



The Bioterrorism Threat and Laboratory Biosecurity

**International Biological Threat Reduction Department
Sandia National Laboratories
October 15, 2006**

**Overview of the Principles of Laboratory Biosecurity
ABSA pre-conference course**

www.biosecurity.sandia.gov

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“A Biological Weapons Risk Assessment”

Scenario	Probability	Consequences	Risk
Biocrimes	High based on historical evidence	Very low by definition	Low
Biological warfare (non-rogues states)	Very low based on historical record	High based on technical sophistication of non-rogue states	Low
Biological warfare (rogue states)	Low based on historical record	Moderate based on technical sophistication of rogue states	Low to moderate
Bioterrorism (non-state actors)	Low to moderate based on historical evidence, but increasing	Low to moderate based on the historical record and technical expertise, but increasing	Low to moderate, but increasing

Salerno et al., *Nonproliferation Review* (Fall-Winter 2004)

Strategies to Counter the Bioterrorist Threat

- **Biodefense**
 - Enhance the ability of a country to respond to the next bioterrorist attack
 - A *domestic* strategy designed to reduce the consequences of bioterrorism
- **Biological Weapons Nonproliferation**
 - Reduce the risk that bioscience and biotechnology could be used maliciously
 - An *international* strategy designed to prevent the acquisition, use, and spread of biological weapons



Development of US Policies to Mitigate the Bioterrorist Threat

- **US policymakers have focused on biodefense**
 - Aims to improve the ability of the US to respond domestically to an outbreak of infectious disease after it has occurred
 - \$35 billion invested since 2001; \$8 billion requested in FY07

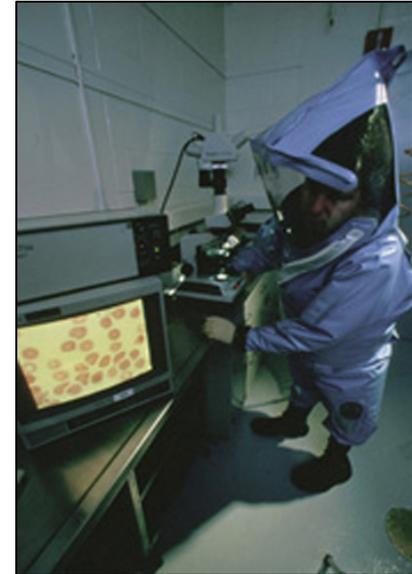
- **Biodefense activities include**
 - Improving diagnostics and disease surveillance
 - Developing detection technologies
 - Strengthening emergency response capabilities
 - Enhancing decontamination and remediation technologies
 - Building public and agricultural health capacities
 - Increasing the effectiveness and availability of vaccines and therapies

- **Recently, the need to develop preventive measures has also been raised:**
 - *“Preventing biological weapons attacks is by far the most cost effective form of biodefense. Prevention requires the continuation and expansion of current multilateral initiatives to limit the access of agents, technology, and know-how to countries, groups, or individuals seeking to develop, produce and use these agents.”*

- Homeland Security Presidential Directive 10

Challenges for the Development of Preventive Solutions

- **Terrorists no longer need sophisticated processing and dissemination systems to threaten international security**
- **Materials, technologies, and expertise are distributed among thousands of legitimate bioscience facilities worldwide**
- **Excessive controls on the biotechnology industry will jeopardize critical research without providing tangible security benefits**



US Domestic Efforts to Reduce Access to Dangerous Biological Materials

- **Realization that bioscience facilities are potential sources of biological weapons material**
- **USA PATRIOT Act of 2001 – US Public Law 107-55**
 - **Restricted Persons**
- **Bioterrorism Preparedness Act of 2002 – US Public Law 107-188**
 - **US Select Agent Rule**
 - **Hazardous Material transport security**
- **No international standards for managing dangerous pathogens internationally**



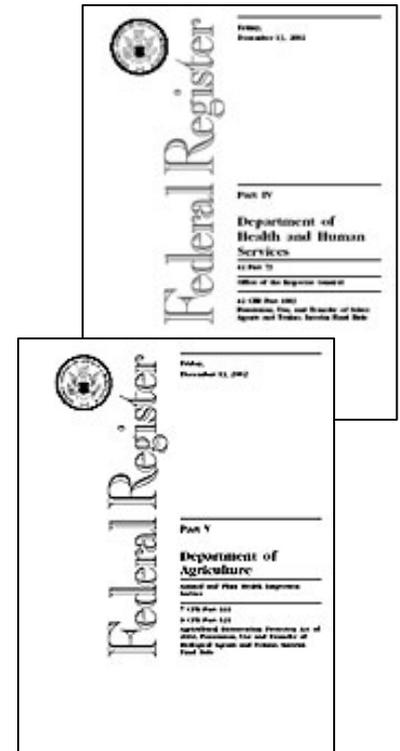
*National Animal Disease Center,
Ames, Iowa*



*Centers for Disease Control and
Prevention, Atlanta, Georgia*

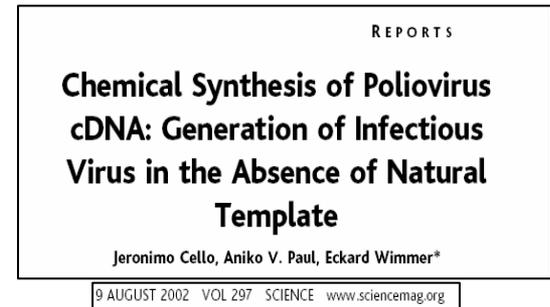
US Select Agent Rule (2005)

- Facility registration if it possesses one of 81 Select Agents
- Facility must designate a Responsible Official
- Background checks for individuals with access to Select Agents
- Access controls for areas and containers that contain Select Agents
- Detailed inventory requirements for Select Agents
- Security, safety, and emergency response plans
- Safety and security training
- Regulation of transfers of Select Agents
- Extensive documentation and recordkeeping
- Safety and security inspections



Concerns About US Select Agent Rule

- **Top-down security regime not tailored to laboratory realities**
- **No need to steal a Select Agent to perpetrate bioterrorism**
- **Fear that security will trump biosafety, increasing the risk of accidental release or exposure**
- **Security requirements increasing operational impediments and compromising research funding**
- **The rule gives no guidance on how to apply graded protection or assess the risk for the listed agents and toxins**
- **No protection if personnel do not understand and accept security**



Heightened Security or Neocolonial Science?

New restrictions on federally funded research involving the world's most dangerous pathogens are hampering foreign collaborations

ALMATY, KAZAKHSTAN—Scott Weaver thought he had a green light for a great research partnership. After an expensive security upgrade of his labs and hours of paperwork, the director for tropical and emerging infectious disease research at the University of Texas Medical Branch (UTMB) in Galveston was ready to resume research on the Venezuelan equine encephalitis (VEE) virus in Colombia, Peru, and Venezuela. The mosquito-borne disease, endemic in all three countries, is not the worst of its kind: The alphavirus kills less than 1% of its human victims. But VEE's potential to incapacitate has landed it on a list of "select agents": several dozen of the nastiest sorts of pathogens that the U.S. government fears could be turned into biological weapons. That designation has thrown up new hurdles for Weaver and his collaborators in South America—and for many other U.S. scientists working overseas.

In August, the U.S. National Institute of Allergy and Infectious Diseases (NIAID) informed Weaver that under the terms of his two VEE grants, the laboratories of his foreign colleagues must have procedures in place for handling select agents that are equivalent to tough U.S. regulations imposed last year. "I seriously doubt whether my collaborators in Caracas or Bogotá could ever meet U.S. standards for select-agent security," says Weaver. "These developing countries cannot afford the kinds of elaborate systems that labs in the U.S. have been required to install," such as sophisticated security and inventory systems and background checks on employees. He's since had to alter his projects to avoid isolating the VEE virus in the labs south of the border. Because the new policy may force some foreign partners to serve as mere sample exporters, it resurrects "the stereotype of the ugly American: arrogant, demanding, and insensitive," Weaver charges: "American collaborations will be unwelcome in many developing countries of the world."

Although his case may be one of the first, Weaver is not the only researcher feeling the

chill. According to a prominent U.S. specialist on select agents, researchers with the U.S. Centers for Disease Control and Prevention (CDC) have seen a curtailment of foreign collaborations on avian flu and viral hemorrhagic fevers. (CDC officials declined to comment.) Scientists at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) in Frederick, Maryland, are experiencing sim-



No picnic. Venezuelan scientists draw blood from rodents to isolate VEE virus. New NIH rules have crippled projects on this and other select agents.

ilar constraints on projects involving Congo-Crimean hemorrhagic fever and related diseases. "The important work we need to do will get done," says USAMRIID public affairs officer Carole Vander Linden, although the details have not been worked out.

U.S. inspectors will soon be heading out to assess lab standards overseas, scientists learned at a closed-door meeting last month. Paul Strickland, acting director of NIAID's Office of International Extramural Activities, told a group at the annual meeting of the American Society of Tropical Medicine and Hygiene (ASTMH) in Miami, Florida, that security teams will include senior microbiologists from CDC's select-agent program. An interagency committee chaired by Strickland with representatives from the U.S. State and Justice departments will determine whether foreign labs "meet minimum biosafety and biosecurity requirements."

The stepped-up regulations are the latest example of the clash between scientists' cher-

ished ways of doing business and the urgent need to reduce the potential for bioterrorism, and some researchers say the rules make sense. "It would be very embarrassing for a U.S. collaborator and a U.S. agency to be funding a facility that had a major accident, or one that was involved in a bioterrorism event," says Paul Keim, an anthrax specialist at Northern Arizona University in Flagstaff.

But others fear that the tightened security could stifle cooperation. "One doesn't develop productive collaborative relationships with foreign counterparts by announcing upon arrival that 'from now on we must do things the American way,'" says UTMB arbovirus specialist Robert Tesh. "Each country has its security priorities. The U.S. cannot demand that they conform to ours."

Adds Weaver: "By inhibiting research on the ecology and epidemiology of potential biological weapons in their natural settings overseas, we will be less prepared to respond optimally to the introduction of these agents by a terrorist."

Clampdown

After letters containing powdered anthrax were mailed to members of Congress and others in the fall of 2001, the U.S. government crafted tough requirements for scientists it funds to study dangerous pathogens. In addition to tightening security at facilities in which the microbes are kept and studied, U.S. regulations now demand rigorous protocols covering security assessments, emergency response plans, training, transfers of materials, and inspections.

Under the new NIAID rules, which the institute began developing in 2003, U.S. grantees must submit a dossier on a foreign collaborating institution detailing its "policies and procedures for the possession, use, and transport of select agents." For what NIAID calls "security risk assessments," grantees "must be willing to provide the names of all individuals who will have access to the select agents."

Weaver says the new rules prompted him to drop his original plan to process field samples potentially infected with VEE virus in South America. Now, he says, he will have all the samples shipped to Galveston. "This seems to have gotten me off the hook for the time being," he says, in that his colleagues at the National Institute of Health in Bogotá and the Central University of Venezuela and the National Institute of Hygiene in Caracas now won't have to adhere to the select-agent

A Selection of Select Agents

Smallpox virus
Crimean-Congo hemorrhagic fever virus
Lassa fever virus
Central European tick-borne encephalitis
Yersinia pestis (plague)
Foot-and-mouth disease virus

Ebola viruses
Ricin
Tetrodotoxin
Bacillus anthracis (anthrax)
Venezuelan equine encephalitis virus
Botulinum neurotoxin



terms. But the change will reduce efficiency and timeliness, he says.

"Basically, the NIH [U.S. National Institutes of Health] left me with little choice," because it would have taken "months or years" to bring overseas labs into compliance, Weaver says. Already, the labs in Colombia and Venezuela store many VEE virus isolates in their freezers: Preventing the isolation of a few more strains, he says, will not deny the virus to a potential terrorist.

Although security at foreign facilities working with select agents generally has been strengthened since the 9-11 attacks, most labs would still run afoul of the new U.S. rules. Many outside the United States appear to be unaware of the regulations. "I haven't heard much," says Lev Soudalchikov, director general of the State Research Center of Virology and Biotechnology, a former bioweapons lab near Novosibirsk, Russia, that collaborates with the United States on smallpox research.

Foreign researchers say they hope to find a way to continue working with U.S. counterparts because it would bolster security in their home countries. "If collaborations will continue, that will inevitably bring the standards up," says Bakyt Atshabar, director of the Kazakh Science Center for Quarantine and Zoonotic Diseases in Almaty, Kazakhstan, which specializes in studying endemic plague with Pentagon funding (*Science*, 17 December, p. 2021).

ASTMH and other societies intend to lobby for a relaxation of the rules. "The approach to this will not be easy," says Peter Weller, an immunologist at Harvard Medical School in Boston and ASTMH's most recent past president. For one, many agencies will want to weigh in on any change of policy. Second, Weller says, "the facile reply is that you scientists gave the Pakistanis nuclear secrets; how do we trust you on these issues?" In an e-mail response to questions from *Science*, NIAID officials say they expect no change to the select-agent terms "in the immediate future."

But some experts such as Keim say raising global security levels to U.S. standards makes sense. "We should not allow U.S. researchers to avoid regulatory oversight by going abroad. This would certainly apply to human subjects in clinical trials and animal-care standards in animal protocols. Why not security of dangerous pathogens?"

Earthquake Preparedness

Some Countries Are Betting That A Few Seconds Can Save Lives

Japan, Mexico, and Taiwan are investing in early warning systems that can offer precious seconds of warning before a major tremor

TOYO—What would you do with 5 to 50 seconds' warning of a major earthquake?

It's not an academic question. Systems that can detect earthquakes near their source and issue warnings before the shaking starts are in place or being deployed in Mexico, Taiwan, and Japan and are being studied for locales from southern California

to Istanbul. Enthusiasts are convinced that short-term warnings can save lives by stopping trains before they pass over damaged track, emptying out elevators, and alerting rescue units. "It is an epoch-making advance in earthquake safety," says Masato Motozuka, a Japanese earthquake engineer at Tohoku University in Sendai.

Not everyone agrees, however. Skeptics note that warning systems don't provide enough time to reduce casualties close to the epicenter of an earthquake. They also worry that such systems could divert spending from earthquake preparedness, which they say has the potential to do much greater good. "Warnings only help in some cases," says Robert Oshinsky, an urban planner at the University of Illinois, Urbana-Champaign. "Investing too much of one's

money and hopes in a short-term warning system is a distraction from the hard and less sexy work, such as upgrading older structures, that is really needed to improve seismic safety."

Faster than a speeding S wave

Early warning systems are not forecasts. Instead, they detect actual quakes near their source and issue warnings to automated systems and humans up to several hundred kilometers away. They work because electronic signals transmitted through wires or air travel faster than seismic waves moving through the earth. Warning schemes also take advantage of the two types of seismic waves that are generated when a fault ruptures. The first—and faster moving—primary (P) waves radiate directly outward from the epicenter. The secondary (S) waves, which cause the oscillating motions responsible for the most damage, lag by tens of seconds over a distance of a few hundred kilometers. "The P waves carry information; the S waves carry energy," explains Hiroo Kanamori, a seismologist at the California Institute of Technology (Caltech) in Pasadena. Unfortunately,



On alert. Newcast stations are being installed across Japan.

Biosecurity Goes Global

The 2001 anthrax letters triggered a strong U.S. response. Now the rest of the world is starting to take biosecurity more seriously—but not necessarily by adopting the U.S. approach

Three years ago, the small number of life scientists using the term “biosecurity” were talking about ways to keep diseased crops and livestock from crossing national borders. Then came the fatal October 2001 anthrax letter attacks against several U.S. targets. In short order, thousands of U.S. scientists were confronted with an avalanche of new and often unpopular rules designed to keep potentially dangerous pathogens and toxins away from bioterrorists. Researchers who break those rules could face significant criminal penalties.

Despite these aggressive steps on the home front, U.S. officials readily acknowledged that unilateral action was insufficient and that the world needed to form a united front against increasingly sophisticated biotechnologies. But many nations were skeptical of the threat. They also doubted the value of what critics call “the guns, guards, and gates” approach to biosecurity. The result, says Reynolds Salerno, a biosecurity expert at Sandia National Laboratories in Albuquerque, New Mexico, has been “tremendous confusion and concern in the international life sciences community about biosecurity.”

That confusion may be giving way to cooperation, however, as an increasingly global effort to define and implement biosecurity is gaining speed. Nations are moving to pass new biosecurity laws, while public health and security experts are hammering out voluntary biosecurity guidelines and debating “codes of conduct” for life scientists. Many countries are thinking about looser rules for less risky agents than in the United States, which critics say has imposed a one-size-fits-all approach, and few are likely to require the extensive criminal background checks carried out by U.S. agencies.

The new world order may not resemble the U.S. model. But like it or not, life scientists worldwide are about to become much more familiar with the term biosecurity.

—DAVID MALAKOFF



Spreading the word. U.K. officials are preparing to host a Bioweapons Convention-related summit in October 2005 on “codes of conduct” for life scientists who work with potentially dangerous pathogens and biotechnologies. Although few believe that such codes will deter evildoers, advocates say they can play an important role in raising awareness of biosecurity. This winter, academic and industrial scientists will gather in Washington, D.C., to sign a pledge to help prevent the misuse of biological research—a theme also stressed in a new public relations campaign (left) by the International Committee of the Red Cross (www.icrc.org). Such efforts are “a way to encourage dialogue,” says Michael Moodie of the Chemical and Biological Arms Control Institute, an organizer of the Washington meeting. In the meantime, the Federation of American Scientists and other groups are preparing biosecurity course materials for undergraduate and graduate students.

Self-help book. Early next year, the 192-member World Health Organization (WHO) plans to unveil its first-ever set of international biosecurity guidelines. The consensus how-to guide, currently in draft form, should help “clear up a lot of confusion ... by clarifying best practices and minimum standards for keeping pathogens secure,” says Brad Kay, a WHO biosafety expert in Lyon, France.

But implementing the voluntary standards is another story. Many poorer nations won’t want to divert precious public health funds to security, and WHO has meager resources to help out. It also isn’t clear what would happen to labs that don’t meet the standards. “WHO has no mandate to become a global enforcer,” says Kay. In the United States, meanwhile, a team of government and academic researchers is writing a new biosecurity chapter for the “bible” of lab safety, *Biosafety in Microbiological and Biomedical Laboratories*.



Center of expertise. The United States and Europe are spending more than \$90 million annually to help Russia secure its sprawling former bioweapons complex and employ an estimated 6000 former bioweapons scientists. But efforts to attract investment from foreign biotech and drug firms have had mixed results, and some critics say more needs to be done to prevent ex-Soviet pathogens and weapons experts from leaking into the black market. “Biosecurity is about limiting the spread of expertise, too,” says Amy Smithson, a nonproliferation specialist at the Center for Strategic and International Studies in Washington, D.C.



Whose resolve? Last April, the United Nations Security Council adopted Resolution 1540, which expresses “grave concern” about bioterrorism and directs UN members to enact tough controls on potential bioweapons. The resolution is intended to help close legal loopholes in dozens of nations—including some with growing biotech industries—with laws that don’t cover all the bases. “They are now obligated to build the legal framework needed for effective biosecurity,” says Barry Kallman, a law professor at DePaul University in Chicago, Illinois. Critics, however, see the measure as a U.S.-backed gambit to sidestep efforts to strengthen the Biological and Toxin Weapons Convention, which is in limbo until at least 2006.

Biocrime fighters. Interpol, the International Criminal Police Organization, has launched a 2-year effort to train police in its 181 member countries on biosecurity and fighting bioterrorism. “You’d be amazed at how little the average police chief knows about the subject,” says Barry Kallman of DePaul University, who is involved in the project, which is funded by the Alfred P. Sloan Foundation. One goal: to teach investigators how to avoid lumping legitimate researchers in with the biocriminals.



Lessons learned. The Republic of Georgia is on the verge of adopting biosecurity rules modeled on the U.S. approach—but with some important differences. For instance, the same agency will regulate both biomedical and agricultural scientists in the United States that job is split between the Centers for Disease Control and Prevention and the U.S. Department of Agriculture. “We’re telling people that our model is often far more complicated than what they need,” says a U.S. State Department official who advises other governments on biosecurity.

Building boom. Kazakhstan is the first of several nations getting new, secure laboratories to store and study dangerous pathogens. The facilities are courtesy of a U.S.-funded effort to reduce the bioterror threat in the former Soviet Union. Construction of the new Human Health Central Reference Lab and Repository in Almaty is set to begin in mid-2005, with Uzbekistan and Georgia next on the list. Meanwhile, talks are under way on long-term strategies for consolidating the 500 or more culture collections around the world that stock dangerous pathogens, with a goal of fewer, more secure facilities.

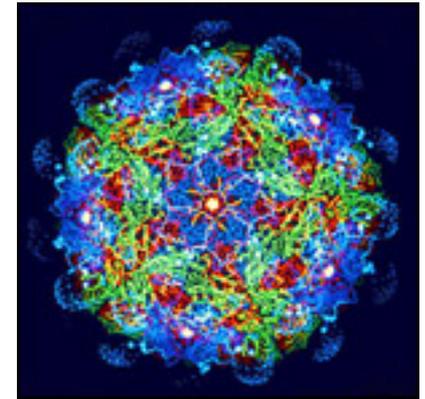


Asia alert. Asian Pacific leaders pledged last year to get tough on biosecurity—in part due to fears that their rapidly growing biotech industries could attract regional terrorist groups along with investors. “Singapore views this threat with grave concern,” Deputy Prime Minister Tan Keng Yam said at a biosecurity conference held in the city-state earlier this year. China, meanwhile, has ratcheted up export controls and is examining both its biosafety and biosecurity rules in the wake of the SARS epidemic and several lab accidents.



A Need for Global Laboratory Biosecurity

- **The International Committee on the Red Cross:**
 - “Alarmed by the hostile uses of biotechnology the ... ICRC appeals ...to all political and military authorities ... to enact effective controls on biological agents with potential for abuse”
- **United Kingdom Legislation:**
 - “There is a need to ensure that terrorists do not have access to premises, which hold substances that may be used in a potentially devastating manner such as pathogens dangerous to human, plant, or animal health”
- **Singapore Ministry of Health:**
 - “Certain biological agents and toxins may be used as weapons of terror and thus pose a threat there is a need for a regulatory framework to provide for proper security of such agents and prevent possible misuse”



Recognized Need for International Biosecurity

- **NAS “Fink Report” – Biotechnology Research in an Age of Terrorism (2003)**
 - Role for the life sciences in efforts to prevent bioterrorism and biowarfare; need to educate the international scientific communities about the nature of the dual use dilemma
 - Demands “harmonized international oversight” for the “protection of biological materials and supervision of personnel who work with those materials”
- **HSPD-10 – Biodefense for the 21st Century (2004)**
 - Endorses international “proactive prevention”
 - “Preventing biological weapons attacks is by far the most cost-effective approach to biodefense”
- **UN Security Council Resolution 1540 (2004)**
 - Urges nations to take preventive measures to mitigate the threat of biological, chemical, and nuclear terrorism
- **Commission on the Intelligence Capabilities of the United States Regarding Weapons of Mass Destruction (2005)**
 - Recommends “encouraging foreign criminalization of biological weapons development and establishing biosafety and biosecurity regulations” internationally



The BWC and Biosecurity

- **Meetings of the Bacteriological (Biological) and Toxin Weapons Convention (BWC) has addressed three relevant issues**
 - **National Implementing Legislation**
 - **National Pathogen Security (biosecurity)**
 - **International Cooperation**

- **Recent technical experts meetings to strengthen the BWC**
 - **States Parties agree to pursue national implementation of laboratory and transportation biosecurity (2003)**



UNSCR 1540 and Biosecurity

- **Urges States to take preventative measures to mitigate the threat of WMD proliferation by non-state actors**
- **UNSCR 1540 requires States to**
 - **Establish and enforce legal barriers to acquisition of WMD by terrorists and states**
 - **Submit reports to the 1540 Committee on efforts to comply**
- **Paragraph 3 is the key provision that supports biosecurity**
 - **“Take and enforce effective measures to establish domestic controls to prevent the proliferation of . . . biological weapons . . .; including by establishing appropriate controls over related materials”**
 - **Develop and maintain appropriate effective measures to account for and secure such items in production, use, storage or transport**
 - **Develop and maintain appropriate effective physical protection measures**



Strengthening Biological Risk Management

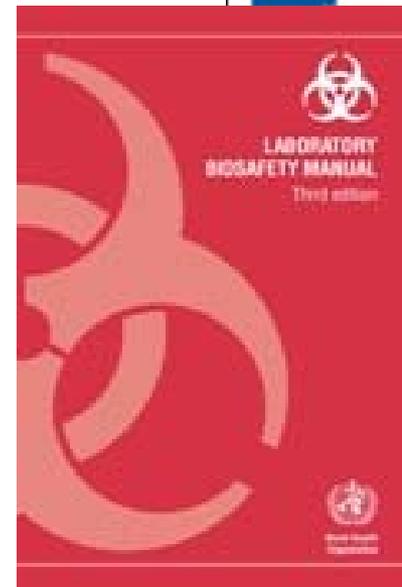
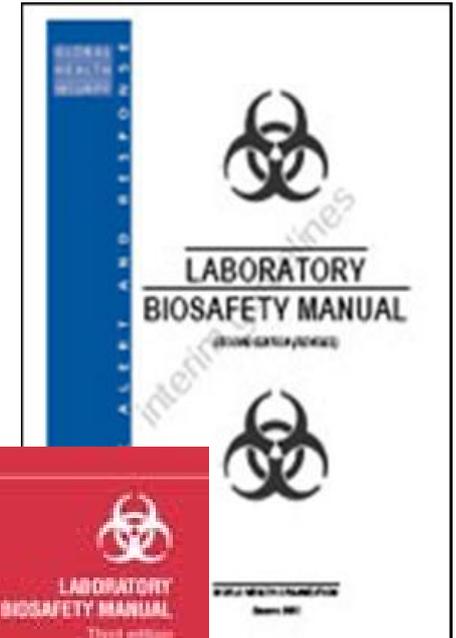


Vision for Integrated BioRisk Management:

- ✓ Increased focus on "awareness" to change current culture
- ✓ Clarify terminology
- ✓ Development of targeted "training strategies"
- ✓ Securing "commitment" from key stakeholders, including government officials, who must be on board
- ✓ Continue increasing "capacity" based on Regional/Country needs and establish accountability through development of Country "report cards"

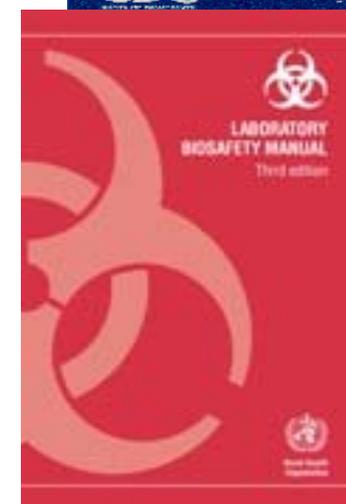
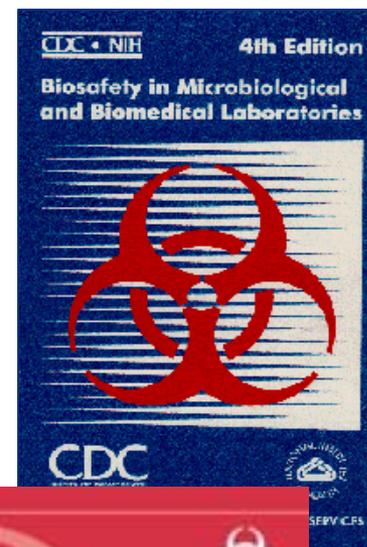
Laboratory Biosecurity Supports Laboratory Biosafety

- **Laboratory biosecurity supports the laboratory biosafety agenda of preventing disease in people, animals, and plants and minimizing the risk of worker injury**
- **Safe and secure laboratories help**
 - **Ensure the containment of hazardous infectious substances in laboratories**
 - **Maintain citizens' confidence in the activities of the bioscience research community**
 - **Increase transparency to investors in the biomedical and biotechnology industries**
 - **Protect valuable research and commercial assets**
 - **Reduce the risks of crime and bioterrorism**



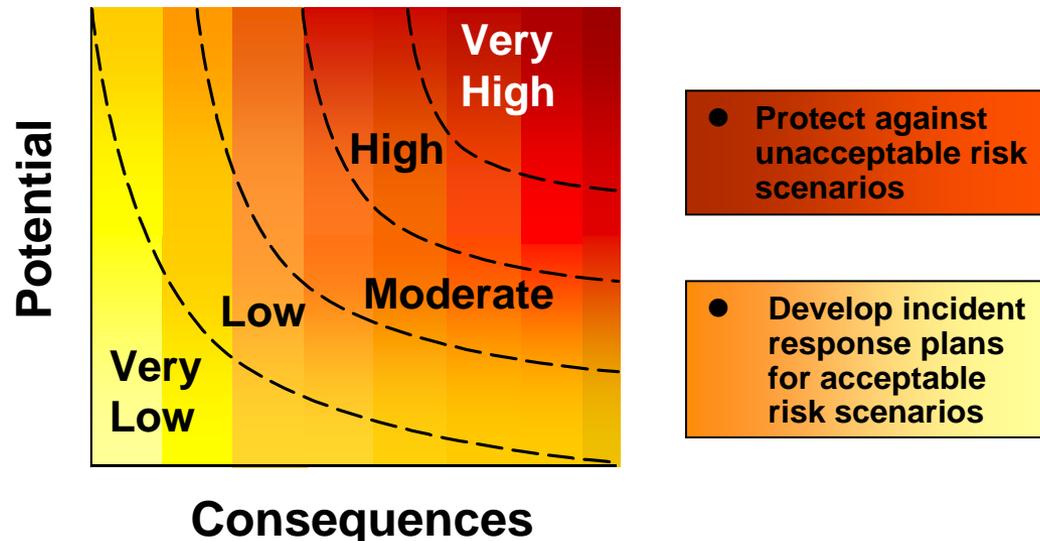
Anticipated Developments

- Next edition of CDC/NIH *Biosafety in Microbiological and Biomedical Laboratories* will include extensive recommendations on biosecurity
- WHO/FAO/OIE developing joint international biosecurity guidelines: Biorisk Management—Laboratory Biosecurity
- Organisation for Economic Co-operation and Development (OECD) is establishing biosecurity guidelines
- Hopefully, these initiatives will
 - Avoid conflicting recommendations
 - Promote the concept of integrated biosafety and biosecurity
 - Introduce a tiered system of protection based on risk assessment and management methodologies



Biosecurity and Biosafety Based on Risk Management

- Laboratory work with pathogens will always involve some level of safety and security risk
- Most biological materials occur in nature and can be isolated from nature
- Critical not to compromise legitimate bioscience operations
 - Systems should be designed to address unique situations
- Resources are not infinite; existing resources should be used efficiently
- Management must distinguish between “acceptable” and “unacceptable” risks
 - Ensure that protection and the cost is proportional to the risk



Conclusions

- **BW threat is evolving and requires new approaches to mitigate**

- **Recommended steps at the national level include:**
 - **BWC Implementing Legislation**
 - Bans development, production, and stockpiling
 - **National Legislation for Laboratory and Transportation Biosecurity**
 - Control use, storage, and transport of dangerous pathogens domestically
 - **Export Controls**
 - Control transport of dangerous pathogens and technology internationally
 - **Biosecurity Implementation Standards or Guidelines**
 - Provide assistance to those who handle, store, or transport dangerous pathogens so that they can comply with legislation while still meeting their biomedical and bioscience research and diagnostic duties

- **Requires cooperation and coordinate of scientific and security communities**

**“Infectious diseases make no distinctions among people and recognize no borders”
President George Bush, November 2001**