that will ensure that all personnel meet institutional expectations for working in high-containment labs. In general, all personnel entering the containment facility will receive job-specific training prior to starting work, and all training will be documented.

The International Centre of Medical Research of Franceville: A Medical Research Center in the Heart of a Tropical Rainforest

Jean-Paul Gonzalez (International Centre of Medical Research of Franceville [CIRMF], Gabon/France) described the history of CIRMF and the work the facility's unique location makes possible.

Dr. Gonzalez started by relaying the history of the CIRMF, which was founded by Omar Bongo, the President of Gabon, in 1974. The facility, which covers 98 acres, became operational in 1979 and added a BSL-3 lab in 1982 for HIV studies. Animal biosafety level (ABSL) -3 primate containment structures followed in 1985, and a BSL-3+ was developed in 1996 to facilitate Ebola research after Ebola outbreaks in Gabon. In 2011 CIRMF began operating a unique BSL-4 glove box[1] whose mission is to diagnose and characterize BSL-4 agents on a regional level. Altogether, CIRMF currently has 60 scientists, 1,500 m^2 of labs, 2 field stations, a primate center with 450 apes, and living accommodations for scientists on site. It receives funding from the Gabonese government (20 percent), the oil company TOTAL-GABON (65 percent), the French Ministry of Foreign and European Affairs (10 percent), and international institutions (5 percent).

Dr. Gonzalez described the work of several of CIRMF's seven research units: emerging viral diseases, retrovirology, medical parasitology, health ecology, sickle cell disease, medical biology and public health, and primatology. The emerging viral diseases research unit, for example, studies viral biodiversity of the Central African tropical rainforest, the emergence of human viral diseases, and the fundamentals of cross-species transmission. Past work examined the phylogeny and natural history of Ebola, suggesting that fruit bats serve as a reservoir for the virus and then infect both great apes and humans. Work also investigated asymptomatic infections and deep immunosuppression caused by the virus. Research tools and methods include molecular virology, *in vivo* immunology, human cohort studies, animal trapping, entomology, and field investigations. In general, CIRMF's field investigations survey

[1] Adding to the confusion is the range of design options used in building such facilities. For instance, the maximum containment labs may be self-contained suites accessed through airlocks and decontaminating showers by researchers wearing one-piece, positive-pressure suits with their own life-support systems. On the other hand, some BSL-4 labs may consist of little more than small glove box isolators in which researchers access samples through glove-enclosed portals.See: *http://www.engineering.com/Library/ArticlesPage/tabid/85/articleType/ArticleView/articleId/92/Level-4-Containment-Labs.aspx*

both of the nearby ecosystems (tropical rainforest and savannah), as each environment has unique pathogens and diseases.

Dr. Gonzalez also highlighted the work of the retrovirology unit and the primate center. The retrovirology unit, which uses BSL-3 facilities, has worked on human immunodeficiency virus (HIV) diagnostics and genotyping, simian immunodeficiency virus (SIV) phylogeny and transmission, retrovirus discovery and characterization, and antiviral drug testing. The primate center, whose facilities include an ABSL-3 lab and a surgery room, has studied anti-HIV drug therapies, characterized the physiopathology of SIV in Mandrill monkeys, and developed a vaccine against Chikungunya virus using macaques.

Dr. Gonzalez provided additional information about CIRMF during the session on BSL-4 labs (Chapter 8).

BREAKOUT SESSION 3: EASTERN EUROPE AND WESTERN ASIA
Chair: Greg Smith
Rapporteur: Alison Hottes

In this session, participants heard talks about containment labs in various stages of their life cycles. Two of the labs have long histories; one is rejuvenating containment facilities that have existed since the lab's founding, while the other is in the last stage of adding BSL-3 facilities. The other two presentations described new labs being built through collaborations between the host country and a foreign partner to address specific regional needs. One is nearing certification, and the other is stalled in the last portion of the design stage. **Greg Smith** (Commonwealth Scientific and Industrial Research Organisation, Australian Animal Health Lab, Australia), the session chair, then led a discussion that elaborated on issues introduced during the talks.

BREAKOUT SESSION PRESENTATIONS

Georgian Central Public Health Reference Laboratory

Colonel Arthur Lyons (United States Army Medical Research and Materiel Command, United States) described the mission and facilities of the Georgian Central Public Health Reference Laboratory (CPHRL) and shared lessons learned from each stage of the development process.

Colonel Lyons explained that CPHRL, which is a collaboration and partnership between the United States and the Republic of Georgia, seeks to promote public and animal health through infectious disease detection, epidemiological surveillance, and research for the benefit of Georgia, the Caucasus region, and the global community. CPHRL will augment current surveillance and diagnostics initiatives with BSL-3 facilities, genomics capabilities, and a vivarium; serve as the hub of a Central Asia regional network; and engage in research on bacteriophages, wound healing, and vector-borne diseases. CPHRL will focus on capacity building and will collaborate with both national and international partners including the National Center for Disease Control and Public Health; the Laboratory of the Ministry of Agriculture; the George Eliava Institute of Bacteriophage, Microbiology, and Virology; the United States Centers for Disease Control and Prevention (CDC), and the World Health Organization (WHO).

Colonel Lyons reported that Georgia and the United States broke ground in 2004, completed construction in 2010, and hope to certify the lab by the end of the 2011. The building (7,500 m^2 including 2,500 m^2 of lab space) contains two separate BSL-3 laboratory suites: one for animal pathogens and one for human pathogens. The human pathogen lab contains animal-

holding rooms that can operate at either BSL-2 or BSL-3 levels. The facility also contains BSL-2 space, a BSL-2 laboratory training suite, and cell culture and media preparation rooms. The surrounding area includes a perimeter fence, an incinerator building, fuel tanks, water tanks, and a natural gas line. The United States Army Medical Research and Materiel Command expects to occupy a portion of CPHRL permanently as a guest of the government of Georgia, and the United States will bring in experts to train Georgians to both establish and maintain operations.

Colonel Lyons then shared lessons learned from each stage in the process. He feels that during the planning and coordination stage it is important to:

- Obtain political buy-in and involve the appropriate political level, as ultimately, Ministers and politicians will need to budget for the lab and defend it publicly;
- Obtain scientific buy-in and have the right partner country scientific personnel begin planning the scientific work and continue planning throughout the construction process to facilitate a quick start-up upon completion; and
- Consider starting public awareness outreach.

During the design phase, Colonel Lyons recommended the following:

- Engage a commissioning agent (preferably 3rd party).
- Document the Basis of Design and describe why and when decisions were made; this will help the project team make good decisions during construction.
- Realize that personnel changes within program offices and the partner nation government will complicate the task.
- Perform a comprehensive utility study.
- Design for sustainability, which includes building in access for maintenance and realizing that biocontainment labs generally have high operating costs.

He believed that the following advice and insights are useful for the construction phase:

- Biocontainment labs are not the same as other complex industrial facilities, so contractors and subcontractors should have appropriate experience with biocontainment labs.
- Local availability of specified parts will be limited, and decisions on using alternate parts or waiting for parts from overseas can be critical to success. The commissioning agent can provide critical input on decisions that may impact commissioning and certification.
- A dedicated project oversight team should be on-site to ensure quality while helping to maintain cost and schedule.

For the commissioning and certification stage, Colonel Lyons recommended scheduling sufficient time (12-18 months minimum) and realizing that the lab certification process in many countries is evolving.

Planning a Cost-Effective and Sustainable BSL-3

Ken Ugwu (Global Partnership Program, Canada) described lessons learned during Canada's recent efforts to engage with the Kyrgyz Republic.

Mr. Ugwu opened by saying that as part of its $1 billion commitment to the Global Partnership Against the Spread of Weapons and Materials of Mass Destruction, which includes $100 million for biological non-proliferation, Canada wanted to undertake a large-impact project

in the former Soviet Union. Canada ultimately chose to assist the Kyrgyz Republic, which has endemic diseases of terrorist concern (e.g., plague, anthrax, and foot and mouth disease), a large number of substandard and insecure labs, and numerous poorly documented pathogen collections. Canada and the Kyrgyz Republic ultimately agreed to undertake a comprehensive assistance program including development of national biosafety guidelines, training, a twinning program with Canada's Winnipeg lab, scientific engagement, help establishing the Biosafety Association for Central Asia and the Caucasus, interim security upgrades, and a new biological containment laboratory.

Early on, the Canada/Kyrgyz Biological Laboratory Working Group (BLWG) was formed to oversee all phases of lab design, construction, and operation. The BLWG, which included participants from all Ministries, underwent an extensive education and training program on the complexities of BSL-3 labs, met every 6 weeks in the Kyrgyz Republic, and worked closely with architects and engineers. During the design process, the BLWG also formulated a sustainability and transition plan that made provisions for long-term financing. The BLWG worked with a community liaison group that included representatives from the Kyrgyz community at large, the city of Bishkek, the province of Chui, the Kyrgyz government, non-governmental organizations (NGOs), academics, and the health and agricultural communities. Additionally, an International Peer Review Group provided expert advice.

Mr. Ugwu also described a number of steps the project took to combat the local scarcity of technical equipment and expertise in an effort to reduce costs and improve sustainability. As much as possible, the facility was planned in accordance with the capabilities of local trades and used local materials. To that end, the project team identified local factories that could manufacture needed equipment (e.g., high-efficiency particulate air [HEPA] boxes), and the architectural and mechanical team made many visits to investigate local capacities and materials.

Mr. Ugwu also presented a number of decisions that were made to both control costs and improve the resulting facility:

- To allow flexibility and the consideration of several BSL-3 design options, Canada chose to use WHO guidelines.
- The BLWG worked to reduce uncertainty about the desired lab capabilities as uncertainty leads to overdesign and increased upfront and maintenance costs.
- Most of the lab space was zoned for BSL-2 work, with BSL-3 space limited to essential functions; architectural and mechanical components of the BSL-2 and support spaces were not over-designed.
- The BLWG targeted the most expensive components—mechanical and electrical—for savings. (Structural, architectural, and fixed equipment are comparatively inexpensive.)
- Human and animal work was placed in the same building to allow the groups to both share common services and to collaborate.
- Instead of building a large vivarium, animal rooms were integrated into the BSL-3 space. Animal containment was designed to use simple filter bonnet cages and flexible isolators instead of a ventilated rack system. While frequent cage changes would be required, the inexpensive labor in the region made the decision economical.
- Workflow analysis was used to optimize the flow of people and wastes. Heating, ventilation, and air conditioning (HVAC) and effluent treatment facilities were placed to limit expensive ductwork and piping and to reduce the length of pipes to maintain.
- After extensive discussion about ventilation, the BLWG chose a simple volumetric offset flow that creates a "leaky" BSL-3 over the more complex differential pressurization control, which produces an airtight facility.
- Type IIB2 BSCs were limited in favor of type IIA2 BSCs.

Mr. Ugwu concluded by noting that the project is on hold due to Kyrgyz Republic politics.

Why We Need a BSL-3 Laboratory at the Pendik Veterinary Control and Research Institute

Aysen Gargili (Marmara University, Turkey), delivering a presentation that was prepared in cooperation with **Ayse Selma Iyisan** (Pendik Veterinary Control and Research Institute, Turkey), described the changes that have taken place at Pendik Veterinary Control and Research Institute in Istanbul, Turkey from its founding in 1894 as a facility for the production of cattle plague serum to its present installation of a BSL-3 lab.

Currently the Pendik Institute works under the Turkish Ministry of Agriculture and Rural Affairs (MARA) and has ties with the Food and Agriculture Organization of the United Nations (FAO), World Organisation for Animal Health (OIE), the European Union (EU), and the WHO Mediterranean Zoonoses Control Center. In addition to its research, diagnostics, education, publishing, and project development duties, Pendik Institute also serves as the national reference lab for sheep and goat pox, animal brucellosis, animal mycoplasmosis, anaerobic diseases, *Theileria annulata*, Marek's diseases, and the detection of drug residues. Pendik Institute also produces 17 vaccines and 22 serums, antigens, and biological materials.

As one of three institutes in Turkey with avian influenza (AI) virus identification capabilities and one of eight with the ability to isolate virus, Pendik Institute has played a major role in detecting and combating AI in Turkey. The first case of AI in Turkey was reported on 5 October 2005 and between 25 December 2005 and 26 February 2007, there were 247 confirmed cases in Turkey of which 246 were highly pathogenic avian influenza (HPAI) H5N1 virus and one of which was H7N1 virus. Overall, 217 outbreaks occurred in domestic poultry and 30 in wild birds. Both OIE and the EU were notified. Overall, Pendik Institute tested 2,278 samples for avian influenza and found 78 positive results.

In response to the outbreaks, an EU-funded project implemented by Conseil Santé helped the Turkish MARA and Ministry of Health formulate a coordinated preparedness and response plan.[2] The project's overall objectives were to minimize the threat to humans in Turkey posed by HPAI infection in domestic poultry and other animals, to diminish the burden of disease and loss of productivity, and to improve influenza pandemic preparedness. Specific tasks included developing and improving the regulatory framework, upgrading surveillance programs, strengthening veterinary services, and raising public awareness about good poultry keeping practices and biosecurity measures. As the three labs responsible for virus identification and pathogenicity characterization under the plan (Pendik Institute and labs at Bornova and Etlik) did not meet the safety recommendations for the proposed work, the General Directorate of Protection and Control decided to upgrade them to BSL-3 capabilities using World Bank funds.

Currently, the new BSL-3 lab at Pendik Institute is involved in the final stages of staff training and equipment installation. More information about the lab is available in Appendix D.

The History and Current Status of the Chumakov Institute of Poliomyelitis and Viral Encephalitides

Evgeniy Tkachenko (Chumakov Institute, Russia) described how the Chumakov Institute of Poliomyelitis and Viral Encephalitides has kept its focus aligned with the current public health threats to Russia.

[2] Technical Assistance to Avian Influenza Preparedness and Response. Available at: *http://www.kkgm.gov.tr/TR_06_AI_SV_new/English/start.htm*. Accessed August 29, 2011.

Dr. Tkachenko explained that Chumakov Institute was founded in 1955 within the USSR Academy of Medical Sciences as a center for the study of poliomyelitis. The Institute subsequently produced both inactivated and oral poliomyelitis vaccine. Using oral poliomyelitis vaccine, the USSR started mass immunizations in 1959, and in 2002, WHO declared Russia free of poliomyelitis. Unfortunately, poliovirus has since been reintroduced to Russia, likely from Tajikistan. Chumakov Institute hosts the WHO Regional Reference Polio Laboratory for Russia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Tajikistan, Turkmenistan, Uzbekistan, and Ukraine.

In addition to polio vaccine, Chumakov Institute has also produced vaccines against yellow fever, influenza A, hepatitis A, rabies, tick-born encephalitis, Crimean-Congo hemorrhagic fever (CCHF), and measles as well as cell culture media and hantavirus test-systems.

As the diseases of epidemiological importance to Russia have changed, Chumakov Institute has modified its research agenda accordingly. For example, Russia now has approximately 3 million carriers of hepatitis B virus, which is currently one of the Institute's areas of emphasis. The impacts of hemorrhagic fever with renal syndrome, CCHF, and West Nile virus on Russia have also increased recently and are now garnering more scientific attention.

Dr. Tkachenko noted that Chumakov Institute has taken a number of steps to maintain and improve its facilities. For example, the Institute recently updated the inventories of its collections of nine virus families that range from hazard groups 2 through 4 in the Russian system. (In the Russian system, hazard group 1 organisms are the most dangerous and hazard group 4 are least dangerous.) Out-of-date infrastructure in the research complex was renovated and a lab for working with hazard group 2 organisms was created and registered according to Russian national safety requirements. The certification was expensive (500,000 rubles) and will soon need to be renewed.

As a reminder of how dangerous the work can be, Dr. Tkachenko ended by showing a picture of six researchers, including himself, who had been infected with hantavirus or arenavirus during their research.

SYNTHESIS OF BREAKOUT GROUP DISCUSSISONS

Throughout the discussion, many participants remarked on the benefits of involving everyone including architects, designers, the lab director, scientists, contractors, certifiers, and the community from the very start and keeping them involved throughout the process. Additionally, individuals made comments on four main topics areas:

Planning, Design, and Construction

Many participants added to the recommendations offered during the presentations. In deciding whether or not a lab should have BSL-3 capabilities, one person argued that while a country may need to study endemic agents that routinely cause health problems, which typically requires BSL-3 facilities, it may be sufficient to simply diagnose imported diseases using molecular techniques in BSL-2 conditions. Others suggested expecting problems and budgeting for them, involving a workflow specialist, training local craftsmen, and identifying good contractors and project managers through a pre-qualification mechanism. Someone else warned that architectural and engineering consultants, who typically receive a percentage of a facility's cost, have a strong incentive to overdesign, which can increase both upfront and maintenance costs.

Maintenance

Much of the discussion about maintenance highlighted the difficulties in finding funds and expertise. Several people observed that obtaining money for new labs was much easier than finding money for maintenance, as maintenance is often considered overhead and the return on specific expenditures is often difficult to quantify. One person advocated creating a facility's maintenance plan as part of the design and construction process, and another observed that there was nothing worse than a good lab in bad condition.

Many people expressed the opinion that ideally parts and qualified workers should be available locally but are often not. Several people noted that more countries are now producing their own HEPA filters and components and that many donors are training local technicians to service BSCs. One person indicated that it might be useful to have a group that certifies BSL-3 equipment in Africa, and others suggested requiring suppliers and manufacturers to train local maintenance and engineering personnel as part of their contract.

Several people also commented on the often-ignored requirement to certify BSCs annually. One person wondered whether expensive, annual certification was really necessary and wondered if simple tests to detect reduced cabinet function could be devised. Another questioned whether workers, lab managers, or countries themselves should take responsibility for equipment, and asked if countries needed legislation to force annual certification.

Certification

Many felt that certification was desirable in theory but pointed to a number of practical problems. The largest difficulty reported was in finding qualified certifiers who were independent of those who built and maintain the lab. Several commented on the lack of competent local certifiers and the prohibitive expense in bringing in external certifiers. One person suggested that certification groups should contain multidisciplinary expertise. Another wondered if perhaps WHO or another organization could oversee the certification of these inspectors.

A frequently expressed frustration was in determining which standards should be used during a certification. Some proposed certifying against a lab's written SOPs, regardless of whether or not they conform to external standards. Others noted that for lack of better options, certification is often done against the WHO Laboratory Biosafety Manual (LBM) or BMBL guidelines.

Training and Human Capacity

Many people remarked that "laboratories" are not just buildings, but also the humans who work in them and that improving the practices of lab workers is often the easiest, most effective, and least expensive way to improve safety and security. Nonetheless, other individuals indicated that often skilled workers are not available, good training is frequently not offered, and that even among trained workers complacency can be a problem. Someone else suggested that "biosafety professional" is not perceived as an attractive career path.

A number of people described difficulties in retaining qualified workers:

- Experienced people may leave a developing country for higher paying jobs abroad.
- Individuals may change jobs when a grant runs out.
- New, well-equipped labs may drain qualified people away from labs in other parts of the country leaving pre-existing labs understaffed.

- Pregnant women may stop working in containment labs due to perceived risks (One participant supported this practice).

Participants then offered a range of suggestions. One person suggested that initial training emphasize routine tasks, such as the proper use of personal protective equipment, and another suggested that some entity certify people as being qualified to work in BSL-3 labs. One argued that institutions, in spite of the expense involved, needed to be willing to fail people during internal training; another added that people who don't follow rules should be removed. Someone else felt that new labs should be willing to train students rather than taking trained people from elsewhere.

6

PUBLIC HEALTH NEEDS: COSTS, EFFECTIVENESS, AND BIOSAFETY REQUIREMENTS FOR DIAGNOSTIC PROCEDURES (BREAKOUT SESSIONS)

This set of breakout sessions sought to (1) describe the public health needs lab workers are attempting to meet, the range of tools being utilized, and the challenges regularly encountered and (2) examine the spectrum of molecular, immunological, and culture-based assays available as well as their associated costs, effectiveness, and biosafety requirements. To inform the discussion, participants in each session first listened to several talks that described examples of the diagnostics currently employed.

BREAKOUT SESSION 1: HUMAN DISEASES PART 1
Chair: Ingegerd Kallings
Rapporteur: Alison Hottes

This session opened with talks that both illustrated the application of current biosafety recommendations to diagnostics and surveillance and looked ahead to the type of detailed, protocol-specific biosafety guidance that might be available in the future. The first talk portrayed the changing set of diagnostic tools available for clinical work and the ability of a BSL-3 lab to allow a clinical group to perform complimentary research. The second talk described a large-scale surveillance operation that seeks to understand influenza strain dynamics. The final talk gave an example of the potential for a detailed risk assessment to provide more nuanced biosafety guidance than that available using the standard World Health Organization (WHO) or "Biosafety in Microbiological and Biomedical Laboratories" (BMBL) four level systems. After the talks concluded, **Ingegerd Kallings** (Swedish Institute for Communicable Disease Control, Sweden) led a discussion.

BREAKOUT SESSION PRESENTATIONS

Preparedness for the Detection of Emerging and Re-emerging Pathogens in Croatia

Alemka Markotić (University Hospital for Infectious Diseases, Croatia) described the diagnostic tools she uses at University Hospital for Infectious Diseases which includes both the largest hospital in the region and a reference center with a new BSL-3 lab.

Dr. Markotić explained that she does both clinical and research work on hantaviruses, Dengue fever virus, tick-borne encephalitis, West Nile virus, Chikungunya virus, and influenza A using several methods including point-of-care (POC) tests, enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) tests, sequencing, and cell culture. She and the other members of her lab staff generally follow United States Centers for Disease Control and Prevention (CDC) recommendations except those that pertain to the United States Select Agents program, meaning that serology is done in BSL-2 conditions in a biological safety cabinet (BSC) and that molecular tests start in BSL-2 conditions and then move to a molecular lab. Cell culture and virus isolation, which are typically part of research, not clinical work, are done in BSL-3 conditions except for small quantities of Dengue virus that are grown and handled in the BSL-2 lab.

Dr. Markotić indicated variable levels of satisfaction with POC tests. When she initially tried using POC tests to detect Puumala and Dobrava hantaviruses, she experienced too many false positives; recently, however, the quality of commercial tests has improved and she has resumed using them. She also uses POC tests to look for influenza A, Dengue fever virus, and Chikungunya. Dr. Markotić emphasized that while POC tests in conjunction with a clinical evaluation can serve as a valuable early indicator, she always proceeds with additional confirmatory testing.

Dr. Markotić also compared the costs of various techniques. For example, given the short shelf life of many ELISA reagents and the frequency with which she does the tests for clinical work, she indicated that PCR tests are comparatively cheaper for her lab. She reported mainly using ELISA tests for research projects when she knows the reagents will be used before they expire. Although University Hospital for Infectious Diseases has in-house sequencing capabilities, she normally uses the equipment at the Institute for Biological Services, which is cheaper. She noted, however, that the cheapest option is to send the samples to South Korea. Dr. Markotić pointed out that, in general, costs in Croatia are extremely high, and reagents often cost 5-6 times more than they would in the United States.

She explained that her research uses a number of culture-based techniques that are performed in BSL-3 conditions and that she would like to pursue more immunopathogenesis research. In particular, she developed a research model for hantaviruses using 293-HEK cells (Markotic et al., 2003). Resource limitations have, however, put this research on hold. Her lab, however, is currently working to develop molecular tests for Crimean-Congo hemorrhagic fever (CCHF), other hemorrhagic fevers, poxvirus, and rickettsia. As the Croatian Ministry of Health has limited opportunities that support research, Dr. Markotić indicated that she relies on international collaborations and foreign research grants for support.

Biorisks Connected with Wild Birds: Results of Avian Influenza Virus Surveillance in Southwest Siberia (Russia) in 2010

Alexander Shestopalov (State Research Center of Virology and Biotechnology, Russia), whose division monitors influenza in humans, wild birds, and poultry and contributes their data to WHO, described his lab's efforts to understand the dynamics of highly pathogenic avian influenza (HPAI) in Eurasia.

Dr. Shestopalov started by explaining that southwest Siberia contains many lakes, three major flyways for migrating birds, and played an important role in the 2005 expansion of influenza A, H5N1 in Eurasia. He believes that the lakes and rivers in the region play an important role in the circulation of avian influenza (AI) and that by monitoring influenza activity in migratory and resident bird there, they could provide an early warning system for HPAI outbreaks in birds in Eurasia.

In 2010, his lab isolated 32 AI viruses from 743 samples collected in western Siberia. Phylogenetic subtyping using PCR and sequencing indicated that 10 were H3N8, 4 were H3N6, and 8 were H4N6, while 10 could not be typed.

Another of the lab's datasets demonstrated that the H5N1 viruses present on Uvs–Nuur Lake in Mongolia near the Russian border shifted from clade 2.2 to clade 2.3.2 (evolutionarily distinct groups) between 2006 and 2009-2010. Hemagglutination inhibition assays using sera from ferrets showed no cross-reactivity between either virus and the opposite sera, suggesting that the viruses produce distinct immunological responses and display distinct antigens. As such, Dr. Shestopalov proposed that the current circulation of clade 2.3.2 and the disappearance of clade 2.2 could be explained by antigenic drift of the hemagglutinin under the pressure of population immunity in the natural host species. Clade 2.3.2 viruses were subsequently found in Russian in 2009, Bulgaria and Romania in 2010, and Japan in 2011, illustrating the potential for the region to function as an early warning system.

Biosafety Recommendations for Laboratory Testing for TB

Thomas Shinnick (Division of TB Elimination, United States CDC) described the Global Laboratory Initiative's (GLI) soon-to-be-finalized consensus guidance for tuberculosis (TB) lab procedures.

Dr. Shinnick started by explaining that TB lab workers are at a 3-fold to 9-fold higher risk of becoming infected with *Mycobacterium tuberculosis* than other lab workers and that infection often results from the unrecognized production of infectious, bacteria-containing aerosols, although infection can also occur in other ways, such as through needle sticks or contact with broken skin. He also reminded the audience that while TB is classified as a risk group 3 organism, different protocols for a single agent may necessitate the use of precautions from different biosafety levels.[1]

Dr. Shinnick explained that GLI performed a systems-based risk analysis and divided TB procedures into one of three sets depending on whether they posed a limited, moderate, or high risk of generating infectious aerosols.

GLI classified direct acid-fast bacillus (AFB) smear microscopy, which involves few cells in a viscous material that impedes aerosolization, as a limited risk procedure.[2] As such, GLI feels AFB smear microscopy can be done on an open bench in a laboratory with restricted access. The laboratory should have adequate ventilation, meaning 6-12 air changes per hour (ACH) from either natural or mechanical ventilation with directional airflow from the worker to the sample to the exterior. Infectious material should be disposed of properly.

In general, however, GLI regards sputum specimen manipulation for smear, culture, or molecular tests as a moderate-risk activity and recommends precautions like separating labs from public areas and restricting access. Surfaces should be impermeable for easy cleaning, infectious material should be disposed of properly, windows should be closed, and air (6-12 ACH) should flow into the lab without recirculation to non-lab areas. Properly installed and annually certified Class I or II BSCs should be used for all open manipulations of agents. Exhaust should be directed outside through a thimble fitting (preferred) or a hard duct; exhaust from a properly functioning BSC may be recirculated into the room. Aerosol-containment rotors should be used for centrifugation and opened in a BSC.

Finally, GLI classified work with cultures, which includes virtually all research, as high-risk due to the extreme likelihood of generating infectious aerosols while manipulating liquid suspensions. The recommendations are similar to those for moderate risk, except an autoclave should be available on site, the lab should have a double door entry (not necessarily an airlock), and windows should be sealed, not just closed. The ability to seal the lab for fumigation, however, was not deemed necessary by GLI; once TB settles it is difficult to re-aerosolize, so making the room amenable to surface decontamination was judged sufficient.

Dr. Shinnick reflected that in general, the new guidance does not map perfectly to any of the four generic BSL levels and represents an effort to move away from the traditional biosafety level boxes.

He closed by mentioning that the GLI expert committee is also considering suitable lab floor plans as well as specific recommendations for appropriate respirator usage, for human immunodeficiency virus (HIV)-positive technicians, and for samples from known or highly suspected extremely drug-resistant (XDR) TB patients.

---

[1] Current guidance on TB work is available in the BMBL (United States HHS, 2009; see pp. 145-147).
[2] GLI also considers Cepheid's Xpert® MTB/RIF molecular test limited risk.

BREAKOUT SESSION 2: HUMAN DISEASES PART 2
Chair: Peter Palese
Rapporteur: Michael Callahan

This session opened with a talk that described the recent outbreak of *Escherichia coli* in northern Germany and the associated epidemiological and diagnostic work. While containment labs are not ordinarily used to process *E. coli* specimens, the experience illustrates many of the challenges associated with emerging infectious diseases, including the need to increase hospital capacity during an outbreak, characterize the causative agent, and identify the outbreak's source. The second talk described a diagnostic network for influenza and emerging infectious diseases. The final talks presented the range of diagnostic tests available and the associated precautions routinely employed for two diseases: severe acute respiratory syndrome (SARS) and Crimean-Congo hemorrhagic fever (CCHF). Following the talks, **Peter Palese** (Mount Sinai School of Medicine, United States) led a discussion.

BREAKOUT SESSION PRESENTATIONS

EHEC O104:H4 in Germany 2011: Large Outbreak of Bloody Diarrhea and Haemolytic Uraemic Syndrome by Shiga Toxin-Producing E. coli via Contaminated Food

Reinhard Burger (Robert Koch Institute [RKI], Germany) described Germany's recent outbreak of enterohaemorrhagic *E. coli* (EHEC) and the associated public health response.

Dr. Burger started by updating the audience on the then on-going outbreak, which included an unusually high incidence of haemolytic uraemic syndrome (HUS). He indicated that as of 7 July 2011, Germany had recorded 3,322 cases of EHEC gastroenteritis that did not include HUS and 859 cases that did. By that time, the outbreak had resulted in 49 deaths. He also noted that Sweden, Denmark, and France had reported multiple cases and that 14 additional countries had reported single cases. He then walked the audience through a timeline of RKI's response to the outbreak (Box 6-1).

Once the outbreak was recognized, Dr. Burger indicated that RKI enhanced EHEC/HUS surveillance. They instituted daily transfer of normal surveillance data, which they augmented with laboratory surveillance of positive EHEC tests and by requesting reports of emergency cases with bloody diarrhea admitted to hospitals.

Dr. Burger then elaborated on the epidemiological investigation, which involved over 85 staff members. The group's early analyses, which were later found to be erroneous, suggested that Spanish cucumbers were the source, and the resulting decrease in consumption caused between 80 and 200 million Euros in losses. Later analyses used novel techniques to obtain more accurate information, including using billing data and digital photographs to remind cases and controls what they ate at a restaurant.

Box 6-1
Initial Events in RKI's Response to Germany's 2011 EHEC Outbreak

May 19: RKI received a call from the Hamburg health department and notified the German Federal Institute for Risk Assessment and the Federal Ministry of Health.[a]

May 20: RKI visited Hamburg and interviewed patients and local public health authorities.

May 21: RKI passed information about the qualitative role of vegetables in the outbreak to the Food Safety Authorities.

May 22: RKI warned WHO and local public health authorities and informed the German Press Agency about the possible involvement of uncooked vegetables.

May 23: RKI began publishing information on their website. Polymerase chain reaction (PCR) tests for the responsible pathogen became available.

May 24: The first official International Health Regulations (IHR) notification took place. The pathogen's serotype was identified as O104.

May 25: RKI identified the pathogen and advised northern Germany to avoid uncooked tomatoes, cucumbers, and lettuce.

[a] German authorities had tracked an increased incidence of HUS since May 2, 2011. See: Outbreak Notice. Shiga toxin-producing E. coli O104:H4 infections in Germany. June 3, 2011. Available at: http://www.vdh.state.va.us/clinicians/pdf/06-03-11%20Clinicians%27%20Letter%20-%20CDC%20Health%20Alert%20Shiga%20Toxin.pdf.

Dr. Burger indicated that the case control studies ultimately pinpointed bean sprouts as the source of the German outbreak, and subsequent cluster and traceback analysis linked the sprouts to a single farm. Bacteriological screening of over 10,000 samples of sprouts, seeds, and materials from the production site, however, produced only a single positive result. Additional work attributed the French outbreak to Egyptian fenugreek seeds and indicated that the German sprout producer and the French seed distributer had a common supplier. As a result of the investigation, imports of Egyptian seeds and beans were temporarily banned.

In addition to surveillance and epidemiology, Dr. Burger indicated that RKI also contributed communications and microbiology expertise to the effort. Seven staff members oversaw communications efforts that included press conferences, outreach to public health authorities, and dissemination of accurate information through the RKI website. Over 10 staff members engaged in primary and reference laboratory typing, and microbiological characterization of the strain indicated that the organism was unusually adherent to the intestine, produced Shigatoxin 2, and had an unusual antibiotic resistance profile. Dr. Burger noted that the strain was likely of natural origin.

In conclusion, Dr. Burger mentioned that retrospective analysis of case reports indicated that it took about two weeks to detect the outbreak and that identifying the source then took another three weeks. By way of comparison, he noted that investigations of similar outbreaks in Japan in 1996 (*E. coli* in radish sprouts) and in the United States in 2008 (*Salmonella* in chili peppers) took longer to accomplish each of those milestones.

Biosafety and the Southeast Asian Clinical Infectious Diseases Network

Rogier van Doorn (Oxford University Clinical Research Unit, Netherlands) described the present and future work of the Oxford University Clinical Research Unit's Ho Chi Minh City, Vietnam (OUCRU-HCM) facility.

Dr. van Doorn opened by saying that the OUCRU-HCM is part of the Southeast Asian Clinical Infectious Diseases Network (SEAICRN), which also has facilities in Thailand, Indonesia, and Singapore. He explained that SEAICRN works to advance the scientific knowledge and clinical management of influenza and emerging infectious diseases through integrated, collaborative clinical research and to produce evidence that will inform health policies and clinical practice. As part of its pandemic preparedness efforts, the network also builds public health capacity for the world.

He noted that OCURU-HCM receives core funding from the Wellcome Trust and started external collaborations in 1991. The facility has BSL-2 diagnostic labs for bacteriology, serology, and molecular virology; BSL-2 research labs for virology culture and molecular work; an insectary; BSL-3 labs for mycobacterial culture and virology; and a U.K. Specified Animal Pathogens Order 4 (SAPO4) containment lab for virology. The facilities were audited and certified by WHO and use closed circuit television, signage, and restricted access for security.

While the existing BSL-3 facilities opened in 2002, Dr. van Doorn explained that in 2008, the lab began the design, construction, and certification of a multifunctional BSL-3 suite that is expected to open in 2011. The new lab is funded by the United States National Institutes of Health (NIH) National Institute of Allergies and Infectious Diseases (NIAID) through SEAICRN and complies with United Kingdom laws and guidelines. An independent party, Oxford University, and Vietnam's Ministry of Health will all certify the lab for operation. He indicated that they are also considering applying to the United States Centers for Disease Control and Prevention (CDC) for Select Agent certification. The lab plans to work on hand, foot, and mouth disease and viral encephalitis and run outbreak investigations, a pathogen discovery program, and a zoonoses program.

In closing, Dr. van Doorn described the OUCRU-HCM's virology reference lab, which works to build state-of-the-art molecular diagnostic units and to disseminate low-biorisk diagnostics. The lab provides a centralized facility for developing assays and standard operating procedures, ordering reagents, and performing high-risk diagnostics involving culture. The reference lab is particularly experienced in influenza diagnostics and offers a range of molecular diagnostics including reverse transcription polymerase chain reaction (RT-PCR), in-house tests for resistance-associated mutations, Sanger sequencing, and pyrosequencing. The reference lab also performs culture-based susceptibility testing and microneutralization assays. The lab trains its staff on site and participates in external quality assessment programs.

SARS-Coronavirus: Diagnosis, Antibody Responses, and Biosafety Concerns

Cheng Cao (Beijing Institute of Biotechnology, China) characterized a range of diagnostic tests for SARS as well as related biosafety and biosecurity precautions.

Dr. Cao started by reminding the audience that the SARS epidemic that started in Guangdong Province in November of 2002 was the first time China had fought against a communicable disease caused by an initially, unidentified pathogen. In spite of intensive public health measures to identify and isolate patients, the outbreak caused more than 8000 cases (more than half in China) and over 700 deaths. Once the etiological agent was confirmed in early April 2003, he and others began developing fast, accurate laboratory diagnostics. Dr. Cao indicated that while China currently has around 30 BSL-3 labs, the small number of BSL-3 labs in China at the time and the lack of an accreditation system for the labs made the initial work more difficult.

Dr. Cao then described a number of the diagnostics that are currently available for SARS:

- RT-PCR assays convert viral RNA into complementary DNA, which is then amplified and detected. The technique requires specialized equipment, often suffers from low sensitivity, and contamination may cause false positives (Di et al., 2005). Since the technique looks for the virus directly instead of waiting for an immune response, it can be used earlier in an infection than other methods, but it cannot be used for retrospective tests.
- Enzyme-linked immunosorbent assays (ELISA) using monoclonal antibodies can look for antigen to the SARS coronavirus nucleocapsid protein (Di et al., 2005). As antigen appears before antibodies, the test is useful for early diagnosis. However, as the antigen becomes undetectable 20 days post onset of symptoms, the test, which does not require viral culture, cannot be used for retrospective work.
- Dr. Cao showed that immunofluorescence assays (IFA) could detect SARS antibodies in 90 percent of the patients 15 days after infection.
- ELISA assays using whole viral lysate as the antigen, like IFA assays, can detect SARS antibodies in serum. Dr. Cao reported that the technique has a higher false positive rate than the comparatively more difficult IFA.
- ELISA assays using recombinant nucleocapsid protein as the antigen can detect SARS in 68 percent of patients 6-10 days after the start of infection and in 90 percent of patients after 10-61 days (Shi et al., 2003). Unlike ELISA with whole viral lysate or IFA, viral culture is not required as the needed protein can be expressed in *E. coli*. Dr. Cao developed the technique in April 2003, and China's State Food and Drug Administration certified it soon after. Antibodies to nucleocapsid protein persist for months (Liu et al., 2004), allowing the assay to be used for retrospective work.

Dr. Cao also shared some biosafety and biosecurity concerns and advice. First, as SARS-coronavirus-like viruses are circulating in the Chinese and Slovenian horseshoe bat populations and the Nigerian leaf-nosed bat population, disease reemergence is a concern. Second, the 2004 laboratory leak in Beijing that resulted in 8 cases of SARS, including one death, and the SARS LAIs in laboratory workers in Singapore and Taiwan illustrate the importance of rigorously following safety procedures. To that end, Dr. Cao argued that SARS coronavirus and infected tissues must be manipulated only in BSL-3 labs by well-trained scientists and technicians. While serum tests can be done in BSL-2 labs in BSCs, he cautioned that sera from SARS patients should be incubated at 56°C for 30 minutes to inactivate the virus.

Dr. Cao also presented data showing the role of nucleocapsid protein in the immune response to SARS coronavirus.

Crimean-Congo Hemorrhagic Fever: Pakistan's Perspective

Birjees Mazhar Kazi (National Institute of Health, Islamabad-Pakistan) described the tests and the accompanying precautions the National Institute of Health in Islamabad, Pakistan uses for CCHF diagnosis.

Dr. Kazi explained that due to the prevalence of the tick vector, Pakistan experiences CCHF outbreaks and that the National Institute of Health, Pakistan tracks reported cases. Current diagnostic tools include immunoglobulin M (IgM) capture ELISA using a kit from Biological Diagnostic Supplies Limited, RT-PCR using a published protocol (Schwarz et al., 1996), and genetic sequencing. Dr. Kazi noted that although the National Institute of Health, Pakistan has the infrastructure and trained personnel for DNA sequencing, reagents for this

protocol are currently limited. Past techniques that are no longer used include electron microscopy, inoculation into suckling mice, and fluorescent microscopy.

When handling CCHF samples, the National Institute of Health, Pakistan employs a number of safety precautions. In general, separate designated areas with restricted personnel access are used for sample receipt, processing, and testing. Diagnostic samples are inactivated at receiving prior to moving them to the lab. The work itself is then done in BSL-2+ laboratories using enhanced personal protective equipment. Finally, waste is destroyed by autoclaving and incineration.

In the future, the lab plans to establish standard guidelines for diagnosis and to establish a separate core laboratory facility.

BREAKOUT SESSION 3: ANIMAL AND LIVESTOCK DISEASES
Chair: David Franz
Rapporteur: Fran Sharples

This session began with presentations describing the work of three institutions that provide surveillance and diagnostic services to both their home country as well as neighboring countries. The first two talks detailed the operations of networks that include high-containment facilities and are responsible for monitoring a wide range of animals for signs of many different diseases. In contrast, the final talk described the diagnostic tools at a lab developed to detect endemic risk group 4 agents without a BSL-4 lab. Following the talks, **David Franz** (MRIGlobal, United States) led a discussion.

BREAKOUT SESSION PRESENTATIONS

The Work and Capabilities of the High Security Animal Disease Laboratory at Bhopal, India

Gaya Prasad (Indian Council of Agricultural Research, India) described the range of diagnostics the High Security Animal Disease Laboratory (HSADL) is developing and using to detect and combat emerging and exotic diseases in India. He noted that the HSADL lab also serves Bangladesh, Nepal, Bhutan, and other nearby nations without analytical lab capabilities on a case-by-case basis subject to government authorization.

Dr. Prasad started by explaining that while India only has one veterinarian for every 20,000 animals, the government runs all veterinary hospitals allowing unusual livestock diseases to be detected and rapidly brought to government notice. The HSADL has operated as a BSL-3+ facility since its commissioning in 2000. With the help of the Food and Agriculture Organization of the United Nations (FAO) and the United Nations Development Program, the facility was recently upgraded to BSL-4 including an animal biosafety level (ABSL)-4 facility with isolators. The new BSL-4 lab allows the facility to work on Nipah virus and other dangerous pathogens.

Dr. Prasad noted that in its capacity as a World Organisation for Animal Health (OIE) reference lab for avian influenza, HSADL has tested over 450,000 samples since 2006 when HPAI H5N1 was first detected in domestic poultry. In addition to molecular and phylogenetic analyses of HPAI isolates, the lab also characterizes the pathogenicity of influenza isolates and engages in surveillance of migratory birds. HSADL developed an avian influenza database and a reverse transcription polymerase chain reaction (RT-PCR) test for the diagnosis of avian influenza H5N1.

HSADL has also been active in the field of swine influenza research and surveillance. The lab conducts antibody detection by hemagglutination inhibition and enzyme-linked

immunosorbent assays (ELISA) and detects strains and subtypes using RT-PCR and sequencing. Overall, sera from 401 pigs have been tested, and 76 were positive for H1N1 antibody. Additionally, 656 nasal swabs were tested, and H1N1 viruses were isolated from two samples.

In addition to its influenza work, HSADL also regularly tests cattle, buffalo, sheep, and goat samples for bovine viral diarrhoea (BVD) and border disease (BD) viruses. The lab isolated and characterized the BD virus using nucleotide sequencing, antigenic analysis, and transmission electron microscopy, and developed a monoclonal antibody-based ELISA test for the diagnosis of BVD virus in cattle and an immunoperoxidase-linked neutralization assay for the detection of neutralizing antibodies to BVD virus. The Department of Animal Husbandry, Dairying, and Fisheries' proposal for OIE reference lab status for BVD virus for HSADL is under the final stages of consideration by OIE.

Dr. Prasad also described a number of other diagnostics that HSADL has developed including a recombinant nucleoprotein-based ELISA test for the detection of porcine reproductive and respiratory syndrome virus antibodies in pigs and real-time PCR tests for the diagnosis of pseudorabies, porcine parvovirus infection, and malignant catarrhal fever. He concluded by mentioning that HSADL also works with international agencies such as FAO, the World Health Organization (WHO), and the International Consortium on Anti-Virals; domestic agencies; leading national pharmaceutical, research and development, and vaccine production firms; and national and international biosafety organizations.

Diagnostic Capabilities for Exotic and Emerging Animal Diseases of Mexico's Official Laboratory Network

Marco Antonio Rico Gaytán (Mexico-US Commission for the Prevention of Foot and Mouth Disease and Other Exotic Animal Diseases [CPA], Mexico) described the organization and diagnostic capabilities of CPA's laboratory network whose mission is to protect terrestrial and aquatic animals from exotic and emerging diseases.

Dr. Gaytán explained that the CPA network contains 13 molecular biology labs, 7 regional labs, and one BSL-3 lab that is located in Cuajimalpa in Mexico City. The molecular biology labs, which are all of the same design, are BSL-2 labs with some enhancements and run serology and molecular biology-based diagnostic tests including standard polymerase chain reaction (PCR), real-time PCR, sequencing (3 labs only), and ELISA tests using commercial kits. He noted that the National Services of Health, Safety, and Food Quality operate an additional three molecular biology labs and that each regional lab has specialized equipment and reagents and performs specific diagnostic tests. The BSL-3 lab was certified in 2006 by the University of Texas Medical Branch, which, in the absence of specific Mexican regulations, checked for compliance to the United States Department of Agriculture Manual and the Containment Standard for Veterinary Facilities from the Canadian Food Inspection Agency. The BLS-3 lab, which was renovated from a lab originally built in 1949, contains a number of biosecurity measures including fingerprint-based access control. The labs, particularly the molecular biology labs, are distributed throughout Mexico.

The network is currently responsible for the diagnosis of 33 diseases and performs a total of 110 tests of 20 different types. As such, the network has multiple ways to diagnose most diseases. The most common techniques are PCR (24 diseases), virus isolation in cell culture (19 diseases), ELISA (13 diseases), and virus isolation in laboratory animals (12 diseases). The CPA network also has a large number of people in the field who perform surveillance and technical training.

While noting that exact costs are difficult to establish, Dr. Gaytán estimated that the network, which receives funding from the Mexican government and CPA and offers free services to its clients, probably requires about $27 million U.S. annually. He explained that over

95% of the laboratory equipment and over half of the laboratory materials and reagents are imported, which increases costs. To provide a frame of reference for participants, he noted that in U.S. dollars the price of diagnostic tests (materials and reagents only) varies from about $120 for sequencing tests to $5 for ELISA tests to $1 for hemmaglutination inhibition assays.

Coping with Deadly Viruses

Supaporn Wacharapluesadee (Chulalongkorn University, Thailand) described diagnostics and procedures she developed for monitoring and diagnosing viral zoonoses in wildlife and humans.

Dr. Wacharapluesadee started by describing the history of Chulalongkorn University, which has been studying encephalitis viruses and serving as a referral hospital for patients with encephalitis since 1989. In 2002, Chulalongkorn University started active wildlife surveillance of Nipah, Lyssa, rabies, and other viruses in Thailand in a project sponsored largely by the Thailand Research Fund. In recognition of this work, the lab was designated as a WHO Collaborating Centre for Research and Training on Viral Zoonoses in 2009. Then, in 2011, the work expanded under the One Health program to include more human and domestic animal components. She noted that the lab partners with the Thai Red Cross, the United States Defense Advanced Research Projects Agency (DARPA), the United States Naval Health Research Center, EcoHealth Alliance, and FAO.

She explained that much of the group's work involves surveillance for Nipah virus, a risk group 4 pathogen that causes encephalitis in humans with a 40-70% mortality rate and severe respiratory disease in pigs.[3] Bats are a natural reservoir for the virus, and human infection can result from drinking palm juice from trees where bats roost. As Thailand has no BSL-4 labs, her group developed a duplex nested RT-PCR test to detect low amounts of viral RNA in bat specimens including urine, saliva, serum, and blood without the need for a containment lab (Wacharapluesadee and Hemachudha, 2007). She described how specimens are taken from urine collected on plastic sheets under trees and from bats captured with mist nets and subsequently released. The samples are put into lysis buffer containing guanidine thiocyanate, which inactivates the virus and protects the RNA until the samples can be transported on ice to the lab for testing. She noted that Nipah RT-PCR tests are also used as a diagnostic tool for encephalitis patients.

Dr. Wacharapluesadee then described how her group performs rabies diagnoses using brain samples obtained during human and animal post-mortems. In the rabies test protocol, she places animal brain samples on Flinders Technology Associates (FTA) cards, which inactivate the virus, allowing safe handling and transport (Picard-Meyer et al., 2007). She noted that FTA cards also stabilize virus nucleic acids, allowing accurate analysis after even months of storage (Wacharapluesadee et al., 2003).

She also mentioned that her group has started using high-throughput sequencing methods and metagenomics to analyze the microorganisms present in bat saliva.

SYNTHESIS BREAKOUT GROUP DISCUSSIONS

Following the presentations, each session was asked to consider a number of questions:

1. As they are performed, what commonly used procedures/assays cause the highest risk for workers and/or the community?

[3] The BMBL recommends that Nipah virus, including diagnostic specimens, be handled at BSL-4 (United States HHS, 2009; see pages 201-202).

2. To what extent can molecular diagnostic tests replace traditional techniques that necessitate working with larger quantities of pathogens?
3. Are an appropriate number of reference pathogen collections available?
4. How do biosafety/biosecurity considerations impact your ability to perform necessary analyses for clinical diagnosis or outbreak investigations?

In addition to elaborating on the opportunities and limitations of molecular diagnostics, including point-of-care tests, participants also discussed how transport restrictions and the availability of reference pathogen collections impact diagnostic and research work.

Molecular Tests

While generally enthusiastic about the potential for molecular tests, which use inactivated pathogens and can safely be performed in BSL-2 labs, multiple people stressed that molecular tests will never completely eliminate the need to isolate and characterize pathogens in high-containment labs. Several people also indicated that molecular tests are best suited for answering routine questions about normal specimens and that only culture offered the flexibility needed to deal with novel situations and outbreaks. As an example of a case where molecular tests are increasing capabilities, one person mentioned that some countries such as India that have historically avoided TB culture capabilities due to biosafety concerns are now embracing TB molecular tests. While some expressed frustration with the low accuracy of some molecular tests, one person countered that some of the tests being replaced, such as direct smear microscopy, which detects 55 percent of TB cases, also have low accuracy. Several people indicated that they were looking forward to the opportunities that will accompany the increasing availability of high-throughput DNA sequencing.

Several participants observed that since diagnostics are developing quickly, biosafety and biosecurity systems must keep pace. TB was discussed as a case in point. As BSL-3 facilities are no longer necessary for most common TB testing (i.e., everything except resistance testing for drugs other than rifampicin), countries with a low incidence of multidrug-resistant tuberculosis (MDR-TB) may need many TB labs but only a single BSL-3 lab for drug-resistance testing. The Global Fund to Fight AIDS, Tuberculosis, and Malaria, however, is just starting to be open to using non-BSL-3 labs for TB work, and many previously approved requests for BSL-3 labs are proceeding.

POC Tests

A number of participants elaborated on the strengths and limitations of point-of-care (POC) tests, which are usually performed in a BSC using blood or sera and typically take 5-30 minutes. Several people remarked that while the quality of individual POC tests is highly variable and the tests are relatively expensive, there is a need for good POC tests in both medical and veterinary practices. One person mentioned that while POC tests cannot be used to rule out an infection, they serve as a useful orientation for clinicians and could reduce the need to transport potentially high-risk patients. Someone else noted that people do tend to believe the positives and that even low-quality tests can be informative about an outbreak. Another pointed out that as POC tests are neither 100% sensitive nor specific, clinicians in the field should be trained to recognize diseases of concern.

Transport

During a number of these sessions, some participants expressed frustration with what they perceived as unnecessarily restrictive transport, import, and export regulations. Individuals

complained about burdensome paperwork, precautions out of proportion to the risk, long delays to obtain permission, and multiple levels of bureaucracy that could block a transfer. They noted that some countries will not allow the import of drug-resistant TB strains while in other cases intellectual property restrictions block pathogen export. One mentioned that most African countries will not allow samples to be transported by air. Another person recounted that even when regulations permit transfer of samples awaiting diagnostics, inadequate transportation infrastructure in some regions may cause life-threatening delays. One person did acknowledge, however, that sample transport, particularly for pathogen collections, does present risks.

Various participants also identified consequences of the current situation:

- Labs that aspire to become international reference labs, which must be able to receive unknown samples, typically need to engage in detailed conversations with regulators to put transfer agreements in place. Additionally, regulations effectively bar some labs from ever serving as reference labs.
- Difficulty in obtaining samples when needed encourages facilities to create or retain their own reference collections.
- An inability to ship samples for timely diagnostics encourages countries and localities to build their own laboratories.
- Particularly burdensome transport regulations, such as the United States Select Agent rules that require individuals who ship select agents within or into the United States to obtain a United States security clearance, discourages potential, foreign collaborators.

To ameliorate some of these problems, several participants suggested continuing to engage the International Air Transport Association (IATA), the U.N. Committee on Dangerous Goods Transport, and national governments in a dialog to better define the requirements for safe transport and to accurately characterize the associated risks. One suggested that TB, due to the large potential number of samples and the comparatively well-characterized risks might be an ideal starting point for a conversation, particularly as transporting TB samples is much less risky than transporting TB patients.

One person indicated that countries are increasingly relying on in-country DNA sequencing capabilities rather than sample export for diagnoses. While valuable for public health independence and IHR compliance, the individual worried that such a model might stymie international characterization of emerging threat pathogens.

Reference Collections

As reference collections present security risks, participants discussed both the demand for pathogen collections as well as the ethics of destroying collections. Many indicated that research, particularly pathogenesis studies, almost always requires viable organisms that are typically obtained from collections. In contrast, many felt that diagnostics, particularly for organisms like TB where the tests are standardized and use internal controls, created much less demand.

Opinions were mixed concerning whether pathogen collections should ever be destroyed, and one person cited that the recent eradication of rinderpest and the accompanying debate over whether or not to destroy all samples as a topical example. One viewpoint maintained that dangerous pathogens are inherently interesting and that we should retain and study them to understand the source of the pathogenicity. Another viewpoint argued for destroying samples when transporting them to more secure, centralized locations represented an unacceptably high risk, particularly when the samples are unlabeled or without context.

7

IDENTIFYING AREAS FOR POSSIBLE ACTION (BREAKOUT SESSIONS)

The goals for this group of breakout sessions were to (1) generate strategies and suggestions for countries building/upgrading or considering building/upgrading labs, (2) consider what data on biosafety would be most useful to generate, and (3) identify areas where current biosafety practices are not well-matched to actual needs. In order to facilitate discussions, participants in each session first listened to several brief talks.

BREAKOUT SESSION 1: DETERMINING NECESSARY AND APPROPRIATE PRECAUTIONS

Chair: Michael Callahan
Rapporteur: J. Craig Reed

In view of the increasing range of available biosafety options, from expensive engineered solutions to lower-cost microbiological techniques, breakout session 1 examined how to select combinations of precautions that best meet individual needs. Each precaution adds to a facility's complexity, and safeguards need to be maintained during both normal operations and emergency conditions including natural disasters.[1] Components, such as backup power systems intended to maintain the required airflow during loss of primary power, may have non-trivial interactions that make understanding and testing the overall system difficult.[2] Personnel require regular refresher training to maintain competencies, and complex regulations can be difficult to implement and verify.[3]

Laboratory authorities, while acknowledging the infeasibility of conducting zero-risk operations, rarely specify the level of risk they consider acceptable. Often the incremental reduction in risk from each layer of precautions is unclear. Lack of quantitative information makes prioritizing options difficult, particularly when constrained by finite budgets for both containment labs and competing priorities. Additionally, complying with funding requirements often requires laboratories to adhere to the recommendations for standard BSL levels, even if some aspects of those recommendations are excessive for a facility's particular mission. Furthermore, universal recommendations, while convenient and simple, do not afford opportunities to factor in additional information about the setting in which the work is performed, such as disease endemicity, local immunity, and community concerns. Unnecessary precautions increase expense, decrease efficiency, and tempt workers to circumvent safeguards (United States HHS, 2009; see page xxxi).

[1] For example, the Shope Lab and the Galveston National Laboratory's BSL-4 facilities at the University of Texas Medical Branch in Galveston developed plans for dealing with hurricanes, floods, and earthquakes (Federal Register, 2005).
[2] The United States Centers for Disease Control and Prevention's new BSL-4 in Atlanta, Georgia has had several problems with its backup power system including nearby construction cutting a grounding cable and whether to share a backup power plant with other facilities or to have its own plant (United States GAO, 2007).
[3] CDC inspections of laboratories at Texas A&M University failed to find any evidence of an occupational exposure that later resulted in a case of brucellosis (United States GAO, 2009).

Before the session opened for general discussion, several speakers addressed a number of issues related to the topic including whether adding additional engineering controls always increases safety, the reality that regulations and guidelines rarely keep up with technology, and the benefits of making risk assessments more quantitative and pathogen-specific. Speakers also commented on the need for and difficulties in obtaining quantitative data and offered suggestions to address this problem. Following the presentations, **Michael Callahan** (Defense Advanced Research Projects Agency, United States) led a discussion.

BREAKOUT SESSION PRESENTATIONS

Evidence-Based Biosafety: Ensuring Precautions are Adequate and Appropriate

Allan Bennett (Health Protection Agency, U.K.) discussed the main causes of laboratory-acquired infections (LAI) and argued that the combination of building engineering, equipment, and practices commonly used today are neither economical nor maximally effective. While the best direct evidence that labs are not serving as sources of infection and that a set of precautions is effective would be accurate counts of the number of LAIs, lack of governmental reporting requirements make such data scarce. In the absence of direct evidence, he suggested that applied biosafety data could serve as indirect evidence.

Mr. Bennett started by pointing out that of the three main routes of laboratory infection—inhalation of aerosols, surface contact with the agent, and punctures from needles or other sharps—aerosols have historically received the most attention. Starting in the early 1980s, regulations began requiring a number of expensive technologies to reduce aerosol exposure including HEPA filters, directional air flow, multiple air exchanges per hour (ACH), and biological safety cabinets (BSC). Since then, materials and practices have evolved to offer additional ways to minimize the creation of aerosols, such as the use of sealed centrifugation rotors and the substitution of plastic flasks and bottles for glass ones. He believes that many research spaces, as a result, are now over-engineered. This can cause both unnecessary expense and a reduction in overall safety. As an example, he pointed out that many of the precautions used to reduce aerosol exposure (e.g., flexible film isolators, half suit isolators, respirators, and Class II BSCs) reduce vision and manual dexterity, which can increase splashes (Sawyer et al., 2006). As such, he believes that when evaluating protocols the whole set of precautions and their side effects should be considered collectively.

Glove usage and hand hygiene constitute another set of practices that Mr. Bennett believes should be altered. For example, the thick household gloves used in Class III BSCs and in BSL-4 conditions significantly decrease both gross dexterity of the hand as well as fine finger dexterity. Similarly, although latex gloves cause no loss in manual dexterity (Sawyer et al., 2006) and are critical for preventing direct contact infections, many BSL-2 lab workers, even in high resource countries, do not use latex gloves consistently. He cited a study conducted at the University of Utah and presented at the 2010 American Biological Safety Association (ABSA) Conference where James Johnston[4] (University of Utah) found that only 46 percent of staff removed gloves on leaving a BSL-2 lab, hand hygiene compliance before exiting a lab was 10 percent, and 72 percent of individuals touched their face while working. In the study, compliance varied widely between labs and could not be predicted by training.

Mr. Bennett also stated that in the developed world, workers might become overly reliant on engineering and let down their guard with respect to biosafety procedures and good

[4] James Johnston, Ph.D., C.I.H.: Hand Hygiene in the Biosafety Level-2 Lab: Is it a Matter of Training? (Tuesday, October 5, 2010) ABSA 53rd Annual Biological Safety Conference, September 30-October 6, 2010 Denver, CO. Available: www.absaconference.org/pdf53/Session8-Johnston.pdf.

microbiological practices. He feels the recent outbreak of *Salmonella typhimurium* in teaching and clinical microbiology labs in the United States is likely an example of the phenomenon.[5]

Due to the development and widespread use of advanced diagnostic techniques, he speculated that improper inactivation is likely to become a major source of infection in the future.

Risk-Based Design of Facilities for High Consequence Animal Pathogen

Uwe Mueller-Doblies (Institute for Animal Health, Pirbright Laboratory, U.K.) described the benefits of taking quantitative, risk-based approaches to laboratory safety and gave examples of how such approaches could be implemented.

Dr. Mueller-Doblies began by suggesting that people should move from a compliance-based approach to a risk-based approach. Compliance-based approaches, he argued, consist largely of checking boxes and often lead to over-engineering. Instead, he feels that we should learn to better understand, quantify, and communicate risks. As eliminating all risk is not achievable, a key component of the approach is defining an acceptable risk level. His institution (Institute for Animal Health), for example, uses one consequential release every 500 years as its target risk level. Other institutions may need to define targets for an acceptable risk of operator exposure or cross contamination. He suggested that communities or countries with multiple facilities may want to consider risk/year/facility (i.e., risk per facility per year).

After selecting a target risk, Dr. Mueller-Doblies feels labs must determine both what their risks are and implement appropriate controls to reduce those risks to an acceptable level. He noted that controls for human pathogens (operator protection) and animal pathogens (requiring environmental and veterinary protection) differ significantly and that plant pathogens present their own challenges. Furthermore, the consequences of an event often depend on issues such as the proximity of the surrounding community and whether or not a particular disease is endemic. Thus, he argued that risk assessments should be specific to regional and local requirements and should not be blindly accepted by facilities in other countries.

Dr. Mueller-Doblies then introduced the bow-tie risk management model for visualizing and calculating risks (Figure 7-1) and gave examples of many types and classes of threats. For example, aerosols, needles and sharps, ingestion from fomites, and infected animals are all threats that could lead to human exposure, while threats that could lead to environmental release include operator error, solid waste, animal carcasses, fomites, effluent, and aerosol escape through ventilation. From a biosecurity point-of-view, deliberate threats such as intruders, insiders, a theft in transit, or illegitimate material receipt could also lead to a release event.

[5] Investigation Announcement: Multistate Outbreak of Human *Salmonella Typhimurium* Infections Associated with Exposure to Clinical and Teaching Microbiology Laboratories. Available at: *http://www.cdc.gov/salmonella/typhimurium-laboratory/042711/index.html*. Accessed October 17, 2011.

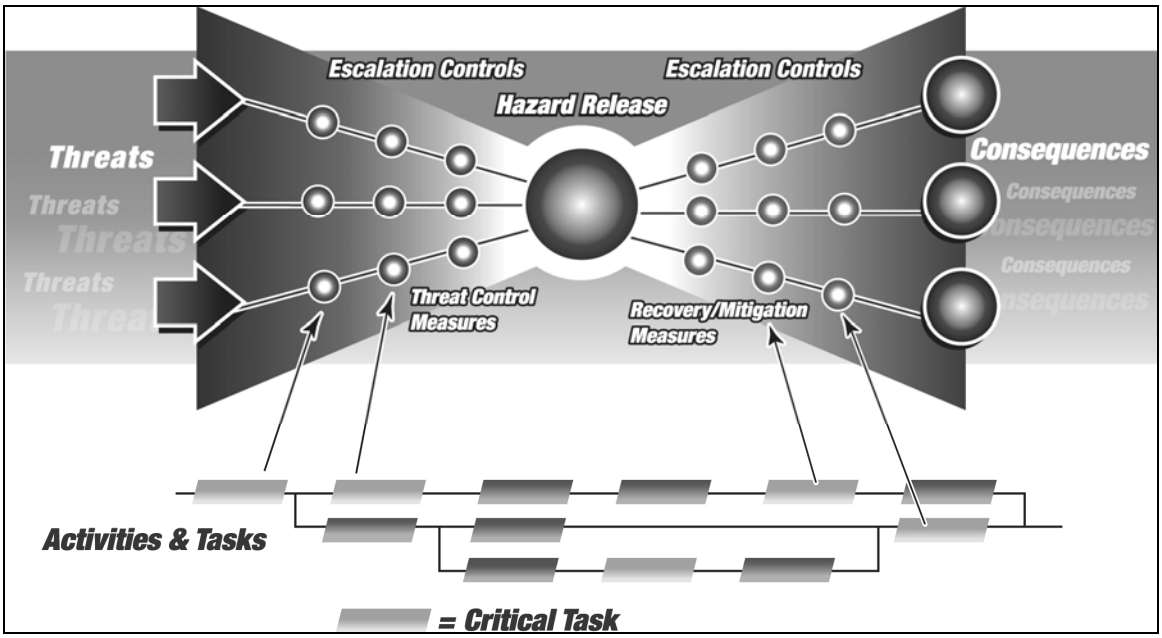

Figure 7- 1 Bow-tie Risk Management Model. The center of the tie represents the hazard release, threats are on the left, and consequences are on the right. Risk paths connect each threat to the release event, and threat control measures are visualized along the appropriate risk path. Paths from the release to consequences have recovery and mitigation measures such as vaccination and isolation of exposed workers for human threats and exclusion zones and quarantine periods for environmental threats. SOURCE: Copyright © 2011 ABSG Consulting Inc. All rights reserved. Used with permission.

Dr. Mueller-Doblies explained that threat control measures often include a number of layers of protection: passive controls, dynamic controls, and management controls. Passive controls include airtight barrier construction and double exhaust HEPA filtration. Dynamic controls include air changes, directional inward airflow, steam autoclaves, leak alarms, and shower protocols. Management controls include alarm response protocols, HEPA filter validation, and protective clothing. Threat control measures for biosecurity threats include physical security, security procedures, inventories, security staff, and security services.

A number of elements go into effectively using the bow-tie model. In particular, one needs to know how much each threat control measure reduces risk and the likelihood and consequences of failure for any measure. Furthermore, Dr. Mueller-Doblies argued that one should be able to detect failure in a control measure, and control measures should be independent, i.e., no two active engineering controls in the same risk path should be dependent upon the same service, such as electricity or steam. He mentioned that a number of assessment methodologies such as failure mode effect analysis and hazard operability studies can assist with such an analysis.

Control of Emerging Infections

Onder Ergonul (Koç University, Turkey) discussed the high incidence of secondary infections, some fatal, among health care workers and demonstrated how examination of data on secondary infections among health care workers in conjunction with details about the precautions used and types of exposures received can provide valuable information about routes of infection and what precautions are necessary and appropriate.

Many emerging and reemerging diseases, including Crimean-Congo hemorrhagic fever

(CCHF), Ebola, and Rift Valley fever are zoonotic diseases. CCHF is transmitted by ticks of the genus *Hyalomma* and has a particularly high incidence in Turkey, Russia, and other countries in the region. Like Ebola and Marburg, CCHF has a high risk of human-to-human transmission in the health care setting, and Dr. Ergonul showed data that since 1950, at least 94 workers have been infected by CCHF, 38 fatally. Both needlesticks and exposure to contaminated blood have caused infections in health care workers (van de Wal et al., 1985). By following up in Turkey on health care workers who had previously treated CCHF patients, Dr. Ergonul found no evidence of infections from inhalation and concluded that standard precautions, including those to protect against bloodborne pathogens, are usually adequate (Ergonul et al., 2007). He feels that use of gloves, gowns, and facial protection for the eyes, nose, and mouth are particularly indicated by risk assessments based on documented transmissions. While N95 respirators are usually not necessary for health care workers, he noted that they might be advisable for lab workers engaged in aerosol-generating activities.

Dr. Ergonul explained that increasing worker use of the recommended standard precautions requires both more resources and more education. For example, needlestick injuries, a major cause of CCHF transmission to workers, can be reduced by safety-engineered devices, appropriate sharps containers, and education on best practices. Dr. Ergonul observed that, unfortunately, increasing compliance with sharps protocols is almost as difficult as increasing compliance with hand hygiene recommendations, another inexpensive, but effective precaution.

To illustrate the general utility of using data to evaluate the effectiveness of potential precautions, Dr. Ergonul described a metaanalysis of studies that examined the ability of various barrier interventions to reduce severe acute respiratory syndrome (SARS) transmission (Jefferson et al., 2008). The work provided strong statistical support for the effectiveness of frequent hand washing and the use of masks, gowns, and gloves to protect against transmission to healthcare workers.

Dr. Erogonul also presented data indicating that treatment of CCHF with ribavirin is most effective during the disease's pre-hemorrhagic stage (Ergonul, 2008), which coincides with the time the virus is detectable by polymerase chain reaction (PCR), but not yet detectable with enzyme-linked immunosorbent assay (ELISA) tests (Ergonul, 2006).

BREAKOUT GROUP 1 DISCUSSIONS

To foster discussion, several questions were posed to the group:

- Are there any common procedures for which specific baseline minimum biosafety requirements have not been determined (and that are likely performed using unnecessary precautions)?
- Are any procedures commonly done using safeguards that do not enhance safety?
- What data on biosafety would be most useful to generate?
- To what extent should the setting in which work is performed (endemicity, local immunity, local risk tolerance, etc.) affect the precautions employed?

In discussing the presentations and the above questions, participants identified two main issues.

Difficulties in Implementing Good Practices

Several participants indicated that it is frequently difficult to convince lab and healthcare workers to use good practices, even in cases where the techniques, such as glove use and hand hygiene, are both inexpensive and known to be effective. To address this issue, one

person pointed out the value of vigorous mentoring programs that workers in some labs must complete (in addition to formal training) before being allowed to work independently. Another suggested that biosafety should be taught as, "This is why we do X, and this is why we do Y," rather than simply as, "We do X and Y." A third proposed that anyone who joins a lab, regardless of his or her previous experience, should undergo an apprenticeship that includes competency testing.

Need for Applied Biosafety Data

Many presenters as well as several members of the attendee group commented on the difficulty in obtaining good data on the effectiveness of particular precautions. To partially satisfy the need, one attendee suggested people make an effort to publish biosafety data they previously generated for their own internal use. Several people indicated that to generate useful data, perhaps a voluntary process for reporting LAIs and near misses to an international authority could be developed. One person cautioned that care must be taken to distinguish LAIs from background infections in regions where certain diseases of concern are endemic. In response to a comment on the need for more funding for applied biosafety research, one person indicated that the United States Defense Threat Reduction Agency (DTRA) plans to fund research on that topic.

Someone else indicated that additional data are needed to determine if current designs, equipment, and procedures are reducing actual risks appropriately. The individual also suggested that evaluations might discover that many components of containment labs are over-engineered and that changes could potentially lead to decreased costs. Routine use of second HEPA filters was suggested as a possible example of engineering that may no longer be necessary given that when this practice started in the 1980s filters were much easier to damage. The participant stated that there is a clear need for data to inform decisions regarding ways to more economically maintain and operate containment laboratories while ensuring their safe and secure operations.

In an attempt to answer the question of how the effectiveness of particular techniques can be measured, someone suggested using proxies for infection such as fluorescent splashes on clothing.

BREAKOUT SESSION 2: IMPROVING ORGANIZATIONAL CULTURE AND PRACTICES

Chair: Serhiy Komisarenko
Rapporteur: Benjamin Rusek

The session opened with three talks that illustrated different approaches to improving safety and security practices. The first focused on the importance of establishing an atmosphere of trust and avoiding over-regulation. The second described the use of twinning programs to "seed" a second lab with successful practices from a more established lab. The final talk described how a nation passed legislation to improve biosafety and biosecurity on a national scale. After the talks, **Serhiy Komisarenko** (Palladin Institute of Biochemistry, Ukraine) led a discussion that further explored the topic.

BREAKOUT SESSIONS PRESENTATIONS

'Enlightened Leadership': More Powerful Than Guns, Gates, and Guards

David Franz (MRIGlobal, United States) warned the group about the dangers of over-regulation and argued that enlightened leadership and an atmosphere of trust should be key elements in any effort to increase biosafety and biosecurity.

Dr. Franz started by reminding the audience that we should be careful to preserve the power of science to do 'good' in our often-dangerous world. He then familiarized the audience with the history of biosafety and biosecurity in the U.S, and explained that prior to the events of 2001; the focus in the United States was on laboratory biosafety. Then, in response to the 11 September 2001 attacks, the anthrax letters (2001), and the subsequent Amerithrax investigation that culminated in the Federal Bureau of Investigation's (FBI) contention that an insider was responsible for the anthrax letters (2008), the focus shifted to biosecurity, and new regulations followed. He noted two:

- The USA Patriot Act of 2001 (Public Law 107-56) and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Public Law 107-188) enhanced controls on dangerous biological agents and toxins and required the registration of persons who work with Select Agents.
- Army Regulation 50-1 (Department of the Army, 2008) established a biological 'surety' program that defined criteria for evaluating personnel reliability.

While acknowledging that if the FBI is correct about the Amerithrax case, then the insider threat is more difficult to combat than he had initially believed, Dr. Franz warned against the "slippery slope" of increasing regulation. In particular, he expressed concern about the growing attention synthetic biology is garnering and wondered if nanotechnology and work on understanding the human immune system might also be targeted for unnecessary regulation that could impact the science. He argued that by reducing the efficiency of scientific research and encouraging scientists to change fields or relocate their research offshore, over-regulation could ultimately impact the security and economy of nations. Furthermore, he cautioned that it could take 5-10 years to realize that we have over-regulated and an additional 15-20 years to reverse course.

Dr. Franz then defined 'enlightened leadership' and compared the 'enlightened leadership' and 'regulatory oversight' approaches to dealing with the insider threat. He explained that enlightened leadership involves *leading with science* and focusing on quality research, safety, vision, education, responsibility, honesty, transparency, and ethics. Ultimately, it creates a culture of trust and accountability. In contrast, the 'regulatory oversight' approach entails *leading with security* and implementing "guns, gates, and guards," background checks, psychological evaluations, and pathogen controls and often results in a culture of mistrust. Dr. Franz acknowledged that while labs need varying levels of regulatory oversight, all labs can benefit from enlightened leadership.

Dr. Franz then recommended ways to reduce the momentum towards unnecessary regulations in the life sciences. He suggested that scientists strive to increase transparency in science and communicate and demonstrate a culture of scientific responsibility to the public. Scientists should work with lawmakers and concerned citizens to regulate real risks, evaluate the value of proposed safety and security solutions, and examine the full costs of proposed regulatory solutions. These steps will help put in place effective regulation that limits the frustration to scientists.

In closing, Dr. Franz observed that completely eliminating the insider threat in a given laboratory can only be done by stopping all research and firing the scientists. This society

cannot afford to do. While we will always live with some risk, he emphasized that we can control the amount and type of regulation that we chose to impose and the leadership and culture of our laboratories in which we work.

Laboratory Twinning – A Tool to Improve Global Disease Security

Keith Hamilton (World Organisation for Animal Health [OIE], France) described OIE, its laboratory network, and the twinning program OIE is using to expand and strengthen that network.

OIE, which is an intergovernmental organization with 178 member countries, produces manuals and international standards for animal health, disease surveillance, laboratory diagnostics, trade, vaccine production, veterinary laboratories, and animal facilities. It also oversees a network of OIE Reference Laboratories (OIE RL) and OIE Collaborating Centers (OIE CC). An OIE RL serves as a center of expertise and standardization for a particular disease and offers technical advice, training, and diagnostic services (e.g., confirmatory testing, agent characterization, pathogen isolation, and production and distribution of reagents) and ultimately disseminates useful information including positive test results to the international community. Rather than focusing on a particular disease, an OIE CC is recognized for a particular sphere of expertise, such as epidemiology or veterinary medicinal products. An OIE CC provides technical advice and training, develops new techniques and procedures, disseminates useful information, and places expert consultants at OIE's disposal. He emphasized that both OIE RLs and OIE CCs provide international support and make an impact far beyond their national borders and pointed to the recent worldwide eradication of rinderpest as a major success of the network.

To expand its current network of 225 OIE RLs and 40 OIE CCs, Dr. Hamilton explained that OIE has instituted a twinning concept[6] that establishes a link between a parent OIE RL or OIE CC and a candidate national laboratory. As OIE does not provide funding for hardware or facility upgrades, the focus is on transferring expertise and improving practices. While formal twinning lasts between 1-3 years, the experience is intended to form lasting links between the two institutions. Dr. Hamilton identified several objectives of twinning:

- To build scientific communities;
- To help countries enter the scientific debate on an equal footing;
- To improve access to high quality diagnostics and technical assistance for OIE members;
- To extend the OIE network of expertise and provide better geographic coverage for priority diseases;
- To strengthen global disease surveillance networks;
- To harmonize procedures globally, allowing for the generation of comparable results and increasing confidence in lab test results; and
- To improve the ability of the candidate lab to meet OIE international standards.

To help achieve the final goal, all twinning projects include subjects such as quality management, biosafety, and biosecurity. Often countries have more specific goals like combating an endemic disease or creating the capacity for pre-export testing to facilitate trade. While another goal of twinning is for candidate labs to successfully apply for OIE RL or OIE CC

[6]A Guide to OIE Certified Laboratory Twinning Projects. Available at: *http://www.oie.int/fileadmin/Home/eng/Support_to_OIE_Members/docs/pdf/A_Twinning_Guide_2010.pdf*. Accessed August 29, 2011.

status, he acknowledged that that will not happen in all cases. Nonetheless, he expects the twinning experience to bring candidate labs closer to OIE RL or OIE CC status. Currently, OIE has about 30 active twinning projects and 10 more waiting to start.

Singapore's Response to Biorisk Events at Home and Abroad

Teck-Mean Chua (Asia-Pacific Biosafety Organization, Malaysia) gave a presentation prepared by **Ai Ee Ling** (Singapore General Hospital, Singapore) describing the events that convinced Singapore that the country needed to improved its national biosafety and biosecurity practices and the actions the country ultimately took.

Dr. Chua explained that while the Malaysian Nipah virus outbreaks in the late 1990s, the Anthrax letters in the United States in 2001, and the country's growing biomedical industry attracted attention to the problem of naturally occurring and deliberate biological threats, the severe acute respiratory syndrome (SARS) epidemic of 2003 was the true wakeup call for Singapore. In addition to causing loss of life, the disease also had a massive economic impact on the country. Furthermore, after the outbreak had been contained, a researcher's laboratory-acquired infection led to the reappearance of SARS in Singapore.

An investigation of that lab revealed structural problems, insufficient training, overcrowding, and the lack of an inventory or tracking system for infectious samples. The investigation also identified the lack of a regulatory framework and national biosafety standards as contributing factors and recommended legislation to create such standards, as well as a process for certifying laboratory structural integrity and operating procedures and a system for tracking agent import, export, and transfer. The Biological Agents and Toxins Act (BATA), which was passed by Parliament in October 2005 and enacted in January 2006, implemented those recommendations in an enforceable way.

Dr. Chua then gave several examples of the changes produced by BATA. As part of the new system, the Internal Security Department of the Ministry of Home Affairs began vetting personnel with access to containment labs that were determined to be protected facilities, and the Singapore Civil Defense Force assumed responsibility for laboratory emergency response. The Ministry of Health approved laboratory certifiers and trainers and required annual certification of BSL-3 labs. He noted that BATA complements the Animals and Plants Act of 1965 and the Genetically Modified Organisms Guidelines of 2006.

The Ministry of Health also issued two sets of guidelines concerning the 2009 H1N1 influenza epidemic. The first set (May 2009) dictated that culture work take place in BSL-3 labs and that diagnostic work be done in BSL-2 labs using BSL-3 practices. The second set, which followed an improved risk assessment, allowed the virus to be handled in BSL-2 conditions in Class II BSCs.

Dr. Chua also described some of the non-regulatory steps Singapore has taken to improve biosafety:

- Delegations took study trips to CDC and the Canadian Biosafety Office and Office of Laboratory Security in 2002.
- Starting in 2002 with the National University of Singapore, many universities established Institutional Biosafety Committees.
- In 2005, the Ministry of Health granted the Asia-Pacific Biosafety Association status as an approved trainer, and the Biorisk Association of Singapore was formed in 2010.

BREAKOUT GROUP 2 DISCUSSIONS

Participants were asked to consider several questions:

1. What organizational culture and practices are desirable? How universal is this list?
2. What types of training and educational programs are most effective? What types of content should be emphasized?
3. What factors are key to successfully changing a lab's culture and practices? What motivates change?

During the discussion many pointed to a lack of funding, demonstrating a lack of priority to improve practices, training, and education, which they attributed to insufficient understanding on the part of senior management and government, as the biggest impediment to change. Individual participants then suggested various solutions:

- Individual "champions" could take up the cause and spread the message in their countries and regions.
- Good biosafety practices could be taught at all levels of life sciences education to help change attitudes and behaviors.
- Biosafety associations could (1) provide neutral, national platforms for discussions among stakeholders from multiple agencies, (2) provide people, including those not in the life sciences, a sense of community, and (3) encourage the adoption of a biosafety culture.
- Scientists could advise politicians. One person noted the benefit of getting involved at the time an agency asks for public comments on a proposal rather than waiting to complain about the final result.

Several people also commented on the legislative approach to affecting change. One person felt that it is difficult, but perhaps not impossible, to legislate human behavior. Others suggested that more thinking is needed about how to enforce national regulations at the local level as implementation is missing in many places.

BREAKOUT SESSION 3: DESIGN AND OPERATIONAL OPTIONS FOR IMPROVING SUSTAINABILITY, BIOSAFETY, AND BIOSECURITY

Chair: Willy Tonui
Rapporteur: Jennifer Gaudioso

Challenges and limitations notwithstanding, many laboratories would like to improve their operations, and this session was intended to offer some practical suggestions. The session started with a presentation that offered tips for each stage in the lab lifecycle from design through maintenance. The second speaker then shared the decision process he used to acquire a BSL-3 lab for his institute and the steps he took to ensure that they would obtain a quality facility that would be affordable to maintain. The third speaker offered suggestions for improving practices and argued that practices are much easier to change than equipment or lab designs, and the final speaker provided another perspective on the design decision process. Following the presentations, **Willy Tonui** (Kenya Medical Research Institute, Kenya) led a discussion to examine some of the issues in more depth.

BREAKOUT SESSION PRESENTATIONS

Design and Operational Options for Improving Sustainability, Biosafety, and Biosecurity in Southeast Asia

Stuart Blacksell (Mahidol University, Oxford University, Australia) proposed solutions to address common sustainability, biosafety, and biosecurity issues in the region.

Dr. Blacksell shared a number of design, construction, and commissioning suggestions:

- Make sure that a BSL-3 facility is really necessary.
- Allow enough time for all aspects of the project.
- Select and prequalify the commissioning agent, general contractors, project managers, biocontainment engineers, and others as soon as possible. Beware of contractors without local experience or who want to design "reverse clean rooms."
- Obtain approvals as soon as possible.
- Document specification compliance, the budget, and contingencies. When multiple sets of standards must be met, make sure that each partner signs off.
- Hire someone familiar with lab workflow.
- Avoid common mistakes including: biosafety cabinets (BSCs) that are of the wrong type, incorrectly placed, or have interrupted air flow; hand sinks in the wrong location or of the wrong type; and rooms that cannot be sealed for decontamination.
- Do not neglect the plant room, which should include sufficient space.
- Keep air-handling systems simple to increase reliability. Make sure HEPA filters are accessible for future service. As single pass air is very expensive and wasteful, he recommended considering recirculating ~85 percent of the air with additional HEPA filtration on the recirculated component.
- Perform accreditation against the design standard(s).

Additionally, Dr. Blacksell made a number of operational suggestions:

- Make sure that everything can be serviced locally.
- Ensure that BSL-3 organisms are stored within the BSL-3 lab.
- Arrange for a maintenance budget, and plan for routine upgrades and replacements.
- Check Type II BSCs annually.
- Increase security by restricting access and/or employing guards, proximity cards, fingerprint readers, iris readers, locks, and closed circuit television monitoring. Perform personnel background checks with the help of the police, security agencies, and previous employers.

Dr. Blacksell also made a number of general suggestions:

- As Asia currently lacks engineers with biocontainment and biosecurity design experience, local universities should develop biosecurity engineering curricula. He added that development funds might be used for training and scholarships and that regional training facilities may be a viable option.
- Increase the number of accredited BSC and HEPA filter testers.
- Donors and partners should increase their role in maintenance. He noted that getting funding for new labs is typically much easier than obtaining maintenance money and believes that part of the problem is the difficulty in seeing how maintenance money is spent. He suggested that more education and awareness be directed towards this issue.

Dr. Blacksell also emphasized that the client has a responsibility to be knowledgeable about what they want.

Enhancing Biosafety and Biosecurity in North Africa and the Middle East: The Pasteur Institute of Morocco Experience

Mohammed Hassar (Institut Pasteur du Maroc, Morocco) described the decision process the Institut Pasteur du Maroc (PIM) used to acquire an affordable, sustainable BSL-3 lab that met its scientific, biosafety, and biosecurity requirements.

Dr. Hassar explained that in response to concerns about troop health and worries about epidemics entering the country, Morocco's King, in collaboration with the army and the Ministry of Health, decided that Morocco needed to conduct disease surveillance. To accomplish that goal, he decided the country should build several BSL-3 labs.

At the time, the PIM had a rudimentary BSL-3 that had been quickly built and had never functioned properly, and the PIM decided that building a new lab would be more economical than repairing the existing facility. Rather than put the project out for open bids, Dr. Hassar, who was then Director of the PIM, recounted that he requested and received special permission from the Minister of Finance to purchase a BSL-3 lab from the supplier that had just finished installing two other labs in Morocco. He felt that using the same supplier, who by that point had Moroccan experience, simplified operations and maintenance training and gave them confidence that they would receive a functional lab.

The PIM built the facility's shell, which has BSL-2 space and room for two BSL-3 suites. The supplier then assembled a single BSL-3 container (36 m^2) in the shell; Dr. Hassar noted that a second suite may be added at a future date if the need arises. The BSL-3 component cost $450,000 U.S., while the whole facility (260 m^2) cost $700,000 U.S. to build.

He explained that the lab's objectives are to isolate and analyze viruses, perform advanced scientific research in the field of viral infectious diseases, and protect workers and the environment from highly pathogenic agents. He indicated that the lab has an annual budget of $160,000 U.S., of which $30,000 goes to maintenance regardless of how much or little the BSL-3 component is used. They also started training a local, private company to perform the necessary maintenance immediately after making the decision to build the lab. He reported that while the lab conducts some training, the overall BSL-3 usage is not high. Nonetheless, he finds it reassuring that the lab will be available when needed and indicated that in the future, the Institut Pasteur plans to install a BSL-3 lab at each of their locations.

A Rational and Attainable Approach to Successfully Implementing Biosafety in Laboratory Settings Worldwide

Barbara Johnson (Biosafety Biosecurity International, United States) discussed the role of good practices in addition to other controls in lowering risk and the need to let a detailed risk analysis rather than blind adherence to a general BSL recommendation or a set of standards guide decision-making. She acknowledged that in some cases regulations do not permit such flexibility.

Dr. Johnson started by reminding the audience that many labs lack funding, well-maintained infrastructure, and equipment yet still need to perform critical public and animal health, medical, and research missions. She then related a number of examples from her experience of situations where lab workers used a risk analysis in combination with a detailed assessment of their needs and resources to develop creative solutions that improved the overall safety of their labs. For example, one group's autoclave was fully used for sterilizing surgical packs, and hence they did not have sufficient capacity to sterilize lab ware like bacteriologic

loops. They decided that rather than flaming their loops inside their BSC, they could flame them outside their BSC and immediately place them inside a sterile can inside the BSC for later use. Other workers have employed homemade sharps containers (she indicated that any puncture and leak proof can is sufficient.) near the point of use. Similarly, she has seen a variety of reusable, resealable containers function as secondary containment to improve the safety of within and between room transport. The need to work in specifics rather than generalities is why Dr. Johnson feels that training that takes place largely inside the trainees' own lab, directly addressing their situation and ultimately improving practices, is particularly valuable.

In determining the appropriate primary containment, Dr. Johnson noted that it is often productive to determine if a lab's procedures will aerosolize an organism that is infectious by inhalation. In resource constrained environments where purchasing and maintaining equipment that employs HEPA filtration is not feasible and when aerosols are not likely to be generated, a fan box without a HEPA filter that vents to the outside away from building air inlets and public spaces may be sufficient. Similarly, when organisms and procedures are not an aerosol risk, extensive HEPA-filtering of the lab itself may not be necessary. Additionally, HEPA-filtered exhaust air may be suitable for recirculation to the laboratory, but one should annually certify the building HEPA filters if this is considered.

Another case where a situation-specific risk assessment can be useful is in determining the appropriate number of air changes per hour (ACH). While labs that work with volatile chemicals may need 10-12 ACH, in other cases the National Institutes of Health (NIH)-mandated minimum of 6 ACH for BSL-3 labs may be sufficient. Furthermore, if regulations and the heat load permit, it *might* be possible to reduce the number of air exchanges even further without compromising safety. While standby modes during times when there is no work ongoing in the lab may be acceptable, maintaining some airflow is usually necessary to prevent mold, humidity, and condensation inside the lab and ducts.

A focus on functional requirements can also help labs avoid unnecessary, high-end construction. For example, 'turnkey' labs are often designed like clean rooms instead of containment labs and contain numerous HEPA filters that are expensive to maintain, impossible to test, and do not increase safety. A key attribute for BSL-2 labs is cleanability and in many cases vinyl flooring and painted gypsum wallboard suffices. In BSL-3 labs, seamless welded vinyl flooring and gypsum board walls covered with epoxy paint are often used to bear the weight of BSCs and allow for gas decontamination. More expensive floor and wall materials (poured concrete with troweled epoxy) can be reserved, if needed, for animal rooms where movement of racks and carts would quickly damage walls and floors. Rather than simply applying N+1 rules for mechanical equipment (e.g., redundant fans), the ease of repairs and the tolerance for downtime should be factored into calculations of the necessary level of redundancy.

Dr. Johnson ended her presentation by observing that facilities, equipment, and practices all contribute to safety and that there is rarely a single correct way to do things.

Engineering Control: Challenges in Maintaining a BSL-3

Pretty Sasono (National Institute of Health Research and Development [NIHRD], Indonesia) described the steps Indonesia has taken to improve its laboratory capabilities, biosafety, and biosecurity.

Dr. Sasono opened by saying that diseases of concern in Indonesia include anthrax, tuberculosis, avian influenza, AIDS, malaria, dengue, typhoid, hantavirus diseases, and Nipah virus infections. To reduce the impact of disease, she explained that Indonesia would like to diagnose diseases in the shortest possible time, prevent diseases through vaccine development, and cure diseases through drug development, all of which require safe and secure labs.

She then explained that to improve national laboratory capabilities, the Indonesian government recently funded construction of a BSL-3 lab. In 2005, an initial plan to retrofit an existing lab BSL-3 lab was considered but deemed infeasible. In 2006, NIHRD, with expert assistance from other countries and support from the United States State Department's Biosecurity Engagement Program (BEP), considered BSL-3 designs based on WHO guidelines. She noted that local conditions, which include frequent floods and earthquakes, coupled with limited Indonesian BSL-3 expertise led to a decision to place a four room modular BSL-3 on the ground level of a new lab building. Construction started in 2007 and finished in 2008, and the lab was certified to international standards in 2009. The new BSL-3 laboratory complements about 20 other laboratories in NIHRD, a 44 lab network for infectious disease diagnosis that was originally assembled to combat avian influenza, 800 private laboratories, 9,000 Central Health laboratories, and other labs within hospitals and universities.

Dr. Sasono went on to describe Indonesia's biosafety and biosecurity efforts, which have included the introduction of training, guidelines, and regulations. Training has discussed weapons of mass destruction, bioterrorism, the National Biorisk Management Program, and biosecurity for avian influenza laboratories. NIHRD created an Instructor's Guide for Biosafety Training based on a translation of WHO guidelines. A number of regulations have also been issued.[7]

She then explained that top managers as well as scientific and facility managers have taken steps to improve laboratory infrastructure and operational management. Facility managers are improving maintenance, control, calibration, certification, validation, and waste management, and security managers are improving physical, information, and personnel security. Occupational health improvements include keeping health records and providing vaccines, lab clothing, and personal protective equipment. Additionally, she reported that Biorisk Management Advisory Committees have been formed.

Dr. Sasono also identified a number of on-going challenges and some possibilities for the future. She indicated that arranging for the rapid collection and testing of patient specimens in response to an outbreak is of the highest priority. Similarly, prompt and accurate reporting of confirmed diagnoses is also important. Another primary focus is making full use of qualified national laboratories and enhancing collaboration and networking within the country. While the Indonesian government has recently increased laboratory capacity, she noted these efforts should continue as should support for laboratory accreditation. She believes that additional technical expertise is needed and reported that Indonesia is considering a number of options including recruiting young engineers, offering special training, and increasing the availability of graduate studies. Possible training methods include in-house, hands-on training provided by an invited expert, training abroad, and participation in laboratory twinning programs.

BREAKOUT GROUP 3 DISCUSSIONS

In addition to discussing the presentations, the breakout session participants were asked to consider several questions:

[7] Regulations include: Decree of the Minister of Trade and Industry of the Republic of Indonesia regarding the export and import of certain dangerous materials, including chemical and biological agents (2000); Decree of the Minister of Health of the Republic of Indonesia regarding safety and security guidelines for microbiology and biomedical laboratories (2009); Decree of the Minister of Health of the Republic of Indonesia regarding the delivery and use of clinical specimens, biological materials, and their information (2009); and Decree of the Minister of Health of the Republic of Indonesia to the National Commission regarding study and research on infectious diseases (2010).

1. What options do countries have to improve the sustainability, biosafety, and biosecurity of their containment laboratories?
2. To what extent do donors influence laboratory design and operation and what is the impact of their involvement?
3. Is it possible to build a "green lab"? (Reducing operating costs increases sustainability.)
4. Are there some local industries that should be encouraged?
5. Should the world establish universal design and operational standards?

Participants identified two topics to explore further.

Green Labs

While some participants felt it was possible to be greener and that "greenness" was generally desirable for economic and environmental reasons, others found discussion of the concept pointless, largely due to its incompatibility with regulations. One person described an existing modular lab capable of being shut down in parts, but most indicated that their labs shut down only for maintenance and inspections, both to comply with regulations and because their missions require them to be ready constantly. One person indicated that communities are often not receptive to the perceived risk of changing or reducing airflow to save energy even if evidence indicates that safety will not be affected. Someone noted that the American Society of Heating, Refrigerating, and Air-Conditioning Engineers[8] publishes guidelines for green designs, including labs.

Custom vs. Off-the-Shelf

Many participants felt that selecting the "right" lab was critical to achieving the needed capabilities and noted that often one of the first decisions a group makes is whether to design a custom facility or to install an "off-the-shelf " modular facility. One person from a country without any prior experience with containment labs recounted choosing a modular lab in the hope that it would be easier and still being surprised by the amount of expertise needed and the number of decisions required. Several people indicated that even with modular labs, there is no one size fits all solution and customers should shop around and make decisions based on their needs using the advice of their own technical advisors. Others cautioned that some modular labs are deceptively simple and include features such as an excessive number of HEPA filters with high maintenance requirements.

Individual participants offered various suggestions for improving safety, security, and sustainability:

- Require personnel to carry passes that track their location within the laboratory.
- Start by focusing on demonstration sites.
- Simulate both accidents and security breaches in order to identify weaknesses and improve; do not simply rely on preventative maintenance.
- If funds allow, build a mock-up to train local workers on construction techniques.
- Use the construction phase as a training opportunity for engineers and maintenance staff.
- Use re-engineering and frugal engineering techniques to design cost-effective alternatives for equipment such as biosafety cabinets.

[8] American Society of Heating, Refrigerating and Air-Conditioning Engineers. Available at: *http://www.ashrae.org/*. Accessed August 29, 2011.

8

REQUIREMENTS FOR AND CHALLENGES ASSOCIATED WITH BSL-4 LABS (PLENARY SESSION)

Chair: James Le Duc

As many of the previous sessions dealt mainly with BSL-3 labs, this session focused on some of the special issues associated with BSL-4 facilities (see Table 8-1 for a list of operational BSL-4 facilities[1]). The session examined a number of topics including how many BSL-4 facilities are needed in a region, construction and maintenance costs, biosecurity issues, environmental risks including the potential for large economic impact, training, strategies to manage an individual who becomes infected with a risk group 4 agent, community relations (see Table 8-2 for laboratories communities have prevented from operating at a BSL-4 level), whether existing and planned networks are adequate, and how much and what kinds of 'surge capacity' are ideal.

James Le Duc (University of Texas Medical Branch, United States), the session's chair, opened the session by reminding the participants that risk group 4 agents include the 'headline viruses' such as Ebola and Marburg and other causes of viral hemorrhagic fevers and that the lack of vaccines and treatments makes safety and security particularly important. He then introduced the session's four talks that provided snapshots of BSL-4 operations in different regions of the world and highlighted some of the current issues. The first talk described a network of BSL-4 labs that provides expertise and services in response to outbreaks, often on-site. The second examined the challenges associated with maintaining an aging facility, while the third looked at efforts required to maintain a permanent presence in an isolated region. The final talk addressed the importance of obtaining and maintaining community support. Following the talks, Dr. Le Duc led a discussion that explored many of the issues in greater depth.

Table 8-1 Locations of selected, operational BSL-4 labs.

Institution	Laboratory	Location
Bernard-Nocht-Institute of Tropical Medicine	Hamburg Bernhard Nocht Institute	Hamburg, Germany
CDC Special Pathogens Branch	CDC Special Pathogens Branch	Atlanta, GA United States
Commonwealth Scientific and Industrial Research Organisation	Australian Animal Health Laboratory	Geelong, Victoria Australia
Georgia State University	National B Virus Resource Center	Atlanta, GA United States
Health Protection Agency	Centre for Infections	London, England U.K.
Health Protection Agency-Centre for Emergency Preparedness and Response	Centre for Emergency Preparedness and Response, Porton Down	Salisbury U.K.
Institut Pasteur/Merieux Foundation/National Institute of Health and Medical Research of France (INSERM)	Jean Mérieux BSL-4 Laboratory	Gerland, Lyon France
International Center for Medical Research of Franceville (CIRMF)	CIRMF	Libreville, Gabon
Laboratory Centre for Disease Control	National Microbiology Laboratory	Winnipeg, Manitoba Canada

[1] It is more difficult to track the number of BSL-3 laboratories worldwide. See pages 15-16 and 26 for more information.

National Institute for Communicable Diseases	Special Pathogens Unit	Sandringham, Johannesburg South Africa
National Institute of Allergy and Infectious Diseases (NIAID)	NIAID Rocky Mountain Lab	Hamilton, MT United States
National Institute of Infectious Diseases	Lazzaro Spallanzani Hospital	Rome, Italy
Philipps Universität Marburg	Institute for Virology	Marburg, Germany
Queensland Health	Queensland Health Forensic and Scientific Services	Brisbane, Queensland Australia
Research Institute of Molecular Biology	Vector--Novosibirsk	Novosibirsk, Russia
Russian Ministry of Defense	Institute of Microbiology	Kirov, Russia
Russian Ministry of Defense	Virological Center of the Institute of Microbiology	Sergiev Possad, Russia
Swedish Institute for Communicable Disease Control	Department of Preparedness/Highly Pathogenic Microorganisms	Solna, Sweden
Teaching Hospital of Geneva	Teaching Hospital of Geneva	Geneva, Switzerland
Texas Biomedical Research Institute [a]	Texas Biomedical Research Institute [a]	San Antonio, TX United States
United States Army Medical Research Institute for Infectious Diseases (USAMRIID)	USAMRIID	Frederick, MD United States
University of Texas Medical Branch	Shope Lab, Galveston National Laboratory	Galveston, TX United States
Victorian Infectious Diseases Reference Laboratory	Victorian Infectious Diseases Reference Laboratory	Melbourne, Victoria Australia
Westmead Hospital	Centre for Infectious Diseases and Microbiology Laboratory Service (CIDMLS) and The Institute for Clinical Pathology and Medical Research (ICPMR)	Sydney, New South Wales Australia

SOURCE: Committee
[a] Formerly Southwest Foundation for Biomedical Research

TABLE 8-2 Laboratories built for BSL-4 work that as of the date of publication community opposition had prevented from operating at a BSL-4 level.

Institution	Laboratory	Location
Boston University	National Emerging Infectious Diseases Laboratories	Boston, MA United States
Central Public Health Laboratory	Central Public Health Laboratory	Etobicoke Ontario, Canada
Institute of Physical and Chemical Research (RIKEN)	RIKEN	Kanto, Tokyo Japan
National Institute of Infectious Diseases (NIID)	NIID	Tokyo, Japan

SOURCE: Committee

PLENARY PRESENTATIONS

From the Detection of BSL-4 Pathogens to the Development of Preventive and Curative Strategies

Gary Kobinger (Public Health Agency of Canada, Canada) described the structure and goals of the Emerging and Dangerous Pathogens Laboratory Network (EDPLN).

EDPLN, as Dr. Kobinger explained, resulted from informal consultations in Libreville, Gabon, in March 2008 and at World Health Organization (WHO) Headquarters in Geneva in February 2009. EDPLN is a network of BSL-4 and BSL-3 human and veterinary laboratories able and willing to share their knowledge, biological materials, reagents, protocols, and experimental results in real time to detect, diagnose, and control novel disease threats (e.g., Ebola, Marburg, SARS, Nipah, etc.). Currently, EDPLN contains 25 laboratories in 18 countries and 6 WHO regions and has infrastructure such as portable glove-box labs that can be rapidly deployed to outbreaks sites anywhere in the world using standard commercial crates suitable for air transport.

The EDPLN network has a number of goals:

- Support diagnostic functions for laboratory response to global epidemic threats of new, emerging, and dangerous pathogens;
- Build capacity and transfer technology for safe and appropriate diagnostics to regional networks and countries in zones of emergence to enhance outbreak detection and management; and
- Provide surge capacity in response to epidemic activity.

He noted that EDPLN has working groups for laboratory outbreak response, assay and reagent development, technology transfer and training, international engagement, and applied research. Biosafety, biosecurity, and shipment of dangerous goods are issues of concern to the international engagement group. He added that in addition to sharing reagents for ELISA-based (enzyme-linked immunosorbent assay) detection of various pathogens in primates, EDPLN also develops post-exposure treatment options for Ebola virus and other agents. Dr. Kobinger ultimately hopes to develop treatments for use both in the lab for post-exposure prophylaxis and in the field to treat naturally infected individuals.

Dr. Kobinger noted that EDPLN is just one element in the WHO-coordinated Global Outbreak Alert and Response Network (GOARN) that also includes clinical networks, mathematical modeling groups, and infection control networks. The overall GOARN approach includes social mobilization, health education, risk communication, case management, safe funerals, death audits, infection control, environment and vector control, logistics, security, communications, epidemiological investigation, and surveillance. He explained that WHO created this multidisciplinary approach for emerging, infectious disease outbreak control to help the affected population and countries take appropriate measures to interrupt the spread of disease and ensure the safety of both the population at risk and the international partners assisting in the outbreak response. Additionally, GOARN also works to ensure that our understanding of new diseases progresses in a manner that will increase global preparedness.

Requirements for and Challenges Associated with BSL-4 Laboratories

Greg Smith (Australian Animal Health Laboratory, Australia) talked about the Australian Animal Health Laboratory (AAHL) and the challenges associated with maintaining and upgrading an aging facility and the lab's biosecurity and public relations efforts.

Dr. Smith started by introducing AAHL, which is located in Geelong, Australia. The lab opened in 1985, cost $200 million to build in 1985 Australian dollars, and would cost $650-700 million Australian dollars to replace today. The facility has 15,000 m^2 of lab space including 2,900 m^2 of BSL-3 space (28 rooms) and 100 m^2 of BSL-4 space. The AAHL also has two BSL-4 animal rooms, one of which can hold up to six horses, and 955 m^2 of animal biosafety level (ABSL)-3 space. The facility is available to scientists across Australia and globally and has government, academic, and commercial clients.

AAHL's staff includes 60 full-time engineers and has annual maintenance and running costs of $6.8 million. He added that the lab just completed a $25 million engineering upgrade that focused on control and monitoring and that changing standards will require additional significant investment. Additionally, the lab would like to add 127 m^2 of ABSL-4 space as well as additional BSL-4 space. He noted that the scientific mission requires continuous operation during refurbishment and expansion, which greatly increases construction costs.

He then addressed the lab's biosecurity features. In addition to employing a microbiology security staff of 10, the building, which is surrounded by a perimeter fence, has infrared cameras and was designed using the box within a box principle. Doors have dual access controls and cyberlocks that record identity of each person who attempts access along with the time and date. AAHL has a dedicated training lab and uses structured competency based training during which all routine and emergency procedures are practiced. The Australian Security Intelligence Organization clears all AAHL staff with security access. Local regulations prohibit residents from keeping cloven-hoofed animals within 5 km of the laboratory, and AAHL staff may not live on farms.

AAHL formed a Medical Advisory Committee (MAC) about 15 years ago following a Newcastle incident to manage any individual who might become infected while working in the facility. The MAC includes the State Chief Health Officer, the State Chief Veterinary Officer, a local general practitioner, and an infectious disease physician. All incidents are referred to the MAC, which can put people in home quarantine or admit them to an infectious diseases ward. The MAC is aware of all pathogens and reagents in use at AAHL.

Dr. Smith observed that the facility's long record of safe operation has led to strong community support. To help maintain that support, he explained that AAHL employs a dedicated public relations officer who facilitates media coverage and actively engages with the community. Activities include school programs and tours for key state and federal politicians. While community support is strong, he admitted that it is not unconditional: Although the lab was built for foot and mouth disease (FMD) diagnosis and vaccine production, FMD virus has never been placed in the lab due to opposition from farmers and ranchers.

Potential and Constraints Associated with Developing an Advanced Laboratory in a Challenging Technical and Social Environment

Jean-Paul Gonzalez (The International Centre of Medical Research of Franceville, Gabon [CIRMF]) talked about the special challenges that accompany the unique location of CIRMF.

Dr. Gonzalez started by reminding the audience that his facility, which contains a glove box BSL-4 lab, is located in the middle of a tropical rainforest and that Libreville, the nearest city, is 3 hours away by small plane or 12 hours by car or train. He described how the lab's location, which is critical for its mission, makes communications, scientific exchanges, and supply and equipment delivery difficult. Field stations, for example, rely on satellite dishes for communications, and the facility's isolation requires them to generate their own liquid nitrogen, make their own dry ice, and maintain two generators to ensure uninterrupted power for their -80°C freezers. In addition to the difficulty of finding technical and scientific personnel in such a small country, all visitors and researchers require on-site accommodations. Furthermore, the low standards of local products make maintenance a challenge.

CIRMF does not, however, rely on its isolation for security. The BSL-4 lab is separated from the other buildings and has electric fences and a guard on duty at all times. For additional control, only three people know the code to the BSL-4 freezer.

Dr. Gonzalez attributed the facility's success to relatively secure funding; local, regional, and international partners; and national political stability. He ended by pointing to the

approximately 700 peer-reviewed papers the facility has produced over the last 30 years as evidence of the scientific return on investments in CIMRF.

The High-containment Laboratory of the National Institute of Infectious Diseases, Tokyo, Japan: Activities, Circumstances, and Future Challenges

Masayuki Saijo (National Institute of Infectious Diseases, Japan) talked about the importance of community support in operating a BSL-4 laboratory.

He opened by explaining that the National Institute of Infectious Diseases (NIID) constructed a glove box BSL-4 facility in its Murayama annex in the early 1980s, but the lab, which is expensive to maintain, has never been used as a BSL-4 due to local opposition. In an effort to increase community support, NIID periodically gives seminars on infectious diseases to community residents and has established a safety committee that includes members of the local municipalities.

In addition to community opposition, Dr. Saijo explained that NIID's situation is also complicated by the Japanese Infectious Diseases Control Law, which restricts importation, possession, transportation, and transfer of many agents including Ebola virus, Marburg virus, Crimean-Congo hemorrhagic fever (CCHF) virus, Lassa virus, South American hemorrhagic fever viruses, and *Yersinia pestis*.

Dr. Saijo argued that NIID, in collaboration with key partners, has an important role to play in the world, and to fulfill that role it must operate as a BSL-4. Specifically, operating the facility as a BSL-4 laboratory would better allow NIID to prepare for possible outbreaks of hemorrhagic fever and other emerging infections in both Japan and other parts of the world. Dr. Saijo recognizes that fulfilling what he views as the NIID's mission will require mutual understanding between NIID and the community about safety and operational risks and will also require mutual collaboration between NIID; the Ministry of Health, Labor, and Welfare of Japan; and the Ministry of Education, Culture, Science, and Technology.

Although NIID has been unable to operate as a BSL-4 lab, Dr. Saijo gave examples of how the facility is still working to combat emerging and exotic infectious diseases by developing diagnostic tests and vaccines, often in collaboration with international partners. Organisms of interest include the CCHF virus, for which NIID developed a recombinant nucleoprotein-based antibody detection system; avian influenza virus, for which they have been testing vaccines using nonhuman primates; and severe acute respiratory syndrome (SARS) coronavirus, for which they are developing diagnostics, vaccines, and animal models. NIID is also engaged in an efficacy assessment of a highly attenuated smallpox vaccine, LC16m8, using nonhuman primate models.

DISCUSSION

During the discussion, participants focused on three main topics:

Community Relations and the Power of Perceived Risks

Participants reported a wide range of reactions to local labs from pride to apathy to intense opposition. Support sometimes stemmed from the associated jobs, and opposition was normally due to fear of accidental or intentional releases. Furthermore, many felt that perceived rather than real risks were the primary drivers of negative community reactions.

The need to distinguish real and perceived risks was mentioned in many discussions, including the one in this session. For example, numerous people noted that pregnant lab workers often quit working in containment laboratories out of fear for themselves and their unborn child, but participants did not agree on whether that fear was justified. (Many felt it was

not.) Another example was whether regulations should be changed to permit recirculation of HEPA-filtered air from the containment laboratory into non-laboratory parts of a building, which could decrease heating and cooling costs. Several people felt the rule existed mainly because office workers did not feel comfortable breathing lab air and that no real risk was present, particularly if filters were tested annually as required. Others considered recirculation unacceptably risky regardless, indicating that some HEPA filters have poor integrity and that while some of the energy used in heating or cooling the air could be recovered, the air itself should not be. In contrast, recirculation of HEPA-filtered air (both from biological safety cabinets [BSCs] and from the lab itself) is currently permitted to a BSL-3 lab, which many people felt was acceptable due to the additional precautions in place and, possibly, more permissive attitudes among lab workers. Several people indicated that often evidence to accurately characterize and assess risks is not available.

Many also felt that perceived risks had a large impact on regulations and enforcement for both BSL-3 and BSL-4 labs. Someone suggested that liability concerns and society's current aversion to risks have made regulators increasingly conservative and that it was far easier for regulators to say 'no' than to understand the real risks. Others expressed a need to educate regulators and felt that caution was a reasonable response to a lack of understanding. One person recommended that inspectors have lab experience and that evidence be collected to serve as a basis for writing sensible regulations. Another pointed out the difficulty in writing regulations or training inspectors in places with only a small number of facilities.

Various participants offered a number of suggestions for improving and maintaining community support. Ideas included educating locals about infectious diseases, particularly those diseases that are endemic to their location, and approaching communities that are comfortable with and support existing labs, rather than communities with no laboratory experience, when new BSL-4 space is needed. One person reported success with having the organization's top leadership engage with the community and answer questions before plans were finalized and before money was spent.

Current BSL-4 Needs

Many people felt that the world had sufficient BSL-4 diagnostic capacity but needed more BSL-4 research space. As threats can arise from anywhere, some felt that the diagnostic capacity could, however, be more widely distributed. Participants were divided concerning the comparable merits of a small number of larger, more economical labs and a larger number of small labs closer to potential endemic sites or existing centers of excellence. Several participants also noted that few BSL-4 labs can work with large animals and that in addition to direct concerns about animal health, livestock and companion species often serve as reservoirs for pathogens (e.g., cattle harbor Crimean-Congo hemorrhagic fever [CCHF] virus) and that the entire human-livestock interface is very important for biosecurity. Additionally, several people pointed to fieldwork with risk group 4 organisms as another area that could benefit from improved safety and security.

Personnel Reliability

The group had a number of thoughts about how to increase personnel reliability and to guard against threats from those working in containment laboratories (insider threats). Ideas included increasing trust among scientists and technicians working within containment facilities, enhancing transparency regarding the work being undertaken, monitoring how well those working within biocontainment facilities adhere to protocols, requiring accurate record keeping, and allowing people to opt-out of containment lab work when under personal stress or otherwise unable to fully concentrate on a particular day with few questions asked. Many indicated that

the facility director had a critical responsibility to set the overall atmosphere and that a director should know and establish relationships with every scientist in a lab. Thoughts on the values of psychological screenings were mixed and concerns were raised about the value and utility of existing testing tools. Some, including a few who expressed skepticism about the accuracy of the tests, felt that given the high costs of even a single accident, not using all possible tools could be considered irresponsible. One person, however, indicated that denying someone the right to work on the basis of a psychological test would be considered a human rights violation in some countries.

9

CONCLUDING PLENARY DISCUSSIONS: MAJOR THEMES AND NEXT STEPS

Chair: Adel Mahmoud

Following brief presentations from rapporteurs on the previous day's breakout sessions, United States National Research Council (NRC) Committee Chair **Adel Mahmoud** (Princeton University, United States) led a final discussion on July 13, 2011 to draw attention to the main themes from the workshop, consider the importance of the various issues raised, and identify possible next steps. In the course of the discussion, the group considered the overarching challenges; connections, drivers, and tensions in the field; the areas of greatest concern; and actions with the potential to generate the largest positive impact.

Many participants commented on various aspects of the on-going global expansion of high-containment laboratory capacity. Construction of new labs is continuing, and with the WHO International Health Regulations (IHR) (2005) coming into force, many countries are deciding whether to create their own diagnostic capabilities or to rely on regional neighbors to meet their needs. Laboratory networks are coalescing as countries and regions decide which capabilities they should share and which they need locally. Inadequate transportation infrastructure, restrictive shipping regulations, and intellectual property concerns, however, often hamper multi-national efforts. Many facilities need improved sustainability strategies some participants noted, as donors and national governments often choose to fund new labs rather than maintain on-going operations at older labs. Furthermore, emerging technologies such as molecular diagnostics and high-throughput sequencing, which unlike culture-based assays do not require viable pathogens or containment labs, are expanding diagnostic options and infrastructure is struggling to keep up. Similarly, regulations and guidance have not always kept pace with developments. In some countries, rules exist but are poorly understood and enforced, and many countries lack national guidelines and regulations altogether. Many felt that while these topics are predominantly national issues, international discussions could facilitate progress.

TRANSITIONING FROM BIO SAFETY LEVEL-BASED TO FULLY RISK-BASED PRECAUTIONS

Some speakers drew attention to limitations of the current World Health Organization (WHO) and "Biosafety in Microbiological and Biomedical Laboratories" (BMBL) systems (i.e., BSL-1, 2, 3, or 4) for characterizing labs and practices. While acknowledging the simplicity of systems with a small number of pre-defined levels, they felt the classification methodologies too coarse to describe the wide spectrum of risks that laboratories must address and indicated that the levels are sometimes negatively perceived as a ranking. Others desired minimal standards that could serve as an attainable goal.[1] Many argued that while BSL levels were created as specific measures to mitigate particular risks, recently BSL levels have often been used as general-purpose, canned solutions. A common complaint was that by strictly enforcing adherence to one of the standard levels, funders often stop engineers and architects from

[1] Global Laboratory Initiative's recommendations for tuberculosis procedures (described in Chapter 6), are an example of guidance that could function as a minimum standard.

considering practical, less expensive construction and equipment options that could be sufficient in specific circumstances.

Many had similar concerns about systems used to classify pathogens (e.g., risk groups 1-4), indicating that prudent handling practices depend not only on the organism, but also the procedures to be performed and the endemic situation.[2] Additionally, one person noted that for precautionary reasons, novel pathogens are usually assumed to be high-risk, and that the initial classification is rarely revisited unless the microbe causes an outbreak that overwhelms the public health system. Hence, the participant said, a systematic reassessment of organisms that downgrades pathogens when appropriate would likely speed research, improve preparedness, and increase the number of potential research collaborators.

As an alternative to the current systems, numerous participants proposed starting over and performing a full, situation-specific risk analysis. Several people pointed to the Global Laboratory Initiative's (GLI) recommendations for tuberculosis (TB) procedures, which are described in Chapter 6, as a good example of the benefits of the risk-based approach. GLI abandoned the traditional BSL framework and instead characterized the risks associated with specific diagnostic and research procedures in detail. Instead of the previous blanket recommendation of BSL-3 labs for most TB work,[3] the result is far more nuanced and allows groups to invest in infrastructure and precautions suited to the type of procedures that they actually perform.

Multiple attendees acknowledged that moving to a fully risk-based system, although desirable, would require an increase in both data and expertise. Some worried that the lack of funding for applied biosafety research and the paucity of formal accident reporting systems would make obtaining accurate information about how well particular precautions function difficult. Similarly, implementing new recommendations and procedures would require more training specific to the staff and the situation.

IMPORTANCE OF COLLABORATION

Many participants indicated that in their experience collaboration is the most successful way to transfer knowledge and expertise and that productive collaborations rely on the recruitment and involvement of credible, experience-appropriate individuals from both the donor and recipient countries. For countries that lack sufficient indigenous expertise, activities like WHO's Train-the-Trainer programs can help fill the gap. Examples of collaborations included individual mentoring programs, such as those offered by many biological safety associations, and laboratory twinning programs like the ones sponsored by the World Organisation for Animal Health (OIE). Several individuals suggested that central (hub) laboratories could use similar mentoring and twinning mechanisms to strengthen the rest of their networks. Such a model would also allow donors and international collaborators to focus their efforts on a small set of hub labs and multiply the return on their investment. Along the same lines, assistance in 'needs' decision making in a region or country might consist of a joint analysis of needs rather than a simple declaration of, "Here's what you need." Some attendees also suggested drawing on the expertise of individuals in related fields such as those who design or work with hospital isolation rooms or members of the pharmaceutical industry who are familiar with working in a disciplined regulatory environment.

[2] The BMBL does augment the classification with specific recommendations for many organisms.
[3] See pages 145-147 of the BMBL (United States HHS, 2009) for current guidance on TB work.

STRATEGIES TO AFFECT IMPROVEMENTS

Many participants identified the Biological and Toxin Weapons Convention (BWC) review in December of 2011 and the subsequent annual "experts meetings," the IHR update in 2014, and the next revision of the WHO Laboratory Biosafety Manual (LBM) as places the biosafety, biosecurity, and public health communities might try to make changes. The IHR, might, for example, add minimum safety and security standards to the current diagnostic capability requirements. The LBM revision might consider adding the GLI TB recommendations as well as rethinking other recommendations on the basis of new risk analyses. Future BWC confidence building measures might consider requesting information about laboratory biosecurity and biosafety for BSL-4 labs and representative BSL-3 labs to help define and baseline this type of research and the current norms in the world.

To increase funds for operations and maintenance and support for regulatory changes from national governments and donors, laboratories might increase their efforts to describe containment laboratories in the context of government priorities, national health systems, and local economies. Both labs and their communities benefit when consumables and equipment are available locally, and a quick response during a public health emergency relies on pre-existing bridges between a containment lab and the public health infrastructure. Additionally, biosafety associations could help by educating scientists as well as policymakers and functioning as a catalyst for rewriting national and international standards.

ABBREVIATIONS AND ACRONYMS

A-PBA	Asia-Pacific Biosafety Organization
AAHL	Australian Animal Health Laboratory
ABSA	American Biological Safety Association
ABSL	Animal biosafety level
ACH	Air changes per hour
AFB	Acid-fast bacillus
AfBSA	African Biological Safety Organization
AI	Avian influenza
AIDS	Acquired immune deficiency syndrome
ANBio	Brazilian Biosafety Association
AusAID	Australian Government Overseas Aid Program
BATA	Biological Agents and Toxins Act (Singapore)
BD	Border disease
BEN	Biocontainment Engineering Network (IFBA)
BEP	Biosecurity Engagement Program (United States)
BLWG	Biological Laboratory Working Group (Canada/Kyrgyz Republic)
BMBL	Biosafety in Microbiological and Biomedical Laboratories
BSA	Biosafety association
BSC	Biological safety cabinet
BSL	Biosafety level
BTRP	Biological Threat Reduction Program
BVD	Bovine viral diarrhoea
BWC	Biological and Toxin Weapons Convention
CAREC	Caribbean Epidemiology Centre
CCHF	Crimean-Congo hemorrhagic fever
CDC	Centers for Disease Control and Prevention (United States)
CEN	European Committee for Standardization
CIRMF	International Centre of Medical Research of Franceville
CMLF	Caribbean Med Labs Foundation
COMSTECH	Ministerial Standing Committee on Scientific and Technological Cooperation (Pakistan)
CPA	Mexico-US Commission for the Prevention of Foot and Mouth Disease and Other Exotic Animal Diseases
CPHRL	Central Public Health Reference Laboratory (Republic of Georgia)
CTR	Cooperative Threat Reduction
CWA	CEN Workshop Agreement
DARPA	Defense Advanced Research Projects Agency
DTRA	Defense Threat Reduction Agency
EDPLN	Emerging and Dangerous Pathogens Laboratory Network
ELISA	Enzyme-linked immunosorbent assay
EHEC	Enterohaemorrhagic *Escherichia coli*
EU	European Union

FAO	Food and Agriculture Organization of the United Nations
FBI	Federal Bureau of Investigation (United States)
FMD	Foot and mouth disease
FTA	Flinders Technology Associates
GAO	Government Accountability Office (United States)
GOARN	Global Outbreak Alert and Response Network
GLI	Global Laboratory Initiative
GMO	Genetically modified organism
GMP	Good manufacturing practice
HEPA	High-efficiency particulate air
HFRS	Hemorrhagic fever with renal syndrome
HIV	Human immunodeficiency virus
HPAI	Highly pathogenic avian influenza
HSADL	High Security Animal Disease Laboratory
HUS	Haemolytic uraemic syndrome
HVAC	Heating, ventilation, and air conditioning
IAP	InterAcademy Panel on International Issues
IAP BWG	InterAcademy Panel on International Issues Biosecurity Working Group
IATA	International Air Transport Association
IBC	Institutional Biosafety Committee
IFBA	International Federation of Biosafety Associations
IHR	International Health Regulations
INTERPOL	International Criminal Police Organization
ICAO	International Civil Aviation Organization
ICLS	International Council of Life Sciences
IEC	International Electrotechnical Commission
IFA	Immunofluorescence assays
IgM	Immunoglobulin M
IPM	Institut Pasteur du Maroc
IPPC	International Plant Protection Convention
ISO	International Organization for Standardization
IVI	International Vaccine Institute
JICA	Japan International Cooperation Agency
KCDC	Korean Center for Disease Control and Prevention
LAI	Laboratory-acquired infection or laboratory-associated infection
LANL	Los Alamos National Lab
LBM	Laboratory Biosafety Manual
LPAI	Low pathogenic avian influenza
LRN	Laboratory Response Network
MAC	Medical Advisory Committee (Australia, AAHL)
MARA	Ministry of Agriculture and Rural Affairs (Turkey)
MDR-TB	Multidrug-resistant tuberculosis
MORU	Mahidol Oxford Tropical Medicine Research Unit

NGO	Non-governmental organization
NIAID	National Institute of Allergies and Infectious Diseases (United States)
NIH	National Institutes of Health (United States)
NIHRD	National Institute of Health Research and Development (Indonesia)
NIID	National Institute of Infectious Diseases (Japan)
NRC	National Research Council (United States)
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
OIE CC	World Organisation for Animal Health Collaborating Center
OIE RL	World Organisation for Animal Health Reference Laboratory
OUCRU-HCM	Oxford University Clinical Research Unit—Ho Chi Minh City
PCR	Polymerase chain reaction
POC	Point-of-care
PPE	Personal protective equipment
RKI	Robert Koch Institute
RT-PCR	Reverse transcription polymerase chain reaction
SAPO	Specified Animal Pathogens Order (U.K.)
SARS	Severe acute respiratory syndrome
SEAICRN	Southeast Asian Clinical Infectious Diseases Network
SIV	Simian immunodeficiency virus
SNL	Sandia National Laboratories
SOP	Standard operating procedure
TB	Tuberculosis
TÜBA	Turkish Academy of Sciences
UNAS	Uganda National Academy of Science
UNESCO	United Nations Educational, Scientific, and Cultural Organization
VSVRI	Veterinary Serum and Vaccine Research Institute
WHO	World Health Organization
XDR	Extremely drug resistant

REFERENCES

Akinfeeva, L.A., O.I. Aksionova, I.V. Vasilevich, Z.I. Gin'ko, K.A. Zar'kov, N.M. Zybavichene, L.R. Katkova, O.P. Kuzovlev, V.I. Kuzubov, L.I. Lokteva, and E.I. Ryabchikova. 2005. A case of Ebola hemorrhagic fever. *Infektsionnye bolezni (Epidemiology and Infectious Diseases)* 1:85-88.

Department of the Army. 2008. *Nuclear and Chemical Weapons and Materiel: Biological Surety*. Army Regulation 50-1. Headquarters, Department of the Army: Washington, D.C. 54 pp. [Online]. Available at: *http://www.fas.org/irp/doddir/army/ar50-1.pdf*.

Di, B., W. Hao, Y. Gao, M. Wang, Y.D. Wang, L.W. Qiu, K. Wen, D.H. Zhou, X.W. Wu, E.J. Lu, Z.Y. Liao, Y.B. Mei, B.J. Zheng, and X.Y. Che. 2005. Monoclonal antibody-based antigen capture enzyme-linked immunosorbent assay reveals high sensitivity of the nucleocapsid protein in acute-phase sera of severe acute respiratory syndrome patients. *Clinical and Diagnostic Laboratory Immunology* 12(1):135-140.

Ergonul, O. 2006. Crimean-Congo haemorrhagic fever. *The Lancet Infectious Diseases* 6(4):203-214.

Ergonul, O. 2008. Treatment of Crimean-Congo hemorrhagic fever. *Antiviral Research* 78(1):125-131.

Ergonul, O., H. Zeller, A. Celikbas, and B. Dokuzoguz. 2007. The lack of Crimean-Congo hemorrhagic fever virus antibodies in healthcare workers in an endemic region. *International Journal of Infectious Diseases* 11(1):48-51.

Federal Register. 2005. *Galveston National Laboratory Record of Decision*. 70(68):18408.

Franz, D.R. and J.W. Le Duc. 2011. Balancing our approach to the insider threat. *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 9(3):205-206.

Franz, D.R., S.A. Ehrlich, A. Casadevall, M.J. Imperiale, and P.S. Keim. 2009. The “nuclearization” of biology is a threat to health and security. *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 7(3):243-244.

Gaidamovich, S.Y., A.M. Butenko, and H.V. Leschinskaya. 2000. Human laboratory Acquired Arbo-, Arena- and Hantavirus infections. *Journal of American Biological Safety Association* 5(1):5-11.

Gaudioso, J., S.A. Caskey, L. Burnett, E. Heegaard, J. Owens, and P. Stroot. 2009. *Strengthening Risk Governance in Bioscience Laboratories*. Sandia Report: SAND2009-8070. Sandia National Laboratories. Albuquerque, NM. 147 pp.

Harding, A.L. and K.B. Byers. 2000. Epidemiology of laboratory-associated infection. *In: Biological Safety: Principles and practices.* Pp. 35-56. Fleming, D.O. and D.L. Hunt (Eds.). 3rd ed. Washington, D.C.: ASM Press.

Heckert, R.A., J.C. Reed, F. Gmuender, M. Ellis, and W. Tonui. 2011. International biosafety and biosecurity challenges: Suggestions for developing sustainable capacity in low-resource countries. *Applied Biosafety* 16(4).

Jackson, R.J., A.J. Ramsay, C.D. Christensen, S. Beaton, D.F. Hall, and I.A. Ramshaw. 2001. Expression of mouse interleukin-4 by a recombinant ectromelia virus suppresses cytolytic lymphocyte responses and overcomes genetic resistance to mousepox. *The Journal of Virology* 75(3):1205-1210.

Jefferson, T., R. Foxlee, C. Del Mar, L. Dooley, E. Ferroni, B. Hewak, A. Prabhala, S. Nair, and A. Rivetti. 2008. Physical interventions to interrupt or reduce the spread of respiratory viruses: Systematic review. *British Medical Journal* 336(7635):77-80.

Kaiser, J. 2011. Taking stock of the biodefense boom. Science 333(6047):1214.

Kruse, R.H., W.H. Puckett, and J.H. Richardson. 1991. Biological safety cabinetry. *Clinical Microbiology Reviews* 4(2):207-241.

Liu, X., Y. Shi, P. Li, L. Li, Y. Yi, Q. Ma, C. Cao. 2004. Profile of antibodies to the nucleocapsid protein of the severe acute respiratory syndrome (SARS)-associated coronavirus in probable SARS patients. *Clinical and Diagnostic Laboratory Immunology* 11(1):227-228.

Markotic, A., L. Hensley, T. Geisbert, K. Spik, and C. Schmaljohn. 2003. Hantaviruses induce cytopathic effects and apoptosis in continuous human embryonic kidney cells. *Journal of General Virology* 84(8):2197-2202.

Medina, R.A., B. Manicassamy, S. Stertz, C.W. Seibert, R. Hai, R.B. Belshe, S.E. Frey, C.F. Basler, P. Palese, and A. García-Sastre. 2010. Pandemic 2009 H1N1 vaccine protects against 1918 Spanish influenza virus. Nature Communications 1:28. doi: 10.1038/ncomms1026. Available at: *http://www.nature.com/ncomms/journal/v1/n3/full/ncomms1026.html.*

National Research Council (NRC). 2007a. The Biological Threat Reduction Program of the Department of Defense: From Foreign Assistance to Sustainable Partnerships. Washington, D.C.: National Academies Press.

National Research Council. 2007b. Technical Input on the National Institutes of Health's Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University: A Letter Report. Washington, D.C.: National Academies Press.

National Research Council. 2009a. A Survey of Attitudes and Actions on Dual Use Research in the Life Sciences: A Collaborative Effort of the National Research Council and the American Association for the Advancement of Science. Washington, D.C.: National Academies Press.

National Research Council. 2009b. Countering Biological Threats: Challenges for the Department of Defense's Nonproliferation Program Beyond the Former Soviet Union. Washington, D. C.: National Academies Press.

National Research Council. 2009c. Global Security Engagement: A New Model for Cooperative Threat Reduction. Washington, D.C.: National Academies Press.

National Research Council. 2009d. The 2nd International Forum on Biosecurity: Summary of an International Meeting, Budapest, Hungary, March 30 to April 2, 2008. Washington, D.C.: National Academies Press.

National Research Council. 2009e. Responsible Research with Biological Select Agents and Toxins. Washington, D.C.: National Academies Press.

National Research Council. 2010a. Infectious Disease Movement in a Borderless World: Workshop Summary. Washington, D.C.: National Academies Press.

National Research Council. 2010b. Evaluation of the Health and Safety Risks of the New USAMRIID High-containment Facilities at Fort Detrick, Maryland. Washington, D.C.:. National Academies Press.

National Research Council. 2010c. Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and *Agro-Defense Facility in Manhattan, Kansas*. Washington, D.C.: National Academies Press.

National Research Council. 2010d. *Challenges and Opportunities for Education About Dual Use Issues in the Life Sciences*. Washington, D.C.: National Academies Press.

National Research Council. 2011a. *Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Anthrax Letters*. Washington, D. C. :National Academies Press.

National Research Council. 2011b. *Trends in Science and Technology Relevant to the Biological and Toxin Weapons Convention: Summary of an International Workshop: October 31 to November 3, 2010, Beijing, China*. Washington, D. C.: National Academies Press.

National Research Council. 2011c. *Protecting the Frontline in Biodefense Research: The Special Immunizations Program*. Washington, D.C.: National Academies Press.

Picard-Meyer, E., J. Barrat, and F. Cliquet. 2007. Use of filter paper (FTA) technology for sampling, recovery and molecular characterisation of rabies viruses. *Journal of Virological Methods* 140(1-2):174-182.

Pike, R.M. 1979. Laboratory-associated infections: incidence, fatalities, causes, and prevention. *Annual Review of Microbiology* 33:41-66.

Public Law 104-132: *Antiterrorism and Effective Death Penalty Act of 1996*. (110 Stat. 1214, 04/24/1996). [Online]. Available: *http://www.gpo.gov/fdsys/pkg/PLAW-104publ132/pdf/PLAW-104publ132.pdf*.

Public Law 107-56: *Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA Patriot Act) Act of 2001*. (115 Stat. 272, 10/26/2001). [Online]. Available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_cong_public_laws&docid=f:publ056.107.pdf.

Public Law 107-188: *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*. (116 Stat. 594, 06/12/2002). [Online]. Available: *http://www.epa.gov/watersecurity/pubs/security_act.pdf*.

Rusnak, J.M., M.G. Kortepter, R.J. Hawley, A.O., Anderson, E. Boudreau, and E. Eitzen. 2004. Risk of occupationally acquired illness from biological threat agents in unvaccinated laboratory workers. *Biosecurity and Bioterrorism: Biodefense Strategy, Practice, and Science* 2(4):281-293.

Sawyer, J., A. Bennett, V. Haines, E. Elton, K. Crago, S. Speight. 2006. Measuring the loss of dexterity during microbiological containment systems use. *Journal of Occupational and Environmental Hygiene* 4(3):166-173.

Shi, Y., Y. Yi, P. Li, T. Kuang, L. Li, M. Dong, Q. Ma, C. Cao. 2003. Diagnosis of severe acute respiratory syndrome (SARS) by detection of SARS coronavirus nucleocapsid antibodies in an antigen-capturing enzyme-linked immunosorbent assay. *Journal of Clinical Microbiology* 41(12):5781-5782.

Schwarz, T.F., H. Nsanze, M. Longson, H. Nitschko, S. Gilch, H. Shurie, A. Ameen, A.R. Zahir, U.G. Acharya, and G. Jager. 1996. Polymerase chain reaction for diagnosis and identification of distinct variants of Crimean-Congo hemorrhagic fever virus in the United Arab Emirates. *The American Journal of Tropical Medicine and Hygiene* 55(2):190-196.

Stavskiy, E.A., B. Johnson, R.J. Hawley, J.T. Crane, N.B. Cherny, I.V. Renau, and S.V. Netesov. 2003. Comparative Analysis of Biosafety Guidelines of the USA, WHO, and Russia (Organizational and Controlling, Medical and Sanitary- Antiepidemiological Aspects). *Applied Biosafety* 8(3):118-127.

Tumpey, T.M., C.F. Basler, P.V. Aguilar, H. Zeng, A. Solórzano, D.E. Swayne, N.J. Cox, J.M. Katz, J.K. Taubenberger, P. Palese, and A. García-Sastre. 2005. Characterization of the reconstructed 1918 Spanish influenza pandemic virus. *Science* 310(5745):77-80.

Uganda National Academy of Science (UNAS). 2008. *Promoting Biosafety and Biosecurity Within the Life Sciences: An International Workshop in East Africa*. Uganda National Academy of Sciences, Kampala, Uganda.

Uganda National Academy of Science. 2009. *Establishing and Promoting Standards and Good Laboratory Practice (GLP) for Running Safe, Secure, and Sustainable Laboratories in Africa*. Uganda National Academy of Sciences. Kampala, Uganda:

Uganda National Academy of Sciences. 2010. *Scope of Biosafety and Biosecurity in Uganda: Policy Recommendations for the Control of Associated Risks: A Consensus Study Report*. Uganda National Academy of Sciences, Kampala, Uganda.

United Nations (U.N.) Security Council, 4956th Meeting. 2004. Resolution 1540. (S/RES/1540). April 28, 2004.

United States Department of Health and Human Services (United States HHS). 2009. *Biosafety in Microbiological and Biomedical Laboratories*. 5th Edition. HHS Publication No. (CDC) 21-1112. Washington, D.C. 438 pp. [Online]. Available: *http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf*.

United States Government Accountability Office (United States GAO). 2007. High-Containment Biosafety Laboratories: Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States. GAO-08-108T. Washington, D.C. [Online]. Available: *http://www.gao.gov/new.items/d08108t.pdf*.

United States Government Accountability Office. 2009. High-Containment Laboratories: National Strategy for Oversight Is Needed. Report to Congressional Requesters. GAO-09-574. Washington, D.C. [Online]. Available: *http://www.gao.gov/new.items/d09574.pdf*.

van de Wal, B.W., J.R. Joubert, P.J. van Eeden, and J.B. King. 1985. A nosocomial outbreak of Crimean-Congo haemorrhagic fever at Tygerberg Hospital. Part IV. Preventive and prophylactic measures. *South African Medical Journal* 68(10):729-732.

Wacharapluesadee, S. and T. Hemachudha. 2007. Duplex nested RT-PCR for detection of Nipah virus RNA from urine specimens of bats. *Journal of Virological Methods* 141(1):97-101.

Wacharapluesadee, S., P. Phumesin, B. Lumlertdaecha, and T. Hemachudha. 2003. Diagnosis of rabies by use of brain tissue dried on filter paper. *Clinical Infectious Diseases* 36(5):674-675.

World Health Organization (WHO). 2004. *Laboratory Biosafety Manual*. 3rd Edition. WHO Press, Geneva, Switzerland. 178 pp.

World Health Organization. 2005. *Enhancement of Laboratory Biosafety*. World Health Assembly resolution WHA58.29. World Health Organization, Geneva, Switzerland. [Online]. Available: *www.who.int/gb/ebwha/pdf_files/WHA58/WHA58_29-en.pdf*.

World Health Organization. 2008. International Health Regulations 2005. 2nd Edition. Geneva, Switzerland WHO Press. 74 pp.

APPENDIX A

WORKSHOP AGENDA

ANTICIPATING BIOSECURITY CHALLENGES OF THE GLOBAL EXPANSION OF HIGH-CONTAINMENT BIOLOGICAL LABORATORIES
Istanbul, Turkey
July 11-13, 2011

This international workshop will examine issues related to the design, construction, and operation of high-containment biological laboratories—equivalent to United States Centers for Disease Control and Prevention Biological Safety 3 or 4 level labs. Although these laboratories are needed to isolate some highly dangerous pathogens, they are complex systems with inherent risks. The workshop will aim to engage scientific experts and policy makers both from countries experienced in operating laboratories and from countries that are contemplating or undertaking the construction of new facilities. Possible areas for discussion include:

- Technological options to meet diagnostic, research, and other goals;
- Laboratory construction and commissioning;
- Operational maintenance to provide sustainable capabilities, safety, and security;
- Measures for encouraging a culture of responsible conduct

Workshop participants will explore possible strategies for enhancing biological safety and security worldwide and will offer practical suggestions to countries considering constructing or expanding their high biocontainment facilities.

AGENDA

JULY 10, 2011

Some Participants Arrive

20:00 *Informal Reception* (Jolly Café, Point Hotel)

JULY 11, 2011
(Main Meeting Room: Fuji II)

8:30 Registration (Remaining Participants Arrive)

9:00 **Plenary:** *Welcome*
Adel Mahmoud (NRC Committee Chair, Princeton University, United States)
Sevket Ruacan (Koç University, School of Medicine, Turkey)
Sumi Paranjape (Biosecurity Engagement Program, United States)

9:20 **Plenary:** *Framing the Issue, Part 1:*
The function of high-containment labs and factors encouraging and constraining the creation of new labs

This session will start by reminding the participants that lab practices are intended to keep the worker safe, buildings are designed to keep the community safe, and that there are often many ways of achieving those objectives. The session will then describe the recent expansion in the number of high-containment biology labs including the types of labs, the standards and designs used, factors driving and restraining the expansion, and safety and security concerns.

Chair: Katsuhisa Furukawa (Rebuild Japan Initiative, Japan)

- Russian and United States biosafety experiences during the last two decades: Lessons and achievements
  Peter Palese (Mount Sinai School of Medicine, United States) and Sergey Netesov (Novosibirsk State University, Russia)
- Containment labs - Who wants them, who funds them, and why
  Jennifer Gaudioso (Sandia National Laboratories, United States)
- Discussion

10:30 *Break*

11:00 **Plenary:** *Framing the Issue, Part 2:*
The current status and opportunities for the future

This session will describe how well currently operating labs are meeting their objectives and what challenges they are encountering. Additionally, speakers will summarize current discussions in the area and ask if we are at the beginning of the next paradigm where countries are looking at new ways of achieving and maintaining the necessary containment.

Chair: Anwar Nasim (Ministerial Standing Committee on Scientific and Technological Cooperation [COMSTECH], Pakistan)

- Laboratory capacity, biosafety, and biosecurity in Africa: Gaps, goals, needs, and progress
  Willy Tonui (Kenya Medical Research Institute, Kenya)
- Current thinking and trends ahead
  Teck-Mean Chua (Asia-Pacific Biosafety Association, Singapore [Malaysia])
- Discussion

12:15 *Lunch*

13:15 **Plenary:** *Assessments of Needs, Challenges, and Resources*
This session will provide an overview of local assessments including: what they are, what purpose they serve, who should be involved in a local assessment, and what information might be included.

Chair: Seval Korkmaz (Abdi Ibrahim, Turkey)

- Challenges and suggestions for sustainable biosafety and biosecurity capacity in low resource countries
  Craig Reed (Inspirion Biosciences, United States)
- Biosafety and biosecurity challenges in the Caribbean region
  Valerie Wilson (Caribbean Med Labs Foundation, Trinidad & Tobago)
- Discussion

14:15 **Breakout Sessions**
(Rapporteurs will prepare brief summaries for later presentation)
Paths from assessments to functional labs

While the previous sessions examined assessments broadly, this session will provide specific examples of the process by which countries and corporations decide where and when to build labs, the degree to which their original objectives have been achieved, and the lessons they have learned along the way.

Each speaker will focus mainly on a single lab and describe that lab's strengths, ongoing efforts to sustain and improve capabilities, and key obstacles that have been successfully overcome. Topics to be discussed may include how well the lab is fulfilling its original research and public health goals; where the lab is situated within country and regional networks; whether initial and on-going costs and funding have been as expected; and ongoing biosafety, biosecurity, and maintenance efforts.

Session #1: Eastern Asia (Room: Babylon I)
Chair: Leila dos Santos Macedo (ANBio, Brazil)
Rapporteur: Fran Sharples

- Meeting international biosafety and biocontainment standards in low-resource settings - The southeast Asian experience
  Stuart Blacksell (Mahidol Oxford Tropical Medicine Research Unit, Thailand [Australia])
- Establishing and operating a BSL-3 facility in South Korea: The International Vaccine Institute experience
  Soh Jin Lee (International Vaccine Institute, South Korea)
- Biocontainment for clinical and research activities
  Sunee Sirivichayakul (Chulalongkorn University, Thailand)
- Discussion

Session #2: Africa (Room: Fuji I)
Michael Ugrumov (Institute of Developmental Biology RAS, Russia)
Rapporteur: Benjamin Rusek

- Veterinary Serum and Vaccine Research Institute in Egypt: Present & future prospects
  Seham El-Zeedy (Veterinary Serum & Vaccine Research Institute, Egypt)
- A medical research center in the heart of a tropical rainforest
  Jean-Paul Gonzalez (CIRMF, Gabon [France])
- Morocco Biopharma RL for diagnostic and veterinary vaccines: Current situation and future challenges
  Mehdi El Harrak (Biopharma, Morocco)
- Discussion

Session #3: Eastern Europe and Western Asia (Room: Fuji II)
Chair: Greg Smith (CSIRO, Australian Animal Health Lab, Australia)
Rapporteur: Alison Hottes

- Central Public Health Research Laboratory
  Art Lyons (WRAIR, United States [Republic of Georgia])
- Planning a cost-effective and sustainable BSL-3, lessons learned- Kyrgyz Republic
  Ken Ugwu (Foreign Affairs and International Trade Canada, Canada)
- Why we need a BSL-3 Laboratory at the Pendik Veterinary Control and Research Institute
  Ayşe Selma İyisan (Pendik Veterinary Control and Research Institute, Turkey), and Ayşen Gargili (Marmara University, Turkey)
- The history and current status of the Chumakov Institute of Poliomyelitis and Viral Encephalitides

Evgeniy Tkachenko (Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russia)
- Discussion

16:00 *Break*

16:30 **Plenary:** *Available resources, regulations, and guidelines*

This session will characterize the international, regional, and local resources available to countries; will describe sources of guidance on how to build, operate, and improve labs; and will examine alternatives to relying exclusively on within-country labs.

Chair: Serhiy Komisarenko (Palladin Institute of Biochemistry, Ukraine)
- International regulatory frameworks, standards, and guidelines
  Ingegerd Kallings (Swedish Institute for Communicable Disease Control, Sweden)
- IFBA's biocontainment engineering network
  Ken Ugwu (Foreign Affairs and International Trade Canada, Canada)
- Sustaining regional & national biosafety associations: Challenges and considerations
  Teck-Mean Chua (Asia-Pacific Biosafety Association, Singapore [Malaysia])
- Discussion

Country Overview Writers: Panel Discussion on Local Resources, Regulations, and Guidelines

Chair: Serhiy Komisarenko (Palladin Institute of Biochemistry, Ukraine)
- Biosafety laws and regulations in Turkey
  Hüseyin Avni Öktem (Middle East Technical University, Turkey)
- High-containment laboratories in Ukraine- Local resources and regulations
  Olena Kysil (Taras Shevchenko National University of Kyiv, Ukraine)
- Overview of biosafety and biosecurity in high-containment labs in Brazil
  Leila dos Santos Macedo (ANBio, Brazil)
- Bio-technology and biosecurity initiatives in Pakistan: A country report
  Anwar Nasim (Ministerial Standing Committee on Scientific and Technological Cooperation [COMSTECH], Pakistan)
- High-containment microbiology laboratories in Europe
  Ingegerd Kallings (Swedish Institute for Communicable Disease Control, Sweden)
- Panel Discussion

Additional Country Overview Writers (Please see workshop binder for these overviews):
- High-containment laboratories - Sweden case study
  Ingegerd Kallings (Swedish Institute for Communicable Disease Control, Sweden)
- Overview of high-containment biological laboratories in Russia
  Michael V. Ugrumov (Russian Academy of Sciences, Russia) and Sergey V. Netesov (Novosibirsk State University, Russia)
- High-containment laboratories – U.K. case study
  Neil Davison (International Committee of the Red Cross, Switzerland [United Kingdom]) and Filippa Lentzos (London School of Economics, United Kingdom [Norway])
- United States high-containment biological labs and regulations
  United States National Research Council Staff

18:30 Break

19:00 Dinner (Point Hotel Restaurant)

20:00 **Keynote Address:** ***Pandemic Influenza: The origin, spread, and response to the 2009 H1N1 strain***
Peter Palese (Mount Sinai School of Medicine, United States)

JULY 12, 2011

9:00 **Summary from Day 1 (Plenary)**
Presentations from Rapporteurs of Day 1 Breakout Sessions and Audience Comments

9:45 *Movement to Breakout Sessions*

10:00 **Breakout Sessions (break from 10:45-11:15)**
(Rapporteurs will prepare brief summaries for later presentation)
Public health needs: Costs, effectiveness, and biosafety requirements for diagnostic procedures

These sessions will (1) describe the public health needs lab workers are attempting to meet, the range of tools being utilized, and the challenges regularly encountered and (2) examine the spectrum of molecular, immunological, and culture-based assays available as well their associated costs, effectiveness, and biosafety requirements.

Session #1: Human Diseases Part 1 **(Room: Babylon I)**
Chair: Ingegerd Kallings (Swedish Institute for Communicable Disease Control, Sweden)
Rapporteur: Alison Hottes

- Preparedness for the detection of emerging and re-emerging pathogens in Croatia
  Alemka Markotic (University Hospital for Infectious Diseases, Croatia)
- Biorisks connected with wild birds: Results of avian influenza virus surveillance in southwest Siberia (Russia) in 2010
  Alexander Shestopalov (State Research Center of Virology and Biotechnology "Vector," Russia)
- Biosafety recommendations for laboratory testing for tuberculosis
  Tom Shinnick (Centers for Disease Control, United States)
- Discussion

Session #2: Human Diseases Part 2 **(Room: Fuji II)**
Chair: Peter Palese (Mount Sinai School of Medicine, United States)
Rapporteur: Michael Callahan (DARPA, United States)

- Biosafety and the southeast Asian infectious diseases clinical research network
  Rogier van Doorn (Oxford University, Vietnam [Netherlands])
- SARS Coronavirus: Diagnosis, antibody responses and biosafety concerns
  Cheng Cao (Beijing Institute of Biotechnology, China)
- Crimean Congo hemorrhagic fever- Pakistan perspective
  Birjees Mazhar Kazi (National Institute of Health, Pakistan) and Sohail Zaidi (National Institute of Health, Pakistan)
- EHEC O104:H4 in Germany 2011: Large outbreak of bloody diarrhoea and haemolytic uraemic syndrome by Shiga toxin-producing *E. coli* via contaminated food
  Reinhard Burger (Robert Koch Institute, Germany)

Session #3: Animal and Livestock Diseases **(Room: Fuji I)**
Chair: David Franz (MRIGlobal, United States)

Rapporteur: Fran Sharples

- The work and capabilities of the High Security Animal Disease Laboratory at Bhopal
  Gaya Prasad (Indian Council of Agricultural Research, India)
- Diagnostic capability on exotic and emerging animal diseases of the Mexico official laboratory network
  Marco Antonio Rico Gaytan (Mexico-US Commission for the Prevention of Foot & Other Exotic Animal Diseases, Mexico)
- Coping with deadly viruses
  Supaporn Wacharapluesadee (Chulalongkorn University, Thailand)
- Discussion

12:30 *Lunch*

14:00 **Breakout Sessions**

(Rapporteurs will prepare brief summaries for later presentation)
Identifying areas for action

Collectively, these sessions will (1) generate strategies and suggestions for countries building/improving or considering building/improving labs (2) consider what data on biosafety would be most useful to generate and (3) identify areas where current biosafety practices are not well-matched to actual needs.

Session #1: Determining necessary and appropriate precautions **(Room: Babylon I)**
Chair: Michael Callahan (DARPA, United States)
Rapporteur: Craig Reed (Inspirion Biosciences, United States)

- Evidence based biosafety - Ensuring precautions are adequate and appropriate
  Allan Bennett (Health Protection Agency, United Kingdom)
- Risk based design of facilities for high consequence animal pathogens
  Uwe Mueller-Doblies (Institute for Animal Health, United Kingdom [Germany])
- Emerging Infections in Turkey: Do we need biosafety labs?
  Onder Ergonul (Koç University, School of Medicine, Turkey)
- Discussion

Session #2: Improving organizational culture and practices **(Room: Fuji I)**
Chair: Serhiy Komisarenko (Palladin Institute of Biochemistry, Ukraine)
Rapporteur: Benjamin Rusek

- Enlightened laboratory leadership: More powerful than guns, gates and guards
  David Franz (MRIGlobal, United States)
- Singapore's response to biorisk events at home and abroad
  Presented by Teck-Mean Chua (Asia-Pacific Biosafety Association, Malaysia/Singapore) on behalf of Ling Ai Ee (Singapore General Hospital, Singapore)
- OIE laboratory twinning - A tool to improve global disease security
  Keith Hamilton (World Organisation for Animal Health [OIE], France [United Kingdom])
- Discussion

Session #3: Design and operational options for improving sustainability, biosafety, and biosecurity **(Room: Fuji II)**
Chair: Willy Tonui (Kenya Medical Research Institute, Kenya)
Rapporteur: Jennifer Gaudioso (Sandia National Laboratories, United States)

- Maintenance, certification and cost-saving issues for BSL-3 labs in southeast Asia

Stuart Blacksell (Mahidol Oxford Tropical Medicine Research Unit, Thailand [Australia])
- The BSL-3 lab at Institut Pasteur du Maroc
  Mohammed Hassar (Institut Pasteur du Maroc, Morocco)
- A rational and attainable approach to successfully implementing biosafety in laboratory settings worldwide
  Barbara Johnson (Biosafety Biosecurity International, United States)
- Engineering control: Challenges in maintaining BSL-3 (country experience)
  Pretty Sasono (Litbangkess, Indonesia)
- Discussion

15:30 *Break*

16:00 **Plenary:** *Requirements for and challenges associated with BSL-4 Labs*
This session will discuss how many BSL-4 facilities are needed in a region; construction and maintenance costs; biosecurity issues, environmental risks (especially for pathogens affecting domestic animals where the potential economic impact is striking); training; strategies to manage an individual who may become infected with a BSL-4 agent; community relations; whether existing and planned networks are adequate; how much and what kinds of "surge capacity" are ideal; whether existing facilities can be re-tasked during a crisis; and if BSL-4 labs can be safely made less technology-intensive or easier to sustain.

(Panel Discussion)
Chair: James Le Duc (University of Texas Medical Branch, United States)
- From the detection of BSL-4 pathogens to the development of preventive and curative strategies
  Gary Kobinger (Public Health Agency of Canada, Canada)
- Requirements for and challenges associated with BSL-4 laboratories: Maintaining an aging facility
  Greg Smith (CSIRO, Australian Animal Health Lab, Australia)
- Needs, potential, and constraints for developing an advanced laboratory in a challenging technical and social environment
  Jean-Paul Gonzalez (CIRMF, Gabon [France])
- The high-containment laboratory in the National Institute of Infectious Diseases, Tokyo, Japan: Activities, circumstances, and future challenges
  Masayuki Saijo (National Institute of Infectious Diseases, Japan)
- Panel Discussion

18:30 *Break*

19:30 *Conference Dinner* (Haci Baba Restaurant)

JULY 13, 2011

9:00 **Summary from Day 2 (Plenary)**
Presentations from Rapporteurs of Day 2 Breakout Sessions and Audience Comments

10:30 *Break*

11:00 **Plenary**: *Workshop Conclusions*
Chair: Adel Mahmoud (NRC Committee Chair, Princeton University, United States)

12:00 Meeting Adjournment/Lunch (Some Participants Depart)

13:00 ***Bus Departs*** *for Optional Group Visit to Pendik Veterinary Control and Research Institute (estimated return to hotel at 18:30)*

APPENDIX B

COMMITTEE, PARTICIPANT, AND STAFF LIST

NRC Workshop Organizing Committee

Mahmoud, Adel (Chair)
Princeton University, United States

Callahan, Michael
DARPA, United States

Chua, Teck-Mean
Asia-Pacific Biosafety Association, Malaysia

Franz, David
MRIGlobal, United States

Furukawa, Katsuhisa
Rebuild Japan Initiative

Gaudioso, Jennifer
Sandia National Laboratories, United States

Johnson, Barbara
Biosafety Biosecurity International, United States

Kallings, Ingegerd
Swedish Institute for Communicable Disease Control

Komisarenko, Serhiy
Palladin Institute of Biochemistry, Ukraine

Le Duc, James
University of Texas Medical Branch, United States

Nasim, Anwar
Ministerial Standing Committee on Scientific and Technological Cooperation, Pakistan

Palese, Peter
Mount Sinai School of Medicine, United States

Reed, J. Craig
Inspirion Biosciences, United States

Tonui, Willy
Kenya Medical Research Institute

Participants

Abdelghani, Ahmed Safwat
Central Public Health Laboratories, Egypt

Antoniadis, Antonios
Greek Pasteur institute

Bennett, Allan
Health Protection Agency, U.K.

Blacksell, Stuart
Mahidol Oxford Tropical Medicine Research Unit, Thailand

Burger, Reinhard
Robert Koch Institute, Germany

Cao, Cheng
Beijing Institute of Biotechnology, China

Chapman, Leonard (Will)
Defense Threat Reduction Agency, United States

Diao, Tianxi
Academy of Military Medical Sciences, China

Dzagurova, Tamara
Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russia

El Harrak, Mehdi
Biopharma Lab, Morocco

El Ouni, Naceur
Institut Pasteur du Tunis, Tunisia

Elyan, Diaa
United States Naval Medical Research Unit #3, Egypt

El-Zeedy, Seham
Veterinary Serum & Vaccine Research Institute, Egypt

Ergonul, Onder
Koç University, School of Medicine, Turkey

Gargili, Aysen
Marmara University, Turkey

Gaytan, Marco Rico
Mexico-US Commission for the Prevention of Foot & Other Exotic Animal Diseases (CPA) – DGSA, Mexico

Gonzalez, Jean-Paul
CIRMF, Gabon

Hamilton, Keith
World Organization for Animal Health (OIE), France

Hassar, Mohammed
Institut Pasteur du Maroc, Morocco

Iyisan, A. Selma
Ministry of Agriculture, Pendik Veterinary Control and Research Institute, Turkey

Kazi, Birjees Mazhar
National Institute of Health Islamabad, Pakistan

Kobinger, Gary
Public Health Agency of Canada

Korkmaz, Seval
Abdi Ibrahim Pharmaceuticals, Turkey

Kumin, Daniel
Spiez Laboratory, Switzerland

Kysil, Olena
Taras Shevchenko National University of Kyiv, Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine

Lee, Soh Jin
International Vaccine Institute, South Korea

Lyons, Arthur (Colonel)
WRAIR, United States

Macedo, Leila
ANBio, Brazil

Markotic, Alemka
University Hospital for Infectious Disease, Croatia

McKinney, Michelle
Defense Threat Reduction Agency, United States

Melboucy, Mohamed Abdeldjallil
Institut Pasteur D'Algerie

Mueller-Doblies, Uwe
Institute for Animal Health, U.K.

Netesov, Sergey
Novosibirsk State University, Russia

Öktem, Hüseyin Avni
Middle East Technical University, Turkey

Paranjape, Suman (Sumi)
Department of State, United States

Prasad, Gaya
Indian Council of Agricultural Research, Krishi Bhawan, New Delhi, India

Ruacan, Sevket
Koç University, Turkey

Saijo, Masayuki
National Institute for Infectious Diseases, Japan

Sasono, Pretty
National Institute of Health Research & Development, Indonesia

Shestopalov, Aleksandr
State Research Centre of Virology & Biotechnology "Vector," Russia

Shinnick, Thomas
United States Centers for Disease Control and Prevention

Sirivichayakul, Sunee
Chulalongkorn University, Thailand

Smith, Greg
CSIRO, Australian Animal Health Lab

Tkachenko, Evgeniy
Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russia

Ugrumov, Mikhail
Institute of Developmental Biology RAS, Russia

Ugwu, Kenneth
Foreign Affairs and International Trade Canada

van Doorn, H. Rogier
Oxford University, Vietnam

Wacharapluesadee, Supaporn
Chulalongkorn University, Thailand

Wilson, Valerie
Caribbean Med Labs Foundation, Trinidad & Tobago

Zaidi, Sohail
National Institute of Health Islamabad, Pakistan

Presentation or Overview Writers not in Attendance

Davison, Neil
Science Adviser, Arms Unit Legal Division, International Committee of the Red Cross, Switzerland

Khan, Erum
Pakistan Biological Safety Association and Aga Khan University Hospital

Lentzos, Filippa
BIOS Centre, London School of Economics, U.K.

Ling, Ai Ee
Singapore General Hospital/Singapore Health Services

Summermatter, Kathrin
Institute of Virology and Immunoprophylaxis (IVI), Switzerland

Staff

Chiarello, Heather
The National Academies, United States

Hottes, Alison
The National Academies, United States

Rusek, Benjamin
The National Academies, United States

Sharples, Fran
The National Academies, United States

APPENDIX C

COMMITTEE, PARTICIPANT, AND STAFF BIOGRAPHIES

NRC Workshop Organizing Committee

Mahmoud, Adel (Chair)
Princeton University, United States

Adel A. F. Mahmoud (M.D., Ph.D.) is at the Woodrow Wilson School of Public and International Affairs and the Department of Molecular Biology at Princeton University. He recently retired as president of Merck Vaccines and a member of the management committee of Merck & Company, Inc. His prior academic services at Case Western Reserve University and University Hospitals of Cleveland spanned 25 years concluding as chairman of medicine and physician-in-chief from 1987 to 1998. Dr. Mahmoud's academic pursuits focused on investigations of the determinants of infection and disease in human schistosomiasis and other infectious agents. In laboratory and field studies in several endemic areas, he developed the scientific bases of strategies to control helminthic infections, which have been adopted globally. At Merck, Dr. Mahmoud led the effort to develop four new vaccines: combination of measles, mumps, rubella and varicella; rota virus; shingles; and human papillomavirus. He is an active contributor to scientific literature and authored and edited several textbooks and reports. Dr. Mahmoud received his M.D. degree from the University of Cairo in 1963 and his Ph.D. from the University of London, School of Hygiene and Tropical Medicine in 1971. He was elected to membership of the American Society for Clinical Investigation in 1978, the Association of American Physicians in 1980, and the Institute of Medicine of the National Academy of Sciences in 1987. Dr. Mahmoud is a fellow of the American College of Physicians and a member of the Expert Advisory Panel on Parasitic Diseases of the World Health Organization. He served on the National Advisory Allergy and Infectious Diseases Council and is a past president of the Central Society for Clinical Research and the International Society for Infectious Diseases. He is currently serving as a member of the National Science Advisory Board for Biosecurity and the Committee on Scientific Communications and National Security (CSCANS) of the National Academy of Sciences.

Callahan, Michael
DARPA, United States

Dr. Callahan has extensive knowledge of biological laboratories in Africa and Asia. He has directed multiple USAID and World Bank-funded projects in Africa and Asia and served as program manager and emergency clinical consult physician for a United States Department of State non-proliferation and biological threat reduction and redirection effort in former biological weapons facilities in Russia. His research interests are in the area of new technology and novel drug development to address catastrophic health events. He received undergraduate degrees from the University of Massachusetts, Amherst in microbiology and environmental toxicology. He received a M.P.H. and a M.D. from the University of Alabama, and he received his tropical medicine training from the London School of Tropical Medicine and Hygiene. Dr. Callahan has been active in disaster medicine, wilderness medicine, and medical care in resource-constrained regions since 1982. In 1988, he co-founded the charter organization Rescue Medicine, which provides emergency air medical evacuation and refugee medical care in austere developing regions. Following the events of 9/11, Dr. Callahan served as director of biodefense and mass-casualty care at the Center for Integration of Medicine and Innovative Technology, a multi-institution rapid medical research consortium, and as staff physician at Massachusetts General Hospital in Boston. His current activities include active clinical consultation for highly dangerous pathogens and envenomation and active duty as command physician for Rescue Medicine Airlift One's international disaster medicine team. He began working with the Defense Advanced Research Projects Agency

(DARPA) in 2005 and was recognized with the DARPA 2008 Achievement Award for his work on emergency and pandemic influenza vaccine manufacture.

Chua, Teck-Mean
Asia-Pacific Biosafety Association, Malaysia

Dr. Chua has experience working for the World Health Organization and the Food and Agriculture Organization of the United Nations on laboratory capacity building in the Asia-Pacific region. Additionally, he serves as a laboratory consultant for the Temasek Life Science Laboratory of the National University of Singapore. He is the current treasurer and past president of the Asia-Pacific Biosafety Association.

Franz, David
MRIGlobal, United States

David R. Franz is vice president and chief biological scientist at MRIGlobal and senior advisor to the Office of the Assistant to the Secretary of Defense for Nuclear, Chemical and Biological Defense Programs. Dr. Franz served in the United States Army Medical Research and Materiel Command for 23 of 27 years on active duty and retired as a colonel. He served as commander of the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) and as deputy commander of the Medical Research and Materiel Command. Prior to joining the Command, he served as group veterinarian for the 10th Special Forces Group (Airborne). Dr. Franz was technical editor for the Textbook of Military Medicine on Medical Aspects of Chemical and Biological Warfare released in 1997. He serves on numerous national committees and boards. Dr. Franz holds an adjunct appointment as professor for the Department of Diagnostic Medicine and Pathobiology at the College of Veterinary Medicine, Kansas State University. The current focus of his activities relates to the role of international engagement in the life sciences as a component of national security policy. Dr. Franz holds a D.V.M. from Kansas State University and a Ph.D. in physiology from Baylor College of Medicine.

Furukawa, Katsuhisa
Rebuild Japan Initiative

Katsuhisa Furukawa has been an adjunct fellow at the Rebuild Japan Initiative since July 2011. From October 2004 through August 2011, he was a fellow of the Research Institute of Science and Technology for Society (RISTEX) in the Japan Science and Technology Agency, which put him in charge of a project on science, diplomacy, and security. He has joined various Japanese government and nongovernmental study groups, including groups at the Office of National Security and Crisis Management of the Cabinet Secretariat; the Ministry of Foreign Affairs; the Ministry of Education, Science, and Technology; the Ministry of Justice; the Ground Self-Defense Force; and the Japan Aerospace Exploration Agency. He was in charge of projects on science and technology for counter-terrorism commissioned by the Ministry of Education, Science, and Technology (2006-2009). He is also a member of the Council of Asian Transnational Threat Research (October 2006-present) and a lecturer for the United Nations Security Council Resolution 1540 Committee Regional Workshop (March 2009-present).

Gaudioso, Jennifer
Sandia National Laboratories, United States

Jennifer Gaudioso manages the International Biological Threat Reduction program at Sandia National Laboratories (SNL) in Albuquerque, NM, USA. This program enhances U.S. and international security by promoting safe, secure, and responsible use of dangerous biological agents. Dr. Gaudioso and her SNL team have worked extensively in laboratory biosafety, biosecurity, biocontainment, and infectious disease diagnostics and control internationally. They have organized many international conferences, trainings, and workshops on these topics. In the last five years, the team has visited biocontainment laboratories in more than 40 countries specifically to consult on laboratory biorisk management issues. She and her SNL team work with international partners, such as the World Health Organization, on the development of international laboratory biorisk guidelines and standards. She served on the National Academies' Committee on Education on Dual Use Issues in the Life Sciences. She is author of numerous journal

articles and has presented her research at national and international meetings. She also co-authored the Laboratory Biosecurity Handbook, published by CRC Press. Dr. Daudioso serves on SNL's Institutional Biosafety Committee and is an active member of the American Biological Safety Association. She earned her Ph.D. at Cornell University.

Johnson, Barbara
Biosafety Biosecurity International, United States

Dr. Barbara Johnson owns the consulting company Biosafety Biosecurity International. She is a microbiologist with over 15 years of experience in the United States government in the areas of biosafety, biocontainment, and biosecurity. Her research areas include biological risk assessment and mitigation, testing the efficiency of respiratory protective devices, and testing novel decontamination methods against biological select agents and toxins. She provides training and consultation in the United States and internationally (over 20 countries) on biosafety and biosecurity matters as they pertain to risk assessment; management and mitigation; emergency response; and BSL/ABSL -2, -3, -4 and ABSL-3 facility design, testing, audit, and construction. Her technical and policy advice and strategies are requested in the United States by various government agencies, companies, universities, and subcommittees (ANSI, Senate, National Biosafety and Biocontainment Training Program, etc.) as well as internationally by Ministries of Health. She has recently served on three National Academy of Sciences panels focused on high and maximum containment laboratories and currently serves on the NRC committee providing continuing assistance to the National Institutes of Health on preparation of additional risk assessments for the Boston University National Emerging Infectious Diseases Laboratory. Dr. Johnson is a Registered Biosafety Professional, approved BSL-3 Facility Certifier and Trainer by the Singapore Ministry of Health, past president of ABSA, past vice president of A-PBA, founding member of IFBA, and co-editor of the peer-reviewed journal *Applied Biosafety*.

Kallings, Ingegerd
Swedish Institute for Communicable Disease Control

Dr. Kallings is a senior medical officer and biosafety advisor for the Swedish Institute for Infectious Disease Control (SMI). Ingegerd Kallings has a medical degree from Karolinska Institutet, with a specialization in clinical bacteriology. She was head of the WHO Collaborating Center on Legionella Infections at SMI. From 1997 until 2004, she was senior medical officer and biosafety officer at SMI, during which time SMI constructed and made operational PCL 3 and 4 laboratories including PCL 3 animal facilities for non-human primates. From 1996 to 2009, she was the head of the WHO Collaborating Centre on Biological Safety at SMI and a member of the WHO Biosafety Advisory Group. She recently coordinated a Swedish government-funded project with China's CDC: *Advanced Biosafety Capacity Building in the Chinese National System for Infectious Disease Control and Prevention.* Dr. Kallings was a council member of the European Biosafety Association (EBSA) 2005-06, EBSA president in 2009-10, and an EBSA honorary member from 2001. She founded the Nordic Network for Biosafety in 2004 and since 2009 has been a member of *BioRisk Information, Communication, Knowledge and Scientific Advice* at the European Centre for Disease Prevention and Control. Dr. Kallings was a temporary advisor and short-term consultant to the WHO on various topics including WHO polio eradication and influenza (avian flu) programs. Her experience with developing countries includes Vietnam (research collaboration on antibiotic resistance surveillance), Russian Federation (surveillance of sexually transmitted diseases for the World Bank, biosafety and biosecurity projects, and establishment of an infection control and laboratory network), and the Baltic Sea States (Council of Baltic Sea States Task Force to Combat Communicable Diseases). She has published and lectured on sexually transmitted diseases, legionella infections, antibiotic resistance control, and biosafety.

Komisarenko, Serhiy
Palladin Institute of Biochemistry, Ukraine

Serhiy Komisarenko is currently the academician-secretary of the Division of Biochemistry, Physiology and Molecular Biology of the National Academy of Sciences of Ukraine (since 2004), the director of the Palladin Institute of Biochemistry (1989-1992 and since 1998) and the head of the Laboratory of

Molecular Immunology at Palladin Institute of Biochemistry (1982-1989 and since 1998). He is also the chairman of the Commission on Biosafety and Biosecurity at the National Security and Defense Council of Ukraine (since 2007). Dr. Komisarenko was formerly the ambassador of Ukraine to the United Kingdom (1992-1998), ambassador of Ukraine to Ireland (simultaneously, 1995-1998); deputy prime minister of Ukraine responsible for the humanitarian sector (1990-1992); the head of the Laboratory of Immunochemistry (1975-1982); scientific secretary of the Institute (1972-1974); as well as a junior scientific researcher in the Institute of Biochemistry of the Ukrainian Academy of Sciences, Kyiv (1969-1972). Dr. Komisarenko has been an invited lecturer at many institutions. Dr. Komisarenko is a Doctor of Medicine with distinction (1966, Kyiv Medical Institute) and holds a Ph.D. in biochemistry (1970). He did his post-graduate course in biochemistry in the Institute of Biochemistry of the Ukrainian Academy of Sciences (1966-1969) and completed courses on advanced immunology at the Pasteur Institute in Paris (1974-1975). Since 1992, he has had the life title of Ambassador of Ukraine. Dr. Komisarenko is the editor-in-chief of the *Ukrainian Biochemical Journal* (1989-1992 and since 1998) and *Biotechnology* (Ukraine) (2008-). He is also the president of the Ukrainian Biochemical Society (1999-).

Le Duc, James
University of Texas Medical Branch, United States

Jim Le Duc, Ph.D. is the director of the Galveston National Laboratory (GNL) located on the campus of the University of Texas Medical Branch (UTMB) in Galveston, Texas and holds the inaugural Robert E. Shope, M.D. and John S. Dunn Distinguished Chair in Global Health. Dr. Le Duc joined UTMB in late 2006 from the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, where he held various positions including influenza coordinator (2005-2006), director of the Division of Viral and Rickettsial Diseases (2000-2005), and associate director for the Center for Global Health (1996-2000). He was a medical officer in charge of arboviruses and viral hemorrhagic fevers at the World Health Organization in Geneva, Switzerland (1992-1996) and he held leadership positions during a 23-year career as a United States Army officer in the medical research and development command, with assignments in Brazil, Panama, and at various locations in the United States, including the Walter Reed Army Institute of Research and the United States Army Medical Research Institute of Infectious Diseases. He is a member of various professional organizations, has published over 200 scientific articles and book chapters, and is well recognized as an expert in viral diseases, biodefense, and global health. Dr. Le Duc earned his M.S.P.H. and Ph.D. degrees from the University of California at Los Angeles.

Nasim, Anwar
Ministerial Standing Committee on Scientific and Technological Cooperation (COMSTECH), Pakistan

Dr. Anwar Nasim is a renowned name in the field of science in Pakistan. He currently works as a science adviser for COMSTECH. Dr. Nasim has been actively involved in the socio-economic development of Pakistan and of other Islamic countries. His main areas of interest are molecular biology, biotechnology and genetic engineering. Dr. Nasim has over 100 scientific publications in prestigious international journals. He is an author of eight books and is a member of the editorial boards of six science magazines. He was an international coordinator and member of the Executive Committee for the XVI International Congress of Genetics, Toronto, Canada (1988). Dr. Anwar Nasim has earned a number of awards. Starting from the Gold Medal in M.Sc. Botany, he has to his credit the Pride of Performance (molecular genetics, 1995) awarded by the president of Pakistan and Sitara-i-Imtiaz (molecular genetics, 1999). He was awarded the Overseas Pakistanis' Institute (OPI) award for outstanding services for promotion of science in Pakistan (1995). He also received a special award during BioAsia2011 for his promotion of biotechnology in Asian countries as the founding president of the Federation of Asian Biotech Associations (FABA). He is an elected fellow of The Academy of Sciences for the Developing World (TWAS) and the Islamic World Academy of Sciences (IAS), and he is a fellow of the Pakistan Academy of Sciences (PAS). Dr. Nasim is playing a key role in bringing about sustainable development in Pakistan through the use of modern techniques in the fields of biotechnology and its allied disciplines in his capacity as the first chairman of the National Commission on Biotechnology of Pakistan.

Palese, Peter
Mount Sinai School of Medicine, United States

Dr. Palese is a professor of microbiology and chair of the Department of Microbiology at Mount Sinai School of Medicine in New York. His research includes work on the replication of RNA-containing viruses with a special emphasis on influenza viruses, which are negative-strand RNA viruses. He established the first genetic maps for influenza A, B and C viruses, identified the function of several viral genes, and defined the mechanism of neuraminidase inhibitors (which are now FDA-approved antivirals). Dr. Palese also pioneered the field of reverse genetics for negative-strand RNA viruses, which allows the introduction of site-specific mutations into the genomes of these viruses. This technique is crucial for the study of the structure/function relationships of viral genes, for investigation of viral pathogenicity, and for development and manufacture of novel vaccines. In addition, he and his colleagues used an improved version of the technique to reconstruct and study the pathogenicity of the highly virulent but extinct 1918 pandemic influenza virus. His recent work in collaboration with Garcia-Sastre revealed that most negative-strand RNA viruses possess proteins with interferon antagonist activity, enabling them to counteract the antiviral response of the infected host. Dr. Palese was elected to the National Academy of Sciences in 2000. At present he serves on the editorial board for the Proceedings of the National Academy of Sciences. He has been a corresponding member of the Austrian Academy of Sciences since 2002 and a member of the German Academy of Sciences Leopoldina since 2006. Dr. Palese was president of the Harvey Society in 2004/2005 and president of the American Society for Virology in 2005/2006. He was the recipient of the Robert Koch Prize in 2006, of the Charles C. Shepard Science Award in 2008, and of the 2010 European Virology Award.

Reed, Craig
Inspirion Biosciences, United States

Craig Reed is the founder and president of Inspirion Biosciences, a Maryland (United States) company that performs international work in support of various United States government agencies as well as for-profit and non-profit entities in the United States and abroad. As a captain in the United States Army, Dr. Reed was stationed at the United States Army Medical Research Institute of Infectious Diseases, Fort Detrick where he worked in biosafety level-2 and -3 laboratories studying the organisms that cause plague and anthrax. For the past 12 years, Dr. Reed has supported multiple scientific engagement programs funded by the Department of State, Department of Defense, the United States Centers for Disease Control and Prevention, and the Defense Research Projects Agency. During this time, he performed or supervised the performance of threat and vulnerability assessments at more than 50 different human and animal epidemiological laboratories as well as high and maximum containment biological research and production facilities throughout Russia, and six countries in Central Asia and the trans-Caucasus region. Dr. Reed has also worked with Ministers of Defense, Agriculture, and Emergency Situations to modernize laboratories in these same countries and to revise biosafety procedures to account for modern equipment and technology. Through Inspirion Biosciences, Dr. Reed has also led the development and delivery of a variety of training workshops in support of the National Biosafety and Biocontainment Training Program at the National Institutes of Health, the only federally-funded biosafety and biocontainment training fellowship of its type. Dr. Reed serves as technical advisor to the Secretariat of the International Federation of Biosafety Associations and as associate to the International Centre for Infectious Diseases (Winnipeg, Canada). Dr. Reed's professional relationships and personal efforts in Central Asia provided the nucleus for the recent formation of the Biosafety Association of Central Asia and the Caucasus (BACAC). Additionally, Dr. Reed is an active member of multiple regional and national biosafety associations and regularly participates in their annual meetings. These associations include the biological safety associations of America (ABSA), Canada (CABS), the Asia-Pacific (APBA), Europe (EBSA), and Central Asia and the Caucasus (BACAC).

Tonui, Willy
Kenya Medical Research Institute

Dr. Willy Kiprotich Tonui is a principal research officer (immunology) and health, safety, and environment coordinator at the Kenya Medical Research Institute (KEMRI) in Nairobi, Kenya. His work specializes in the safety and security of high-risk pathogens, occupational health, fire safety, environmental audits, hazardous chemicals, and laboratory risk management. Dr. Tonui is co-chair to the International Federation of Biosafety Associations (IFBA). IFBA is a forum for biosafety professionals of different nations that coordinates and develops a global biosafety agenda aimed at international harmonization, sharing of information, development of common standards, and collaboration in all aspects of biological safety. IFBA's mission is to support and promote biosafety on a national and international level through collaboration among national and regional biosafety organizations worldwide. He is also a founding member and president of the African Biological Safety Association (AfBSA), a three-year old professional association that seeks to congregate practitioners of biological safety, promote biosafety and biosecurity as a discipline through awareness, and to facilitate the sharing of biosafety and biosecurity information in the African region. He is also a member of the American Biological Safety Association (ABSA) and the Asia Pacific Biosafety Association (APBA). Willy studied for his B.S. (biological sciences and chemistry) at Kurukshetra University (India), earned his M.S. and Ph.D. in immunology (specialty in vaccine development) from Kenyatta University (Kenya) and did his post-doctoral training at the School of Veterinary Medicine at Colorado State University, United States. Willy has a career-long history of supporting national programs, regulations, and policies in Kenya. He is a registered expert on Environmental Impact Assessment and Audit (EIA/EA) by the National Environmental Authority. In general, his work at KEMRI supports national programs in developing laws and regulations in hazardous waste management, biosafety, occupational health and safety, disaster management, quality management, and cleaner productivity enhancement. He is a member of several national committees including the Kenya Medical Laboratory Quality Assurance Advisory Body, the Kenya National Accreditation Services, and the National Biosafety Committee. He is currently the vice chairman of the National Biological and Toxins Weapons Convention Committee, which aims to implement UN 1540 in Kenya. He is an author of a laboratory safety handbook and three other books on fire safety and prevention.

Participants

Abdelghani, Ahmed Safwat
Central Public Health Laboratories, Egypt

Dr. Abdelghani is a medical microbiologist who serves as the head of the Microbiology Department of Central Public Health Laboratories, Egypt. He has previously worked in the fields of serology and the molecular diagnosis of viruses, particularly viral hepatitis, HIV, and influenza. He is also experienced in the laboratory diagnosis of tuberculosis. He has participated in many research studies including full genome sequencing of highly pathogenic avian influenza H5N1 virus in Egypt, molecular epidemiology of highly pathogenic avian influenza H5N1 Egyptian viruses, surveillance for measles and rubella infections in Egypt, surveys of the prevalence of hepatitis C virus in Egypt, and tuberculosis drug resistance surveillance.

Antoniadis, Antonios
Greek Pasteur institute

Dr. Antonios Antoniadis (M.D., Dip. Bact-Lond, Ph.D.) is a professor emeritus of the Medical School of the Aristotelian University of Thessaloniki, Greece. For 14 years he was the director of the 'A' Microbiology laboratory of the same school and head of the WHO Collaborating Centre for Reference and Research on Arbovirus and Hemorrhagic Fever Viruses, which he created in 1996. He is currently acting director and president of the Executive Board of the Hellenic Pasteur Institute in Athens. As a medical doctor, he specialized in medical microbiology and obtained the Diploma in Bacteriology from the London School of

Hygiene and Tropical Diseases. He also trained at the Yale Arbovirus Research Unit (Yale University, United States), at the Department of Disease Assessment of the United States Army Medical Research Institute for Infectious Diseases (Fort Detrick, United States), at the Central Public Health Laboratory in London, UK, and at the National Laboratory of Microbiology in Stockholm, Sweden. Since 1980, his research has focused on viral tropical diseases, particularly viral hemorrhagic fevers. The outcome of his research was the laboratory diagnosis of several "new" diseases in Greece leading to a rapid public health response during outbreaks and/or epidemics. In the context of this research, he has collaborated with laboratories of the Central African Republic, Senegal, Nigeria, Russia, and China. For nearly seven years, Dr. Antoniadis was a member of the Executive Board of the Hellenic Center for Diseases Control and Prevention, and he participated and participates in boards of the Greek Ministry of Health and Solidarity concerning public health issues. Since 1992, he is National Expert at the UN, Geneva, for the Biological Weapons Convention and the ad hoc meetings of experts, National Representative for Poliovirus Containment of the WHO Poliovirus Global Eradication Program, and during the Athens 2004 Olympic Games he coordinated the laboratory network against bioterrorism. As a WHO consultant, he lead WHO missions in Iraq during a Crimean-Congo hemorrhagic fever epidemic, he participated as an expert in boards of the European Union for issues concerning viral hemorrhagic fevers, he participated in EU missions to Russia and China, and he coordinated the EU workshop in Xian, China for the collaboration of EU and China in the field of viral hemorrhagic fevers.

Bennett, Allan
Health Protection Agency, U.K.

Allan Bennett is a general project manager of biosafety at the Health Protection Agency at Porton Down in the United Kingdom. His professional background includes heading a research group of 10 scientists undertaking research in the fields of aerobiology, biocontainment, infection transmission, and bioresponse. He also was the coordinator of the European Centres for Disease Control and Prevention Biorisk Expert Group (2009-present) and worked as a package manger on the FP7 project "European Research Infrastructure on Highly Pathogenic Agents" on a package titled "Design considerations and estimating construction costs for new BSL-4 areas." Dr. Bennett has 20 years of experience in the study of the behavior of airborne microorganisms, biocontainment design, and validation of containment systems. He led research projects for the European Space Agency in planetary protection and was a council member of the European Biosafety Association (2005-2007). He also led environmental microbiology response teams for fatal anthrax cases in Scotland and England. He has over 30 peer-reviewed scientific publications.

Blacksell, Stuart
Mahidol Oxford Tropical Medicine Research Unit, Thailand

Adjunct Associate Professor Stuart Blacksell is an Australian with more than 27 years working experience in microbiology research activities who has been actively been involved in studies in Asia (Thailand, Laos, Cambodia, Vietnam, China) since 1989. He has been employed by the Nuffield Department of Clinical Medicine at the University of Oxford since August 2001 and is based at the Mahidol-Oxford Tropical Medicine Research Unit (MORU) in Bangkok, Thailand. From 1983-2001, prior to moving to the University of Oxford, he worked at the BSL-4 CSIRO Australian Animal Health Laboratory (AAHL) in Geelong, as well as the organization's Thai and Lao-based projects. He holds Bachelor of Applied Science (Charles Sturt University), M.P.H., and Ph.D. degrees (both University of Queensland). He is also qualified as a Registered Biosafety Professional (RBP) by the American Biological Safety Association. He also holds adjunct associate professorships at the School of Population Health, University of Queensland and the School of Veterinary & Biomedical Science, Murdoch University in Australia and is an honorary research lecturer at the University of Oxford. He is a fellow of the Australian Society of Microbiology, fellow of the Australasian College of Tropical Medicine, and fellow of the Royal Society for Tropical Medicine and Hygiene. He has served as a member of the Asia-Pacific Biosafety Association (A-PBA) committee (2009/2010) and has lectured at A-PBA training courses. He has also been a committee member of the Biosafety and Biosecurity Network of Thailand (BSNT). In his position at MORU, he is the senior expatriate microbiologist and the head of biosafety and biocontainment. He has been responsible for the design, construction, and certification (Oxford and BMBL standards) as well as the management of the

new BSL-2 and BSL-3 laboratories in Bangkok and Laos that are essential for laboratory studies of scrub typhus, murine typhus, and melioidosis. He is also responsible for biological safety at MORU's Thai, Lao, and Cambodian laboratories. Dr. Blacksell has authored or co-authored more than 70 scientific papers.

Burger, Reinhard
Robert Koch Institute, Germany

Dr. Reinhard Burger is the president of the Robert Koch Institute in Germany. He is the former head of both the Department for Immunology and the Department for Infectious Diseases. He received his Ph.D. (1976) and habilitation (1982) at the Institute for Medical Microbiology at the University of Mainz. From 1983-1987 he served as a professor for immunology at the Faculty for Theoretical Medicine at the University of Heidelberg. Since 1989 he has been a professor for immunology at the Free University of Berlin (University Hospital Benjamin Franklin). Dr. Burger was also a visiting scientist in various institutions abroad, such as the National Institutes of Health in Bethesda, MD, United States, and later at Harvard Medical School in Boston, and at the Medical University in Wuhan, China. He is a member of a number of scientific societies, including the German Society for Immunology, the German Society for Hygiene and Microbiology, the American Association of Immunologists, the German Society for Transfusion Medicine and Immune Hematology, and the American Association of Blood Banks. In 1993 Dr. Burger was appointed as chairman of the National Advisory Committee on Blood of the German Federal Ministry for Health. This national committee of experts gives advice to the federal government on all aspects of the safety and efficient use of blood components and plasma derivatives. Dr. Burger has many immunological publications, particularly concerning the detection of infectious agents and the safety of blood and blood products, and is a member of many national and international expert committees.

Cao, Cheng
Beijing Institute of Biotechnology, China

Cheng Cao, Ph.D., graduated from the Department of Biology in Wuhan University and was awarded the Ph.D. degree from the Beijing Institute of Biotechnology. He finished his postdoctoral training at the Dana Farber Cancer Institute at Harvard Medical. Dr. Cao was then appointed to the position of professor at the Beijing Institute of Biotechnology. His work focuses on molecular cell biology and the diagnosis of viral diseases.

Chapman, Leonard (Will)
Defense Threat Reduction Agency (DTRA), United States

As the deputy program manager for the Cooperative Biological Engagement Program, Mr. Chapman is the lead for the program's expansion activities as it moves out of the former Soviet Union. He has been a leader in the biological threat reduction field for the last five years and is active on several interagency and White House-level working groups. Mr. Chapman's efforts have often focused on the question of sustainability of international biological capacity building efforts, and he has several publications on this work. He has worked in the threat reduction sphere for the past nine years with direct implementation experience in 15 countries.

Davison, Neil
Science Adviser, Arms Unit Legal Division, International Committee of the Red Cross, Switzerland

Neil has over ten years experience in research and policy work on international security issues. From 2007 to 2011 he was responsible for policy work on science and international security at the Royal Society, the U.K.'s national academy of science. There he focused on nuclear, biological, and chemical arms control, non-proliferation, and security issues, as well as the security impacts of developing science and technology such as neuroscience. He is author of *'Non-Lethal' Weapons*, published by Palgrave Macmillan in 2009. Prior to joining the Royal Society, Neil was in the Department of Peace Studies at the University of Bradford for five years. There he was lead researcher on "non-lethal" weapons and contributed to work on chemical and biological arms control policy. In 2000 he completed training as a biological weapons inspector with the United Nations Monitoring, Verification and Inspection Commission.

Neil holds a B.S. in biology from University College London and a Ph.D. in peace studies from the University of Bradford.

Diao, Tianxi
Academy of Military Medical Sciences, China

Tianxi Diao holds a Ph.D. in preventive medicine. He is a professor at the Academy of Military Medical Science. His current research field is policy and strategy for technology development for preventive medicine.

Dzagurova, Tamara
Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russia

Dr. Dzagurova holds an M.D. and Ph.D. in virology. She is the head of the Laboratory of Hemorrhagic Fevers at the Chumakov Institute of Poliomyelitis and Viral Encephalitides at the Russian Academy Medical Sciences. She has been in this position since 2006. She attended the Medical Institute of Vladikavkaz (Russia), Licentiate in 1973. From 1973-1977 she was a post-graduate student, then a junior researcher, senior researcher, and lead researcher at the Laboratory of Hemorrhagic Fevers, Institute of Poliomyelitis and Viral Encephalitides (USSR Academy of Medical Science, Moscow, USSR). Her research interests include virology, laboratory diagnosis, vaccines, and hantaviruses. In particular, she has studied the ecology and biology of hantaviruses, the epidemiology of hantaviral infections, hantavirus vaccination, and methods for laboratory diagnosis of hantavirus infections.

El Harrak, Mehdi
Biopharma Lab, Morocco

Mehdi El Harrak, D.V.M., Ph.D., has been the technical manager of Biopharma, the national reference laboratory for veterinary diagnostic and vaccine production in Morocco since 2005. He was the head of the Virology Department at Biopharma from 1985 to 2005 and has been the secretary general of the Laboratory Commission at the World Organization of Animal Health (OIE) since 2006. Dr. El Harrak is also a consultant for the United Nations Food and Agriculture Organization (FAO) and the World Bank.

El Ouni, Naceur
Institute Pasteur of Tunis, Tunisia

Dr. El Ouni holds a degree in industrial engineering from the National Engineers School of Tunis (1986). He is currently engineer-in-chief at the Institute Pasteur of Tunis, Tunisia (IPT). He began at the IPT in 1987 as a technical engineer and has served IPT in many different roles ever since. He became a member of the Board of Directors of IPT in 1999, was a project manager for the construction and design of a new good manufacturing practices (GMP) production unit for vaccines and serums (2000), and recently became the deputy director of studies and shared services (including safety services). Dr. El Ouni has a wide range of technical skills in the following areas: analysis and biomedical research equipment, industrial pharmaceutical processes, water treatment and purification, and air handling. In 2010, he provided technical assistance for a French-Tunisian biotechnology project on vaccine production. In 2006, he worked on the design and installation of a P2+ laboratory for the research department of the National School of Veterinary Medicine, Sidi Thabet, Tunis. In 2000, he designed a sera purification process chain. He also supervised the technical component of the vaccine production unit's renovation project at the Institute Pasteur of Tunis (IPT) and has worked abroad on many projects.

Elyan, Diaa
United States Naval Medical Research Unit #3, Egypt

Dr. Elyan has close to 25 years of lab experience in the field of virology and is an expert in handling highly infectious materials in P3 enhanced and P3+ conditions and in preparing diagnostic reagents. He also has been engaged with outbreak investigation and control and has worked with select agents in BSL-3 and BSL-4 facilities. He has lead biosafety decontamination teams for 10 years. Currently, Dr.

Elyan is a special assistant to the head of the cooperative biological engagement program at United States Naval Medical Research Unit No. 3 (NAMRU-3). He holds dual appointments as NAMRU-3's country manager for Pakistan and as the capacity building and enhancement coordinator for Afghanistan and is experienced in medical diplomacy. Dr. Elyan implements total quality (TQ) systems, quality control & quality assurance (QC&QA), and good laboratory practices (GLPs) with a special focus on safety, biosurety, and biosecurity strategies. As a senior researcher, Dr. Elyan also conducts trainings and workshops for local and international trainees and medical researchers. Much of his work takes place in conflict areas where security and safety are of the highest concern.

El-Zeedy, Seham
Veterinary Serum & Vaccine Research Institute, Egypt

Since 2010, Seham Abd El-Rasheed Sayed El-Zeedy has served as director of the Veterinary Serum and Vaccine Research Institute (VSVRI). VSVRI was established in 1903 on an area of about 23 square hectares in the Abassia district, East Cairo. The main goals of VSVRI are to produce the highly efficient viral vaccines, bacterial vaccines, diagnostic biological reagents, and antisera needed to immunize farm animals, poultry, and companion animals against infectious diseases prevalent in Egypt and exotic diseases introduced to the country. VSVRI produces about 72 products and contains 14 research departments: five departments for bacterial vaccines, eight departments for viral vaccines, and a genetic engineering research department.

Ergonul, Onder
Koç University, School of Medicine, Turkey

Onder Ergonul is a professor of infectious diseases at Koç University, School of Medicine in Istanbul, Turkey. He graduated from Hacettepe University School of Medicine in 1989 and completed his residency in 1996 in the Infectious Diseases and Clinical Microbiology Department of Ankara University in Ankara, Turkey. He received a M.P.H. degree from Harvard University School of Public Health in 2003. In 2000-2002, he worked as a research fellow in the Clinical Epidemiology Division of the Infectious Diseases Department at the University of Utah, School of Medicine, United States. He is a member of the steering committee of the EU-FP7 project "International Network for Capacity Building for the Control of Emerging Viral Vector Borne Zoonotic Diseases," and a partner of the European Research Infrastructure on Highly Pathogenic Agents project. He received the Public Health Scientific award from the Turkish Medical Association in 2007. He is the program director of the research methodology course of Koç University, School of Medicine in collaboration with Harvard Medical School and the Istanbul branch of the Ministry of Health.

Gargili, Aysen
Marmara University, Turkey

Aysen Gargili is currently a professor at the Marmara University Infectious Diseases Epidemiology Research Center (MEHAM). She graduated from Istanbul University's Veterinary Faculty in 1989 and completed her doctorate in 1995 at the Institute of Health Sciences, Istanbul University. Prior to joining MEHAM, she was a lecturer at Istanbul University's Veterinary Faculty (1995-2001) and Istanbul University's Cerrahpasa Medical School (2001-2007). She is currently responsible for directing research projects, teaching medical and-premedical students, and training graduate and post-graduate students. She works collaboratively with related staff of the Ministry of Agriculture and the Ministry of Health (MOH). She is a referee board member of The Scientific and Technological Research Council of Turkey (TUBITAK) and responsible for the scientific evaluation of national and international projects. She is a member of the Tick Surveillance Study Group at MOH, the Lyme Disease Study Group at MOH, and a counselor for the MOH Istanbul Branch. She has experience at Gifu University Medical School, Japan (1999) as a scientific trainee, the International Center for Genetic Engineering and Biotechnology, Malaria Department, New Delhi, India (2000) as a postdoctoral fellow, and the Ludwig Maximillien University, Tropical Diseases Institute, Molecular Parasitology Section, Munich, Germany (2005) as a visiting scientist. She has presented 14 talks as an invited speaker in international congresses and published 27 scientific papers in journals indexed in SCI/SCI expanded lists. She has conducted 4 national research

projects funded by TUBITAK and 2 international research projects funded by the EU FP6 framework in the last 5 years. She currently is involved with 2 international research projects. She has been employed by the WHO for the short term mission, Support for Molecular Diagnosis of CCHF, in Tajikistan in November 2009. She was a co-author on the WHO Health Impact Assessment of Climate Change in Turkey.

Gaytan, Marco Rico
SENASICA - CPA, Mexico

Marco Antonio Rico Gaytán has been with the Mexican-American Commission for Foot and Mouth Disease and other Exotic Diseases Prevention since 2003. He works in a BSL-3 laboratory performing serological diagnostic tests. In 2008, he was designated as a biosafety officer for the BSL-3 activities. He earned a veterinarian degree in 1997 from the Universidad Nacional Autonoma de Mexico (Mexico National University). From 1995-2002 he collaborated with several institutions and companies in the public and private sector doing activities such as teaching, investigation animal viral diseases, and performing animal disease diagnostic tests.

Gonzalez, Jean-Paul
CIRMF, Gabon

Jean-Paul Gonzalez graduated as a medical doctor from the Medical School of Bordeaux in 1974. After completing his internship in French Guyana, he spent most of his career out of France as a medical researcher. He received his Ph.D. in viral ecology in 1984 from the University of Clermont-Ferrand, in Auvergne, France. As a researcher at the Institute for Research for the Development (IRD, Paris) he dedicated his career to research and training in many developing countries throughout the Americas, Africa, and Asia. His main fields of research encompass several domains of viral disease epidemiology and virus ecology, including vector transmitted viral diseases, viral hemorrhagic fevers, emerging viral diseases and the study of domains of disease emergence. Since the late 70s, he has been leading international teams of researchers from his own institute and institution partners in developing countries. For a decade he led teams of virologists at the Dakar Pasteur Institute (Senegal) and also at the Bangui Pasteur Institute (Central African Republic). He has spent several years in the United States, working as a guest researcher at the CDC in Atlanta, Georgia and as a visiting professor of epidemiology and public health at Yale School of Medicine. In both institutions he was involved in high security laboratory practices and research and the initial development and application of geographical information systems in the field of health. For the past decade he acted as a visiting professor of microbiology at Mahidol University (Bangkok, Thailand), founded a research center for emerging viral diseases, and developed a multidisciplinary technical platform dedicated to research and training for vectors and vector borne diseases. With his group of researchers he identified several new pathogens for humans and animals and described new viruses, vectors, and hosts of diseases from different tropical domains. He contributed to developing tools and implementing strategies for the control and prevention of transmitted diseases. He and his team studied the spread and dynamics of several viral hemorrhagic fevers, adding spatial and temporal dimensions to a dynamic study of epidemiology. He also developed several scientific concepts including postulating that germs and hosts co-evolve on geologic time scales. He has more than 170 scientific papers in peer-reviewed journals. In September 2008, the Gabonese government appointed him the general director of the International Center for Medical Research in Franceville, Gabon.

Hamilton, Keith
World Organization for Animal Health (OIE), France

Keith Hamilton, B.V.Sc., M.Sc., M.R.C.V.S., is a veterinarian from the British Iles. Having worked in mixed animal practice, field disease control programs, and with an NGO in India, he went on to study infectious disease control at the London School of Hygiene and Tropical Medicine, including field work relating to the control of zoonotic African trypanosomiasis in Uganda. In 2003, he joined the U.K. government as an advisor on the control of veterinary exotic diseases and in 2007 was seconded to the World Organisation for Animal Health (OIE) where he works on a range of topics including laboratory capacity building, animal influenza, and biological threat reduction.

Hassar, Mohammed
Institut Pasteur du Maroc, Morocco

Professor Mohammed Hassar is honorary director of the Institut Pasteur du Maroc (IPM) and emeritus professor at the Rabat School of Medicine and Pharmacy. He is an internist and a clinical pharmacologist. He served as director of the Institut National d'Hygiène from 1989 to 1993 and director of IPM from 2001 to 2010. Professor Hassar has been active in global public health for the past two decades. He serves on several WHO committees and panels and is also a board member of IANPHI (the Public Health Institutes of the World). His interests include capacity building in health research, rational drug use and drug safety, food and environmental safety, and biosafety.

Iyisan, A. Selma
Ministry of Agriculture, Pendik Veterinary Control and Research Institute, Turkey

Dr. Ayse Selma Iyisan graduated with a degree in Veterinary Faculty from the University of Istanbul in 1983 and started working at Pendik Veterinary Control and Research Institute (PVCRI) in 1984. From 1989-1992 she specialized in bacteriology at PVCRI. From 1985 to 1993, she was a Ph.D. candidate at the Department of Microbiology in Veterinary Faculty at the University of Istanbul. Since 1993, she has worked as the chief of the Laboratory in Serological Diagnosis and the Epidemiology and Statistics Unit at PVCRI. She became the Technical Deputy Director of the Institute in 2004. She obtained additional training at the Veterinary, Epidemiology, and Economic Research Unit of Reading University in the U.K. She has extensive experience with the development and implementation of control and epidemiological survey projects for livestock diseases such as avian influenza, brucellosis, and bovine spongiform encephalopathy. Dr. Iyisan has authored 20 publications.

Kazi, Birjees Mazhar
National Institute of Health (NIH), Islamabad, Pakistan

Dr. Birjees Mazher Kazi is working as executive director at the National Institute of Health (NIH), Islamabad, Pakistan. He is a pathologist, hematologist, and public health laboratory specialist. He is also the chief of Public Health Laboratories, Division of NIH, which is a WHO collaborating centrer for research and training in viral diagnostics. Dr. Kazi is the national technical coordinator and a faculty member of the Field Epidemiology and Laboratory Training Program, CDC-NIH, Pakistan. He is a member of the Advisory Board of Directors of the Training Program for Epidemiology and Public Health Interventions, United States. Dr Kazi is the principal investigator of NIH-CDC's National Lab-based Influenza Surveillance Project. Dr. Birjees Kazi is a medical graduate and joined NIH Islamabad Pakistan after completing a postgraduate diploma in clinical pathology. He underwent postgraduate training at Manchester Royal Infirmary, Manchester University as a WHO fellow. Later on, he earned a M. Phil. He is a fellow of the Pakistan College of Pathologists. Dr. Kazi is a member of the WHO Expert Advisory Panel on Health Laboratory Services. He introduced HIV and hepatitis B and C blood screening in public sector blood banks in Pakistan during 1995. Dr. Kazi played a leading role in the development of federal and provincial legislation on blood safety, HIV/AIDS, and the public health laboratory network. He also worked as principal investigator of WHO Tropical Diseases Research Program projects on leishmaniasis and bacterial meningitis. Dr. Kazi has written 87 scientific papers and compiled 4 national guidelines including the National Standards and Guidelines for Blood Transfusion Services of Pakistan and National Guidelines on Quality Assurance in Laboratory Medicine.

Khan, Erum
Pakistan Biological Safety Association and Aga Khan University Hospital

Erum Kahn is an associate professor in the Department of Pathology & Microbiology at Aga Khan University in Karachi, Pakistan and the president of the Pakistan Biological Safety Association. She also acts as the head of clinical microbiology in the Department of Pathology and Microbiology and is a

consultant clinical microbiologist in the Clinical Microbiology Laboratory at Aga Khan University Hospital. Additionally, Dr. Kahn is a visiting lecturer at the College of Physicians and Surgeons Pakistan and serves as co-chair of the academic program of IFBA. Dr. Kahn attended Dow Medical College (Pakistan), where she received her M.B.B.S. in medicine; Imperial College (London, U.K.), where she received her M.S. in molecular biology and pathogenesis of viruses; and the Royal College of Pathologists (London, U.K.); and the Fellow College of Physicians and Surgeons (Pakistan), where she studied medical microbiology. She is a member of the editorial boards for both the *Journal of Microbiology and Biology Education* and the *Journal of Applied Biosafety*. She is also a member of the national task force for national biosafety activities in Pakistan. Dr. Kahn has received numerous awards and grants and has participated in many biosafety activities at the local, national, and international levels. She has over 75 peer-reviewed publications.

Kobinger, Gary
Public Health Agency of Canada

Gary Kobinger obtained his Ph.D. with honors from the University of Montreal in 1998 before completing a post-doctoral fellowship at the University of Pennsylvania. In March 2005, Gary was recruited by the National Microbiology Laboratory in Canada where he is the chief of the Special Pathogens Program and has an adjunct professor appointment at the University of Manitoba. Gary was granted several awards including the 2010 Research Merit Award from Public Health Canada. He currently holds funding from several agencies and has been elected by WHO to serve as co-director of the WHO Collaborating Centre for Emerging and Zoonotic Diseases Detection, Diagnostics, Reference and Research and to co-chair the Emerging and Dangerous Pathogens Laboratory Global Network for Outbreak Response and Readiness.

Korkmaz, Seval
Abdi Ibrahim Pharmaceuticals, Turkey

Seval Korkmaz is a cell culture and in vitro screening supervisor at Abdi Ibrahim Pharmaceuticals Inc. in Istanbul, Turkey. During the first years of her scientific career (1996-2006), Dr. Korkmaz was a researcher and assistant professor at the Pharmacology Department of Anadolu University and the Faculty of Pharmacy. She later established the first cell culture laboratory in the Turkish pharmaceutical industry in 2006 at FARGEM Inc. to allow permeability studies of generic drugs. She has been working at Abdi Ibrahim Pharmaceuticals since March 2010 where she has just established the second cell culture laboratory in the Turkish pharmaceutical industry. While most of her university studies were on high-throughput screening of natural and synthesized substances, recently she has worked on permeability studies, in vitro high-throughput studies of drugs and drug candidates, and models of biological barriers. She just developed and is seeking to patent a new in vitro blood-brain barrier model that is 2-fold more successful than the best currently available blood-brain barrier models.

Kumin, Daniel
Spiez Laboratory, Switzerland

Daniel Kümin studied microbiology at the University of Berne in Switzerland before moving to the Ecole Supérieure de Biotechnologie de Strasbourg in France, where he obtained his master's degree in biotechnology, specializing in molecular biology (1999). For his master's thesis, he studied the tropism of porcine adenoviruses looking for ways to improve the vector potential of these viruses. This work was done at the Australian Animal Health Laboratory (AAHL) in Geelong, Australia. His Ph.D. project on the biology and vector potential of ovine adenoviruses was performed at a private biotechnology company in Berlin, Germany. He received his Ph.D. from Humboldt University in Berlin, Germany in 2003. He then returned to Switzerland for his post-doc, working at the Institute of Veterinary Virology of the University of Berne. In 2007 he left research and joined the Federal Office for the Environment where he was responsible for, among other things, the development of a national biosafety curriculum and was also involved in the review of notifications and permits for work with genetically modified and pathogenic organisms according to the Containment Ordinance. In 2008 he was offered the Biosafety Officer (BSO) position at Spiez Laboratory. Spiez Laboratory is the national center of competence for nuclear, biological, and chemical protection. Spiez Laboratory is currently constructing a new high-containment

facility, the first of its kind in Switzerland. Daniel Kümin has been involved in biosafety training for a number of years, nationally as well as internationally. He has collaborated with WHO providing expertise in biosafety training for several courses.

Kysil, Olena
Taras Shevchenko National University of Kyiv, Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine (NASU)

Olena Kysil, who has a Ph.D. in biology (2004), is an advanced doctoral level student and assistant professor at National Taras Shevchenko University of Kyiv and a researcher at the Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine. She has a strong background in the life sciences and practical training in the political sciences having served an internship in the Parliament of Ukraine. A biologist by training, her current research interest is Ukraine's biosafety and biosecurity system. Since October 2008, as an assistant to the chairman of the Commission on Biosafety and Biosecurity of the National Security and Defense Council of Ukraine, she has been directly involved in generating analysis and recommendations that will guide the development of the national strategy on biosafety, biosecurity, biopreparedness, and public health.

Lee, Soh Jin
International Vaccine Institute, South Korea

Soh Jin Lee holds a M.S. in medical laboratory science from Inje University and is a special research student at Kyoto University in Japan with a scholarship from Ministry of Environment, Japan. She joined the International Vaccine Institute (IVI) as general manager of the ABSL-3/BSL-3 in March 2010. Prior to appointment at IVI, she worked for GreenCross Vaccine in Korea and RheinBiotech in the Netherlands. She also performed regulatory affairs and WHO prequalification consulting for vaccines at Innopath International Inc. After that, she moved to the biosafety field by transferring to Institut Pasteur Korea in 2005. As a biosafety officer, Ms. Lee obtained the first BSL-3 certificate in Korea. Based on her experience, she was asked to participate in the construction of a new building that included BSL-3 facilities and obtained the second certificate for it. After moving to IVI, she made the systematic changes necessary to obtain a BSL-3 certificate for the facility. She's been developing a BSL-3 manual, standard operating procedures, user protection systems, and several kinds of biosafety training programs, including ABSL-3/BSL-3 training. She received her biosafety and biosecurity training from Institut Pastuer-Paris, Institut Pastuer-Shanghai, the National Institute of Infections Diseases (Japan), the Korean Centers for Disease Control and Prevention (KCDC), the Korean Biological Safety Association, and A-PBA. Ms. Lee was a member of the Biosafety Advisory Committee, KCDC and has been invited to speak to several government agencies and at international workshops.

Lentzos, Filippa
London School of Economics, U.K.

Filippa Lentzos is a senior research fellow in the BIOS Centre at the London School of Economics. Originally trained in human sciences before switching to sociology, she focuses on social, political, economic and legal questions in the fields of biosecurity and synthetic biology.

Ling, Ai Ee
Singapore General Hospital/Singapore Health Services

Dr. Ling Ai Ee currently chairs the SingHealth IBC (Institutional Biosafety Committee), which provides advice and guidance for all institutional biosafety committees of the constituent health institutes in the SingHealth group, which includes Singapore General Hospital, KK Women's and Children's Hospital, five National Specialist Centers, and the SingHealth Experimental Medical Center. The SingHealth IBC also appoints an expert panel to review all research protocols relating to biological agents and toxins pursuant to the Biological Agents and Toxins Act, 2005. She also is director of the Office of Safety Network, Singapore General Hospital, which provides oversight of all safety issues in research laboratories in the SingHealth group and is directly involved in all safety issues in Singapore General Hospital. A committee

member of the National Biosafety Committee, Ministry of Health, Singapore, she also sits on two of its subcommittees: the Select Agents Technical Working Group and the Training Technical Working Group (co-chair). In addition, she is a committee member of the Genetic Modification Committee (GMAC), Singapore.

Lyons, Arthur
WRAIR, United States

Colonel Arthur Lyons holds a B.S. degree from the College of William and Mary, United States (1985), a Ph.D. degree in organic chemistry from the University of Iowa, USA (1991), and an M.D. from the University of Iowa, USA (1995). He is board-certified in internal medicine (2000, 2009) and infectious diseases (2001, 2010). Colonel Lyons is a military research physician with 16 years of active duty military service developing therapeutics, prophylactics, diagnostic devices, surveillance and laboratory systems against infectious disease threats of military and global health importance, especially flaviviruses (Japanese encephalitis and dengue), adenovirus, influenza, and other pathogens of regional and global public health importance. He is a subject matter expert on Japanese encephalitis, adenovirus vaccine development, and operational medicine. He establishes national and international research collaborations with United States federal agencies, non-governmental organizations, international Ministries of Public Health, biotechnology firms, management consulting firms, and leading universities. Additionally, he initiates and leads basic, clinical, and field medical research in the United States, Europe, Asia, and Africa in accordance with local IRB, United States Food and Drug Administration, and host nation guidelines. Colonel Lyons publishes work in peer-reviewed scientific journals and represents the United States Army Medical Research and Materiel Command at national and international scientific and policy meetings. He is an attending physician at Walter Reed Army Medical Center and National Naval Medical Center. Colonel Lyons is also an assistant professor of medicine at Uniformed Services University of the Health Sciences responsible for teaching medical students. He is currently the director of United States/Georgia Laboratory Operations, which is responsible for a primary mission to develop a new Department of Defense laboratory in the country of Georgia.

Macedo, Leila
ANBio, Brazil

Leila dos Santos Macedo has been a senior researcher on biosafety at the Oswaldo Cruz Foundation in Brazil since 1982. She holds a Ph.D. in microbiology and immunology. She established the quality control system of human vaccines in Brazil from 1983 to 1988 and established the Biosafety Program at the Ministry of Health in Brazil from 1988-1994. She was chair of the National Biosafety Committee at the Ministry of Science and Technology from 1996-1998. Dr. Macedo founded the Brazilian Biosafety Association (ANBio) in 1999, and she has been its president since that time.

Markotic, Alemka
University Hospital for Infectious Disease, Croatia

Dr. Alemka Markotic is an associate professor and lecturer in postgraduate studies at the medical school of the University of Rijeka and she teaches at medical schools in Zagreb, Osijek and Split, Croatia. She is also head of the Research Department and head of the Department for Clinical Immunology, University Hospital for Infectious Diseases (UHID) in Zagreb, Croatia. She received her M.D. at the University of Sarajevo, Bosnia and Herzegovina (1989), an M.S. in medical microbiology and parasitology (1996), and a Ph.D. in infectious diseases (1999) from the University of Zagreb Medical School. Dr. Markotic began her biomedical research career at the University of Sarajevo Medical School in Bosnia and Herzegovina studying ribavirin treatment of hantaviruses during which time she collaborated with the United States Army Medical Research Institute for Infectious Diseases (USAMRIID) in Frederick, Maryland. She later received a National Academy of Sciences, National Research Council Postdoctoral Fellowship at USAMRIID to conduct research on the immunopathogenesis of hantaviruses. Based on this work she received the Joel Dalrymple Memorial Award (American Society of Virology) and the USAMRIID Coin. Dr. Markotic's research on hantaviruses has earned her seven national and nine international awards. She has published 56 peer-reviewed papers and delivered over 90 presentations at national and international

conferences. She has been the principal investigator on research projects studying immune responses to intracellular pathogens, zoonoses, and apoptosis in hantavirus-infected 293HEK cells. At the UHID, Dr. Markotic established the Center for Emerging and Re-emerging Infection Diseases with nine international and six national partners, and she is responsible for managing the first Croatian BSL-2+ and BSL-3 laboratory that recently was completed at the UHID. She is trained and certified for work in BSL-3 facilities and received training in BSL-4 level work at USAMRIID. At the request of the EU Commission, Dr Markotic designed, organized, and presented a biosafety/biosecurity training workshop in Beijing, China in May 2009. She worked for several years at the Institute of Immunology in Zagreb as a head of the Viral Vaccines and Interferon Quality Control Unit. She is a member of the Council of the International Society for Hantaviruses, the Board for Allergy and Clinical Immunology at the Croatian Academy of Science and Arts, and was a member of the Committee of the Croatian Science Foundation, the National Council for Science, and vice-president of the Scientific Council in the Scope of Biomedicine and Health. In 2004, 2005, and 2009 she was an expert evaluator for FP6 projects (EU Commission, Brussels) in immunology and emerging infectious diseases. In the 1990s, during the war in Bosnia and Herzegovina, she helped organize the “Caritas” Pharmacy and Health Care Unit that addressed the health needs of those affected by the conflict.

McKinney, Michelle
Defense Threat Reduction Agency, United States

Michelle McKinney is the biorisk lead for the United States Defense Threat Reduction Agency’s (DTRA) Cooperative Biological Engagement Program supporting partners around the world in the sustainable implementation of risk-based laboratory biosafety and biosecurity practices. She has also served as a principal member of the technical staff in the International Biological Threat Reduction Program (IBTR) at Sandia National Laboratories. Prior to joining the IBTR, she was a principal life scientist with SAIC supporting a variety of customers regarding biorisk issues, most recently DTRA’s international cooperative threat reduction program. While at SAIC she also served as the safety and biosecurity manager for the National Bioforensic Analysis Center. Previously, Michelle was a research scientist at the United States Medical Research Institute of Infectious Diseases where she conducted novel research on molecular diagnostics of select agents and also has experience working in a variety of university and private industry settings researching infectious diseases. She received her B.S. in cellular and molecular biology from Tulane University and her M.S. in microbiology from Clemson University. Michelle has been a Certified Biological Safety Professional and Specialist Microbiologist in Biological Safety Microbiology, National Registry of Certified Microbiologists since 2000. She is an active member of ABSA having served as an instructor, committee chair, and team leader. She is currently a member of the ABSA Council and was recently appointed co-chair of the Biosafety Professional Accreditation Working Group with the International Federation of Biosafety Associations.

Melboucy, Mohamed Abdeldjallil
Pasteur Institute of Algeria

Mohamed Abdeldjallil Melboucy is currently in charge of quality assurance and biosafety at the Pasteur Institute of Algeria. He has a diploma in public health quality and risk management from the Lille Institute of Health Engineering. He has worked in both the pharmaceutical and hospital fields. He is experienced in implementing Good Manufacturing Practices (GMP) for safety and hygiene, pharmaceutical production, analytical chemistry, and controlled atmosphere processes. He has developed protocols for assessing the performance of mobile decontamination techniques for air contaminated with *Aspergillus* and other microorganisms.

Mueller-Doblies, Uwe
Institute for Animal Health, U.K.

Dr. Uwe Mueller-Doblies studied veterinary medicine at the Free University of Berlin and virology and immunology at the University of Cambridge, U.K. He received a doctorate in veterinary virology from the University of Zurich, where he also completed a postdoctorate degree in parasitology. With a fellowship from the Swiss Science Foundation he joined the Microbial Pathogenesis Center at the University of

Connecticut studying the immunology of pathogen transmission by hard ticks. In 2003, Dr. Mueller-Doblies was appointed as head of biosecurity and named veterinary surgeon for the Institute for Animal Health at the Pirbright Laboratory. He is a diplomat of the European College for Veterinary Public Health and chairman of the International Veterinary Biosafety Workgroup. At the Pirbright Laboratory, Dr. Mueller-Doblies interacts closely with research groups and reference laboratories working in the high-containment facilities. In his current role, he participated in the working group of the Advisory Committee for Dangerous Pathogens to develop the guidance for the deliberate work with biological agents in the U.K., participated in the EU foot and mouth disease (FMD) working group to revise the EU minimum standards for laboratories working with FMD virus, worked for the EU Food and Veterinary Office as a national expert on numerous missions to inspect veterinary high-containment facilities, and served as an external member on the National Bio and Agro-Defense Facility design review team for the United States government. Aside from managing the biocontainment aspects of the IAH Pirbright Laboratory, Uwe specialized in technical risk assessments of biocontainment facilities and maintains a strong interest in vector-borne diseases.

Netesov, Sergey
Novosibirsk State University, Russia

Sergey V. Netesov, Ph.D., D.Sci. (1953) has been vice rector (research) of the Novosibirsk State University since November, 2007 and is also head of the university's Bionanotechnology Laboratory. Prior to this position, he served for 30 years at the State Research Center of Virology and Biotechnology ("Vector") becoming deputy director in 1990. He graduated from Novosibirsk State University and joined Vector in 1977. He later received a Ph.D. (1983) and a Doctor of Biology degree (1993). He is a member of the Russian Biotechnology Association; the American Society for Virology; the Russian Society of Epidemiologists, Microbiologists, and Parasitologists; the American Society for Virology; AAAS; the American Biosafety Association; the European Biosafety Association; and the Filovirus Study Group of the International Committee on Taxonomy of Viruses. He is a corresponding member of the Russian Academy of Sciences (since 1997) and the European Academy of Sciences (since 2004). In the beginning of his research career, he developed original methods for isolating restriction endonucleases and reverse transcriptases. Later, Dr. Netesov headed Russian projects that sequenced the genomes of the Marburg, Ebola, Venezuelan equine encephalitis (VEE) virus, and Eastern and Western equine encephalitis viruses. He was a leader of the reverse genetics project on the VEE virus reconstruction from cDNA fragments. He also led the work on sequencing Russian strains of tick-borne encephalitis and influenza viruses and was involved in the development of an inactivated vaccine for hepatitis A. Recently, he completed projects focused on the molecular diversity and epidemiology of viral hepatitis in Siberia and currently participates in other molecular epidemiological and biotechnological projects. He, together with his colleagues, received two Russian government awards (1998 and 2006) for the development and production of modern ELISA diagnostic kits against viral hepatitis and HIV and for development of bioterrorism prevention measures in Russia. His research interests include virology and biotechnology. Dr. Netesov has more than 140 publications in Russian and international scientific journals and 12 patents.

Öktem, Hüseyin Avni
Middle East Technical University, Turkey

Professor Öktem got his B.Sc. (biological sciences) and M.Sc. (biochemistry) degrees from Middle East Technical University (METU) in Ankara, Turkey, followed by a neurochemistry certificate and Ph.D. in biochemistry from Josef Attila University in Hungary (1990). He worked for a year at the Plant Biotechnology Institute of Texas Tech University. He established one of the first plant genetic transformation research facilities in Turkey, and at 36 years old he became a full professor of biochemistry at METU. He was involved in more than 100 academic and industrial research and development (R&D) projects as either project director or researcher. He has more than 50 scientific publications and 6 utility models/patents (1 pending patent) applications. Dr. Öktem acts as a referee and consultant for various governmental and private organizations, and he is the chairman of the Turkish Biotechnology Association. Professor Öktem is the co-founder and owner of two technology companies: OBiTEK-Middle East United Technologies Ltd. Co. and NANObiz NanoBioTechnological Systems R&D

and Consultancy Ltd. Co. Currently, he holds a full professor position in the Molecular Biology and Genetics Department of Middle East Technical University. He is responsible for strategic planning and R&D operations at NANObiz Ltd. Co. His fields of expertise include biosensing technologies, homeland security, molecular diagnostic, array technologies, biosensors, and transgenic plant technology.

Paranjape, Suman (Sumi)
Department of State, United States

Dr. Sumi Paranjape is an American Association for the Advancement of Sciences (AAAS) Fellow and a program officer at the Bioengagement Program (BEP) of the United States Department of State. Sumi currently manages the India and Pakistan portfolios for BEP and leads efforts for several international collaborations with the World Health Organization and the European Committee for Standardization. Sumi is the focal point for the Department of State's efforts on United States initiatives on the International Health Regulations and laboratory capacity. Before beginning at the State Department, Sumi performed research spanning the areas of infectious diseases, biochemistry, molecular biology, and public health. As a President's Postdoctoral Fellow at the University of California, Berkeley, Sumi studied dengue virus and collaborated with scientists at the Nicaragua Ministry of Health to increase dengue and West Nile virus diagnostic and surveillance capacity. Sumi earned her Ph.D. in biomedical sciences from the University of California, San Diego and a M.P.H. from the University of California, Berkeley.

Prasad, Gaya
Indian Council of Agricultural Research (ICAR), Krishi Bhawan, New Delhi, India

Dr. Gaya Prasad obtained a bachelor of veterinary sciences and animal husbandry (1977), a master's in veterinary sciences (microbiology) (1980), and a Ph.D. in microbiology and public health (1984) from G.B. Pant University of Agriculture & Technology in Pantnagar, India. He worked as a postdoctoral fellow (1986-1988) at M.D. Anderson Hospital and Cancer Institute at the University of Texas, Science Park Research Division in Smithville, United States. He started his career as a teaching associate at G.B. Pant University of Agriculture & Technology in 1982 and became an assistant scientist in 1983 at Chaudhary Charan Singh Haryana Agricultural University, Hisar. Dr. Prasad became a scientist and associate professor in 1995 and professor and head of the Department of Animal Biotechnology in 2003. Dr. Prasad became the assistant director general (animal health) of ICAR at Krishi Bhawan, New Delhi in July 2010. Dr. Prasad is a distinguished veterinary microbiologist and has made significant contributions in the fields of animal rotaviruses and bluetongue virus epidemiology and diagnostics. Dr. Prasad was also founder and head of the Department of Animal Biotechnology at Haryana Agricultural University. He served as principal investigator and co-principal investigator of several projects funded by ICAR, USAID, the United States Department of Fish and Wildlife Service, and the Ministry of Environment and Forests. He has published over 100 research papers in national and international journals and written several book chapters, laboratory manuals, conference proceedings, and books. He has been a keynote and invited speaker in several national and international conferences, symposia, and seminars and has received many awards. Dr. Prasad has served as the volume editor of the international review series "Progress in Vaccinology," editor of the *Indian Journal of Microbiology*, managing editor of the *Indian Journal of Virology*, and president of the Association of Microbiologists of India. Dr. Prasad has been awarded fellowships from the National Academy of Agricultural Sciences, the National Academy of Veterinary Sciences, and the Association of Microbiologists of India.

Ruacan, Sevket
Koç University, Turkey

Professor Ruacan graduated from Hacettepe University Faculty of Medicine in Ankara in 1969. He then completed postgraduate studies at the University of Pennsylvania and New York University. He later served as the dean of the Medical School and director of the Institute of Oncology at Hacettepe University. He was also a member of the Executive Board of the Turkish Scientific and Technical Research Council. Currently, he is the dean of Koç University Medical School, vice president of the Association of Asian Academies of Science, and a member of the Executive Council of the Interacademy Medical Panel. Professor Ruacan has been a member of the Turkish Academy of Sciences since 1994.

Saijo, Masayuki
National Institute for Infectious Diseases, Japan

Dr. Masayuki Saijo is a medical doctor and received his Ph. D. degree in pediatrics under the directorship of Professor Yoshioka H. and Professor Okuno A. at Asahikawa Medical University in Japan (1991). His primary research field is viral infections. He has studied clinical infectious respiratory diseases in children and antiviral-resistant herpesvirus infections in immunocompromised subjects. He joined the National Institute of Infectious Diseases (NIID) in Tokyo, Japan in 1997 and has studied viral hemorrhagic fevers such as Ebola, Marburg, Lassa, and Crimean-Congo hemorrhagic fevers as well as orthopoxvirus infections. He leads the Department of Virology 1 at NIID.

Sasono, Pretty
National Institute of Health Research & Development, Indonesia

Pretty Multihartina D. Sasono has been a researcher at the National Institute of Health Research and Development (NIHRD), Ministry of Health, Republic of Indonesia since 1989. She received her Ph.D. in biology from the University of Leeds, U.K. in 1997. She was part of the postdoctoral program at the Center for Biologic and Evaluation Research, United States Food and Drug Administration within the United States NIH Campus from 2008 to 2010. She was a project leader for building the BSL-3 laboratory at NIHRD from 2007 to 2008. Presently, she is a laboratory manager and the head of basic technology of the Health Division at the Center for Biomedical and Basic Technology of Health under the NIHRD.

Shestopalov, Aleksandr
State Researcher Centre of Virology & Biotechnology "Vector," Russia

Dr. Shestopalov has served from 1991 to the present day as the director of the Division of Influenza and Zoonotic Infections at the Federal State Research Center of Virology and Biotechnology "Vector" in Koltsovo, Novosibirsk region (Russia) and also as a senior researcher at Novosibirsk State University. In 1979 he received an M.S. from Novosibirsk State University, Department of Natural Sciences, and in 1983 he received a Ph.D. from the Siberian Computer Center, Novosibirsk Specialization. In 1984 the Irkutsk Antiplague Institute gave him a certificate on work with especially dangerous infections. In 2005 he was at the World Health Organization Collaborating Center for Studies on the Ecology of Influenza in Animals and Birds located at the Division of Virology Department of Infectious Diseases at St. Jude Children's Research Hospital in Memphis, Tennessee, United States where he earned a certificate on work with influenza viruses. His research experience includes the study of epidemiology; virus and bacterial diseases dangerous to humans and animals; field epizotology and epidemiology; search, isolation, and identification of new strains of viruses and bacteria; research of immune pathogenesis of viral diseases; and development of medical, preventive and diagnostic preparations. His main research directions include immunopathogenesis of haemorrhagic fevers (Marburg, and CCHF), development of the means for haemorrhagic fever prophylaxis (Marburg, CCHF), and therapy (Marburg). Recent international projects led by Dr. Shestopalov include Russian flu surveillance from 2004-2010; the epidemiology of influenza A in wild birds, poultry and pigs in the Novosibirsk region, Siberia (2005-2006); monitoring of influenza A viruses in wild birds, poultry, and pigs in the Novosibirsk region (2007-2010); and measuring, monitoring, modeling, and predicting avian influenza in the Pacific Rim (2010-2012).

Shinnick, Thomas
United States Centers for Disease Control and Prevention

Thomas M. Shinnick, Ph.D., is the associate director for global laboratory activities in the Division of Tuberculosis Elimination at the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention at the Centers for Disease Control and Prevention and an adjunct professor at the Department of Microbiology and Immunology at Emory University. He received a B.S. from the University of Wisconsin-Madison, a Ph.D. (biochemistry) from the Massachusetts Institute of Technology, and did postdoctoral training at the Research Institute of Scripps Clinic. His honors include the Johnson and Johnson Pre-

doctoral Fellowship (1977); Helen Hay Whitney Foundation Postdoctoral Fellowship (1978-1980); Arthur S. Flemming Award (1990); Fellow, American Academy of Microbiology (1994); and Senior Biomedical Research Service (1997). He has been chairman of Division U, American Society for Microbiology (1994); member of the National Tuberculosis Task Force; and member of the scientific advisory board for the Heiser Program. He is also co-chair of the Global Laboratory Initiative Working Group of the Stop TB Partnership, WHO Stop TB Working Group on Diagnostics, WHO Supranational Laboratory Network. Editorial activities include being the associate editor of *International Journal of Tuberculosis and Lung Diseases* and serving on the editorial board of *Emerging Infectious Diseases*, *Tuberculosis*, and *Current Microbiology*. Dr. Shinnick's scientific interests include understanding the biology and genetics of the pathogenic mycobacteria, elucidating mechanisms of pathogenicity and drug resistance of *Mycobacterium tuberculosis*, developing rapid methods for the diagnosis of mycobacterial infections, and using genotyping to support TB control programs and elucidate the dynamics of transmission. He is the author/co-author of more than 150 publications and the editor of one book.

Sirivichayakul, Sunee
Chulalongkorn University, Thailand

Sunee Sirivichayakul works in the Department of Medicine, Faculty of Medicine at Chulalongkorn University in Bangkok, Thailand. She holds three degrees from Chulalongkorn University (B.S. in medical technology, M.S. in medical microbiology, Ph.D. in medical microbiology). Her current work is on molecular and immunologic studies of HIV (i.e., HIV genotypic drug resistance testing using in-house assays, pre-clinical development of HIV-1 DNA vaccines, development of low-cost viral load assays, and intracellular cytokine staining for immunologic evaluation of HIV-infected individuals).

Smith, Greg
CSIRO, Australian Animal Health Lab

Dr. Greg Smith is responsible for microbiological security at CSIRO's Australian Animal Health Laboratory (AAHL) in Geelong, Victoria. Dr. Smith is the leader of the Microbiological Security Group at AAHL. He is currently the chair of the Institutional Biosafety Committee and the Security Sensitive Biological Agent Management Committee. AAHL includes high-containment BSL-3 and BSL-4 facilities to support its major role of diagnosing potential outbreaks of exotic (foreign) animal diseases and is a cornerstone of Australia's emergency disease response capability. It is the only laboratory in Australia licensed by the Commonwealth Government for experimental work with exotic animal disease agents. Dr. Smith is responsible for ensuring exotic disease and other high risk agents are handled safely, that the building and laboratories are maintained and function according to specification, that staff are trained appropriately to operate without breaching microbiological security, and that AAHL is quarantine compliant. Dr. Smith has more than 30 years of experience in medical and veterinary virology, specializing in virus research and diagnostics. Prior to joining CSIRO in April 2009, Dr. Smith was the director of forensic and scientific operations at Queensland Health Forensic and Scientific Services in the Queensland Health Department. Dr. Smith commenced his career at the United States Army Medical Research Institute for Infectious Diseases at Fort Detrick, Maryland, in the early 1980s. He then spent 13 years as a molecular virologist with the Queensland Department of Primary Industries and Fisheries followed by 12 years with Queensland Health. At Queensland Health, he oversaw the construction of BSL-3 and BSL-4 facilities and managed the operation of those facilities for over a decade, which allowed him to acquire extensive knowledge of the operational and regulatory frameworks surrounding high-containment facilities. His academic qualifications include a B.A. degree from the University of Queensland in St. Lucia, Australia (1980), a M.S. in biomedical sciences from Hood College, Frederick, Maryland, United States (1985), and a Ph.D. in biochemistry from the University of Queensland in St. Lucia, Australia (1992). He is also currently a member of the National Association of Testing Authorities, a member of the American Biological Safety Association, and a member of the Association of Biosafety for Australia and New Zealand. Dr. Smith has published more than 75 peer reviewed scientific papers or book chapters on virology research and biocontainment topics.

Summermatter, Kathrin
Institute of Virology and Immunoprophylaxis (IVI), Switzerland

Kathrin Summermatter has been involved in biosafety for more than 15 years. Since 2002, she has been the head of biosafety and the deputy director at the Institute of Virology and Immunoprophylaxis (IVI), the Swiss reference lab for highly infectious animal diseases (ABSL-3). Specifically, IVI is responsible for the diagnosis, surveillance, and control of highly contagious epizootics such as avian influenza, foot-and-mouth disease, and classical swine fever. In addition, the IVI pursues research both on these viruses and emerging viral diseases, as well as their potential transmission to man. The IVI is also the competent authority issuing the licenses required for the sale of veterinary immunobiological products. In addition, Kathrin was the coordinator of BIOSAFETY-Europe. She has been a long-standing member of ABSA, the International Veterinary Biosafety Workgroup, EBSA, and was the president of EBSA in 2003/2004. Along with providing expertise and consultative services to both private companies and government institutions on matters of biosafety and biosecurity, containment issues, and safe operating procedures, she has given many lectures and taught courses to national and international audiences.

Tkachenko, Evgeniy
Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russia

Evgeniy Tkachenko, M.D. and Ph.D., is a professor of virology and epidemiology. Since 2006, he has been the deputy director of the Chumakov Institute of Poliomyelitis and Viral Encephalitides, Russian Academy Medical Sciences and head of the Center on Hemorrhagic Fever with Renal Syndrome of the Russian Ministry of Public Health. He graduated from the Medical Institute of Moscow (Russia), Licentiate in 1965. Following graduation, he was a post-graduate student and later a junior researcher and senior researcher at the Laboratory of Hemorrhagic Fevers at the Institute of Poliomyelitis and Viral Encephalitides, USSR Academy of Medical Sciences (Moscow, USSR). In 1977, Dr. Tkachenko became the head of the Laboratory of Arenaviral Infections and in 1988 the head of the Laboratory of Hemorrhagic Fevers. His research interests include virology, epidemiology, laboratory diagnosis, vaccines, hantaviruses, and epidemiology.

Ugrumov, Mikhail
Institute of Developmental Biology, Russian Academy of Sciences (RAS), Russia

Prof. Ugrumov graduated from Moscow University Medical School in 1970 and received a Ph.D. from the Institute of Evolutionary Physiology and Biochemistry, USSR Academy of Sciences in 1974. He was a senior researcher at the Institute of Human Morphology, Russian Academy of Medical Sciences (RAMS) (1974-77) and the Institute of Developmental Biology, RAS (1977-87). Prof. Ugrumov has been head of the laboratory at the Institute of Developmental Biology since 1987 and of the Institute of Normal Physiology since 1996. He got a professorship in pharmacology and radiobiology in 1996 at the State Medical University, Moscow, Russia and was elected as a corresponding member of the Russian Academy of Sciences in 1997 and as a full academician in 2006. Prof. Ugrumov is the advisor to the president of the RAS on international scientific cooperation, a member of the Scientific-technical Council of the chairman of the Federal Assembly of the Russian Federation, and vice president of the Russian Physiological Society. He was a visiting professor at the University Medical School, Tokushima (Japan) in 1988-89; the Medical University of Ulm (Germany) in 1993; the University of Tours (France) in 1998, 2000; and the University P. et M. Curie (Paris, France) in 1993-2010. His honors include the Orbeli Prize of the Russian Academy of Sciences in physiology (1995), a professorship from the Burroughs Wellcome Fund, and a prize from the Federation of American Societies for Experimental Biology (2001). His field of expertise is neurosciences, and his main studies are devoted to: (i) the development of neuroendocrine regulation in ontogenesis; (ii) the regulation of neurogenesis and differentiation by extracellular signals including morphogenetic factors; and (iii) the mechanisms of the brain plasticity and their regulation by signaling molecules in normal individuals and in neurodegenerative diseases (e.g., Parkinson's disease).

Ugwu, Kenneth
Foreign Affairs and International Trade Canada

Ken Ugwu is the senior biocontainment specialist with Foreign Affairs and International Trade Canada working with the Global Partnership Program. Ken is an internationally recognized expert on engineering matters relating to the planning, design, construction, operation, and inspection of biocontainment facilities. Ken has over 25 years experience in this field and has been providing expert authoritative advice, training, and recommendations on these matters to professional scientific staff, engineering firms, and government decision makers in many parts of the world. Ken is a Registered Professional Engineer in the Province of Ontario, Canada. He is a member of the American Society of Heating Refrigeration and Air Conditioning Engineers, the American Biological Safety Association (ABSA), and the National Fire Protection Association and the co-chair of the Biocontainment Engineering Network of the International Federation of Biosafety Associations. Ken holds a B.A.Sc. in mechanical engineering from the University of Ottawa and a diploma in engineering management and industrial instrumentation.

van Doorn, H. Rogier
Oxford University, Vietnam

Rogier van Doorn is a Dutch clinical microbiologist who trained at the Academic Medical Center in Amsterdam, Netherlands. He works at the Oxford University Clinical Research Unit (OUCRU) in Ho Chi Minh City, Vietnam. Rogier did a Ph.D. on diagnostics and susceptibility of *Mycobacterium tuberculosis*, has worked and published on parasitology diagnostics, and currently heads the respiratory infections group at OUCRU. Rogier's Ph.D. students work on antibiotic use in respiratory infections, respiratory syncytial virus, viral encephalitis, and H5N1 influenza. The virology lab at OUCRU is the reference virology lab of the Southeast Asian Infectious Disease Clinical Research Network and has recently started work in a newly built BSL-3/SAPO4 lab, funded by NIH and the Wellcome Trust, with labs for tuberculosis and animal and human virus work. Rogier was part of the team that supervised the design and realization of this lab and was responsible for the biosafety aspects during construction and certification.

Wacharapluesadee, Supaporn
Chulalongkorn University, Thailand

Supaporn Wacharapluesadee, Ph.D., is head of the Molecular Biology Laboratory for Neurological Diseases, King Chulalongkorn Memorial Hospital and the WHO Collaborating Centre for Research and Training on Viral Zoonoses, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand. During 1994-1997, she worked on malaria research at the Department of Entomology, Armed Forces Research Institute of Medical Sciences. In 1997, she worked at Chulaporn Research Institute on cancer research. In 1998, she worked in the HIV research laboratory at the HIV/AIDS Collaboration Thai-USA. Since 2001, she has developed molecular techniques for detecting viral pathogens in clinical specimens, especially from encephalitis patients. Her particular areas of interest are viral encephalitis and emerging viral zoonoses carried by wildlife, especially bats and rodents. She holds an undergraduate degree in medical technology from Chiang Mai University, a master's degree in biochemistry from Mahidol University, and a Ph.D. in biomedical sciences from Chulalongkorn University, Thailand.

Wilson, Valerie
Caribbean Med Labs Foundation, Trinidad & Tobago

Ms. Valerie Wilson is a trained immunologist and public health professional who has provided leadership and technical advisory services to Ministries of Health, private and public sector laboratories, and staff in 23 countries within the Caribbean region through her work at the Caribbean Epidemiology Centre, particularly in the areas of laboratory management, quality improvement, laboratory safety and strategic management. She has been involved in a leadership role in raising awareness of governments and laboratories in the Caribbean region with respect to the need for medical laboratory standards and quality

management systems including safety, has developed many training materials and approaches utilized within and external to the Caribbean, and has trained and mentored laboratory managers and supervisors within the region. Ms. Wilson is the director of a non-governmental organization, Caribbean Med Labs Foundation (CMLF), which is focused on strengthening laboratory services within the Caribbean region. CMLF has been successful in attracting funding under Round 9 of the Global Fund against HIV/AIDS as a sub-recipient under the Pan Caribbean Partnership against HIV/AIDS (PANCAP) grant and has recently begun to implement this five-year project for the strengthening of laboratory support for HIV/AIDS programs within the Caribbean region. CMLF is currently working with its Caribbean network of laboratory professionals and the International Federation of Biosafety Associations (IFBA) to establish a Caribbean Association for Biological Safety (CABSA) to promote and improve laboratory safety standards within the region.

Zaidi, Sohail
National Institute of Health Islamabad, Pakistan

Syed Sohail Zahoor Zaidi is the head of the Department of Virology at the National Institute of Health, Pakistan. He is proficient in viral studies using classical as well as modern virological tools. He has been a focal person for many national as well as international public health projects like the WHO Polio Eradication Initiative, the WHO Measles Elimination Initiative, the United States CDC lab-based influenza project, and a number of national projects on rotavirus, dengue virus, Crimean-Congo hemorrhagic fever, hepatitis, and other diseases.

Staff

Chiarello, Heather
The National Academies, United States

Heather Chiarello joined the United States National Academy of Sciences in July 2008. She graduated magna cum laude from Central Michigan University in 2007 with a B.S. in political science with a concentration in public administration. Ms. Chiarello is currently a senior program assistant with the Ocean Studies Board in the Division on Earth and Life Sciences and the Committee on International Security and Arms Control in the Policy and Global Affairs Division of the National Academies. She is pursuing a master's degree in sociology and public policy analysis at Catholic University of America in Washington, D.C.

Hottes, Alison
The National Academies (Consultant), United States

Alison Hottes holds Ph.D. (2005) and M.S. (2000) degrees in electrical engineering from Stanford University and a B.S. (1998) in electrical engineering and mathematics from Utah State University. She just completed a postdoc at Princeton University where she developed experimental and computational methods to enable systems-level studies of bacteria. Her work, which spans the fields of genomics, bioinformatics, and microbiology, examines how mutations propagate through a bacterium's cellular network, altering a range of phenotypes including antibiotic tolerance. She has authored peer-reviewed journal articles and a book chapter. In the winter of 2011, she was a Christine Mirzayan Science and Technology Policy Fellow at the United States National Academies and currently works as a consultant for the Committee on International Security and Arms Control of the United States National Academies.

Rusek, Benjamin
The National Academies, United States

Benjamin Rusek works as a program officer for the Committee on International Security and Arms Control (CISAC) at the United States National Academy of Sciences (NAS) on issues related to nuclear and biological nonproliferation and arms control and the misuse of science and technology. Ben manages CISAC's interaction with its counterpart in Beijing, China, CISAC's programs examining threats related to biological weapons and dual use biotechnology, and serves as program staff on CISAC's "Track II"

dialogues and CISAC-administered National Research Council (NRC) studies. Outside of the NAS, Ben is the chair of the executive board of International Student Young Pugwash (ISYP). Ben has political science degrees from The Ohio State University and Purdue University.

Sharples, Fran
The National Academies, United States

Dr. Frances E. Sharples has served as the director of the National Academy of Sciences' Board on Life Sciences since October 2000. Since spring of 2010, Dr. Sharples has also served as acting director of the Institute for Laboratory Animal Research. The Board on Life Sciences serves as the National Academies' focal point for a wide range of technical and policy topics in the life sciences, including bioterrorism, genomics, biodiversity conservation, and key topics in basic biomedical research, such as stem cells. In 2003, Dr. Sharples directed a study on the organizational structure of the National Institutes of Health that led to the publication of the report *Enhancing the Vitality of the National Institutes of Health: Organizational Change to Meet New Challenges*, which resulted in major management and budgetary changes at NIH. In 2005, Dr. Sharples served as the study director for the preparation of the National Academies' report *Guidelines for Human Embryonic Stem Cell Research,* which had a major impact on the oversight of stem cell research in the United States. Most recently she served as co-study director on the report *Review of the Scientific Approaches Used During the FBI's Investigation of the 2001 Anthrax Letters*. Immediately prior to coming to the National Academies, Dr. Sharples was a senior policy analyst for the Environment Division of the White House Office of Science and Technology Policy (OSTP) from October 1996 to October 2000. Dr. Sharples came to OSTP from the Oak Ridge National Laboratory, where she served in various positions in research and management in the Environmental Sciences Division between 1978 and 1996. Dr. Sharples received her B.A. in biology from Barnard College (1972) and her M.A. (1974) and Ph.D. (1978) in zoology from the University of California, Davis. She served as an American Association for the Advancement of Science (AAAS) Environmental Science and Engineering Fellow at the Environmental Protection Agency during the summer of 1981, and served as a AAAS Congressional Science and Engineering Fellow in the office of Senator Al Gore in 1984-85. She was a member of the National Institutes of Health's Recombinant DNA Advisory Committee in the mid-1980s and was elected a fellow of the AAAS in 1992.

APPENDIX D

DESCRIPTION OF TOUR OF PENDIK VETERINARY CONTROL AND RESEARCH INSTITUTE

Summary prepared by Barbara Johnson (Biosafety Biosecurity International, United States)

Following the conclusion of the workshop, many of the participants visited the nearby Pendik Veterinary Control and Research Institute (PVCRI) and toured its BSL-3 lab, which was undergoing the final stages of construction. PVCRI, which is located in the Asian part of Istanbul, Turkey, was founded in 1894 and moved to its present location in 1912. PVCRI produces veterinary vaccines, serums, antigens, and biological materials and serves as a national reference lab for the Turkish Ministry of Agriculture and Rural Affairs (MARA). The lab's mission includes research, diagnostics, and community education.

As one of three labs in Turkey with the ability to both isolate and identify avian influenza virus, PVCRI played a key role in recent efforts to detect and combat avian influenza in Turkey. In 2006, MARA and the Turkish Ministry of Health produced a new coordinated preparedness and response plan for avian influenza that called for PVCRI and two other labs to expand their capabilities and begin performing virus pathogenicity characterization on-site. At the time of the decision, none of the three labs met the safety recommendations for the proposed work, so the General Directorate of Protection and Control decided to upgrade them to BSL-3 capabilities

For the BSL-3 lab at PVCRI, MARA chose to renovate a portion of the existing facility. Initial construction began in 2008, and the current construction company, HTL, took over from the previous firm in 2010. HTL is a Turkish company with experience constructing not only clean rooms but also containment facilities.

As shown by the floor plan (Figure D-1) personnel enter through a clean corridor. They then pass through a change room where a complete change of clothing is provided prior to transiting through the shower and dirty side change room into a set of corridors that allow entry to bacteriology, virology, necropsy, procedure, and diagnostic laboratories. Sample accessioning is accomplished in a clean room outside the containment zone, and samples enter the BSL-3 via a pass-through box to the adjacent procedure lab. A decontamination airlock is available for decontamination and movement of large pieces of equipment, and waste is passed through a double door bioseal autoclave prior to disposal. For safety, an emergency egress door is provided at the far end of the containment corridor. To facilitate sealing the decontamination airlock and as an added measure of safety above that required for BSL-3, gasketed pneumatic airtight doors are installed on both sides of the decontamination vestibule, the emergency exit, and at the containment boundary from each clean change room to the shower. Viewing windows are provided to the labs and the containment office space.

The floors, walls, and ceilings in the containment area are coved, were constructed to facilitate cleaning, and employ materials resistant to commonly used decontaminating agents (Figure D-2). The entire lab can be sterilized using gas, and each room can also be sterilized separately. Class II biological safety cabinets (BSCs) are used for all manipulations of infectious materials, and procedure rooms are equipped with HEPA-filtered poultry isolators with pass-through chambers for the movement of supplies, animals, and waste. Hands-free sinks and eyewashes are located near the exit of the labs. Doors are self-closing and equipped with locks for biosafety as well as biosecurity. In keeping with international best practices, additional biosecurity features have also been installed.

The exhaust air passes through welded, stainless steel ducts to two HEPA filters in series in the mechanical room that is accessible from outside the containment area (Figure D-

3). The HVAC system is supported by an emergency generator and has a redundant exhaust fan as well as redundant HEPA filter banks, as PVCRI's mission requires it be operational every day with the exception of scheduled maintenance shut downs. Potentially contaminated liquid effluent is gravity fed to an Actini continuous flow liquid sterilization system, which also features a second system for N+1 redundancy.

Ayse Selma Iyisan (PVCRI) hosted the tour and was assisted by **Aysen Gargili** (Marmara University), **Naci Sivri** (HTL), and **Sevil Erdenlig** (PVCRI).

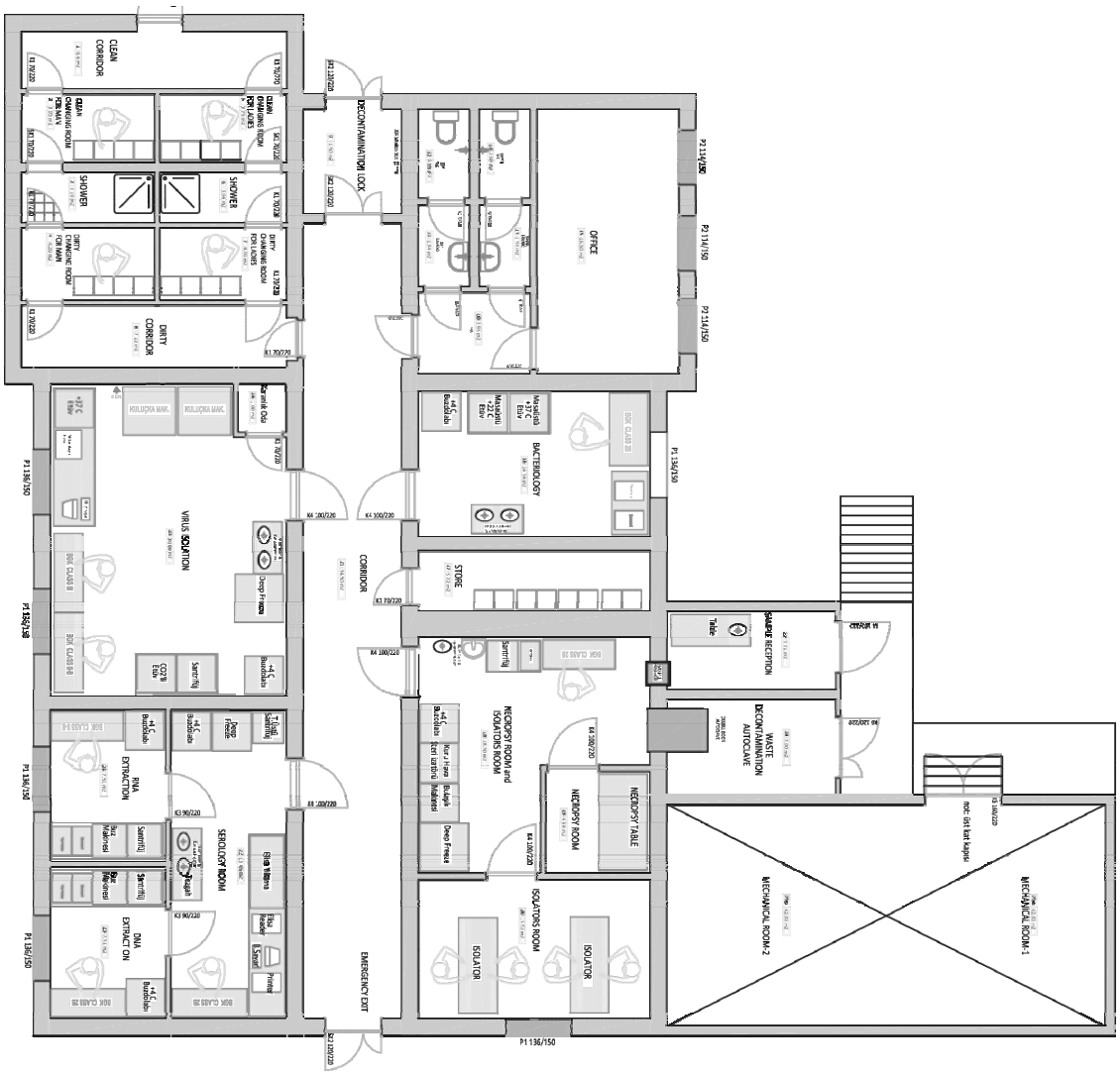

Figure D- 1 Floor plan of PVCRI BSL-3 laboratory.
SOURCE: HTL Gebze Plastic Manufacturer Organization.

Figure D-2 Interior corridor of PVCRI BSL-3 lab.
SOURCE: Barbara Johnson, committee member.

Figure D-3 PVCRI HEPA filter bank.
SOURCE: Barbara Johnson, committee member.

APPENDIX E

COUNTRY AND REGION OVERVIEWS

Phase I of the project allowed National Academies staff to work with international partners to develop country and region overviews in advance of the Phase II international workshop. Staff engaged partners in countries that have developed BSL-3 and/or 4 laboratories and countries planning to construct BSL-3 and 4 labs. Staff asked all of the country study writers to describe a country's facilities, capabilities, and regulations as well as past accidents, safety and security issues, and lessons learned.

Project staff collected nine country and region overviews during the project from authors writing about Brazil, the European Union (region), Pakistan, Russia, Sweden, Turkey, Ukraine, the United Kingdom and the United States. The country and regional overviews vary in the amount and type of information they provide. The overviews were used to inform the discussion at the workshop and the authors of the workshop summary. The final versions are appended below as they were provided to the National Academies.

E1

Overview of Biosafety and Biosecurity in High-containment Labs in Brazil: A Report of the Brazilian Biosafety Association

Leila dos Santos Macedo, Ph.D.
Brazilian Biosafety Association

Background and Disclaimers:

1- The Brazilian Biosafety Association (ANBio), whose main objective is to improve biosafety and biosecurity in Brazil, prepared this report in response to a 2 April 2009 letter from the United States National Academy's Committee on International Security and Arms Control (CISAC). The Brazilian Government has no responsibility for this report or for the information in it.

2- ANBio recognizes the importance of CISAC's project on the risks and responsibilities associated with the international expansion of high-containment laboratory accidents, as well as the importance of following international guidance and agreements to reduce biological threats.

3- This report was produced from survey data collected by ANBio as part of their capacity building program on biosecurity (Figure E1.1). The survey took place from May 2008 through February 2009. Overall, 237 questionnaires were received, which included responses from two institutions in other South American countries (Peru and Equator). The data presented reflects that submitted by survey responders; as such, ANBio is not responsible for any misleading or incomprehensive information.

4- In producing this report, ANBio also considered presentations exhibited by representatives of the Brazilian Government during ANBio's capacity building program.

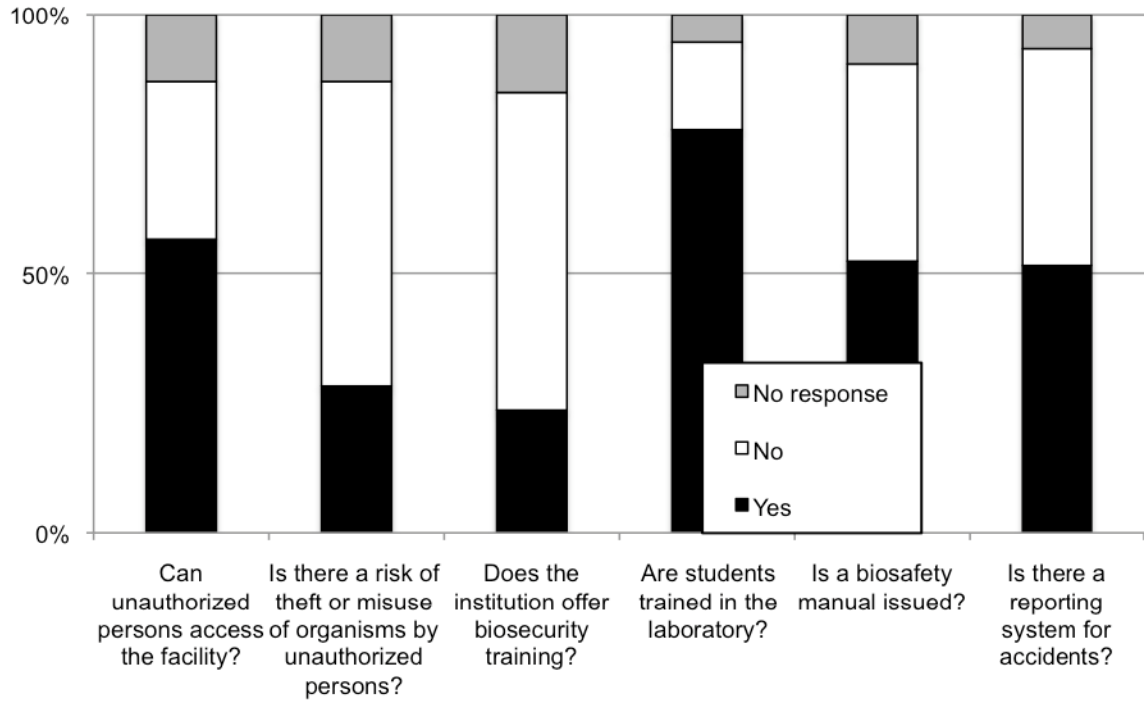

Figure E1-1 The results of a survey conducted by ANBio about the state of biosafety and biosecurity in biological research institutions across Brazil (including two from Peru and Equator). The survey took place from May 2008 to February 2009, and 237 questionnaires were received.
SOURCE: Data are the result of a survey conducted by ANBio.

1- What high-containment biological research facilities exist in your country?

In Brazil, only those laboratories conducting research related to public health, agriculture, and genetically modified organisms (GMOs) are subject to government regulation. There is no oversight or evaluative mechanism for laboratories, high-containment or otherwise, that are established at public or private universities for research activities with biological agents (other than GMOs). So, the answer here refers to public health, agriculture, and GMO laboratories only.

There are a total of 12 BSL-3 laboratories under the responsibility of the Ministry of Health and 8 BSL-3 laboratories under the responsibility of the Ministry of Agriculture (Table E1-1). Brazil currently has no BSL-4 laboratories, although there has been ongoing discussion about building one.

Table E1-1 List of known BSL-3-capable laboratories and microorganisms in Brazil.

Item	Institution	Microorganism	Risk Class[a]	Lab BSL
1	Universidade Federal do Amazonas Laboratório de Genética Animal	Aspergillus *M. tuberculosis MDR*	2 3	BSL2 BSL-3
2	Fiocruz – IOC Laboratorio de AIDS e Imunologia Molecular	HIV	3	BSL-3
3	LACEN – CE Laboratório de Microbiologia	*Micobacterium tuberculosis MDR* *Yersinia pestis* *Burkholderia pseudomallei*	3 3 3	BSL-3
4	Embrapa Suínos e Aves - SC Lab. Virologia/ Laboratório de Sanidade	Avian Flu virus, New Castle virus, virus of respiratory and reproductive syndrome in swine (PRRS), Mycobacteria	3,4	BSL1 BSL2 BSL-3[b]
5	Merial Saúde Animal LTDA - SP Departamento Qualidade - Segurança Biológica	*Brucella abortus* FMDV	3 4	BSL-3
6	FIOCRUZ – IOC Laboratório de Biologia e Parasitologia de Mamíferos Silvestres Laboratórios	*T. cruzi* *Leishmanias*	2 3	BSL-3
7	Instituto Nacional de Salud - Peru	*M. tuberculosis* MDR *Leishmania* Yellow fever virus Hepatitis, A,B,C virus	3 3 2 2	BSL-3
8	Universidade Federal do Rio de Janeiro Departamento de Diagnóstico Oral e Patologia	HIV	3	BSL-3
9	Embrapa Gado de Corte - MS Lab. Sanidade Animal e Virologia	FMDV *Brucella spp.* *Mycobacterium bovis*	4 3 3	BSL1 BSL2 BSL-3[b]
10	Universidade de São Paulo Núcleo de Pesquisas em Raiva do Lab. Virologia Clínica e Molecular do Depto Microbiologia	Arbovirus Hantavirus	3 3	BSL-3 BSL2
11	LANAGRO/SP Setor de Sanidade Aviária	Avian Influenza virus Newcastle virus	4 4	BSL-3
12	Universidade Federal de Pernambuco Departamento de Antibióticos/Laboratórios de Fármacos e Processos microbianos e laboratório de Processos Fermentativos	*Escherichia coli* *Chlostridium botulinum* *Coccidioides immitis* *Penicillium spp.* *Aspergillus spp.* *Candida spp* *Salmonella spp.*	2 2 3 2 2 2 2	BSL1 BSL2 BSL-3
13	Fundação de Medicina Tropical do Amazonas Lab. Virologia	*M. tuberculosis MDR* *Hepatitis virus* *Dengue virus* *Oropoche- and Mayaro virus*	3 2 2 4	BSL2 BSL-3
14	Fiocruz Centro de Pesquisas Aggeu Magalhães Biotério Central	*Yersinia pestis* *Hantavirus*	3 3	BSL2 BSL-3
15	Fiocruz - Centro de Pesquisas Aggeu Magalhães Lab. serviço de referencia em peste	*Yersinia pestis*	3	BSL-3
16	UNESP - Faculdade de Ciências Farmacêuticas Araraquara	HIV *M. tuberculosis MDR*	3 3	BSL2 BSL-3

	Depto Análises Clínicas	Hepatitis virus	2	
17	Ouro Fino Saúde Animal	FMDV	4	BSL-3
18	FIOCRUZ – Centro de Pesquisas Aggeu Magalhães, Lab. IMUNOLOGIA	Hantavirus	3	BSL-3
19	Universidade Federal de Pernambuco Lab. Virologia	HIV HTLV *Chamydia trachomatis*	3 3 2	BSL-3
20	Universidade Federal de Pernambuco Lab. Microbiologia	*E. coli* *Salmonella* *Listeria monocytogenes* *Vibrio parahemoliticus* *Vibrio cholera*	2 2 2 2 2	BSL-3

SOURCE: Data was a result of a survey conducted by ANBio from June 2008 to March, 2009.
MDR: multi-drug resistant
[a] according to Brazilian rule
[b] undergoing validation and commissioning

2- What government organizations are responsible for safety and security of high-containment biological (high BSL) laboratories?

The Ministry of Health is responsible for public health laboratories; the Ministry of Agriculture is responsible for agriculture laboratories. For university labs (except GMO labs), there is no oversight body. For laboratories working with GMOs, the National Biosafety Committee (CTNBio) is the responsible organization.

In March 2008, the Brazilian Ministry of Science and Technology published a resolution with a list of selected agents. The definition of "selected agent" is the same used by the United States Centers for Disease Control and Prevention: "selected agents are those considered by the Health and Human Services to pose a severe threat to human and/or animal health." With the exception of camel pox virus, *Phoma glycinicola*, and *Rathayibacter toxicus*, the Brazilian selected agent list includes all of the agents and toxins on the United States Health and Human Services and United States Department of Agriculture lists. The Brazilian list also includes additional microorganisms, toxins, and some equipment used in BSL-2 and BSL-3 laboratories (Table E1-2). Labs using select agents may voluntarily notify the government. Notification results in informal government visits and additional training.

Table E1-2 Brazilian selected agents that are not also on the United States selected agents list.
SOURCE: HHS And USDA Select Agents and Toxins: 7 CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73 (2008) and the Brazilian Ministry of Science and Technology: Office of the Minister: Resolution No. 10 of 13, March 2008. The Interministerial Commission: Export Control: Sensitive goods, CIBES, using the powers granted to it by Article 4. º, II, of Decree No. 4214 of April 30, 2002.

Microorganisms

African cassava mosaic virus
Agrobacterium ruby
Amanita muscarina
Amapari virus
Apiosporina morbid
Apple Chat Fruit
Apple proliferation
Aspergillus flavus
Aspergillus ochraceus
Aspergillus parasiticus
Aujeszky disease virus
Banana bunchy top virus
Bartonella sp.
Borna disease virus
Bursaphelenchus sp.
Cadang-cadang viroids
Candidatus liberobacter africanus
Candidatus liberobacter asiaticus
Chikungunya fever virus
Chlamydia psittaci
Chondrostereum purpureum
Citri spiroplasma
Citrus leper virus
Clavibacter iranicus
Clavibacter michiganensis subspecies *insidiosus*
Clavibacter michiganensis subspecies *nebraskensis*
Clavibacter michiganensis subspecies *sepedonicus*
Clostridium perfringens epsilon toxin producers
Cochliobolus miyabeanus
Cocoa swollen shoot virus
Coriomeningite Linfocítica virus
Cowdria ruminatum
Coxiella burnetii
Crinipellis pernicious
Curtobacterium flaccumfaciens pv. poinsettiae
Dengue hemorrhagic fever virus
Deuterophoma tracheiphila
Duck hepatitis virus, types 1, 2 and 3
Eastern equine encephalitis virus
Encephalitis virus of Powassan
Enteritis virus of Ducks, Geese and Swans
Enzootic encephalomyelitis flu virus
Ephemeral fever virus of cattle
Erwinia amylovora
Erwinia cypripedii
Erwinia raphontici
Escherichia coli producing verotoxins
Fusarium graminearum
Fusarium moniliforme
Fusarium oxysporium f. sp. lies lycopersici
Fusarium sporotrichioides
Gibberella fujikuroi
Gibberella xylarioides
Globodera sp.
Glomerella manihotis
Grapevine flavescence pains

Guignardia bidwellii
Guignardia citricarpa
Guinea grass mosaic virus
Gymnosporangiumm spp.
Haemophilus equigenitalis
Hemileia coffeicola
Hemorrhagic fever virus of Rabbit
Hepatitis D virus (Delta)
Herpesvirus including rhadinovírus
Herpesvirus of ATEL
Herpesvirus of Saimiri
Histoplasma capsulatum all kinds, including the variety *duboisii*
Kahawae Colletotrichum (Colletotrichum coffeanum var. Virulans)
Latino virus
Lethal yellowing (lethal yellowing of coconut palm)
Linfotróficos *virus of adult T cells, HTLV-1 and HTLV-2*
Longidorus sp.
Lyss virus
Microcyclus ulei
Monilinia fructigena
Moniliophthora roreri
Murray Valley encephalitis virus
Mycobacterium bovis strains except BCG strains
Mycobacterium tuberculosis
Mycoplasma agalacteae (goats and sheep)
Mycosphaerella fijiensis
Nacobbus sp.
Nairobi sheep disease virus
Nectria galligena
Oncobasidium theobromae
Oncornavirus *C and D* of non-human Primates
Oropouche virus
Pantoea stewartii
Paracoccidioides braziliensis
Parana virus
Pasteurella multocida type B SAMPLE Buffalo and other virulent strains
Peach Rosette
Pear decline
Penicillium verrucosum
Peronosclerospora sorghi
Petequial fever virus Infectious Bovine
Phakopsora meibomiae
Phakopsora pachyrhizi
Phoma exigua var. foveata
Phoma tracheiphila
Physopella ampelopsidis (Phakopsora euvitis)
Phytophthora boehmeriae
Phytophthora erythroseptica
Pichinde virus
*Plamospara halstedii (*except strain 2*)*
Pluteus glaucus
Potato latent virus Bookshelves
Potato Spindle Tuber Viroids
Pseudomonas syringae pv. passiflorae
Pseudomonas tolaasii
Psilocybe cubensis
Psilocybe Mexican
Puccini graminis
Puccini melanocephala
Puccini striiformis
Pyricularia grisea
Retroviruses including Human immunodeficiency virus HIV-1 and HIV-2
Rickettsia Akari
Rickettsia australis
Rickettsia canada
Rickettsia conorii
Rickettsia montana
Rickettsia siberica
Rickettsia tsutsugamushi
Rickettsia typhi
Rustic *Xanthomonas pv. cassavae*
Rustic *Xanthomonas pv. citri biótipos B and E*
Salmonella enteritidis
Salmonella paratyphi types a, b, c
Salmonella typhi
Salmonella typhimurium
Severe acute respiratory syndrome virus
Shigella dysenteriae
St. Louis encephalitis virus
Sugarcane Fiji disease virus
Thecaphora solani
Theileria annulata, bovis, hirci, parva and related agents
Tilletia controversial
Tilletia indicates
Tomato ringspot virus
Trichodorus sp
Urocystis agropyri
Vibrio cholerae
Viruses of hemorrhagic fever with Renal or pulmonary syndrome (Hantaan, Seoul, Sin Nombre, Puumala, Prospect Hill, Dobrava, Thailand, and Tottapalayam Muerto Canyon virus)
Viruses related to Ganjam and Dugbe
Wesselsbron disease virus
Western equine encephalitis virus
White pox viruses
Xanthomonas albilineans
Xiphinema sp.
Xylophillus ampelinus
Yellow fever virus
Yellow Peach
Yersinia enterocolitica
Yersinia pseudotuberculosis

Toxins

aflatoxins
Cholera toxin
microcystin
Modecina
ochratoxin A
Toxins of *Clostridium perfringens*
verotoxin
Viscumina
Volkensina

Genetic Elements

All genetic elements that contain nucleic acid sequences associated with the pathogenicity or toxin of any selected agent.

Equipment

Class II and Class III Biological safety cabinets
Chambers designed for aerosol challenge testing with a capacity 1 m^3 or greater
Tangential filtration equipment, except those used for reverse osmosis
Fermenters for the production of microorganisms (>20 liters)
Freeze dryers (condenser capacity between 10 and 1000 kgs in 24 hours)
Sprayer and fumigation aircraft that can generate 50 μm droplets at a rate of 2 liters/ minute
Units that provide complete BL3 or BL4 containment as specified in the Biosafety Manual of the World Health Organization
DNA sequencers
Hybridization ovens
Equipment for producing genetic probes
Centrifugal separators with flow rates greather than 100 L / h

3- If there are BSL laboratories in your country, are there established criteria for deciding:

a. Whether or not to establish such facilities?

The specific criteria are established by the corresponding Ministry as described in the previous answer. For universities, as referenced earlier, it is difficult to evaluate those criteria as they work independently except for laboratories working with GMOs.

b. What criteria are used to select the placement of such facilities? What criteria are used to decide what research will be done in such facilities?

The following are considered: public priorities, prevalence of a specific biological agent, police priorities of the state, institutional support, and institutional capacity to maintain the project.

c. What scientific, technical, and management advice is available to governments when making their decisions.

Each Ministry has advisory groups composed of specialists with a variety of expertise. Those specialists are scientists from the Ministries who can give advice to specific projects when required. Also, the Ministry of Health works closely with the World Health Organization (WHO), Pan-American Health Organization (PAHO) and the Centers for Disease Control (CDC) and can consult these organizations for specific projects when necessary.

4- What standards exist for BSL laboratories?

a. For engineering and construction? For licensing? For safety and security?

Different Ministries have produced some manuals and documentation. The biggest challenge, in our opinion, is to disseminate those materials broadly and make them available to all of the relevant institutions. Again, there is a gap in the case of universities (excluding GMOs labs) for which regulation does not exist. Furthermore, the focus is on biosafety. Biosecurity as a separate issue has only recently been addressed in Brazil.

b. For regular oversight and re-certification?

There is almost no information on these issues and certification is pending for most of the BSL-3 labs within the country.

5- Have there been any BSL accidents in your country?

Yes. Some are reported in master's and doctoral theses and Brazilian journals, but there is no regular system for notification from which to produce a comprehensive report. Thus, the available data significantly underestimates the actual cases. For hospital workers, however, there is a formal system for accident notification. Thus, most published data on accidents are related to hospital professionals (mainly nurses). For health care workers, some studies have shown that most of the accidents are due to overwork, inadequate personnel protective devices, and working with sharp materials.

a. If yes, how and why did accidents at high-containment facilities occur?

About 55 percent of the reports mention absent or non-fitted personnel protective equipment. Overwork was the second most common contributing factor.

b. How, to whom, and when are they reported?

In some cases, accidents are reported to the Institutional Biosafety Committees or to the Commission on Prevention of Hospital Infections. There are no specific guidelines for labs not working with GMOs, and there is no regular and mandatory system for accident notification or for notification of liability measures. However, some voluntary guidance is available (Ministry of Health publication in 2010).

c. Who has authority to investigate accidents?

For GMO work, authority rests in the Institutional Biosafety Committee and/or CTNBio (Law 11.105/2005). For other types of work with biological agents, there are no provisions.

d. What disciplinary or legal actions can be taken?
There are only provisions for working with GMOs.

6- Have any steps been taken to minimize BSL laboratory accidents?
Since its foundation in 1999, ANBio, a non-profit society, has dedicated the bulk of its work to training researchers and biological science students on biosafety measures and procedures.

As part of ANBio's effort, the Brazilian Government has taken a step forward in establishing a biosafety program at public health laboratories and added biosafety university courses to the graduate and post-graduate curriculum. The courses concentrate on biosafety for GMOs but discuss biosafety generally and last between 40 and 420 hours. The courses are multidisciplinary and have attracted pharmacy, biology, medicine, veterinary science, chemistry, agronomy, and engineering students. The courses include the following topics:

- A review of microbiology, biochemistry, immunology, and plant physiology
- Risk classification, assessment, and management
- Personal protective clothing and equipment
- Biosafety regulations
- Biosafety of GMOs
- Animal biosafety
- Waste treatment and transport
- Bioethics, intellectual property rights, and biosecurity
- Design of facilities and commissioning
- Case studies

Most recently, the Brazilian Ministry of Education (Coordination of Post-Graduation Courses-CAPES), the U.S Biosecurity Engagement Program, and the Oswaldo Cruz Foundation (Fiocruz) supported ANBio's development of a new post-graduation course on biosafety and biosecurity (specialization with a total of 180 hours). Forty students took the course the first time it was offered.

Additionally, in 1999, the Ministry of Health started a project to enhance the capacities of BSL-3 public health laboratories. Since then, 12 facilities have been reviewed and more than 4,000 professionals have been trained. In our opinion, however, an important challenge is the lack of regular equipment maintenance and facility certification. Also, training should be regular and frequent. In particular, regular training should be included in the biosafety program of all laboratories working with selected agents.

7- Have any steps been taken to increase security at BSL facilities?
In 2004, Brazil established the National Program for Sensible Goods (PRONABENS) in order to meet Resolution 1540/2004 of the UN Security Council. Since then, the PRONABENS team has conducted site visits, which included presenting talks on biosecurity. ANBio has worked together with this team, and they have participated in ANBio's capacity-building program on biosecurity since 2007.

In 2007, ANBio, with the support of the United States Biosecurity Engagement Program, offered Brazil's first biosecurity course.

Currently, ANBio is organizing our VII Brazilian Biosafety Congress and a "Biosafety and Biosecurity Conference for Latin America and the Caribbean" to be held from September 19-23, 2011 in Joinville, Brazil.

Additionally, ANBio is starting to plan and seek support for a project on "Virtual and in situ training on procedures for detection and control of biological threats" in order to support the 2014 World Cup and the 2016 International Olympiad, both which will be held in Brazil.

Even in light of these actions, Brazil should still create a long-term biosafety and biosecurity program with a dedicated budget, in which all stakeholders should take part. The main gaps that should be addressed are maintenance, certification, waste management, and the lack of a global inventory of samples. Brazil also needs to decide how and whether to destroy its polio samples post-eradication.

E2

HIGH-CONTAINMENT MICROBIOLOGY LABORATORIES IN EUROPE

Ingegerd Kallings,[a] M.D. and Kathrin Summermatter,[b] Ph.D.
[a]Swedish Institute for Communicable Disease Control, Stockholm, Sweden
[b]Institute for Virology and Immunoprophylaxis, Mittelhaeusern, Switzerland

This report is partly based on the final report from the Consortium project BIOSAFETY-EUROPE, funded by the 6th Framework Program of the European Commission: Co-ordination, harmonization and exchange of biosafety and biosecurity practices within a pan-European network.[1]

BIOSAFETY-EUROPE, a coordination action within the European Commission 6th Framework, had the aims to explore harmonization and exchange of biosafety and biosecurity practices within a pan-European network. The consortium included expertise in biosafety, biosecurity, risk assessment and control, containment measures, and on the underlying legal frameworks of the European Union and its Member States (MS). The consortium was comprised of 18 partners from 10 European countries representing industry, academia, and government agencies. It commenced in April 2006 and lasted until the end of 2008. Through detailed questionnaires, information was gathered on the implementation of European biosafety legislation on the national level and on physical containment, practices, and procedures at containment levels 3 and 4. Laboratory biosecurity was addressed as well.

High-containment biological facilities in Europe

A first questionnaire (Q1) was sent to 319 containment level (CL) 3 and 4 laboratories in the 27 EU MS identified through national regulatory agencies and through personal knowledge by consortium partners (see Figure E2-1). Responses were received from 98 laboratories (13 CL 4; 85 CL 3) in 18 countries. Questions were asked on lab type (government, private, academia, or industry), lab activities (clinical, public health, research, human and/or animal, food, defense), the national regulatory framework and the implementation of EU legislation, the implementation of biosafety and biosecurity management and associated controls, and inspection regimes.

EU and national governance of high-containment biological facilities

At the highest EU level, many departments (DGs) deal with laboratory biosafety and biosecurity e.g., DG Health and Consumers, DG Research and Innovation, DG Home Affairs, DG Environment, DG Mobility and Transport, DG Employment, and Social Affairs and Inclusion. More directly, safety at work with biological agents is the responsibility of the EU Occupational Health and Safety Agency (EU-OSHA) that developed the EU Directive 2000/54/EC *on the protection of workers from risks related to exposure to biological agents at work.*[2]

EU MS are obliged to implement EU Directives, and all 27 MS have reported to the EU they have adopted and implemented Directive 2000/54/EC. MS must not delete any requirements from EU legislation when adopting it into national legislation, but some countries have additional requirements.

[1] www.biosafety-europe.eu.
[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:262:0021:0045:EN:PDF.

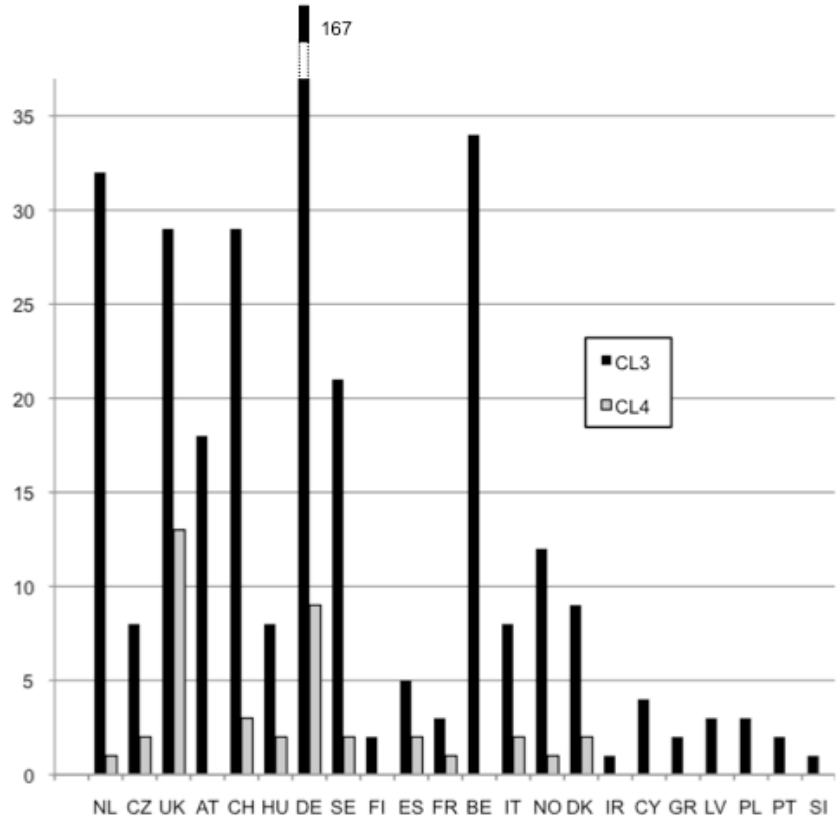

Figure E2-1 Country distribution of CL3 and CL4 laboratories that received the first questionnaire (Q1). The CL3 labs follow a variety of different standards. Additionally, the term "CL4" is not used consistently throughout Europe. CL4 labs may be glove box labs or suit labs. In some countries, a lab (e.g., a veterinary lab) that works with foot and mouth disease virus is automatically considered CL4. The numbers reflect all laboratories to which the questionnaire was sent, including some that were in the planning phase at the time.
SOURCE: BIOSAFETY-EUROPE
NL: Netherlands; CZ: Czech Republic; UK: United Kingdom; CH: Switzerland; HU: Hungary; DE: Germany; SE: Sweden; FI: Finland; FR: France; BE: Belgium; IT: Italy; NO: Norway; DK: Denmark; IR: Ireland; CY: Cyprus; GR: Greece; LV: Latvia; PL: Poland; PT: Portugal; SI: Slovenia

In many countries, several ministries, agencies, and organizations are involved in oversight of biosafety and the regulatory framework for biosafety (e.g., Ministry of Health, Ministry of Agriculture, Ministry of Environment, Ministry of Internal Affairs/Occupational Health) whereas the Ministry of Defense and the Ministry of Foreign Affairs usually are involved in biosecurity in a wider sense. In some countries, there is a department within the Ministry of Health (occasionally the Ministry of Defense) whereas other countries have an independent government agency as the main authority for biosafety matters as in Sweden where this responsibility lies with the Swedish Work Environment Agency. It was clearly shown by the

BIOSAFETY-EUROPE findings that the interpretation and implementation at the actual laboratory level of the common EU legislation varied greatly between MS.

A recent inventory made by the European Biosafety Association (EBSA) found that 20 of 27 countries have a body (agency, commission, or committee) regulating or providing advice on the contained use of Genetically Modified Microorganisms (GMM). For the remaining seven countries, no information was available.

In addition, there are a number of agencies at the EU level dealing with the implementation of biosafety and biosecurity regulations and guidelines: the European Agency for Safety and Health at Work (EU-OHSA), the European Centre for Disease Control and Prevention (ECDC), the European Food Safety Authority (EFSA), the European Food Information Council (EUFIC), the European Commission's Joint Research Centre (JRC), the European Medicines Agency/European Agency for the Evaluation of Medicinal Products (EMEA), and the European Molecular Biology Laboratory (EMBL). Several non-governmental organizations are involved: the European Federation of Biotechnology (EFB); the Federation of European Microbiological Societies (FEMS); the Confederation of the Food and Drink Industries of the EU (CIIA); the International Centre for Genetic Engineering and Biotechnology (ICGEB); the European Association for Bio industries (EuropaBio); EU News, Policy Positions & EU Actors online (EurActiv.com); and the European Society of Gene Therapy (ESGT).

Internationally, the World Health Organisation (WHO), the World Organisation for Animal Health (OIE), and the Food and Agriculture Organisation (FAO) issue guidelines in biosafety and biosecurity. These guidelines have recommendatory character, but they often influence the development of EU-wide and national regulatory frameworks.

BIOSAFETY-EUROPE - Biosafety Findings

National biosafety regulations and practices derived from EU Directives 2000/54/EC[1] and 98/81/EC[2] varied from country to country. In many countries, the regulatory framework for genetically modified microorganisms (GMMs) was more strongly enforced than that for biological agents in general. There is often no specific biosafety regulation for epizootics except for those microorganisms regulated under the two guidelines mentioned above.

Facilities and practices in containment level 3 laboratories throughout the EU are not of a comparable standard, e.g. a large range of different terminologies for "containment level (CL)" were used within the MS. Many laboratories referred to the WHO term 'biosafety level (BSL). It was concluded that EU Directives 2000/54/EC[3] and 98/81/EC require revision and updating to reflect the current state-of-the-art including continuous review of the classification list of microorganisms and the definition of harmonized best practices. (*The Directive 98/81/EC has since been revised and replaced by 2009/41/EC,*[4] *but many inconsistencies remain).*

Moreover, biosafety responsibilities appear often to be attributed to staff in management positions with functional roles that could be in conflict with strict biosafety considerations. Less than half of the respondents were subject to oversight by a biosafety committee.

EC legislation on biological agents and GMMs is often not specific enough to ensure harmonization of the implementation on the national level. There is a lack of European-wide harmonized practical guidance on how to implement the European Directives on biological agents and GMMs. A few EU Member States have developed their own national guidance based on the EC Directives. In other cases, these gaps are filled by e.g., U.S. Biosafety in Microbiological and Biomedical Laboratories (BMBL) and Canadian guidelines. The varying interpretation of the EU Directives allows different approaches to biosafety and

[1] Op. cit. see note 2
[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1998:330:0013:0031:EN:PDF
[3] Op. cit. see note 2
[4] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:125:0075:0097:EN:PDF

laboratory biosecurity. This and differences in terminology make the exchange of scientists between member states problematic.

BIOSAFETY-EUROPE - Biosecurity Findings

Laboratory biosecurity is a relatively new concept that is still developing, and during the project period there was little consensus across Europe as to what biosecurity means, even within the laboratory environment. BIOSAFETY-EUROPE used the term "Laboratory Biosecurity" to describe protection against, control of, and accountability for biological agents and toxins within laboratories, in order to prevent their loss, theft, misuse, diversion, unauthorized access, or intentional unauthorized release (adapted from WHO[5]).

In contrast to this more laboratory-focused definition, it has to be mentioned that the term "livestock biosecurity" has long existed in the veterinary field and describes the prevention of disease-causing agents entering or leaving any place where farm animals are present.

No EU level legislation exists that has been specifically developed to address the protection of biological agents in the laboratory from loss or willful misuse. However, due to the many synergies between biosafety and biosecurity, the EU Directives developed to protect workers from exposure to biological agents or GMMs address most of the issues related to laboratory biosecurity. Only a few Member States are known to have introduced special laboratory biosecurity legislation i.e. England and Denmark. Many facilities implement some biosecurity controls, but these are often focused on physical security and often are not based on a specific risk assessment. Less attention is paid to information security or organizational security issues, despite the fact that internal threats from individuals with authorized access to the laboratory must be recognized.

The recently adopted *Minimum standards for laboratories working with FMDV in vitro/in vivo* (Council Directive 2003/85/EC[6]) is the only binding European document including some aspects of biosecurity. The implementation of this standard is mandatory for laboratories handling live foot and mouth disease virus (FMDV).

Criteria for establishing containment facilities

There are currently no common criteria on the European level for the establishment of containment facilities with regard to rationale, work to be performed, and placement of the facility. However, the EU Directive 2000/54/EC[7] classifies microorganisms into 4 risk groups, based on the WHO criteria, and states that the application of Directive requirements will follow a risk assessment. Some countries may have national regulations, rules, or guidelines.

As indicated above, the differences between MS are huge in biosafety and laboratory biosecurity regulatory framework implementation. Most countries have a National Board of Health, a Central Public Health Institute, and a National Veterinary Institute providing expert advice on the handling of biological agents and toxins.

Standards

There are several ISO/EN standards available in the EU that can be applied for containment laboratory planning, construction, and operation e.g., ISO/EN 15189:2003 *Medical laboratories—Particular requirements for quality and competence,* CEN/CR 12739:1998 *Biotechnology—Laboratories for research, development and analysis—Report on the selection of equipment needed for biotechnology laboratories according to the degree of hazard*. In addition there are CEN standards developed for biosafety equipment e.g., autoclaves, biosafety cabinets, and personal protective equipment. National standards may cover the construction and the licensing of containment facilities, but there is no harmonization of licensing across Europe. Regular oversight and re-certification mainly depends on

[5] http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_EPR_2006_6.pdf.
[6] http://www.fao.org/ag/againfo/commissions/docs/genses38/Appendix_10.pdf.
[7] Op. cit. see note 2

national specifications. Member States have a national standardization institute making CEN standards available in the country.

Laboratory-associated Infections (LAI)

No harmonized system for the reporting of laboratory incidents and accidents is in place in the EU. Few laboratory-associated infections (LAI) and laboratory incidents/accidents have been reported in the literature from Europe during the recent decade (see Box E2-1). There is reason to believe that a serious underreporting is at hand. National reporting systems are not easily accessible. Historically, Northern European countries report higher numbers of LAI than other parts of Europe, presumably reflecting failure to recognize LAI as such as well as reporting inefficiencies. There is a variation between MS regarding to whom and when to report, who investigates the incident, and if there is a possibility for legal actions. Many MS are taking steps to improve the status of biosafety in their laboratories, and awareness of biosecurity issues is increasing.

Box E2-1

During 2000-2010, only 5 incidents of release and/or exposure to infectious agents in risk class 3-4 were reported in the literature from EU Member States:

- In 2000, a broken centrifuge tube caused 12 cases of brucellosis in Italy;[1]
- In 2003, work with genetically modified vaccinia strains in Germany caused vaccinia infection;[2]
- In 2005, a survey of 1,240 laboratory staff in Spain revealed 75 cases of brucellosis (43 microbiologists and 32 technicians);[3]
- In 2007, in the UK, inefficient decontamination of industrial material/leakage in the sewer system caused a release of FMDV causing infections in cattle and sheep, and huge costs to the Government and the British livestock industry;[4]
- In 2009, in Germany, a needle stick injury with Ebola led to no signs of infection after administration of an experimental vaccine.[5]

[1]Fiori P, Mastrandrea S, Rappelli P, Capuccinelli P. Brucella abortus infection acquired in microbiology laboratories. *Journal of Clinical Microbiology* 2000; 38: 2005-2006.
[2]Mempel M, Isa G, Klugbauer N*, et al.* Laboratory acquired infection with recombinant vaccinia virus containing an immunomodulating construct. *J Invest Dermatol* 2003; 120: 356-358.
[3]Bouza E, Sanchez-Carrillo C, Hernangomez S, Gonzalez MJ. Laboratory-acquired brucellosis: a Spanish national survey. *J Hosp Infect* 2005; 61**:** 80-83.
[4]Spratt, B Independent Review of the safety of UK facilities handling foot-and-mouth disease virus, Presented to the Secretary of State for Environment, Food and Rural Affairs and the Chief Veterinary Officer 31 August 2007
[5]Tuffs A. Experimental vaccine may have saved Hamburg scientist from Ebola fever. *Bmj* 2009; 338: 1223.

Future outlook - EU CBRN Action Plan

On June 24, 2009, the European Commission adopted its communication on strengthening chemical, biological, radiological, and nuclear (CBRN) security in the European Union—as an *EU CBRN Action Plan.*[8] The overall goal is an all-hazard approach to reduce the threat of and damage from CBRN incidents of accidental, natural, or intentional origin, including acts of terrorism. The Action Plan has set up a number of goals within three areas: prevention, detection, and preparedness and response:

Prevention

- Develop EU lists of high risk CBRN materials and risk-based approaches to security;
- Enhance the security of high risk CBRN facilities;

[8] http://register.consilium.europa.eu/pdf/en/09/st15/st15505-re01co02.en09.pdf .

- Enhance control over high risk CBRN materials;
- Contribute to the development of a high security culture among staff;
- Improve the identification and reporting of suspicious transactions and behavior;
- Enhance the security of transport;
- Improve information exchange;
- Strengthen the import/export regime; and
- Strengthen cooperation on the security of nuclear materials.

Detection

- Establish a scenario-based modeling approach to identifying work priorities in the detection field;
- Establish trialing, testing, and certification schemes for CBRN detection in the EU;
- Develop minimum detection standards;
- Identify good practices related to the detection of CBRN materials, awareness-raising, and training; and
- Improve the exchange of information.

Preparedness and response

- Improve emergency planning;
- Strengthen countermeasure capacity;
- Improve domestic and international information flows regarding CBRN emergencies;
- Develop improved modeling tools and strengthen decontamination and remediation capacity; and
- Improve the capacity to conduct criminal investigations.

Actions encompassing all CBRN fields are listed as 67 horizontal actions whereas there are 14 B-specific actions listed, among them:

- To assist the MS in the proper implementation of applicable procedures at "the laboratory bench level" and in developing mechanisms for assessing and monitoring its correct implementation;
- The MS should establish:
    - a registry of facilities possessing any of the substances on the EU list of high risk biological agents and toxins;
    - a process to verify whether security arrangements of facilities are adequate, including diagnostic laboratories handling and possessing any of the EU list of high risk biological agents and toxins;
    - a mechanism within facilities storing biological agents and toxins on the EU list of high risk biological agents and toxins to regularly review the need for such biological agents and toxins;
- The Commission together with the MS should take relevant steps so that:
    - a comprehensive overview of the relevant regulations or standards at hand and their relevance to biosecurity and biosafety is achieved;
    - facilities possessing substances on the EU list of high risk biological agents and toxins consider as appropriate the implementation of the CEN Workshop Agreement (CWA 15793[9]), WHO Laboratory Biosecurity Guidance, or their national equivalent standards - unless equal or more stringent national regulations have to be considered;
    - appropriate national regulations or standards are met as part of a national authorization or accreditation process or as a condition for issuing licenses for work with substances on the EU list of high risk biological agents and toxins.
- The Commission together with the MS should encourage professional and other relevant associations working on bio-issues to develop and adopt codes of conduct for their members;
- The Member States together with the Commission should define requirements for biosafety officers (roles, competences, and training).

[9] ftp://ftp.cenorm.be/PUBLIC/CWAs/wokrshop31/CWA15793.pdf .

Other areas addressed in the B-specific list of actions are: transport, detection, and validation of methods, establishment of reference material for quality assurance, international cooperation and networking, research, implementation of good practices, and improved cooperation between relevant agencies in crisis situations.

It is the responsibility of each Member State to protect its population against CBRN incidents and to implement the action plan, whereas the European Union can provide added value and support projects across the EU, to ensure a coherent and consistent approach to cooperation on this issue between the Member States.

The implementation of the EU CBRN Action Plan is now in its second year. Meetings with MS experts are frequently arranged by the Department of Home Affairs (former JLS).

E3

BIOTECHNOLOGY AND BIOSECURITY INITIATIVES IN PAKISTAN: A COUNTRY REPORT

Anwar Nasim,[1] Ph.D. and Erum Khan,[2] MBBS, FCPS, M. Sc.
[1]Ministerial Standing Committee on Scientific and Technological Cooperation
[2]Pakistan Biological Safety Association and Aga Khan University Hospital

What high-containment biological research facilities exist in your country? What are the facilities' main goals and priorities?

In Pakistan, many institutes work using BSL-1 and BSL-2 level facilities. The National Institute of Health, Islamabad has been working at BSL-2+ and is constructing BSL-3 facilities. BSL-3 facilities exist at Aga Khan University and Indus Hospital Karachi.

Priorities and goals vary among facilities. The National Institute of Health, for example, fulfils the 22 objectives defined in ordinance No. XLIII of 1980 including advising the Federal Government on disease control, investigating epidemics, developing an Institute of Tropical Diseases for Research and Training, developing a National Virus Reference Center, and functioning as a National Type Culture Collection Centre (http://www.nih.org.pk/). The BSL-2 and BSL-3 laboratories at Aga Khan University are private diagnostic laboratories that process routine clinical samples. The BSL-3 laboratory is primarily used for processing samples from patients suspected of *Mycobacterum tuberculosis* (TB) infection. The BSL-3 lab at Indus Hospital is used mainly for TB diagnosis.

What government organizations are responsible for safety and security of high-containment biological (high BSL) laboratories?

Responsible organizations include the Disarmament Division, the Ministry of Foreign Affairs, and the National Biosafety Committee. Additionally, the Pakistan Biosafety Rules 2005 require organizations involved in biotechnology or genetic manipulation to have Institutional Biosafety Committees and to designate a Biosafety Officer.

If there are BSL laboratories in your country, are there established criteria for deciding:

a. **Whether or not to establish such facilities?**
b. **What criteria are used to select the placement of such facilities?**
c. **What criteria are used to decide what research will be conducted in such facilities?**
d. **What scientific, technical and management advice is available to governments when making their decisions?**

The Pakistan Biosafety Rules, 2005, which concerns genetically modified organisms, established the following entities:

- **The National Biosafety Committee** whose responsibilities (related to genetically modified organisms) include establishing procedures and standards for risk-assessments, facilitating the exchange of technical advice, developing guidelines for assessing biohazards, informing individuals engaged in genetic manipulations about new biosafety guidelines, coordinating efforts to prepare for biological emergencies, and certifying and inspecting laboratories that intend to perform high-risk work.
- **The Technical Advisory Committee** that examines applications and provides advice concerning work on and the release of genetically modified organisms.
- **Institutional Biosafety Committees**

Criteria used to decide what research will be conducted vary between facilities. Research at the National Institute of Health, for example, fulfils the 22 objectives defined in ordinance No. XLIII of 1980.

1. **What standards exist for BSL laboratories?**
   No standard formulations have been devised or received from the Government of Pakistan. The National Institute of Health, Islamabad, for example, follows the criteria and standard guidelines devised by WHO, the United States CDC's Biosafety in Microbiological and Biomedical Laboratories (BMBL), and ABSA-Canada (Canadian Association for Biological Safety).

   Additionally, in May 2005, The Pakistan Environmental Protection Agency issued National Biosafety Guidelines. The document provides guidelines on laboratory research, field trials, and release of genetically modified organisms.

2. **Have there been any BSL accidents in your country?**
   a. **If yes, how and why did accidents at high-containment facilities occur?**
   b. **How, to whom and when are they reported?**
   c. **Who has authority to investigate accidents?**
   d. **What disciplinary or legal actions can be taken?**

   According to the Pakistan Biosafety Rules, 2005, the Technical Advisory Committee must be notified following any accident that could lead to the release of genetically modified organisms.

3. **Have any steps been taken to minimize BSL laboratories accidents? If so, by whom (i.e., regulation, voluntary measures, individual laboratory practices)?**
   In his December 6, 2010 address to the BWC Meeting of the States Parties, Ambassador Zamir Akram stated that, "The subject of Biosafety has been incorporated in the curricula of relevant university disciplines."

   The Pakistan Biosafety Rules 2005 require an organization involved in bio-technology or genetic manipulation to designate a Biosafety Officer.

   Pakistan currently has three Biosafety organizations including the Pakistan Biological Safety Association (PBSA), which is affiliated with the National Core Group in Life Sciences (NCGLS) of the Higher Education Commission and the Organization of the Islamic Conference (OIC) Committee on Scientific and Technological Cooperation (COMSTECH) and was started in 2008.

   Additionally, a number of training activities and seminars on biosafety have taken place in Pakistan, and Pakistanis have participated in similar events abroad. For example, in 2009, Aga Khan University in Karachi held two seminars on Laboratory Biosafety and a National Training Seminar on Biosafety and Biosecurity Initiatives took place in 2007 in Islamabad. Similarly, Pakistanis attended the Asia Conference on Laboratory Biosafety and Biosecurity (Bangkok, Thailand, 2007); the Biosafety and Biosecurity International Conference: Healthier and More Secure Communities in the Middle East and North Africa Region (Casablanca, Morocco, 2009); the Biosafety and Biosecurity Risk Assessment and Risk Mitigation Training Event for Pakistani Bio-scientists (Dubai, United Arab Emirates, 2010); and the ICLS-COMSTECH-PAS International Conference on Conduct of Responsible Science: Safety, Security and Ethics (Islamabad, Pakistan, 2010).

4. **Have any steps been taken to increase security at BSL facilities? If so, by whom (i.e., regulation, voluntary measures, individual laboratory practices)?**
   In 2010, the Government of Pakistan's Planning Commission issued a report on Biosafety and Biosecurity in Biological Laboratories that describes good microbiological practices and suggests that one lab in each province be brought into full compliance with BSL-2 practices and then used as a model.

   In his December 6, 2010 address to the BWC Meeting of the States Parties, Ambassador Zamir Akram stated that, "the Inter-Agency Task Force on BWC issues has finalized 'Guidelines for development of Code of Conduct for the Life Scientists' and circulated them to all our national stakeholders." Additionally, the documents were translated into the national language, Urdu.

E4

OVERVIEW OF HIGH-CONTAINMENT BIOLOGICAL LABORATORIES IN RUSSIA

Michael V. Ugrumov[1] and Sergey V. Netesov[2]
[1]Councilor of the President of RAS on Foreign Affairs and Biology, Moscow, Russia
[2] Vice Rector, Research, Novosibirsk State University, Novosibirsk, Russia

Russia's extensive experience in working with dangerous pathogens in high-containment laboratories can be traced back to the country's early efforts to improve public health through research, vaccine production, and development and implementation of vaccination strategy.[1] The work led to success in antiplague efforts during the 1920s and 1930s, national eradication of smallpox in 1939, and the successful start of measles and poliomyelitis control through vaccine development followed by mass long-term vaccinations. That expertise has continued to the present day where the Russian Federation is home to 19 World Health Organization (WHO) Collaborating Centers including the WHO Collaborating Centre for Tuberculosis at the Central Tuberculosis Research Institute (CTRI), Russian Academy of Medical Sciences; the WHO Collaborating Centre for Orthopoxvirus Diagnosis and Repository for Variola Virus Strains and DNA at the State Research Center of Virology and Biotechnology ("Vector" Center) in Koltsovo (Novosibirsk Region), under Rospotrebnadzor supervision; and the WHO Collaborating Centre for Training in Multidrug-Resistant Tuberculosis at the Novosibirsk TB Research Institute.[2] The Vector Center also hosts a WHO Influenza H5 Avian Influenza Reference Center,[3] and the WHO National Influenza Center is functioning actively in the St. Petersburg Institute of Influenza, which since last year has been supervised by the Ministry of Public Health and Social Development of the Russian Federation.[4] Additionally, the Russian Federation also has two World Organization for Animal Health (OIE) Collaborating Centers[5] and three OIE Reference Laboratories, which are responsible for dourine, equine rhinopneumonitis, and foot and mouth disease.[6]

The current practice of monitoring, studying, and controlling infectious diseases outbreaks in Russia is based on the following regulatory documents:

- Charter of Federal Service on Customers' Rights Protection and Human Well-being Surveillance (Rospotrebnadzor) approved on 30.06.2004,[7]
- the 2005 International Health Regulations,[8] and
- the State Order #60 dated 2 February, 2006.[9]

---

[1] E.A. Stavskiy, N.B.Cherny, A.A. Chepurnov, S.V. Netesov, Anthology of Some Biosafety Aspects in Russia (up to 1960), in Anthology of biosafety V. BSL-4 laboratories, J.Y. Richmond, Editor. 1999, American Biological Safety Association: Mundelein, IL. p. 29-91.
[2] WHO. World Health Centers Global Database. [cited April 28, 2011]; Available from: http://apps.who.int/whocc/Search.aspx.;
State Research Center of Virology and Biotechnology-Vector. [cited 5 May 2011]; Available from: http://www.vector.nsc.ru/DesktopDefault.aspx?lcid=9&tabindex=1&tabid=52.
[3] [cited October 26, 2011]; Available from: http://www.who.int/influenza/gisrs_laboratory/h5_reflabs/h5_reference_laboratories/en/index.html
[4] [cited May 23, 2011]; Available from: http://www.influenza.spb.ru/en/influenza_surveillance_system_in_russia/who_national_influenza_centre/.
[5] OIE. List of Centres: OIE -World Organization for Animal Health. [cited April 28, 2011]; Available from: http://www.oie.int/our-scientific-expertise/collaborating-centres/list-of-centres/.
[6] OIE. List of Laboratories: OIE -World Organization for Animal Health. [cited April 28, 2011]; Available from: http://www.oie.int/our-scientific-expertise/reference-laboratories/list-of-laboratories/.
[7] http://old.rospotrebnadzor.ru/department/regulations/ (Charter of Rospotrebnadzor)
[8] International Health Regulations -2005. http://www.who.int/ihr/en
[9] Russian State Order #60: http://www.rg.ru/2006/02/17/monitoring-dok.html.

Building on these primary regulating documents, the special Order of Rospotrebnadzor #88 dated 17 March 2008 issued instructions about the measures on monitoring for infectious and parasitary diseases agents.[10] This last order lists four types of research and monitoring centers:

1. The list of regional centers for monitoring the infectious and parasitic disease agents of pathogenicity groups 2-4 (roughly equivalent to BSL1-3 according to WHO classification)—Appendix 1 in;[11]
2. The list of regional centers for monitoring the infectious and parasitic disease agents of pathogenicity groups 1-2 (roughly BSL-3-4 according to WHO classification)—Appendix 2 in;[12]
3. The list of reference centers for monitoring the infectious and parasitic disease agents with functions under the International Health Regulations (20050—Appendix 3 in;[13]
4. The list of national centers for verification of diagnostic work and national centers that fulfill the functions of State Collections of Rospotrebnadzor—Appendix 4 in.[14]

All Russian BSL-3 and BSL-4 laboratories are listed in these Appendices, including Russia's 17 regional anti-plague centers. Additionally, this Order also describes the area of responsibility of each Institute/Center and charters types of these Institutes/Centers. The special national Sanitary Regulations (SR) one of which is the SP 1.3.1285-03 on "Safe handling of micro-organisms in pathogenic hazard groups I-II",[15] whose observance is mandatory, form the foundations of Russian laboratory practices for these Institutes/Centers as well as public health and educational university laboratories.[16] The SR specify a full spectrum of biosafety practices including disinfection procedures, sewage water testing, safe transport of pathogens, and safe practices for hospital work. The SR also describe procedures for obtaining permission to work with recombinant DNA and Hazard Groups I-IV microorganisms from the State Sanitary-Epidemiological Inspection Committee[17] and make provisions for laboratory inspections and compliance monitoring.[18] Hazard groups I, II, II, and IV in the Russian classification system are roughly equivalent to the WHO's risk groups IV, III, II, and I, respectively.[19]

Russia has stringent standards to prevent accidents at high-containment facilities, and the Sanitary and Epidemiological Regulations SP 1.3.1285-03 on "Safe handling of micro-organisms in pathogenic hazard groups I-II" describe the procedures to follow in response.[20] It is a result of a long history of work with dangerous pathogens in Russian microbiological laboratories during which time laboratory accidents took place a few times; some important laboratory infection cases that occurred in Russia between 1950 and

[10] Russian State Order #88: http://old.rospotrebnadzor.ru/docs/order/?id=1832.
[11] Russian State Order #88: http://old.rospotrebnadzor.ru/docs/order/?id=1832.
[12] Russian State Order #88: http://old.rospotrebnadzor.ru/docs/order/?id=1832.
[13] Russian State Order #88: http://old.rospotrebnadzor.ru/docs/order/?id=1832.
[14] Russian State Order #88: http://old.rospotrebnadzor.ru/docs/order/?id=1832.
[15] Russian Sanitary Regulations for special and other dangerous pathogens of 1-2 pathogenicity groups: http://www.lytech.ru/articles_31.htm.
[16] E.A. Stavskiy, B. Johnson, R.J. Hawley, J.T. Crane, N.B. Cherny, I.V. Renau, S.V. Netesov, Comparative Analysis of Biosafety Guidelines of the USA, WHO, and Russia (Organizational and Controlling, Medical and Sanitary- Antiepidemiological Aspects). Applied Biosafety, 2003. 8(3): p. 118-127.
[17] Russian Sanitary Regulations for special and other dangerous pathogens of 1-2 pathogenicity groups: http://www.lytech.ru/articles_31.htm.
[18] Russian Sanitary Regulations for special and other dangerous pathogens of 1-2 pathogenicity groups: http://www.lytech.ru/articles_31.htm. (page 12)
[19] E.A. Stavskiy, B. Johnson, R.J. Hawley, J.T. Crane, N.B. Cherny, I.V. Renau, S.V. Netesov, Comparative Analysis of Biosafety Guidelines of the USA, WHO, and Russia (Organizational and Controlling, Medical and Sanitary- Antiepidemiological Aspects). Applied Biosafety, 2003. 8(3): p. 118-127.
[20] Russian Sanitary Regulations for special and other dangerous pathogens of 1-2 pathogenicity groups: http://www.lytech.ru/articles_31.htm.

1990 are described in the paper of S. Gaidamovich et al.[1] As the result of this experience, during the recent two decades, in the rare cases when an accident occurred, treatment began immediately and the incident was thoroughly investigated. For example, in May 2004, an experienced technician who worked at the Vector Center pricked herself with a syringe needle containing blood from a guinea pig infected with Ebola virus. In spite of extensive prophylaxis and treatment she died. A commission including experts from two governmental agencies, the Russian Federal Service for Surveillance in the Sphere of Consumer Rights Protection and Human Well-being (Rospotrebnadzor) and the Federal Medical and Biological Agency (FMBA), subsequently conducted an investigation that revealed multiple violations of laboratory regulations by this experienced technician.[2] The additional lesson learned from this case was the need for more thorough training courses for experienced workers to prevent complacency.

Several Russian Universities, in collaboration with Health Canada and the Canadian Science Centre for Human and Animal Health, recently updated their biosafety curriculum.[3] For example:

- The Saratov Anti-Plague Institute developed 13 new advanced training programs including a specialized primary training program in biosafety, a program for training specialized anti-epidemic teams to work in emergency situations, and a program for training bacteriologists and epidemiologists in the field of bioterrorism counteraction.
- A Train the Trainers Biosafety/Biosecurity Program organized with assistance of Canadian biosafety experts from Health Canada took place November 17-19, 2008 at the Moscow Medical Academy. As a result, the Moscow Medical Academy added a biosafety component to their advanced virology course.
- The Vector Institute re-established an advanced course for medical, biological, chemical (biotechnology), and veterinarian specialists. The 540-hour course focuses on virology, but also provides a basic microbiological background. The current course includes an expanded biosafety component as well as educational materials from the WHO and examples of biosafety regulations from other countries including the United States and Canada. In the experimental portion of the class, students work with vaccine strains using real laboratory equipment, real BSL-3 facilities, and real personal protective equipment.
- A few universities in Russia including M. V. Lomonosov Moscow State University and Novosibirsk State University (NSU) decided to include biosafety, biosecurity, and bioethics courses in their Master of Biotechnology educational programs. Recently, ISTC project #4060 (Establishment of a Center for personnel training in principles of biosafety in work with viral agents, on the basis of international recommendations and national biosafety requirements and guidelines) started at the NSU with the help of Health Canada specialists to assist Russian specialists to make this Center the most modern in Russia.

Specialists from M. V. Lomonosov Moscow State University, NSU, and a few other Moscow research institutes have also suggested modernizing the Russian educational standard in biotechnology during 2011-2012.
To facilitate biosafety education, the first Russian Glossary of Biosafety Terms was published in 2007; another variant of the Glossary was issued later in the same year. Finally, the first English-Russian Harmonized Dictionary in Biosafety and Biosecurity was published in November 2010.

Furthermore, Russia played a major role in sponsoring and preparing United Nations Security Council Resolution 1540, which requires all countries to take the necessary steps to prevent the proliferation of

[1] S. Ya. Gaidamovich, A. M. Butenko, and H. V. Leschinskaya. Human laboratory Acquired Arbo-, Arena- and Hantavirus infections. Journal of American Biological Safety Association. -2000. -V.5 (1)-P. 5-11.
[2] L. A. Akinfeeva, O. I. Aksionova, I. V. Vasilevich, Z. I. Gin'ko, K. A. Zar'kov, N. M. Zybavichene, L. R. Katkova, O. P. Kuzovlev, V. I. Kuzubov, L. I. Lokteva, E. I. Ryabchikova. A case of Ebola hemorrhagic fever. Infektsionnye bolezni.-2005-No.1-P.85-88.
[3] Netesov, S.V. The Current Situation with Education in Biosafety and Biosecurity in Russia. in Situation and Perspectives of Education in the Field of Biotechnology, Biosafety and bioethics at the Novosibirsk State University and other Russian Universities. 2009. House of Scientists, Novosibirsk, Russia.

weapons of mass destruction,[4] and hence Russia takes its biosecurity responsibilities very seriously. As a result, all, "biological materials are securely protected using modern technology, and the necessary counter-terrorist measures are taken."[5] Furthermore, the national legal framework details procedures to account for the production, use, storage, and transport of biological weapons and related materials and specifies how violators can be penalized.[6] Additionally, microbiological and virological research facilities in Golitsino, Pokrov, Vladimir, Koltsovo (Vector Center), Obolensk, and Kazan recently upgraded their security through their participation in the United States Biological Threats Reduction program,[7] and in collaboration with the International Science and Technology Center (ISTC), seven institutes invested over $18 million in upgraded operating procedures and physical security.[8] During the last three years, two institutes—Vector Center and the Microbiolgical Center in Obolensk —additionally upgraded their biosecurity equipment and services.

The Russian Federation will undoubtedly continue its efforts to modernize its microbiological laboratories and biotechnological facilities in accordance with international standards and new achievements in biosafety and biosecurity will follow.

CONCLUSIONS:

1. Periodical biosafety and biosecurity upgrades in laboratories working with dangerous pathogens are needed to better protect the environment, personnel, and to prevent possible terrorism cases.
2. The modernization of educational courses in all areas of biotechnology and medicine should include basic educational modules on biosafety, biosecurity, and bioethics.
3. The easiest and fastest way to upgrade the national level of biosafety/biosecurity is to study the modern international recommendations and textbooks in this area, to upgrade national biosafety regulations and standards, to modify the national educational programs, and to participate actively in international biosafety meetings and associations.

[4] Note verbale dated 26 October 2004 from the Permanent Mission of the Russian Federation to the United Nations addressed to the Chairman of the Committee. November 2, 2004, Permanent Mission of the Russian Federation to the United Nations.
[5] Second report of the Russian Federation on the implementation of Security Council resolution 1540 (2004). 2004, Permanent Mission of the Russian Federation to the United Nations. (page 6)
[6] Second report of the Russian Federation on the implementation of Security Council resolution 1540 (2004). 2004, Permanent Mission of the Russian Federation to the United Nations;
National Research Council (United States). Committee on Prevention of Proliferation of Biological Weapons., The Biological Threat Reduction Program of the Department of Defense: from foreign assistance to sustainable partnerships. 2007, Washington: National Academies Press. ix, 109 p.
[7] National Research Council (United States). Committee on Prevention of Proliferation of Biological Weapons., The Biological Threat Reduction Program of the Department of Defense: from foreign assistance to sustainable partnerships. 2007, Washington: National Academies Press. ix, 109 p. (page 34)
[8] Weaver, L.M., Biosafety and Biosecurity Activities of the International Science and Technology Center in the Republics of the Former Soviet Union: Accomplishments, Challenges, and Prospects. Applied Biosafety: Journal of the American Biological Safety Association, 2010. 15(2): pp. 56-59.

E5

HIGH-CONTAINMENT LABORATORIES – SWEDEN CASE STUDY

Ingegerd Kallings, Swedish Institute for Communicable Disease Control
SE-171 82 Solna, Sweden

High-containment biological facilities in Sweden

Work with risk class 3 or 4 biological agents requires a permit from the competent authority, which reviews and evaluates that the containment measures chosen are adequate. Thus, one way to address the question of the number of containment laboratories is to look at the number of applications for such a work permit. There are currently 32 employers in Sweden with (one or more) permits to work in 40 sites with (one or more) risk class 3 biological agents. The risk classification in EU Directive 2000/54/EC applies. Most of these permits are for clinical diagnostic work with biological agents that are not airborne e.g., HIV, EHEC, and other gastrointestinal biological agents and thus requirements are less than for a complete containment level (CL) 3 laboratory. One permit is for storage of biological agents in a culture collection. Eleven employers have a permit to work in full CL 3 at 11 sites e.g., clinical mycobacterial laboratories. One employer may have one or more permits for work in one or more laboratories at different sites. There is one containment level 4 facility in Sweden.

National governance of high-containment biological laboratories

Government agencies in Sweden subordinate to a Government Department (Ministry) are responsible for implementing public policies, overseeing the provision of public services, and executing a range of regulatory functions. The Government decides on the preconditions for agencies' operations through appropriation directions and ordinances.

The Swedish Work Environment Authority (SWEA)[1] is an independent government agency authorized by the Labour Ministry. With regard to biosafety, SWEA is responsible for the implementation of the EU Directive 2000/54/EC *on the protection of workers from risks related to exposure to biological agents at work*[2] and EU Directive 2009/41/EC *on the contained use of genetically modified micro-organisms* (GMM).[3] EU Directives contain minimum requirements and Member States may add national requirements. Sweden has done so. EU Directive 2000/54/EC is implemented through national provisions: AFS 2005:01 *Microbiological Work Environment Risks—Infection, Toxigenic Effect, Hypersensitivity*.[4] Regarding GMM, the SWEA provisions AFS 2000:05 *Contained Use of Genetically Modified Micro-organisms*[5] following the previous EU Directive 98/86/EC are still in use but will be reviewed and updated to reflect changes in the most recent EU Directive 2009/41/EC[6] on GMM. The regulatory text of the SWEA statute books is complemented by extensive recommendations on how to interpret and implement the law. A statute book on blood-borne infections will be updated shortly to follow the recent EU Directive,[7] which will also be reflected in the AFS ordinance regulating biosafety.

Criteria for establishing containment facilities

There are no national criteria for the establishment of containment facilities in Sweden, neither for justification of the work nor for selection of sites. The respective management/owner of a facility in any sector (government/university/county level public health /private industry) decides what they intend to do and makes a proposal to SWEA for a work permit. SWEA does not question the rationale for the intended work; they check that safety criteria are pertinent for the work planned and that safety measures will be effective. Thus, the work permit is based on a case-by-case risk assessment and does not strictly follow a checklist for different containment levels.

---

[1] www.av.se
[2] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2000:262:0021:0045:EN:PDF
[3] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:125:0075:0097:EN:PDF
[4] http://www.av.se/dokument/inenglish/legislations/eng0501.pdf
[5] http://www.av.se/dokument/inenglish/legislations/eng0005.pdf
[6] Op. cit. see note 3
[7] http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:134:0066:0072:EN:PDF

Different Government Departments (e.g., Ministries of Defense, Foreign Affairs, Social Affairs, and Health) and agencies are usually involved in the process of funding high-containment facilities, seeking competent advice from several national expert agencies e.g. Swedish Institute for Communicable Disease Control,[1] National Veterinary Institute,[2] Swedish Defense Research Agency,[3] National Board of Health and Welfare,[4] universities, and committees.

Standards

The EU Directive 2000/54/EC[5] and the SWEA statute book AFS 2005:1[6] provide the overarching regulatory framework for construction of containment facilities. In addition there are numerous EN standards for construction and engineering. It is not mandatory for EU Member States to follow the EN standards, but Sweden has adopted most EN standards as national standards (SIS), which makes compliance necessary.

AFS 2000:05[7] and AFS 2005:01[8] specify how and when to apply to SWEA for permission to work with risk class 3 and 4 biological agents. Application has to be renewed every 3-5 years. There are no specific laboratory biosecurity regulations in Sweden but the AFS 2000:5 and 2005:1 dealing extensively with biosafety cover most aspects of laboratory biosecurity. The Ministry of Defense with the Swedish Defense Research Agency as an adviser ensures compliance with the Biological and Toxin Weapons Convention but with little application for laboratories. There is a dialogue between the Swedish Institute for Communicable Disease Control (SMI), where the CL 4 facility is located, and the Swedish Security Service,[9] who informs SMI about any changes in the terrorism situation that may call for additional biosecurity provisions. SWEA has 10 regional inspectorate offices with general work environment inspectors, but biosafety competence is rather scarce and containment facilities are rarely inspected.

Laboratory-associated Infections (LAI)

There is mandatory notification to SWEA of work-related illness, including laboratory-associated infections, as well as of serious incidents with a potential for harm. Employers that run containment labs are required to have a system in place for internal reporting and authority notification when deemed necessary. The employer is required to investigate incidents and accidents and take corrective actions. SWEA can inspect any time they choose to do so. In practice this is done if the safety representative, mandatory in every work place with >5 employees, requests an inspection or if misconduct is suspected. According to the Work Environment Act, the employer is always accountable for the conditions in the workplace and legal actions can be taken if safety precautions are not in place. Imprisonment is possible but is extremely rarely effectuated.

Actions to prevent laboratory incidents

The Swedish Institute for Communicable Disease Control (SMI) and other Government expert authorities together with the profession conduct awareness raising events. SMI initiated the Nordic Biosafety Network in 2004. Work is underway to foster the implementation of The Laboratory Biorisk Management standard, CWA 15793.[10] As in other countries, underreporting and lack of communication of laboratory incidents is an unresolved issue.

No specific actions have been taken on the national level to increase laboratory biosecurity, but there is an increased awareness of the need for precautionary measures among government agencies, the

[1] www.smi.se
[2] www.sva.se
[3] www.foi.se
[4] www.socialstyrelsen.se
[5] Op. cit. see note 2
[6] Op. cit. see note 4
[7] Op. cit. see note 3
[8] Op. cit. see note 4
[9] www.sakerhetspolisen.se
[10] ftp://ftp.cenorm.be/PUBLIC/CWAs/wokrshop31/CWA15793.pdf

profession, and the management of containment facilities. An example of this is the publication *Handbook of Applied Biosecurity for Life Science Laboratories*[11] issued by the Stockholm International Peace Research Institute (SIPRI).

The European Commission has adopted an *EU CBRN Action Plan*[12] on strengthening chemical, biological, radiological, and nuclear (CBRN) security in the European Union. The overall goal is an all-hazard approach to reduce the threat of and damage from CBRN incidents of accidental, natural, or intentional origin, including acts of terrorism. The Action Plan has set up a number of goals in three areas: prevention, detection, and preparedness and response. The implementation of the EU CBRN Action Plan is now in its second year. Sweden is a keen participant in frequent meetings with Member States experts.

[11] http://books.sipri.org/product_info?c_product_id=382
[12] http://register.consilium.europa.eu/pdf/en/09/st15/st15505-re01co02.en09.pdf

E6

COUNTRY OVERVIEW FOR TURKEY: BIOSECURITY LAWS AND REGULATIONS IN TURKEY

Hüseyin Avni Öktem, Ph.D.
Middle East Technical University, Turkey

What high-containment biological (high BSL) laboratories exist in your country? What are the facilities' main goals and priorities?

- The Ministry of Agriculture and Rural Affairs has four BSL facilities that are focused on animal diseases and vaccines.
- The Refik Saydam National Public Health Agency, Sihhiye/Ankara has one lab that focuses on infectious disease surveillance and prevention on a national basis.
- The Gulhane Medical Military Academy, Etlik/Ankara has a medically focused lab.
- The TUBITAK Marmara Research Center, Genetic Engineering and Biotechnology Institute, Gebze/Kocaeli has a research-focused lab.

What government organizations are responsible for the safety and security of high BSL laboratories?

The Ministry of Agriculture and Rural Affairs, General Directorate of Protection and Control and the Ministry of Health are responsible.

If there are high BSL laboratories in your country, are there established criteria for deciding:

a. Whether or not to establish such facilities?
b. Where to place such facilities?
c. What research will be done in such facilities?
d. What scientific, technical, and management advice is available to governments when making their decisions?

In Turkey there are rules and legislation about establishing and running analysis laboratories for food, animal feed, water, genetic testing, etc. These analysis laboratories are controlled by the Ministry of Agriculture and Rural Affairs and by the Ministry of Health. However, there is not yet legislation about establishing a high BSL laboratory in Turkey.

What standards exist for high BSL laboratories for:

e. Engineering and construction?
f. Licensing?
g. Safety and security?
h. Regular oversight and re-certification?

As there isn't any established legislation for such laboratories, internationally established standards and guidelines (CDC's Office of Safety, Health and Environment, National Institute of Health, World Health Organization's Center for Applied Biosafety, etc.) are being used and followed.

Have there been any accidents at high BSL labs in your country?

i. If yes, how and why did the accidents occur?
j. How, to whom, and when are they reported?
k. Who has authority to investigate accidents?
l. What disciplinary or legal actions can be taken?

No accidents.

Have any steps been taken to increase security at high BSL facilities? If so, by whom (i.e., regulation, voluntary measures, individual laboratory practices)?

Security has been increased through individual laboratory practices.

Furthermore, as a result of an increase in research and commercial activities in biotechnology along with the commencement of membership negotiations with the European Union, Turkey has passed biosecurity-related legislation in recent years. Among these laws, the most relevant ones are given below.

Biosecurity-related laws and directives:

- Directive About the Field Studies of Transgenic Culture Plants (05/08/1998)
- The Cartagena Protocol on Biosafety (01/24/2004)
- Directive on Import, Process, Export, Control, and Regulation of Genetically Modified Organisms for Human and Animal Consumption (10/26/2009)
- Biosecurity Law (no.5997 – 09/26/2010)
- Directive on Operational Procedures and Principles of Biosecurity Board and Committees (no.27671 – 08/13/2010)
- Directive on Genetically Modified Organisms and Their Products (no.27671 – 08/13/2010)

Like their equivalents in other countries, biosecurity laws and directives in Turkey are mostly concerned with Genetically Modified Organisms (GMOs) and their distribution, use, import, and export. One of the earliest examples of such a directive was the "directive about the field studies of transgenic culture plants" by the Ministry of Agriculture and Rural Affairs (MARA) in 1998. This directive aimed to prevent the import of GMOs for human consumption that had not first being tested in a field study in Turkey. In addition, all GMOs to be imported were required to have a certification from a country having biosecurity legislation.

In the absence of a national law on biosecurity, in 2000, Turkey signed The Cartagena Protocol on Biosafety and it was ratified in the Turkish Parliament in 2003. In 2002, Turkey started to prepare a "Biosecurity Law" in compliance with The Cartagena Protocol and received project money from the United Nations Environment Program—The Global Environment Facility (UNEP-GEF) to prepare a draft. This project, entitled "Project on the Development of the National Biosafety Framework of Turkey" was started on September 18th, 2002 and finished on March 18th, 2005. Later in 2009, MARA finalized the Biosecurity Law, and it was passed by parliament in 2010. The law does not cover medical or cosmetic products that are approved by the Ministry of Health, but bans the production and release of any GMOs and their use in baby food. The Law also specifies terms of 5 to 10 years of imprisonment for unlawful acts related to unapproved use of GMOs.

A "Biosecurity Board" involving scientists and experts was established by a directive from MARA and held its first meeting on September 27th, 2010. The Board started a web site called "Information Exchange in Biosecurity" at http://www.tbbdm.gov.tr. So far, the Biosecurity Board has had five meetings and accepted only one GMO (A2704-12 soy bean for use in animal feed). The board contains 9 members that are selected by the related ministries as follows: 4 by the Ministry of Agriculture and Rural Affairs (2 from the Ministry, 1 from a University, 1 from a NGO), 2 by the Ministry of Forestry and Hydraulic Works, 1 by the Ministry of Health, 1 by the Ministry of Science, Industry, and Technology, and 1 by the Ministry of Economy.

Directives concerning BSL Labs are under development.

E7

HIGH-CONTAINMENT LABORATORIES IN UKRAINE: LOCAL RESOURCES AND REGULATIONS

Olena Kysil[1,2], Serhiy Komisarenko[1]
[1]Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine and
[2]National Taras Shevchenko University of Kyiv, Ukraine
bs.conf@gmail.com

What high-containment biological (high BSL) laboratories exist in your country? What are the facilities' main goals and priorities?

There are over 4,000 registered microbiological laboratories in Ukraine, but only 2 of them have a permit to work with microorganisms of the first pathogenic group, 402 laboratories have a permit to work with the microorganisms of the second pathogenic group, and all others are allowed to work only with microorganisms of the third and forth pathogenic groups. Here it is necessary to note that the classification of pathogenic organisms and therefore classification of the laboratories in Ukraine differs from the international one. It is inverted (i.e., in Ukraine "one" is the highest risk and "four" is the lowest risk) and also has some additional differences. That is why when speaking about high-containment laboratories according to Ukraine's official classification we need to consider the laboratories that have a permit to work with the microorganisms of the first and the second pathogenic groups. At the same time it is not possible to say that a laboratory that has a permit to work with microorganisms of the first pathogenic group in Ukraine is equivalent to an international BSL-4 lab or that one working with microorganisms of the second pathogenic group is equivalent to a BSL-3 lab.

According to the available data, there are no laboratories in Ukraine that fulfill BSL-4 requirements. One of the laboratories that has a permit to work with the microorganisms of the first pathogenic group did, however, recently undergo an international audit as a BSL-3 laboratory and received a preliminary positive evaluation. This is one of the laboratories of the SI (State Institution) "Ukrainian I. I. Mechnikov Anti-Plague Research Institute" of the Ministry of Health of Ukraine (Odessa), which is responsible for the identification of especially dangerous biological pathogens. This laboratory was reconstructed and technically updated up to the BSL-3 level through a cooperative agreement between the United States Department of Defense and the Ministry of Health of Ukraine that started in 2005. The collaboration focuses on preventing the spread of technologies, pathogens, and knowledge that can be used in the development of biological weapons. The updated laboratory serves as Interim Central Reference Laboratory with a depozitarium (pathogen collection). According to Ukrainian regulations, it has a permit to work with both bacteria and viruses of the first and second pathogenic groups. A second laboratory of the SI "Ukrainian I. I. Mechnikov Anti-Plague Research Institute" of the Ministry of Health of Ukraine also has a permit to work with microorganisms of the first pathogenic group, but it is not updated to the BSL-3 level. This laboratory works only with the especially dangerous infections of bacterial etiology. The third laboratory upgraded to the BSL-3 level belongs to the Central Sanitary Epidemiological Station of the Ministry of Health of Ukraine. This laboratory was updated within the State program and the above-mentioned cooperative agreement between Ukraine and the United States. It has a permit to work with microorganisms of the second pathogenic group and is intended for work with especially dangerous infections.

According to the information received from the Central Regime Commission, the main authority that is responsible for the registration of microbiological laboratories in Ukraine, among the 402 laboratories that have permits to work with microorganisms of the second pathogenic group, 37 are subordinate to the Ministry of Health of Ukraine. Out of these 37 laboratories, 6 laboratories belong to research institutions, and therefore their main goals are scientific and practical investigations, while 31 laboratories belong to the Sanitary Epidemiological Service of Ukraine. These 31 laboratories are responsible for epidemiological and diagnostic investigations. Three hundred sixty two laboratories that have a permit to work with microorganisms of the second pathogenic group are subordinate to the Ministry of Agrarian Policy and Food of Ukraine. Out of them, 358 laboratories are responsible for diagnostic investigations,

while 4 belong to research institutions and perform scientific and practical investigations. The four laboratories of the National Academy of Agrarian Sciences of Ukraine, which have a permit to work with microorganisms of the second pathogenic group, are research oriented. The one laboratory of the Ministry of Defense of Ukraine that has a permit to work with microorganisms of the second pathogenic group performs diagnostic investigations.

What government organizations are responsible for the safety and security of high BSL laboratories?

According to the existing regulations, the main authority that is responsible for the registration of microbiological laboratories and their biosafety and biosecurity is the Central Regime Commission, which works together with regional Regime Commissions of the State Sanitary Epidemiological Service of Ukraine and regional chief state sanitary doctors of Ukraine (according to the State Sanitary Rules 9.9.5.035-99 and 9.9.5-153-2008).

If there are high BSL laboratories in your country, are there established criteria for deciding:

a. Whether or not to establish such facilities?
b. Where to place such facilities?
c. What research will be done in such facilities?
d. What scientific, technical, and management advice is available to governments when making their decisions?

In the case of state subordination of a new laboratory, the decision to establish it or not needs to be taken by the State based on recommendations of a Ministry or a state institution. Then, for example, the decision to establish a new laboratory needs to be included into a state program. To our knowledge there are no established criteria for such a decision.

What standards exist for high BSL laboratories for:

a. Engineering and construction?
b. Licensing?
c. Safety and security?
d. Regular oversight and re-certification?

These are the main regulations that set the high BSL laboratory standards:

1. The State Sanitary Rules 9.9.5.035-99 "The safety of work with microorganisms of the I-II pathogenic groups" (1999)
2. The State Sanitary Rules 9.9.5.-080-02 "The rules of the organization and the safety of work at microbiological laboratories (departments, units)" (2002)
3. The State Sanitary Rules 9.9.5-153-2008 "The organization of laboratories' work in the case of investigation of materials containing the biological pathogenic agents by molecular-genetic methods" (2008)
4. The Order of Ministry of Health of Ukraine N183 from 14.12.1992 "On regime of work with pathogenic microorganisms"
5. The Order of Ministry of Health of Ukraine N452 from 06.11.2001 "On strengthening of anti-epidemical regime of work at microbiological laboratories"

The project of the Regulation of Cabinet of Ministers of Ukraine, proposed by the Ministry of Health of Ukraine "The question of permit issue for work with the microorganisms of the I-IV pathogenic groups for microbiological laboratories and the functioning of regime commissions on biosafety" (2008) is currently undergoing public discussion.

Have there been any accidents at high BSL labs in your country?

According to the information received from the Central Regime Commission during the last twenty years, there were no registered accidents at high-containment laboratories in Ukraine.

Have any steps been taken to minimize high BSL laboratory accidents?

A few virology laboratories of the State Sanitary Epidemiological Service of Ukraine were updated with equipment to fulfill international biosafety requirements for working with poliomyelitis, measles, and influenza as part of a World Health Organization (WHO) Program. The laboratories of the Central Sanitary

Epidemiological Station of the Ministry of Health of Ukraine and the SI "Ukrainian I. I. Mechnikov Anti-Plague Research Institute" of the Ministry of Health of Ukraine were also reconstructed and equipped as part of an agreement with the United States. Over the next years, a few of the regional Sanitary Epidemiological Stations of the Ministry of Health of Ukraine and laboratories of the National Academy of Agrarian Sciences of Ukraine are also scheduled to be updated as part of the same agreement with the United States.

It is also important to mention activities connected with training of laboratory personnel. For example, intensive training programs are running as part of an agreement with the United States. There is also a new Training Centre on Biosafety in Odessa functioning as part of SI "Ukrainian I. I. Mechnikov Anti-Plague Research Institute." Its creation was supported by Canada's Global Partnership Program through the Science and Technology Center in Ukraine (STCU) to ensure modern biosafety and biosecurity training programs.

There are also some projects to increase the biosafety and biosecurity, which are being run by individual laboratories. For example, the Central Sanitary Epidemiological Station of the Ministry of Health of Ukraine laboratory that works with especially dangerous infections is implementing the Laboratory Biorisk Management Standard CWA 15793:2008 with support from Canada through STCU.

All these steps aim to minimize the risk of accidents and to increase laboratory security.

Have any steps been taken to increase security at high BSL facilities? If so, by whom (i.e., regulation, voluntary measures, individual laboratory practices)?
Besides the above-mentioned activities, which are intended to both minimize accidents and increase of security at high BSL facilities, there is also a project to strengthen the education of life scientists on biosafety, biosecurity, and dual-use issues. The project is run by the Palladin Institute of Biochemistry of the National Academy of Sciences of Ukraine in close collaboration with the University of Bradford with support of Canada through STCU. The aim of the project is to strengthen support for the prohibition of the misuse of the modern life sciences by pioneering the formulation and implementation of a national system of biosafety, biosecurity, and dual-use issues education.

E8

HIGH-CONTAINMENT LABORATORIES—UK CASE STUDY

Dr. Neil Davison, Science Policy Centre, the Royal Society
Dr. Filippa Lentzos, BIOS Centre, London School of Economics

Royal Society contribution to a project of the Committee on International Security and Arms Control (CISAC) and the Board of Life Sciences at the US National Academy of Sciences: "Anticipating Biosecurity Challenges of the Global Expansion of High-containment Biological Laboratories"

What high-containment biological research facilities exist in your country?
The UK has both Biosafety Level 3 (BSL-3) and Biosafety Level 4 (BSL-4) laboratories. In the UK these are referred to as Containment Level 3 and 4 (CL3 & CL4). Most work with dangerous pathogens is carried out in Government and Research Council laboratories.[1]

There are approximately 600 laboratories around the UK that are built to operate at BSL-3. Of these around 150 are in research institutes and 150 at universities, although differentiating between research institutes and university laboratories is difficult. There are around 75 BSL-3 laboratories operated by private companies. A large proportion of BSL-3 capacity is held by a small number of universities and research institutes, e.g. two universities have 84 BSL-3 laboratories between them; and one institute has 60 BSL-3 laboratories. The National Health Service (NHS) has 170 BSL-3 laboratories mainly for diagnostics.[2]

Table E8-1 shows data collected by the Health and Safety Executive (HSE**)** for the number of *organisations* with BSL-3 laboratories and their operators as of December 2007. Note that an organisation is at the employer level (e.g. University of Oxford), and a given organisation may have multiple facilities.[3]

Table E8-1 Number of organisations with BSL-3 laboratories (December 2007)[a]

	Government	***Private***	***Research Council***	***University***
BSL-3	202	98	7	40

SOURCE: Contains Parliamentary information licensed under the Open Parliament Licence v1.0.
[a] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp 24-25 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 52

In December 2007, HSE figures showed ten *sites* in the UK with BSL-4 laboratories as shown in Table E8-2. These figures referred to seven government or government sponsored research institutes, one government clinical diagnostic site, and two commercial veterinary vaccine manufacturers.[4] However, as of April 2009 there is only one privately operated BSL-4 site since the Intervet Schering-Plough laboratory in Middlesex, which previously carried out research on Newcastle disease, has now closed. This brings the total number of BSL-4 sites to nine.

[1] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 160-162.
[2] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf pp Ev 162.
[3] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp 24-25 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 52.
[4] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 162.

Table E8-2 Number of sites with BSL-4 laboratories (December 2007)[a]

	Government	***Private***	***Research Council***	***University***
BSL-4	5	2* (Now 1)	3	0

* There is now only one private BSL-4 site.

SOURCE: Contains Parliamentary information licensed under the Open Parliament Licence v1.0.

[a] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp 24-25 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 52

Of the eight government sites, five can operate at BSL-4 for human pathogens (ACDP4), although only four actually operate at this level, and three at BSL-4 for animal pathogens (SAPO4). Seven sites have facilities to work with infected animals.[5] The facilities at each site vary in size from a single room to multiple suites or even individual buildings of BSL-4 laboratories.[6] All BSL-4 facilities are located in the South East of England, ranging from rural settings to suburban areas and cities (there are three BSL-4 sites in or near London).[7] In addition to these BSL-4 laboratories for research and diagnostics, there are also two High Security Disease Isolation Units (HSDUs) for the care of patients with viral haemorrhagic fevers, such as Ebola or Lassa. One is in Coppetts Wood, London, which would also be used for a post-mortem requiring BSL-4, and the other is under development at the Royal Victoria Infirmary, Newcastle.[8]

Details of eight of the UK BSL-4 sites are provided in the UK Government Confidence Building Measure (CBM) submission to the Biological and Toxin Weapons Convention (BTWC), as shown in Table E8-3.[9]

Table E8-3 Details of UK BSL-4 laboratories, covering data for 2010[a]

Type	**Operator**	**Funding**	**Facilities**	**Activities**
Government	Defence science and technology laboratory (Dstl), Porton Down, Wiltshire	Ministry of Defence	Two BSL-4 laboratories (335 m^2 total)	R&D into protective measures against biological weapons
Government	Centre for Emergency Preparedness and Response, Health Protection Agency (HPA), Porton Down, Wiltshire	Department of Health	Two BSL-4 units (59 m^2; and 46 m^2)	Diagnosis and research on viruses including Lassa, Ebola, Marburg and other haemorrhagic fever viruses.
Government	Health Protection Agency (HPA), Colindale, London	Department of Health	One BSL-4 unit (30 m^2)	Applied diagnostic R&D, and diagnostic services for Herpes B; viral haemorrhagic fever infections (Lassa fever, Ebola, Marburg, Congo-Crimean haemorrhagic fever); avian influenza; and SARS
Government	National Institute for Biological	Department of Health and	Two BSL-4 units (each 59 m^2)	Activities related to development of assays and testing of reagents

[5] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev162.
[6] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp 24-25 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 162.
[7] http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1227688128129.
[8] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp 24-25.
[9] UK BWC CBM 2009: http://www.unog.ch/80256EDD006B8954/(httpAssets)/5D42C16D75CA84D4C12575A0002A5A7A/$file/BWC_CBM_2009_UK.pdf.

	Standards and Control (NIBSC), Department of Health, Potters Bar, Hertfordshire	Home Office		including: highly pathogenic influenza virus – reagent development; *Bacillus anthracis* – vaccine testing, reagent development, development of in vitro assays; *Yersinia pestis* – molecular structural work; Botulinum toxins (serotypes A-G) – control, standardisation and assay development for vaccines and anti-toxins
Government	Veterinary Laboratories Agency, Addlestone, Surrey	Department for Environment, Food and Rural Affairs (Defra)	Specified Animal Pathogens Order (SAPO) Level 4: Three avian flu laboratories (each 50 m^2); one classical swine fever laboratory (15 m^2); one Newcastle disease virus laboratory (50 m^2); one rabies virus laboratory (45 m^2); one suite of serology labs capable of increasing to SAPO level 4 (approximately 100 m^2)	Diagnosis and applied research on livestock diseases and wild animal reservoirs.
Research Council	National Institute for Medical Research (NIMR), NIMR Containment 4 Building C, London	Medical Research Council	One BSL-4 unit (298 m^2)	Research and diagnostics on highly pathogenic avian influenza virus and pandemic influenza viruses.
Research Council	National Institute for Medical Research (NIMR), NIMR Containment 4 Building C, London	Medical Research Council	One BSL-4 unit (298 m^2)	Research and diagnostics on highly pathogenic avian influenza virus and pandemic influenza viruses.
Research Council	Institute for Animal Health, Pirbright Laboratory, Pirbright, Surrey	Biotechnology and Biological Sciences Research Council (BBSRC), EU, Defra	SAPO Level 4 laboratory space and plant areas (5,173.87 m^2); SAPO Level 4 animal accommodation including plant (4,327 m^2)	Research on exotic animal virus diseases: foot and mouth disease (FMD), bluetongue, swine vesicular disease, African horse sickness, capripox, African swine fever, peste des petits ruminants and rinderpest.
Private	Merial Animal Health Ltd, Pirbright Laboratory, Pirbright Surrey	Private	One SAPO Level 4 facility	Production of inactivated FMD and bluetongue vaccines.

SOURCE: UK BWC CBM 2011: United Kingdom of Great Britain and Northern Ireland: Confidence Building Measure Return for 2011 (covering data for 2010) for the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and their Destruction, 10 April 1972 (Submitted to the United Nations on 31 March 2011).

[a] UK BWC CBM 2011: http://www.unog.ch/80256EDD006B8954/(httpAssets)/009540B24174AC38C12578930057FF00/$file/BWC_CBM_2011_United+Kingdom.pdf

A 2008 review of the UK's BSL-4 laboratories, Chaired by Professor George Griffin and sponsored by the Health Protection Agency, the Medical Research Council, the Biotechnology and Biological Sciences Research Council, and the Department for Environment, Food and Rural Affairs, identified six building or renovation plans for BSL-4 facilities that were in planning or under consideration as of October 2008:

> "Two of these are in major universities, one involving the up-grading of a yet to be licensed SAPO3 facility to a SAPO4 level, the other, the construction of a completely new ACDP [Advisory Committee on Dangerous Pathogens] CL4 laboratory."[10]

2 What government organizations are responsible for safety and security of high-containment biological (high BSL) laboratories?

The Health and Safety Executive (HSE)[11] is the main government authority that regulates standards and compliance relating to general health, safety and the environment including most matters relating to biological agents, biosafety, and genetic modification. HSE fulfils advisory, regulatory, and enforcement roles.

HSE has sole responsibility for inspections and enforcement at facilities handling dangerous human and animal pathogens and Genetically Modified Microorganisms (GMMs) in the UK.[12] Until 2008 the Department for Environment, Food and Rural Affairs (Defra) regulated standards and compliance for animal and plant diseases, and it continues to license premises for work with animal pathogens under the Specified Animal Pathogens Order (SAPO).[13] The Home Office is responsible for standards and compliance relating to biosecurity.[14] The Advisory Committee on Dangerous Pathogens (ACDP) provides independent scientific advice (see Section 3).

The June 2008 report of a House of Commons inquiry on *Biosecurity in UK research laboratories* expressed concern that there was no ministerial oversight of biosecurity and recommended:

> "... that in view of the cross-cutting nature of these issues, the Government establish a ministerial group to meet periodically to discuss issues of biosecurity. A single Minister, for example the Minister for Science and Innovation, should take responsibility for co-ordinating biosecurity and the provision of high-containment laboratories and should act to convene this ministerial group and the inter-agency body we have recommended be set up."[15]

The government response to this recommendation noted:

> "Where scientific and technical issues are involved, the Chief Scientific Advisers' Committee is best placed to oversee cross-cutting issues and receive reports from the interagency group from time to time.
>
> We agree with the Select Committee that a collective Ministerial overview would be appropriate, at least until Ministers are confident that coordination by officials and Chief Scientific Advisers is working well. We will therefore establish a Ministerial group, to be convened when the need arises."[16]

---

[10] http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1227688128129.
[11] http://www.hse.gov.uk/biosafety/.
[12] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 20 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 53 & http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1227688128129.
[13] http://www.hse.gov.uk/biosafety/callaghan.htm.
[14] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf & http://www.opbw.org/new_process/mx2008/BWC_2008_MX_Docs/BWC_MSP_2008_MX_WP.6_En.pdf.
[15] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 31.
[16] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/1111/1111.pdf p 9.

Regulations and associated responsibilities are currently undergoing significant changes. In the aftermath of the foot and mouth disease (FMD) outbreak in Surrey in 2007 (see Section 5), a single regulatory framework for human and animal pathogens will replace relevant elements of existing regulations.[17] Consultations on the new regulations, termed *The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations*, are now complete, and it is expected that the new regulations will be introduced in 2012.[18] The Advisory Committee on Dangerous Pathogens (ACDP) (see Section 3) is producing guidance to accompany the new regulations that will encompass a common set of containment measures for human and animal pathogens.[19] The guidance is currently in draft form.[20]

As of July 2011, and prior to the introduction of the new regulations, biosafety in UK laboratories is covered by three pieces of legislation:[21]

- *The Control of Substances Hazardous to Health Regulations 2002 (COSHH)*[22]

COSHH regulations come under the European Communities Act 1972 and the Health and Safety at Work etc Act 1974.[23] COSHH regulations are wide-ranging and are not limited to regulation of dangerous pathogens. They are enforced by HSE.[24] Under COSHH, pathogens are classified into Hazard Groups 1-4 based on the risk to human health as defined in *The Approved List of Biological Agents*.[25] This list is produced in consultation with the Advisory Committee on Dangerous Pathogens (ACDP).[26] Biosafety level categories under COSHH are often referred to as ACDP1-4. COSHH is primarily aimed at preventing exposure of workers to dangerous pathogens and places duties on employers to carry out risk assessments and ensure that exposure is prevented or controlled.[27]

- *The Specified Animal Pathogens Order 2008 (SAPO)*[28]

SAPO regulates the use of animal pathogens and until recently was administered by Defra. SAPO is aimed at preventing the escape of pathogens from the laboratory and not with the protection of laboratory workers. It is a licensing system that specifies conditions for handling animal pathogens following inspection of the laboratory and documentation. Licenses are usually valid for five years. Conditions cover: safe containment and disposal; the areas of the laboratory in which various types of work may be done; and the people responsible for the work.[29] Following recommendations of the Callaghan Review,[30] HSE is now responsible for inspection and enforcement across the UK while Defra remains responsible for licensing. SAPO was based on the ACDP 1-4 recommendations (animal pathogens are consequently classed in four categories: SAPO1-4[31]) and the regulations covering work with animal pathogens was

[17] http://www.hse.gov.uk/biosafety/callaghan.htm.
[18] Consultative document http://consultations.hse.gov.uk/inovem/gf2.ti/f/11362/306085.1/pdf/-/cd230.pdf & draft regulations http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[19] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf pp13-15.
[20] Draft CU2010: http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[21] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 51 & http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.7_En.pdf.
[22] http://www.opsi.gov.uk/si/si2002/20022677.htm.
[23] http://www.hse.gov.uk/legislation/hswa.htm.
[24] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p10.
[25] http://www.hse.gov.uk/pubns/misc208.pdf.
[26] http://www.dh.gov.uk/ab/ACDP/index.htm.
[27] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf.
[28] http://www.opsi.gov.uk/si/si2008/uksi_20080944_en_1.
[29] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf p11.
[30] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf.
[31] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p.10.

therefore interlined with those covering human pathogens even before the decision to develop a single regulatory framework.

- *The Genetically Modified Organisms (Contained Use) Regulations 2000 [GMO(CU)]*[32]

GMO(CU) regulations[33] come under the European Communities Act 1972 and the Health and Safety at Work etc Act 1974. GMO(CU) regulates genetically modified pathogens, categorising them in Class 1-4, according to an assessment of risks to both the worker and the environment (thereby differing from COSHH and SAPO). HSE and Defra are responsible for this regulation in England and Wales, and HSE and the Scottish Executive in Scotland.[34]

Table E8-4 below shows data from HSE for the number of *organisations* (for BSL-3) and number of *sites* (for BSL-4) working with dangerous pathogens and their regulation as of December 2007. (Note: These data were provided before HSE took on responsibility for SAPO).

Table E8-4 Number of organisations (BSL-3) and sites (BSL-4) working with dangerous pathogens and their regulation in the UK. (December 2007)[a]

BSL	***COSHH and/or GMO(CU) regulated only***	***SAPO only***	***HSE & SAPO combined***	***Total***
	Number of organisations			
3	323	5	19	347
	Number of sites			
4	1	2	7	10

SOURCE: Contains Parliamentary information licensed under the Open Parliament Licence v1.0.

[a] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p10 & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev52

The Home Office is responsible for biosecurity in UK laboratories. The regulatory framework is Part 7 and Schedule 5 of the Anti-terrorism Crime and Security Act 2001 (ATCSA),[35] which is implemented by the National Counter-Terrorism Security Office (NaCTSO),[36] a police unit reporting to the Association of Chief Police Officers (ACPO). ATCSA allows the police to impose security measures in laboratories handling dangerous pathogens and toxins included on a list of just over 100 pathogens in Schedule 5, which was extended in 2007 to include animal pathogens.[37] ATCSA covers around 400 laboratories including university and hospital laboratories.[38] Guidelines governing these measures are provided in restricted circulation documents published jointly by the Home Office and NaCTSO: "Security Standards for Laboratories"; and "Personnel Security Measures for Laboratories."[39]

ATCSA requires laboratories to:

- Register with the Home Office their holdings of Schedule 5 substances.
- Inform the police of the security measures in place and the personnel who have access to the Schedule 5 substances in certain circumstances.
- Ensure that Schedule 5 substances and the premises in which they are kept, stored, worked on, and disposed of are secure.

[32] http://www.opsi.gov.uk/si/si2000/20002831.htm.
[33] http://www.hse.gov.uk/biosafety/gmo/law.htm.
[34] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p.10.
[35] http://www.opsi.gov.uk/acts/acts2001/ukpga_20010024_en_1.
[36] http://www.nactso.gov.uk/.
[37] http://www.nactso.gov.uk/SiteCollectionDocuments/AreasOfRisk/Implementation%20Guidance%20for%20Labs.pdf.
[38] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p11 &http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev52.
[39] http://www.dh.gov.uk/prod_consum_dh/idcplg%3FIdcService%3DGET_FILE%26dID%3D137088%26Rendition%3DWeb.

- Ensure that access to said substances is authorised and controlled.[40]

If there are BSL laboratories in your country, are there established criteria for deciding:

a. Whether or not to establish such facilities?

Establishment of new BSL-3 and BSL-4 facilities is at the discretion of the relevant organisation, company, or government department. Consulting HSE at an early stage is considered advisable when building new BSL-3 and BSL-4 facilities. For BSL-3 facilities, the organisation is encouraged to contact HSE, and for BSL-4 HSE is always consulted. HSE has the power to prevent the construction of a BSL-4 laboratory if it considers the plans for its construction, operation, or maintenance to be unsafe.[41]

The 2008 House of Commons inquiry recommended that "...HSE be a statutory consultee in any planning application for a CL3 or CL4 laboratory."[42] The report also urged "...HSE to engage as early as possible with those building and operating high-containment facilities to avoid resorting to enforcement action."[43] The UK government has stated that it does not intend to amend current requirements for planning permission but that, in the development of the new single regulatory framework (SRF), consideration will be given to the information that should be provided to HSE and the extent of consultation required for a new facility or change of use of an existing facility.[44]

What criteria are used to select the placement of such facilities?

There are no universal criteria used to select the placement of high-containment facilities. The location of BSL-3 and BSL-4 laboratories is part of an overall risk assessment that would consider other factors including the availability of scientific and maintenance staff and proximity to emergency services.[45] The 2008 House of Commons inquiry concluded "there is no reason in principle why CL4 laboratories should not be built in urban areas, provided that the correct risk assessment is undertaken and biorisk is managed appropriately. As each case will be unique, we recommend that such applications be treated on an individual basis."[46]

As regards the highest level of containment, an October 2008 independent review of UK BSL-4 facilities Chaired by Professor George Griffin concluded:

> "The geographical locations of the existing high-containment facilities have arisen for historic operational reasons and few opportunities exist to alter this situation. When such opportunities do arise then decisions on their location should be based on a robust, multi-faceted risk assessment in which microbiological science and all aspects of security, safety, and public opinion are considered and on the existence of good links to academic centres of excellence."[47]

The review emphasised the importance on taking into account public opinion when locating or renovating high-containment facilities.

HSE's guidance, *Biological agents: The principles, design and operation of Containment Level 4 facilities*, notes that local authorities are responsible for adequate planning and public consent and that those designing the BSL-4 laboratory may want to consider conducting a local public consultation.[48]

HSE provides more specific guidance on factors that influence the positioning of a BSL-4 building at a given location including: headroom; access; daylight and visibility; utilities; and air handling.[49] The guidance also notes:

---

[40] http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[41] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdfp34.
[42] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdfp35.
[43] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p22.
[44] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/1111/1111.pdf p11.
[45] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p34.
[46] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p35.
[47] http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1227688128129 p17.
[48] http://www.hse.gov.uk/pubns/web09.pdf p9.

> "The CL4 [BSL-4] facility will consist of either a separate building or a clearly demarcated and isolated zone within a building. Activities can be separated by locating the laboratory away from main public thoroughfares of the building. The rooms in the unit should be arranged to ensure passage through the changing and decontamination area before entering rooms where work is done with HG4 [Hazard Group 4] agents."[50]

b. What criteria are used to decide what research will be done in such facilities?

Decisions on research to be undertaken are taken by the organisation, company, or government department that is responsible for the laboratory. There are specific requirements for containment measures for BSL-3 and 4 laboratories, as detailed in Section 4. ACDP guidance, *Biological agents: Managing the risks in laboratories and healthcare premises*,[51] provides criteria for selecting appropriate control measures for different types of research and different pathogens.

c. What scientific, technical, and management advice is available to governments when making their decisions.

Advice and guidance is provided to the UK government by the Biological Agents Unit at HSE.[52] Independent scientific and technical advice is provided by the Advisory Committee on Dangerous Pathogens (ACDP), a non-departmental public body with a Chairman and up to 17 members comprising scientific experts, employer representatives, and employee representatives. ACDP's terms of reference are:

> "To advise the Health and Safety Executive, and Ministers for the Department of Health and the Department for Environment, Food and Rural Affairs, and their counterparts under devolution in Scotland, Wales and Northern Ireland, as required, on all aspects of hazards and risks to workers and others from exposure to pathogens."[53]

ACDP's two main areas of work are: "Production of guidance relating to safety at work and protection of public health; and Provision of advice to Government on the formulation and implementation of policy and legislation, relating to specific pathogen risks and their impact." [54]

There are three main guidance documents in current use, which were produced by ACDP and published by HSE:

- *The management, design and operation of microbiological containment laboratories* (2001),[55] aimed at those responsible for the management and operation of BSL2 and BSL-3 laboratories.
- *Biological agents: Managing the risks in laboratories and healthcare premises* (2005),[56] aimed at the healthcare sector; and
- *Biological agents: The principles, design and operation of Containment Level 4 facilities* (2006),[57] which is aimed at high-hazard containment facilities, mainly those that present a risk to human health under COSHH. Genetically modified and animal pathogens are discussed only in the context of human health.

---

[49] http://www.hse.gov.uk/pubns/web09.pdf p33.
[50] http://www.hse.gov.uk/pubns/web09.pdf p41.
[51] http://www.hse.gov.uk/biosafety/biologagents.pdf
[52] http://www.hse.gov.uk/biosafety/infection.htm
[53] http://www.dh.gov.uk/ab/ACDP/index.htm
[54] http://www.dh.gov.uk/ab/ACDP/index.htm
[55] http://www.hse.gov.uk/pubns/books/microbio-cont.htm
[56] http://www.hse.gov.uk/biosafety/biologagents.pdf
[57] http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4135258

As discussed in Section 2, ACDP and HSE are currently developing guidance to accompany the new single regulatory framework to be introduced during 2012.[58]

4 What standards exist for BSL laboratories?

In the UK there are legal requirements under COSHH, SAPO, GMO(CU), and ATCSA (see Section 2). These are supported by guidance from ACDP (see Section 3 (d)). A new single regulatory framework for biosafety, which will replace GMO(CU) and elements of COSHH and SAPO, is under development for introduction during 2012. ATCSA related standards for biosecurity regulated by the Home Office will remain the same.

a) For engineering and construction?

The minimum containment requirements under COSHH regulations for BSL-3 and BSL-4 laboratories are summarised in Table E8-5, which is taken from the ACDP guidance *Biological agents: Managing the risks in laboratories and healthcare premises.*[59]

Table E8-5 Minimum containment requirements under COSHH for work in BSL-3 and BSL-4 laboratories.[a]

Containment Level	***BSL-3***	***BSL-4***
Air Handling		
The workplace is to be maintained at air pressure negative to atmosphere	Yes	Yes
Input air and extract air to the workplace are to be filtered using high efficiency particulate absorption (HEPA) filters or equivalent	Yes, on extract air	Yes, on input and double on extract air
Security and Access		
The workplace is to be separated from any other activities in the same building	Yes	Yes
Access is to be restricted to authorised persons only	Yes	Yes, via air-lock key procedure
Efficient vector control, e.g. rodents and insects	Yes, for animal containment	Yes
Safe storage of a biological agent	Yes	Yes, secure storage
An observation window, or alternative, is to be present, so that occupants can be seen	Yes	Yes
A laboratory is to contain its own equipment	Yes, so far as is reasonably practicable	Yes
Disinfection and Disposal Procedures		
The workplace is to be sealable to permit disinfection	Yes	Yes
Specified disinfection procedure	Yes	Yes
Surfaces impervious to water and easy to clean	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls and ceiling
Surfaces resistant to acids, alkalis, solvents, disinfectants	Yes, for bench and floor (and walls for animal containment)	Yes, for bench, floor, walls and ceiling
Incinerator for the disposal of animal carcasses	Accessible	Yes, on site

[58] http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf
[59] http://www.hse.gov.uk/biosafety/biologagents.pdf

Protective Equipment and Procedures		
Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable equipment	Yes, where aerosol produced	Yes

SOURCE: © Crown copyright: Health and Safety Executive.
a http://www.hse.gov.uk/biosafety/biologagents.pdf

The minimum containment requirements under COSHH, SAPO and GMO(CU) regulations for work in BSL-4 laboratories are shown in Table E8.6, which is taken from the ACDP guidance *The Principles, Design and Operation of Containment Level 4 Facilities*. [60]

Table E8-6 Containment requirements under COSHH, SAPO and GMO(CU) regulations for work in BSL-4 laboratories.[a]

Containment Measures	**COSHH**	**SAPO**	**GMO(CU)***
The workplace is to be separated from any other activities in the same building	Yes	Yes	Yes
Input air and extract air to the workplace are to be filtered using HEPA or equivalent	Yes, on input and double on extract air	Yes, single on input and double on extract air	Yes, extra requirements for viruses
Access is to be restricted to authorised people only	Yes, via airlock key procedure	Yes, restricted and entry through an airlock, clean/dirty area. Shower on exit	Yes, via airlock key
The workplace is to be sealable to permit disinfection	Yes	Yes	Yes, sealable for fumigation
Specified disinfection procedure	Yes	Yes	Yes
The workplace is to be maintained at air pressure negative to atmosphere	Yes	Yes, pressure to be maintained at not less than -75 Pa	Yes
Efficient vector control, e.g. rodents and insects	Yes	Yes, and proofed against entry or exit of animals and insects	Yes
Surfaces impervious to water and easy to clean	Yes, for bench, floor, walls and ceiling	Yes, for working surfaces, walls and ceiling	Yes, for bench, floor, walls and ceiling
Surfaces resistant to acids, alkalis, solvents, disinfectants	Yes, for bench, floor, walls and ceiling	Yes, for working surfaces, walls and ceiling	Yes, for bench, floor, walls and ceiling
Safe storage of a biological agent	Yes, secure storage	Yes, secure storage in the laboratory suite. Inventory to be maintained	Yes, secure storage
An observation window, or alternative, is to be present, so that occupants can be seen	Yes	Yes	Yes
A laboratory is to contain its own equipment	Yes	Yes	Yes
Infected material, including any animal, is to be handled in a safety cabinet or isolator or other suitable containment	Yes	Yes	Class III cabinet required
Incinerator for the disposal of animal carcasses	Yes, on site	Yes, or some other validated means of pathogen inactivation and	Yes, on site

[60] http://www.hse.gov.uk/pubns/web09.pdf pp 14-16.

		safe carcass disposal	
Treatment of liquid and solid wastes	All waste should be made safe or safe to handle before leaving the laboratory	All wastes to be sterilised by a procedure known to inactivate the pathogen(s). For solids this requires autoclaving followed by incineration	Inactivation by validated means
Laboratory security		Laboratory and animal rooms to be kept secure and locked. Intruder alarm system to be fitted	

SOURCE: © Crown copyright: Health and Safety Executive.
[a] http://www.hse.gov.uk/pubns/web09.pdf pp 14-16. *Note: GMO(CU) Regulations specify additional control measures for work with genetically modified micro-organisms in animal units, plant growth facilities and for large-scale work.

These two ACDP guidance documents provide further guidance for the design, construction, and operation of BSL-3 and BSL-4 laboratories. They also refer to publications that provide more detailed information on laboratory construction: Richmond, J Y (ed) (2000) *Anthology of Biosafety II – BSL 2 Facility design considerations*. American Biological Safety Association; and Richmond, J Y (ed) (2002) *Anthology of Biosafety V – BSL 4 Laboratories.* American Biological Safety Association.

The ACDP note that:

> "...it must be remembered that each CL4 [BSL-4] laboratory will be unique and that the number of publications and people (e.g. architects, designers and engineers) with experience of building a CL4 facility will be limited. Consequently, extensive liaison and consultation between all parties, including regulators, at a very early stage is highly recommended for a successful build – the aim being to eliminate problems at the design stage rather than rectifying problems once the facility is built."[61]

b) For licensing? (Also see Section 2)

SAPO is a licensing regime, work covered by COSHH requires notification and, work under GMO (CU) requires permission.[62] Laboratory work covered by ATCSA requires notification.

There is no formal licensing system under COSHH regulations, which are enforced by HSE. However, there is a requirement for those wishing to work on dangerous pathogens in the laboratory to notify and receive acknowledgement from HSE.[63] Evidence submitted by the government to the 2008 House of Commons inquiry noted:

> "In addition to using specific control measures, those working with dangerous pathogens need to notify HSE at least 20 days in advance of any planned work where HG [hazard group] 2, HG3 and HG4 are used for the first time, at particular premises. Notification is also required of the subsequent use of certain organisms (i.e. those in HG3 and HG4 and those in HG2 that are listed in Part V of Schedule 3 of COSHH are used for the first time).
>
> Although this is not an approval system, HSE requires the notification to include sufficient information to demonstrate that duty holders have identified hazards associated with the organism which might arise from carrying out the work."[64]

[61] http://www.hse.gov.uk/pubns/web09.pdf p 31
[62] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 13
[63] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf p 8
[64] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 55

Defra remains responsible for licensing under SAPO (although HSE is now responsible for oversight). SAPO prohibits the possession or introduction of any animal pathogens listed in Part I of the Schedule, or any carrier of that pathogen, except under license. These are primarily exotic diseases that can affect farmed livestock and poultry. No license is needed to possess a pathogen listed in Part II of the schedule but its introduction to any animal is prohibited except under license. Conditions in licenses also place restrictions on domestic transfer of animal pathogens.[65] Government evidence to the House of Commons inquiry provides more details on SAPO licensing:

> "The SAPO licensing process includes inspection of the applicants' laboratories and review of supporting documentation (i.e. the operating procedures for work, risk assessment and appropriate containment measures) prior to the licence being issued. Licences are usually valid for five years. Inspections of laboratories licensed under SAPO may be carried out at any time to ensure full compliance with license conditions and the Order."[66]

GMO (CU) regulations require anyone carrying out genetic modification to conduct a risk assessment for human health and the environment and assign containment accordingly. Activities are assigned a risk class equating to the containment level (1-4). Prior to Class 2, 3 or 4 activities commencing, a notification must be submitted including an assessment of the hazards and planned containment measures. HSE and Defra review these notifications and request additional information where necessary. Written consent from HSE is required before work in class 3 or 4 begins.[67]

Under ATCSA, laboratories are required to register their holding of Schedule 5 substances with the Home Office and provide information to the police on their security measures and, in certain conditions, personnel. Liaison with laboratories is carried out by police Counter Terrorism Security Advisors (CTSAs) from the National Counter-Terrorism Security Office (NaCTSO). Security requirements are dependent on the organism(s) being handled. BSL-4 laboratories have extensive security measures with extremely limited access and all staff must have security clearances. Access to pathogens is restricted at BSL-3 laboratories, which are also subject to security measures and are provided with advice on staff security checking.[68]

c) For safety and security?

There are regulatory requirements for biosafety, covered by COSHH, SAPO and GMO(CU), and biosecurity, covered by ATCSA (see Section 2) and supporting guidance from ACDP (see Section 3 (d)). Minimum containment requirements are outlined in Section 4 (a).

In addition there are relevant standards and guidance around staffing and training. ACDP highlights the important role of Biological Safety Officers/Advisors (BSOs/BSAs):

> "The recruitment of a biological safety advisor (BSA) is pivotal in ensuring management are provided with sufficient information and advice to ensure risks related to biological agents are either controlled or prevented."[69]

The 2008 House of Commons inquiry on biosecurity noted that there was "...widespread support for a more high profile role for BSOs and for giving them professional status."[70]

Training is essential for work at high containment and employers are required to provide this under health and safety law and specific regulations such as COSHH. The House of Commons inquiry found that

---

[65] http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.7_En.pdf
[66] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 57
[67] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf,
http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 56
[68] http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.6_En.pdf
[69] http://www.hse.gov.uk/pubns/web09.pdf p 22
[70] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 18

training could be better coordinated[71] and, following the Griffin review, the government's inter-agency group that is reviewing staffing of high-containment laboratories will also address training issues.[72]

The House of Commons inquiry also reviewed the issue of vetting staff, noting that:

> "...security clearance for scientists working with dangerous pathogens is still not harmonised in the UK and for Home and EU staff or students security-vetting is not always a prerequisite for work with dangerous pathogens."[73]

Those working in government laboratories are subject to government vetting programmes but standards in universities, Research Council institutes, and the private sector vary.[74] The National Counter-Terrorism Security Office (NaCTSO) liaises with laboratories on security checks under ATCSA.

The Foreign and Commonwealth Office (FCO) administers the Academic Technology Approval Scheme (ATAS),[75] which was introduced November 2007 as a replacement for the Voluntary Vetting Scheme. It requires all non European Union (EU) students applying for certain postgraduate programmes at UK universities to receive an ATAS certificate specific to their course and place of study before they apply to enter the UK or extend their stay. ATAS covers a wide range of science and engineering Masters and Doctorate research programmes and a more limited number of taught Masters courses.[76]

According to *Nature*, the FCO had rejected 100 applications in the period up to November 2008, representing 0.5 percent of around 20,000 applications.[77] There is limited publicly available information about the operation of ATAS. An internal FCO review concluded that ATAS is a useful contribution to security at modest cost but noted concerns that handling times for applications are taking significantly longer than the planned ten working day processing time. The review recommended that the FCO ATAS Unit should conduct a biannual review of subject coverage to coincide with UK universities' own review.[78]

d) For regular oversight and re-certification?

The requirement for notifying HSE under COSHH regulations does not automatically lead to an inspection but the information is used to inform inspections and HSE expect to inspect BSL-4 laboratories once a year and BSL-3 laboratories at least once every three years.[79] However, the House of Commons inquiry observed that:

> "...we received evidence that inspections are often infrequent unless problems are reported and that the frequency should increase. Concerns have also been expressed that the HSE may not have sufficient resources, especially with the new burden envisaged by the Callaghan Review, to inspect sufficiently,..."[80]

Under SAPO, inspections may be carried out at any time to ensure compliance with the licence conditions. In April 2008 HSE took over from Defra as the lead inspector and regulator.[81]

Under GMO (CU) all activities in Class 4 or novel genetic modification activities are brought to the attention of the Scientific Advisory Committee for Genetic Modification (SACGM), which provides advice to HSE on the risk assessment that has been submitted. Site inspection may be required if novel

[71] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 46
[72] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/1111/1111.pdf p 15
[73] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 46
[74] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 47
[75] http://www.fco.gov.uk/en/about-us/what-we-do/services-we-deliver/atas/.
[76] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 61-62.
[77] http://www.nature.com/news/2008/081107/full/news.2008.1211.html.
[78] Communication with ATAS Unit, FCO, August 2009.
[79] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 55.
[80] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 20.
[81] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 56.

containment requirements are proposed. HSE issues consent for work to proceed once satisfied with the risk assessment and proposed containment measures.[82]

Under ATCSA, laboratories working with Schedule 5 agents must notify the Home Office and will then be visited by Counter Terrorism Security Advisors (CTSAs). Visits are used to assess physical security and make recommendations. CTSAs produce a written assessment including security advice, which is then provided to the laboratory. Any security improvements required are specific to the laboratory. Often advice is focused on personnel security and procedures with information about security checks and monitoring of staff. (Police can request the details of those with access to Schedule 5 materials if they have specific intelligence.) CTSAs visit registered laboratories once a year or more often if security improvements are required. As of July 2008 there had been issues at two sites, both related to a shortage of funds to improve security at university facilities.[83]

5 Have there been any BSL accidents in your country?

a) If yes, how and why did accidents at high-containment facilities occur?

Foot and mouth disease outbreak in Surrey, UK in August 2007

Pirbright is the site of an Institute for Animal Health (IAH) laboratory and the vaccine manufacturer Merial Animal Health Ltd. A company called Stabilitech that carried out work with FMDV in a laboratory within the IAH facility left the Pirbright site in 2008. The preliminary investigation of an outbreak of FMD in August 2007 indicated that the Pirbright site was the likely source.[84] The Health and Safety Executive (HSE) was then tasked with investigating: "potential breaches of biosecurity at the Pirbright site; whether such breaches may have led to a release of any specified animal pathogen; whether any such breaches had been rectified to prevent future incidents."[85] The December 2007 report of the investigation concluded that wastewater containing live virus leaked out from the drainage pipes and contaminated the surrounding soil. The investigation found evidence of long term damage and leakage from the waste system, including cracked pipes, tree branches breaching pipes, and unsealed manholes. The virus is thought to have spread by vehicles and been exacerbated by mud and slurry due to heavy rainfall in July 2007.[86]

Merial were engaged in large-scale FMDV vaccine production and the waste from this process containing live virus was passed into the site drainage system along with smaller quantities from IAH and Stablitech operations, as permitted under the Defra licence. However, the investigators found that the condition of the site drainage system breached biosecurity for the site as a whole and did not meet requirements for BSL-4 containment. Ownership of the drainage system rests with IAH but the investigators found a difference in opinion between IAH and Merial over responsibility for maintenance of a key section of pipe. (Detailed information about the investigation can be found in the December 2007 report by the HSE, *Final report on potential breaches of biosecurity at the Pirbright site 2007.)*[87]

In addition to recommending a review of the regulatory framework for animal pathogens (see Section 2 and Section 5 (e)), HSE made specific recommendations to the site operators on: whether a high-containment laboratory could be sealed for fumigation; the testing of filters; the need to investigate whether liquid waste could be effectively sterilized; and improvements to the effluent drainage system.[88]

---

[82] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 56.
[83] http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.6_En.pdf & http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 56-57.
[84] http://www.hse.gov.uk/news/archive/07aug/pirbright.pdf.
[85] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf.
[86] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf & http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.7_En.pdf.
[87] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf.
[88] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf & http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.7_En.pdf.

Another well-documented example from the UK is the Birmingham University Medical School smallpox outbreak in 1978.

b) How, to whom and when are they reported?

The Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995 (RIDDOR)[89] requires laboratories to report to HSE certain accidents and near misses involving high hazard biological agents[90] that pose a risk to human health. It covers wild-type human pathogens, zoonotic pathogens, and genetically modified versions of these. RIDDOR requires reporting of infections due to work with live or dead humans or animals, exposure to body fluids, or any potentially infected material derived for any of these. A separate report is required for any release or escape of a biological agent likely to cause severe human disease (i.e., hazard group 3 or 4 biological agents or Class 3 or 4 GMMs). Infections that could have been acquired outside work are not reportable. The following types of accidents require reporting:

- Accidents where the person dies, suffers major injury, or is absent or unable to work for more than three days;
- Accidents where a person not at work suffers an injury and is taken to hospital;
- A person suffering one of the specified work-related diseases; and
- A "dangerous occurrence", which may not necessarily result in injury but has potential to cause significant harm. These encompass any accident or incident that causes or could have caused the release of a biological agent that could cause severe human disease (i.e., hazard group 3 and 4 agents and certain hazard group 2 agents).[91]

Guidance on RIDDOR last updated in 2008 is provided by HSE: *A guide to the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations 1995*.[92]

In addition to RIDDOR requirements for a given accident, there are requirements under GMO(CU)[93] regulations to report certain accidents involving Genetically Modified Organisms (GMOs) to HSE, described as "... an accident involving a significant and unintended release of genetically modified organisms in the course of an activity involving genetic modification which presents an immediate or delayed hazard to human health or the environment."[94] Such accidents might include:

- "the spillage of any Class 3 GMM outside of a microbiological safety cabinet (MSC) or other primary container;
- a major spillage of a Class 3 GMM within a MSC;
- the spillage of any Class 2 GMM outside of a MSC or other primary container, where it is thought likely that an individual or the environment could have been exposed during the spill or during decontamination;
- the release or escape of a GMO, other than a GMM that could cause harm to human health, for example, by acting as a novel disease reservoir;
- infection (classical) of a person with a (replication competent) GMM, as this constitutes a significant and unintended release."[95]

After an accident notification, HSE is required to investigate and provide a report to the European Commission.[96]

[89] http://www.hse.gov.uk/riddor/.
[90] http://www.opsi.gov.uk/SI/si1995/Uksi_19953163_en_5.htm#sdiv3.
[91] http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[92] http://www.hse.gov.uk/pubns/priced/l73.pdf .
[93] https://www.hse.gov.uk/forms/genetic/index.htm.
[94] https://www.hse.gov.uk/forms/genetic/cu3.pdf .
[95] https://www.hse.gov.uk/forms/genetic/cu3.pdf.
[96] http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.

HSE must also be notified of any accident while working with specified animal pathogens, which has or may have caused the release of a specified animal pathogen that could cause serious disease in susceptible animals. For any release into the environment, Defra should also be notified.[97]

c) Who has authority to investigate accidents?

HSE has authority for investigating accidents.

d) What disciplinary or legal actions can be taken?

Under COSHH and GMO(CU) where significant breaches are identified, HSE, "Specialist Inspectors can use a full range of enforcement powers conferred by the Health and Safety at Work Act 1974, which include stopping work activities, issuing notices requiring specific improvements by specific dates and prosecution."[98]

Under SAPO, if HSE inspectors identify non-compliance under the licence conditions they can recommend the license is amended, suspended, or revoked by Defra. Any prosecution would be undertaken by the relevant local authority, when alerted to non-compliance by inspectors.[99]

Under ATCSA, the police CTSAs can demand security requirements, and failure to comply with these is a criminal offence.[100]

e) Have any steps been taken to minimize BSL laboratory accidents?

Following the HSE investigation of the Pirbright FMD outbreak,[101] the government instigated a review of the safety of facilities handling FMDV, carried out by Professor Brian Spratt and published in August 2007, which highlighted a potential conflict of interest for Defra as regulator, licensor, and inspector of the facilities and also their major customer.[102]

Subsequently, the government asked Sir Bill Callaghan to carry out a "...review of the regulatory framework for handling animal pathogens and to make recommendations to Government for changes that would strengthen the regulation of animal pathogens."[103] In addition, the Prime Minster commissioned Dr Iain Anderson to lead an independent review of the lessons learned from the response to the 2007 outbreak.[104]

The Callaghan Review – accepted in full by the government – recommended a three-phase approach to changes leading towards a single regulatory framework (SRF) for human and animal pathogens.[105]

The recent status of the changes is summarised in a June 2009 HSE paper:

> "Phase 1, for HSE to formalise support to Defra and the Devolved Administrations for SAPO inspections, is now complete; Phase 2 saw changes made to the Specified Animal Pathogens Order (SAPO) to designate HSE as the inspection and enforcement body by means of Agency Agreements with Defra and the Devolved Administrations. These arrangements were implemented successfully and are working well.

---

[97] http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[98] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 58.
[99] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 58.
[100] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 57.
[101] http://www.hse.gov.uk/news/archive/07aug/finalreport.pdf.
[102] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/spratt_final.pdf.
[103] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf.
[104] http://webarchive.nationalarchives.gov.uk/20100807034701/http://archive.cabinetoffice.gov.uk/fmdreview/.
[105] http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/fmd/documents/callaghan-reviewreport071213.pdf.

> We are now working on the third and most complex phase of the project that will deliver:
> a. the SRF comprising a single set of regulations to govern work with human and animal pathogens based on a Legislative Reform Order (LRO) to provide HSE with the viruses to make regulations in relation to animal pathogens;
> b. a common set of containment measures based on advice from ACDP (HSE is leading the work);
> c. appropriate cost recovery and integrated notification systems."[106]

These new regulations, to be introduced in 2012, are termed *The Biological Agents and Genetically Modified Organisms (Contained Use) Regulations*.[107] They will replace will replace GMO(CU) and elements of COSHH and SAPO, and will be accompanied by guidance from ACDP, which is currently in draft form.[108]

Government evidence to the 2008 House of Commons inquiry provided some information on the inspection activity that followed the 2007 FMD outbreak:

> "Following the publication of the investigation report following the 2007 outbreak of FMD, HSE and Defra released a Safety Alert on 7 September 2007. This was aimed at all high-containment laboratories, to draw attention to the issues arising from the investigation. In addition, HSE and Defra committed to undertake a programme of inspections.
>
> The first phase of the Safety Alert inspection programme focused on CL4 facilities where work is undertaken with Hazard Group (HG) four dangerous pathogens, including both human and animal pathogens.
>
> The inspections revealed no breaches of the legislation and no formal enforcement action was taken. This process has provided both the regulatory bodies and the operators of the laboratories with the assurance that their facilities are well managed. The inspections have also provided a useful opportunity to provide advice and guidance on good practices. HSE will continue this series of Safety Alert inspections to consider CL3 facilities based on risk. The inspections will begin in January 2008 and will be completed by the end of the year."[109]

Another issue raised in the 2008 House of Commons inquiry was a concern over under-investment in certain UK high-containment laboratories, noting:

> "We have observed at first hand the extent to which the quality of facilities can vary, even those designated CL4. Some of the UK's facilities are world-class; for example the state-of-the-art facilities at the DSTL, Porton Down. In contrast, we found other facilities, at IAH Pirbright and at the HPA in Porton Down, to be in need of significant investment given their age..."[110]

In July 2009 the BBSRC and the government announced £100 million in funding to be allocated to the redevelopment of the IAH facilities at Pirbright.[111]

---

[106] http://www.hse.gov.uk/aboutus/meetings/hseboard/2009/230609/p-jun-b09-57.pdf.
[107] http://www.hse.gov.uk/aboutus/meetings/hseboard/2009/230609/p-jun-b09-57.pdf.
[108] Draft CU2010: http://www.hse.gov.uk/aboutus/meetings/committees/acdp/080609/acdp-92-p13a-annex1.pdf.
[109] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360ii.pdf Ev 54.
[110] http://www.publications.parliament.uk/pa/cm200708/cmselect/cmdius/360/360i.pdf p 25.
[111] http://www.bbsrc.ac.uk/news/archive/2009/090727-pr-100-million-boost-for-animal-health-research.aspx.

f) Have any steps been taken to increase security at BSL facilities?

In 2007 Schedule 5 of ATCSA was updated to include animal pathogens.[112] In July 2008, the government noted plans to review Schedule 5 of ATCSA every two years to update the list of agents covered, and also to review whether any further changes should be made to primary and secondary legislation.[113]

Acknowledgements

The Royal Society would like to thank the Advisory Group for reviewing this document:

- Professor Keith Gull FRS, Wellcome Trust Principal Research Fellow, Sir William Dunn School of Pathology, University of Oxford
- Dr John McCauley, Division of Virology, National Institute of Medical Research, Medical Research Council
- Sir John Skehel FRS
- Professor Geoffrey Smith FRS (**Chair**), Wellcome Principal Research Fellow and Head, Department of Virology, Imperial College London; and Chair, Royal Society Advisory Group on the Scientific Aspects of International Security (SAIS).
- Professor Robin Weiss FRS, Professor of Viral Oncology, University College London.

We would also like to thank Katie Wookey, intern at the Science Policy Centre in 2009, for conducting background research.

Please send any comments to: Dr Filippa Lentzos, BIOS Centre, London School of Economics, Houghton Street, London WC2A 2AE, UK; e-mail: f.lentzos@lse.ac.uk.

[112] http://www.opsi.gov.uk/si/si2007/uksi_20070926_en_1.
[113] http://www.opbw.org/new_process/mx2008/BWC_MSP_2008_MX_WP.6_En.pdf.

E9

UNITED STATES HIGH-CONTAINMENT BIOLOGICAL LABS AND REGULATIONS

United States National Research Council Staff

1. What high-containment biological research facilities exist in the United States?

Since 2001, the number of facilities that can conduct high-containment biological research (United States Centers for Disease Control [CDC] and Prevention Biological Safety 3 or 4 level—BSL 3-4) in the United States has increased and is expected to continue increasing in the immediate future as planned labs are completed and become operational (United States GAO, 2009a).

A rough estimate of the number of BSL-3 labs can be based on the number of labs registered with the Select Agent Program, the main regulatory program for United States high-risk biological research, which is described in the next section. As of 2010, 1,495 laboratories were registered with the Select Agent Program through the CDC (Kaiser, 2011). This provides only a rough estimate of the number of BSL-3 labs as some select agents can be handled at the BSL-2 level, while some pathogens that necessitate BSL-3 precautions are not select agents.[1] Also, some laboratories registered with the Select Agent Program reside outside of the United States.

In 2011, 6 United States entities collectively contained 8 laboratories operating at the BSL-4 level (Table E9-1). Six other BSL-4 laboratories were in the planning or construction phase, one of which will replace an existing laboratory (Table E9-2). BSL-4 facilities, such as the National Institutes of Health's (NIH) small BSL-4 lab in Bethesda, Maryland, that currently operate only at a lower containment level (United States GAO, 2007) were not included in those totals.

Table E9-1 Operational BSL-4 Labs in the United States.

Laboratory	Location
National Institute of Allergy and Infectious Diseases (NIAID) Rocky Mountain Lab	Hamilton, MT
Texas Biomedical Research Institute[1]	San Antonio, TX
University of Texas Medical Branch: Robert E Shope Lab and Galveston National Laboratory	Galveston, TX
Georgia State University	Atlanta, GA
CDC Special Pathogens Branch: Building 15 and Building 18	Atlanta, GA
United States Army Medical Research Institute for Infectious Diseases (USAMRIID)	Fort Detrick, MD

[1] Formerly Southwest Foundation for Biomedical Research

SOURCE: Kaiser, 2011; United States GAO, 2009a

Table E9-2 Planned BSL-4 Labs in the United States That Were not Operational as of September 2011.

Laboratory	Location
NIAID Integrated Research Facility	Fort Detrick, MD
National Biodefense Analysis & Countermeasures Center	Fort Detrick, MD
USAMRIID Recapitalization[a]	Fort Detrick, MD
Boston University National Emerging Infectious Diseases Laboratories (NEIDL)[b]	Boston, MA
Virginia Division of Consolidated Laboratories[c]	Richmond, VA
National Bio- and Agro-Defense Facility	Manhattan, KS

SOURCE: Kaiser, 2011.

[a]This lab will replace the existing USAMRIID facility, which will be decommissioned.

[b] For more information see: *http://www.bu.edu/dbin/neidl/en/*. Accessed October 6, 2011.

[c]The Virginia DCLS facility will be built according to BSL-4 specifications, but due to lack of funding for personnel, will likely operate as a BSL-3+. See: *http://vaperforms.virginia.gov/agencylevel/stratplan/spReport.cfm?AgencyCode=194*. Accessed October 6, 2011.

[1] For a list of Select Agent Pathogens, see: *http://www.selectagents.gov/resources/List%20of%20Select%20Agents%20and%20Toxins_111708.pdf* . Accessed October 6, 2011.

Private companies, non-profits, academic institutions as well as state, local, and federal agencies maintain high-containment facilities. The Department of Defense (DOD), the Department of Homeland Security (DHS), and the Department of Health and Human Services (HHS) operate the main government facilities, sometimes through contracts with private organizations. DOD operates the United States Army Medical Research Institute for Infectious Diseases (USAMRIID).[2] DHS operates the new National Biodefense Analysis and Countermeasures Center (NBACC) through a contract with Battelle National Biodefense Institute and maintains the Plum Island Animal Disease Center, which is scheduled to be replaced eventually by the National Bio and Agro-Defense Facility (NBAF) in Manhattan, Kansas.[3] HHS funds multiple BSL-3 facilities at the NIH and BSL-4 facilities at the CDC. In addition, HHS, through the National Institute of Allergy and Infectious Diseases (NIAID), partially funded construction of the Galveston and Boston University National Laboratories (BSL-4) and 13 BSL-3 Regional Biocontainment Laboratories (Table E9-3).[4] These laboratories are distributed across the United States to conduct research and assist with public health efforts during emergencies. Additionally, HHS funds the Laboratory Response Network (LRN) that includes over 140 Reference Laboratories that have BSL-3 capabilities and can perform confirmatory testing.[5] LRN Reference Laboratories include state and local public health labs as well as military, federal, and international (i.e., Canada, Australia, and United Kingdom) facilities.

Table E9-3 Regional Biocontainment Laboratories (RBL).

Laboratory	**Location**
Tufts Regional Biosafety Laboratory	North Grafton, MA
Regional Biocontainment Laboratory at Biomedical Science Tower 3	Pittsburgh, PA
Center for Predictive Medicine	Louisville, KY
Colorado State University Regional Biocontainment Laboratory	Ft. Collins, CO
George Mason University RBL	Manassas, VA
Global Health Research Building	Durham, NC
Howard T Ricketts Laboratory RBL	Chicago, Il
Pacific RBL (under construction)	Honolulu, HI
Southeast Biosafety Laboratory	Birmingham, AL
Tulane National Primate Research Center	Covington, LA
University of Missouri- Columbia RBL	Columbia, MO
University of Tennessee RBL	Memphis, TN
New Jersey Medical School Center for Infectious Disease Research RBL	Newark, NJ

SOURCE: Kaiser, 2011 and *http://www.niaid.nih.gov/LabsAndResources/resources/dmid/NBL_RBL/Pages/site.aspx*. Accessed October 6, 2011.

2. What government organizations in the United States are responsible for oversight, safety, and security of high-containment biological (high BSL) laboratories?

No single government entity has total responsibility for the safety and security of high-containment laboratories (United States GAO, 2007; see page 4). Instead, oversight is provided by multiple organizations under a number of regulatory frameworks, including:

[2] To learn more about USAMRIID, see: *http://www.usamriid.army.mil/*. Accessed October 6, 2011.
[3] To learn more about NBACC see: *http://www.bnbi.org/*. To learn more about NBAF see: *http://www.dhs.gov/nbaf*. Accessed October 8, 2011.
[4] Available at: *http://www.niaid.nih.gov/LabsAndResources/resources/dmid/NBL_RBL/Pages/site.aspx*. Accessed October 6, 2011.
[5] See: *http://www.bt.cdc.gov/lrn/pdf/lrn-overview-presentation.pdf*. Accessed October 6, 2011.

Select Agent Program

One of the major regulatory programs for high-containment labs in the United States is the Select Agent Program. The program was established in 1996 via the Antiterrorism and Effective Death Penalty Act (P.L. 104-132).[1] This law required the Department of Health and Human Services (HHS) to identify a set of organisms and toxins ("Select Agents") that could be used for bioterrorist attacks and to regulate the transport of those pathogens. Later, the 2001 Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act (USA PATRIOT Act: P.L. 107-56) and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (P.L. 107-188) added restrictions on the possession, use, and transfer of select agent pathogens and toxins. More information on the history of the Select Agent Program may be found in the National Research Council report on Responsible Research with Biological Select Agents and Toxins (NRC, 2009).

The current Select Agent Program covers two lists of pathogens and toxins. The agents on the HHS list are human health threats while those on the United States Department of Agriculture (USDA) list are animal and plant pathogens. Some agents are on both the HHS and USDA lists (overlap agents). The listed agents are to be reviewed every two years. The program also addresses two other areas—*people* who have access to select agents and *facilities* where select agents are used. Additionally, the program monitors the quantity of each agent held by each person at each facility. Scientists who conduct research with pathogens on the select agent list must undergo a background check called a Security Risk Assessment (SRA) with the Department of Justice (DOJ). These clearances are pathogen and institution specific, nontransferable, and valid for three years.[2] (Prior to June 1, 2011, clearances were valid for five years.) Facilities that possess or use select agents must develop and implement a security plan to protect the select agents from theft or improper access and identify a Responsible Official (RO). The RO has the authority and responsibility to ensure compliance with the regulations and report any incidents to the proper authorities.[3] Depending on the pathogen, security plans are submitted either to CDC, USDA's Animal and Plant Health Inspection Service (APHIS), or both for overlap pathogens. A plan must include a site-specific risk assessment, an agent-specific risk assessment, a threat assessment, a vulnerability assessment, and information about physical security, inventory control, and information systems control.[4] CDC and APHIS conduct routine inspections every three years (annually for BSL-4 labs) and may conduct additional inspections at any time if an entity requests a change to its registration.[5] During inspections, both APHIS and CDC use standardized checklists to ensure compliance.[6] Any problems found during an inspection are reported to the institution and must be addressed. If, for example, CDC finds significant problems at a laboratory the following actions may be taken:

> "Administrative actions: CDC can decide to suspend or revoke a registered entity's certificate of registration (a suspension can be for all work at a registered entity or be specific to particular agents or particular types of experiments). Also, CDC can deny an entity's application to possess, use, or transfer select agents;
>
> Referral to HHS-Office of the Inspector General (OIG): CDC can refer possible violations of the select agent regulations to HHS-OIG. HHS-OIG can levy civil monetary penalties (up to $250,000 for an individual for each violation and up to $500,000 for an entity for each violation) or recommend criminal enforcement (imprisonment for up to five years, a fine, or both).

[1] To view the law see: *http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=104_cong_public_laws&docid=f:publ132.104*. Accessed October 6, 2011.
[2] To learn more about SRAs, see: *http://www.selectagents.gov/sra.html*. Accessed October 6, 2011.
[3] See: *http://www.selectagents.gov/resources/Session%201%20-%20RO%20Responsibilities.pdf*. Accessed October 6, 2011.
[4] For more information see: *http://www.selectagents.gov/resources%5CSecurity%20Information%20Document.pdf*. Accessed October 6, 2011.
[5] See: *http://www.hhs.gov/asl/testify/2007/10/t20071004c.html*. Accessed October 6, 2011.
[6] To view the checklists see: *http://www.selectagents.gov/Checklists.html*. Accessed October 6, 2011.

> Referral to FBI: CDC can refer possible violations involving criminal negligence or a suspicious activity or person to the FBI for further investigation."[7]

Through June 29, 2011, the HHS Office of Inspector General (OIG) had accepted a total of $2,127,000 from 16 different organizations to settle allegations of failure to comply with select agent regulations.[8]

To provide oversight of the CDC and APHIS's implementation, the HHS and USDA OIG also conduct audits of the Select Agent Program. In a 2006 HHS audit of 15 universities, OIG found that 8 had inventory weaknesses, 6 had weak security plans, and 6 had access control problems.[9] In a 2006 USDA audit, OIG found multiple weaknesses with the methods that APHIS was using to oversee and regulate the Select Agent Program including an inadequate review of security plans, use of an out-of-date list of individuals with access, and inadequate facility inspections (OIG, USDA, 2006).

In July 2010, Executive Order (EO) 13546, "Optimizing the Security of Biological Select Agents and Toxins in the United States," created the Federal Experts Security Advisory Panel (FESAP), which was tasked to make recommendations to improve the Select Agents Program (Obama, 2010). To better match precautions to actual risks and reduce the impact of excessive security, EO 13546 instructed FESAP to (1) designate a subset of the select agent list as "Tier 1" agents and propose appropriate additional precautions and (2) consider whether any current select agents or toxins might be removed from the list. FESAP subsequently recommended 12 agents and toxins be designated as Tier 1 and 25 agents and toxins be removed from the list (FESAP, 2010).

NIH

The NIH's Guidelines for Research Involving Recombinant DNA Molecules (RAC)[10] provides oversight of laboratories whose investigators receive NIH funding and conduct experiments with recombinant DNA. While many experiments can be reviewed at the institutional level, some experiments require approval from the NIH. Many institutions that do not receive NIH funds voluntarily comply with the RAC guidelines as these are viewed as establishing best practices.

The RAC guidelines require institutions to establish an Institutional Biosafety Committee (IBC) to review research proposals that would require the use of recombinant DNA. Reviews should include an assessment of the procedures, facilities, and practices that would be used in the experiment. The IBC can approve proposals or make recommendations for modifying experiments. In addition, the institution must have a biological safety officer who periodically inspects laboratories, reports violations to the IBC, and prepares emergency plans for dealing with accidental exposures or spills.

OSHA

The Occupational Safety and Health Administration (OSHA) has several mandatory laboratory standards. For example, OSHA Standard 29 CFR 1910.1450 (Occupational Exposure to Hazardous Chemicals in the Laboratory) requires, among other things, that laboratories have a Chemical Hygiene Plan, mandatory employee training, personal protective equipment (PPE) for certain chemicals, and accessible material safety data sheets for all hazardous chemicals.[11] OSHA has also issued a Bloodborne Pathogen Standard, which provides guidance on preventing and responding to worker

---

[7] See: *http://www.hhs.gov/asl/testify/2007/10/t20071004c.html*. Accessed October 6, 2011.
[8] See: *http://oig.hhs.gov/fraud/enforcement/cmp/agents_toxins.asp*. Accessed October 6, 2011.
[9] See: *http://oig.hhs.gov/oas/reports/region4/40502006.pdf*. Accessed October 6, 2011.
[10] For the full NIH Guidelines for Research Involving Recombinant DNA Molecules, see: *http://oba.od.nih.gov/oba/rac/Guidelines/NIH_Guidelines.htm*. Accessed October 6, 2011.
[11] Available at: *http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=10106*. Accessed October 6, 2011.

exposure to blood.[12] OSHA standards apply to public health laboratories and research laboratories at all biosafety levels.

Other Regulators

Many other government entities also play a role in regulation of biosafety and biosecurity in high-containment laboratories. The Departments of State, Commerce, and Treasury, for example, oversee export controls on biological products. Additionally, the Department of Transportation, the United States Postal Service, the International Civil Aviation Organization,[13] and the International Air Transport Association[14] all have regulations regarding the transportation of biological agents.

3. In the United States, are there established criteria for deciding:

a. Whether or not to establish high-containment facilities?

b. Where to place such facilities?

The decision to establish facilities depends on whether the facility is funded by the federal government or will be privately funded. There are, in general, no established criteria for privately funded facilities at universities or private sector institutions on when and where to build facilities. Government facilities or facilities at universities or elsewhere that are funded by the government are established based on the needs and research agendas of individual agencies, and no single government agency has the overall responsibility for determining needed laboratory capacity (United States GAO, 2009a). For example, the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 increased laboratory construction to support research efforts in several areas, including antimicrobial resistance and countermeasures research. Decisions on where to locate facilities are often made through a competitive bid process that solicits proposals from competing entities. The final location is picked based on the scientific and technical merit of a proposal as well as other factors, such as public support, transportation, and site accessibility. Risk assessments are conducted to assess the likelihood and consequences associated with possible pathogen releases (NRC, 2008). Construction of federally funded facilities also requires preparation of environmental impact statements and increasingly involves engaging the local community.

c. What research will be done in such facilities?

High-containment biological laboratories are used for basic research, applied research, medical product testing and evaluation, and animal efficacy[15] studies (United States GAO, 2007). The research done at government-funded facilities includes both investigator-proposed projects and projects proposed by the sponsoring agencies. Grants are awarded competitively. DOD, NIH, and other government entities fund research grants.

d. What scientific, technical, and management advice is available to governments when making their decisions?

A number of groups and organizations provide advice on the subject including:

National Research Council

The National Research Council (NRC), which is a part of the National Academies, writes independent, expert reports to advise the government and increase public understanding on matters

[12] Available at: *http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051*. Accessed October 6, 2011.

[13] For more information, see: *http://www.icao.int*. Accessed October 6, 2011.

[14] For more information, see: *http://www.iata.org*. Accessed October 6, 2011.

[15] Information about "Animal Rule" studies to demonstrate efficacy for Food and Drug Administration (FDA) product licensure may be found in 21 CFR Parts 314 and 601: *http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=314* and *http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=601*. Accessed October 6, 2011.

related to science, engineering, and medicine.[16] The NRC has commented on risk assessments for several high-containment labs including facilities at Fort Detrick, Maryland (NRC, 2010a); Boston, Massachusetts (NRC, 2007); and Manhattan, Kansas (NRC, 2010b). The NRC has also issued a number of reports on biosafety and biosecurity.

NSABB

The National Science Advisory Board for Biosecurity (NSABB) was formed by 42 U.S.C. 217a, section 222 of the Public Health Service Act and is governed by the Federal Advisory Committee Act. The NSABB was created in response to the recommendations made in the 2004 NRC report, *Biotechnology Research in an Age of Terrorism*.[17] It includes non-governmental voting members and non-voting members from 15 federal agencies and departments. Members' areas of expertise cover a wide range of topics, including: microbiology, biodefense, food production, export controls, law, and others.[18] The NSABB advises the Secretary of HHS and other government leaders on policies related to dual use research in the life sciences by issuing reports and recommendations. For example, in September 2011, NSABB released a report on *Guidance for Enhancing Personnel Reliability and Strengthening the Culture of Responsibility* (NSABB, 2011).

Working Group on Strengthening the Biosecurity of the United States

Executive Order 14386,[19] Strengthening Biosecurity of the United States, created the Working Group on Strengthening the Biosecurity of the United States on January 9, 2009. The Secretary of Defense and Secretary of HHS chair the group, which also consists of the Director of National Intelligence, the Director of the National Science Foundation, the Attorney General, and the Secretaries of State, Commerce, Agriculture, Transportation, and Energy. The group reviewed existing laws, regulations, and practices and made recommendations to the President in November 2009 in a report titled *National Strategy for Countering Biological Threats*.[20]

4. What standards exist for high biological containment laboratories in the United States for engineering and construction, licensing, safety, security, regular oversight, and certification?

General Standards

The CDC-NIH publication *Biosafety in Microbiological and Biomedical Laboratories* (BMBL), which is currently in its 5th edition, has served as the standard code of practice for biosafety since 1984 (United States HHS, 2009). The BMBL provides guidance on all areas of biosafety and biosecurity including decontamination, transportation, containment level recommendations, and agent-specific practices. BMBL guidelines have been widely adopted and are mandatory for research conducted using federal grants. Noncompliance may result in the loss of funding (CRS, 2009). Federal laboratories, and most other facilities built using federal funds, are built to standards established by the funding agency. For example, to receive NIH money, laboratory engineering and construction must comply with the NIH

[16] See: *http://www.nationalacademies.org/about/*. Accessed October 6, 2011.
[17] To view the report, go to: *http://www.nap.edu/catalog.php?record_id=10827*. Accessed October 6, 2011.
[18] For more information on the NSABB see: *http://oba.od.nih.gov/biosecurity/PDF/NSABB_Charter_508_accessible.pdf* or *http://oba.od.nih.gov/biosecurity/biosecurity.html*. Accessed October 6, 2011.
[19] To view the Executive Order see: *http://edocket.access.gpo.gov/2009/E9-818.htm*. Accessed October 6, 2011.
[20] The report can be found at: *http://www.whitehouse.gov/sites/default/files/National_Strategy_for_Countering_BioThreats.pdf*. Accessed October 6, 2011.

Design Requirements Manual.[21] Additionally, those laboratories that work with select agents or recombinant DNA must abide by those programs' previously mentioned standards.

Training

Training is required for personnel whose labs fall under the jurisdiction of the OSHA standards, the NIH guidelines, or the Select Agent Program. Rather than being standardized, training is specialized to the agents, risks, and activities in which the trainee will engage. In the case of select agent work, refresher training must be provided annually (CRS, 2009). High-containment labs commonly supplement didactic training with mentored, within-laboratory training (Le Duc et al., 2008).

Many organizations provide resources and guidelines for biosafety and biosecurity training:

- The Sandia National Laboratories' International Biological Threat Reduction Program aims to reduce biological threats worldwide by, among other things, promoting the responsible use of biological agents, equipment, and expertise and improving the understanding of accidental and deliberate biological risks.[22]
- The CDC has online course modules and exercises for training in biosafety and biosecurity.[23]
- University of Texas Medical Branch maintains the National Biocontainment Training Center that provides training in biosafety and biosecurity to United States and international students, as well as on-site fellowships offering mentored training for individuals preparing for work at BSL-4 and for containment laboratory managers and engineers.[24]
- Yale Center for Public Health has online course resources for biosafety training based on a course taught at the school, designed in part for those interested in implementing biosafety and biosecurity courses at their own facilities.[25]
- Biosafety and animal safety training tools are available on the American Biological Safety Association (ABSA) website.[26]

Commissioning Labs

Although there is no formal regulatory requirement for "commissioning," when a new lab is built, a commissioning process may take place to ensure the lab meets safety standards. Agencies often contract out the process of commissioning a laboratory. Some agencies, for example the NIH, have specific checklists[27] and guidelines[28] for commissioning. A similar process occurs in other agencies and generally follows the recommendations of the BMBL. The commissioning documents are part of what must be presented during the select agent inspection that will eventually authorize high-containment labs to begin work with select agents (CRS, 2009).

5. Have there been any high-containment lab accidents in the United States?
   a. If yes, how and why did accidents at high-containment facilities occur?
   b. How, to whom and when are they reported?
   c. Who has authority to investigate accidents?

---

[21] See: *http://orf.od.nih.gov/NR/rdonlyres/AF690C46-0388-4180-9603-3060F3078F5F/25782/NIHDesignRequirementsManualver711.zip*. Accessed October 6, 2011.
[22] See: *http://biosecurity.sandia.gov/*. Accessed October 6, 2011.
[23] See: *http://www.cdc.gov/od/ohs/biosecurity_training/page2790.html*. Accessed October 6, 2011.
[24] See: *http://www.utmb.edu/nbtc*. Accessed October 6, 2011.
[25] See: *http://publichealth.yale.edu/ycphp/biosafety/biosafety.html*. Accessed October 6, 2011.
[26] See: *http://www.absa.org/trainingtools.html*. Accessed October 6, 2011.
[27] Department of Health and Human Services, National Institutes of Health, *Biosafety Level 3-Laboratory Certification Requirements*.
[28] The NIH is currently working on a new version of *The NIH Model Commissioning Guide*. Section 1-7 of the NIH Design Requirements Manual discusses commissioning: *http://orf.od.nih.gov/NR/rdonlyres/AF690C46-0388-4180-9603-3060F3078F5F/25782/NIHDesignRequirementsManualver711.zip. Accessed October 6, 2011.*

d. What disciplinary or legal actions can be taken?

e. Have any steps been taken to minimize BSL laboratory accidents?

Accidents, some of which result in laboratory-acquired infections (LAIs), occur regularly albeit at a low level in United States high-containment laboratories. For example, between 1982 and 2003, personnel at NIAID intramural laboratories worked with microorganisms for more than 3 million hours in BSL-3 laboratories or BSL-2 laboratories with BSL-3 practices and experienced a total of 29 exposures of which only 1 resulted in a clinical infection and 4 resulted in silent infections (Johnson, 2004). Laboratory accidents may result from either human error or equipment or engineering malfunction, and often the specific cause of a suspected LAI cannot be determined (Pike, 1979). FESAP recently proposed that occupational health programs be mandatory for individuals with access to Tier 1 agents, which would aid in identifying LAIs (FESAP, 2010). Table E9.4 contains a partial list of United States laboratory accidents. Additional information about LAIs observed in conjunction with United States containment lab work may be found in the NRC report, *Protecting the Frontline in Biodefense Research: The Special Immunizations Program* (NRC, 2011).

Table E9-4 Examples of Accidents in United States Biosafety Labs.

Location	Agent	Description	Date	Source
Human Error				
New Hampshire	Vaccinia	Accidental exposure from needlestick	9/2007	CDC, 2008
unknown	*Yersinia pestis*	Potential exposure when employee stuck self with broken scalpel blade	8/2007	Field, 2007
Maryland	Vaccinia	Accidental exposure from needlestick	8/2007	CDC, 2008
University of South Alabama	*Ricketssia prowazekii*	Worker drops plate and splashes self	7/2007	Field, 2007
U.C. Davis	*Brucella*	Potential exposure due to needlestick	7/2007	Field, 2007
University of Iowa	Tularemia	Potential exposure due to needlestick	5/2007	Field, 2007
Iowa	Vaccinia	Accidental exposure from needlestick	5/2007	CDC, 2008
UT San Antonio	Tularemia	Workers entered lab wihout PPE, unlikely exposure	4/2007	Field, 2007
unknown	*Brucella*	Researcher ill because of improper decontamination procedures	4/2007	Field, 2007
Pennsylvania	Vaccinia	Accidental exposure from needlestick	10/2006	CDC, 2008
Saint Louis University	monkeypox	Worker exposed from needlestick	8/2006	CDC, 2008
University of Chicago	Anthrax	Worker exposed to Anthrax after needlestick	7/2006	CDC, 2008
Connecticut	Vaccinia	Accidental exposure from needlestick	3/2005	CDC, 2008
Children's Hospital and Research Center Oakland, CA	Anthrax	Scientists exposed after live anthrax samples accidentally get shipped to the lab	6/2004	CDC, 2008
USAMRIID	Ebola	Accidental exposure from needlestick	2/2004	Kaiser, 2007
unknown	West Nile Virus	Lab worker contacts virus after accidentally cutting finger with scalpel	12/2002	CDC, 2008
unknown	West Nile Virus	Lab worker contracts virus after needlestick	8/2002	CDC, 2008
University of Texas	*Anthrax*	Cutaneous anthrax of lab worker	4/2002	Field, 2007
USAMRIID	Junin virus	Bone fragment from monkey punctured finger during autopsy	12/1982	Johnson, 2004
USAMRIID	Lassa virus	Accidental needle stick in finger	11/1979	Johnson, 2004
Equipment/Engineering Error				
University of GA	none	Flooding occurred twice of high-containment laboratory after sterilizer failed to shut off	2008	Schneider and Hart, 2008
CDC	*Coxiella burnetii*	CDC used duct tape to secure facility after air filtration system failed during maintenance	2007	Young, 2008

University of Mississippi Medical Center	Anthrax	Potential exposure from broken flask spill	8/2007	Field, 2007
University of Texas Health Science Center	Anthrax	Potential exposure after fluid discovered in bottom of centrifuge	5/2007	Field, 2007
unknown	*Brucella*	Potential exposure after cap came off tube	8/2006	Field, 2007
University of Virginia	Tularemia	Potential exposure from cracked tube	8/2006	Field, 2007
University of Kentucky	*Yersinia Pestis*	Worker exposed after autoclave bag leaked	5/2006	Field, 2007
Tufts University	Botulinum neurotoxin	Potential exposure after broken vial found in centrifuge	4/2006	Field, 2007
unknown	*Coccidioides immitis*	Potential exposure after broken vial containing agent found in centrifuge	9/2005	Field, 2007
Plum Island		3 hour power failure	12/2003	Santora, 2002
Rocky Mountain Laboratory	*Yersinia pestis*	Open container fell off shaker	2001	Johnson, 2004
Unknown/Miscellaneous Error				
unknown	*Coxiella burnetii*	Blood tests show potential exposures of 10 people to agents	2007	Field, 2007
unknown	Tularemia	Potential exposure after bitten by infected animal	7/2007	Field, 2007
unknown	*Yersinia pestis*	Lab worker potentially scratched by infected animal	4/2007	Field, 2007
Lovelace Respiratory Research Institute	*Yersinia pestis*	Lab worker bit by infected animal	9/2006	Field, 2007
Texas A&M	*Brucella*	Lab workers infected while cleaning aerosol chamber; failure to report to CDC	2/2006	United States GAO, 2007
Public Health Research Institute at UMDNJ	*Yersinia pestis*	Infected mice missing	8/2005	Field, 2007
UNC-Chapel Hill	Venezuelan equine encephalitis	Blood test show possible exposure	9/2004	Field, 2007
Medical College of Ohio	*Coccidioides immitis*	Lab worker contracts coccidioidomycosis, unknown route of exposure	8/2004	Field, 2007
Boston University Medical Center	Tularemia	3 scientists infected with Tularemia over 5 months	2004	Field, 2007
Rocky Mountain Laboratory	*Mycobacterium tuberculosis*	Skin test converted; cause was likely improperly inactivated samples	2000	Johnson, 2004
Rocky Mountain Laboratory	*Chlamydia trachomatis*	Worker hospitalized and successfully treated with antibiotics; no specific cause determined	1998	Johnson, 2004
Yerkes Primate Center	Simian Herpesvirus	Exposed research assistant dies	6/1998	Wrobel, 1998
Rocky Mountain Laboratory	*Mycobacterium tuberculosis*	Skin test converted; no specific cause determined	1996	Johnson, 2004
Yale University	Sabia	Researcher contracts virus and exposes 75 other co-workers	8/1994	Glass, 1994
Plum Island	Foot and mouth disease	Accidental release of virus into holding pens	1978	Margasak, 2008

SOURCE: NRC Staff.

In the event of a theft, loss, or release of a select agent, the Select Agent Program currently requires a laboratory to notify the CDC and/or APHIS immediately (within 24 hours).[29] Appropriate federal, state, or local law enforcement must also be notified in the event of loss or theft; health agencies, such as local employee health services, must be notified if there is a risk of human infection. Additionally, the facility must submit APHIS/CDC Form 3 within seven days of the incident.[30] CDC or APHIS then conducts an investigation into the incident to determine the cause, actions that can be taken to mitigate future accidents, and whether further actions such as revocation of approval to work with select agents, fines, and/or potential criminal enforcement actions are needed.

Laboratories not in the select agent program typically have their own rules for accident reporting. For example, overt or potential exposures in BSL-3 and BSL-4 labs that occur in the course of research subject to NIH Recombinant DNA guidelines must be reported to the NIH Office of Biotechnology Activities immediately.

Increasingly, laboratories are making data on accidents publically available. For example, since 2002, University of Texas Medical Branch has published all incidents of laboratory accidents and potential exposures occurring in its research laboratories quarterly on its website.[31]

There have been several recent cases in which laboratories failed to report accidents in a timely manner. In 2006, Texas A&M did not report laboratory-acquired infections of *Brucella* and *Coxiella burnetii* that were later exposed through a Freedom-of-Information Act (FOIA) request.[32] The CDC ultimately shut down select agent research at the laboratory until all problems identified in the subsequent investigation were addressed and the university agreed to pay a $1 million fine (Kaiser, 2008). At Boston University in 2004, three individuals who worked with a vaccine strain of *Francisella tularensis* (not a select agent) became ill with tularemia.[33] While two of the cases occurred in May and one in September, none was reported to the public health authorities until November. An investigation revealed that their stock of the vaccine strain had became contaminated by unknown means with Type A *F. tularensis*, which is a select agent. OSHA proposed fines of $8,100 for each of Boston University and Boston Medical Center Corporation for their failure to ensure proper use of personal protective equipment.[34] The lack of transparency at Boston University has greatly increased public concern about the new National Emerging Infectious Diseases Laboratory, for which the United States government is preparing additional risk assessments with advice from the National Research Council.[35]

6. Have any steps been taken to increase security at high biological containment facilities?

While select agent rules do not mandate specific physical security requirements, BSL-4 laboratories are increasingly employing visible 24/7 armed guards, controlled access, vehicle barriers, and closed-circuit television monitoring (United States GAO, 2009b). Additionally, since 2008 many Department of Defense containment laboratories have been subject to Army Regulation 50-1, which established a biological 'surety' program that defines criteria for evaluating personnel reliability (Department of the Army, 2008).

---

[29] See: *http://www.selectagents.gov/resources/CDC-APHIS_Theft_loss_Release_Information_Document.pdf*. Accessed October 6, 2011.

[30] CDC/APHIS Form 3 is available at: http://www.selectagents.gov/TLRForm.html. Accessed October 6, 2011.

[31] Safety and Security/Incident Reports. Available at: http://www.utmb.edu/gnl/safety/report.shtml. Accessed October 17, 2011.

[32] To learn more about the Texas A&M incident see: *http://www.cidrap.umn.edu/cidrap/content/bt/bioprep/news/sep1907biolab.html* and *http://www.sunshine-project.org/TAMU/CDCTAMUReport.pdf*. Accessed October 6, 2011.

[33] See: *http://www.bphc.org/programs/cib/environmentalhealth/biologicalsafety/forms%20%20documents/tularemia_report_2005.pdf.* Accessed October 6, 2011.

[34] See: *http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=NEWS_RELEASES&p_id=11351*. Accessed October 6, 2011.

[35] To view the NAS report, see: *http://www.nap.edu/catalog.php?record_id=12208*. Accessed 6 October 2011.

Additionally, FESAP made a number of security recommendations that will be considered during the next revision of the Select Agent Regulations (FESAP, 2010). In particular, FESAP:

- Defined appropriate personnel reliability practices, including provisions for on-going monitoring, for individuals with access to Tier 1 agents and toxins and for individuals with access to other select agents and toxins;
- Specified physical and cyber security requirements for facilities with Tier 1 agents and for facilities with other select agents and toxins; and
- Recommended that facilities document protocols for shipping, storing, and receiving select agents and toxins.

REFERENCES

Centers for Disease Control and Prevention (CDC). 2008. Laboratory-Acquired Vaccinia Exposures and Infections—United States, 2005-2007. *Morbidity and Mortality Weekly Report* 57(15):401-404.

Department of the Army. 2008. Nuclear and Chemical Weapons and Materiel: Biological Surety. Army Regulation 50-1. Headquarters, Department of the Army: Washington, D.C. 28 July 2008. 54 pp. [Online]. Available: http://www.fas.org/irp/doddir/army/ar50-1.pdf.

Federal Experts Security Advisory Panel (FESAP). 2010. *Recommendations Concerning the Select Agent Program*. [Online.] Available: http://www.phe.gov/Preparedness/legal/boards/fesap/Documents/fesap-recommendations-101102.pdf.

Field, K. 2007. After Accidents, Laboratory Safety Is Questioned. *The Chronicle of Higher Education* 54(8):A19.

Glass, S. 1994. Researcher at Yale gets virus after spill. Pittsburgh Post-Gazette August 22, 1994. [Online.] Available: http://news.google.com/newspapers?id=SIgNAAAAIBAJ&sjid=3m8DAAAAIBAJ&pg=6700,3927504&dq=high+containment+lab+accident.

Johnson, K.M. 2004. Appendix D: Review of Biocontainment Laboratory Safety Record. In: *Final Environmental Impact Statement Integrated Research Facility Rocky Mountain Laboratories Hamilton, Montana / Biosafety BSL-4: More than 20 Years Experience at Three Major Facilities*. National Institutes of Health, Bethesda, MD. pp D1-D18.

Kaiser, J. 2007. Accidents Spur a Closer Look at Risks at Biodefense Labs. *Science* 317:1852-1854.

Kaiser, J. 2008. Texas A&M to Pay $1 Million for Biosecurity Breaches. *ScienceNOW* February 20, 2008. [Online.] Available: http://news.sciencemag.org/sciencenow/2008/02/20-01.html.

Kaiser, J. 2011. Taking stock of the biodefense boom. *Science* 333:1214-1215.

Le Duc, J.W., K. Anderson, M.E. Bloom, J.E. Estep, H. Feldmann, J.B. Geisbert, T.W. Geisbert, L. Hensley, M. Holbrook, P.B. Jahrling, T.G. Ksiazek, G. Korch, J. Patterson, J.P. Skvorak, and H. Weingartl. 2008. Framework for Leadership and Training of Biosafety Level 4 Laboratory Workers. *Emerging Infectious Diseases* 14(11):1685-1688.

Margasak, L. 2008. Accidents at Disease Lab Acknowledged. The Associated Press April, 11, 2008. [Online.] Available: http://www.foxnews.com/wires/2008Apr11/0,4670,AnimalDisease,00.html.

National Research Council (NRC). 2007. *Technical Input on the National Institutes of Health's Draft Supplementary Risk Assessments and Site Suitability Analyses for the National Emerging Infectious Diseases Laboratory, Boston University: A Letter Report*. Washington, D.C.: National Academies Press.

National Research Council. 2008. *Technical Input on Any Additional Studies to Assess Risk Associated with Operation of the National Emerging Infectious Diseases Laboratory, Boston University: A Letter Report*. Washington, D.C.: National Academies Press.

National Research Council. 2009. *Responsible Research with Biological Select Agents and Toxins*. Washington, D.C: National Academies Press.

National Research Council. 2010a. *Evaluation of the Health and Safety Risks of the New USAMRIID High-containment Facilities at Fort Detrick, Maryland*. Washington, D.C.: National Academies Press.

National Research Council. 2010b. *Evaluation of a Site-Specific Risk Assessment for the Department of Homeland Security's Planned National Bio- and Agro-Defense Facility in Manhattan, Kansas*. Washington, D.C.: National Academies Press.

National Research Council. 2011. *Protecting the Frontline in Biodefense Research: The Special Immunizations Program*. Washington, D.C.: National Academies Press.

National Science Advisory Board for Biosecurity (NSABB). 2011. Guidance for Enhancing Personnel Reliability and Strengthening the Culture of Responsibility. [Online.] Available: http://oba.od.nih.gov/biosecurity/pdf/CRWG_Report_final.pdf.

Obama, B. 2010. *Optimizing the Security of Biological Select Agents and Toxins in the United States*. Executive Order 13546. July 2, 2010. [Online.] Available: http://www.gpoaccess.gov/presdocs/2010/DCPD-201000572.pdf.

Office of Inspector General, United States Department of Agriculture (OIG, USDA). 2006. Audit Report: Animal and Plant Health Inspection Service Evaluation of the Implementation of the Select Agent or Toxin Regulations Phase II. Report No. 33601-3-AT. [Online.] Available: http://www.usda.gov/oig/webdocs/33601-3-AT.pdf.

Pike, R.M. 1979. Laboratory-associated infections: incidence, fatalities, causes, and prevention. *Annual Review of Microbiology* 33:41-66.

Public Law 107-56: *Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism (USA Patriot Act) Act of 2001*. (115 Stat. 272, 10/26/2001). [Online]. Available at: http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=107_cong_public_laws&docid=f:publ056.107.pdf.

Public Law 107-188: *Public Health Security and Bioterrorism Preparedness and Response Act of 2002*. (116 Stat. 594, 06/12/2002). [Online]. Available: http://www.epa.gov/watersecurity/pubs/security_act.pdf.

Santora, M. 2002. Power Fails for 3 Hours at Plum Island Infectious Disease Lab. *The New York Times* December 20, 2002. [Online.] Available: http://www.nytimes.com/2002/12/20/nyregion/power-fails-for-3-hours-at-plum-island-infectious-disease-lab.html?src=pm.

Schneider, C. and A. Hart. 2008. Flooding at UGA germ lab revealed. *The Atlanta Journal-Constitution* November 2, 2008. [Online.] Available: http://www.ajc.com/metro/content/metro/stories/2008/11/02/lab_1102_2DOT.html.

United States Congressional Research Service (CRS). 2009. *Oversight of High-Containment Biological Laboratories: Issues for Congress*. By: Gottron, F. and D.A. Shea. R40418, May 4, 2009. [Online.] Available: http://www.fas.org/sgp/crs/terror/R40418.pdf.

United States Government Accountability Office (United States GAO). 2007. *High-containment biosafety laboratories: Preliminary observations on the oversight of the proliferation of BSL-3 and BSL-4 laboratories in the United States*. Testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. GAO-08-108T. Washington, D.C. [Online. Available: http://www.gao.gov/new.items/d08108t.pdf.

United States Government Accountability Office. 2009a. *High-containment laboratories: National strategy for oversight is needed*. Report to Congressional Requesters. GAO-09-574. Washington, D.C. [Online]. Available: http://www.gao.gov/new.items/d09574.pdf.

United States Government Accountability Office. 2009b. *Biosafety Laboratories: BSL-4 Laboratories Improved Perimeter Security Despite Limited Action by CDC*. GAO-09-1038T. Washington, D.C. [Online.]. Available: http://www.gao.gov/new.items/d091038t.pdf.

United States Department of Health and Human Services (United States HHS). 2009. *Biosafety in Microbiological and Biomedical Laboratories*. 5th Edition. HHS Publication No. (CDC) 21-1112. Washington, D.C. 438 pp. [Online]. Available: http://www.cdc.gov/biosafety/publications/bmbl5/BMBL.pdf.

Wrobel, S. 1998. Yerkes 'family' pulled together after death of young researcher from rare Herpes B infection. *Emory Report* 50(16).

Young, A. 2008. CDC action at germ lab questioned. *The Atlanta Journal-Constitution* June 22, 2008. [Online.] Available: http://www.ajc.com/search/content/news/stories/2008/06/22/cdclab.html.