

High-Containment Biosafety Laboratory Safety Breaches a Growing Concern

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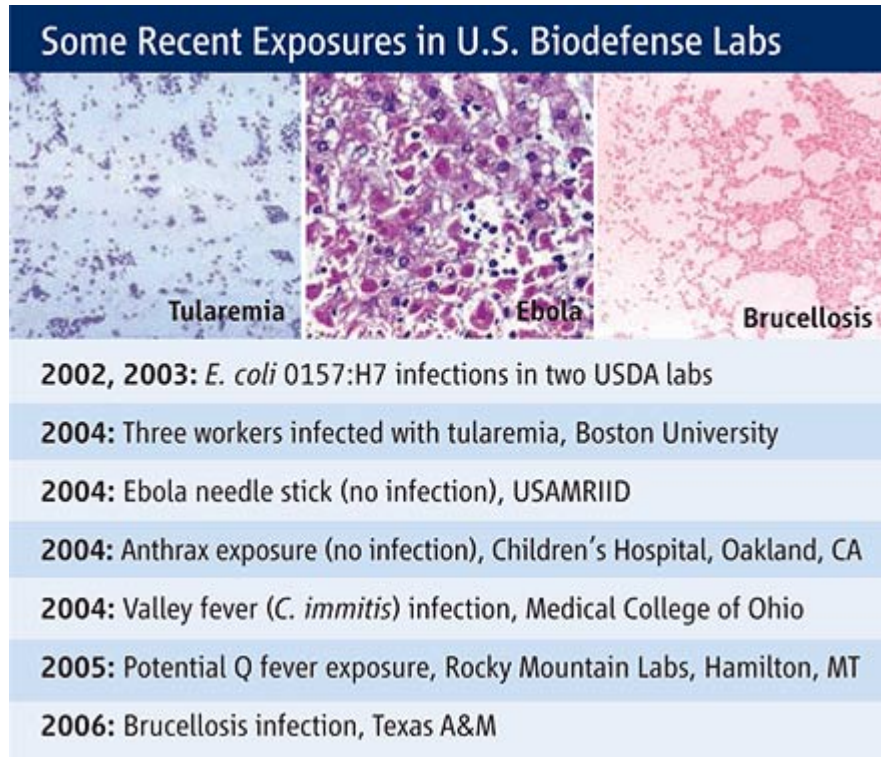
U.S. Government Accountability Office (GAO) chief technologist Keith Rhodes (Center for Technology and Engineering, Applied Research and Methods, GAO), in his written testimony before the U.S. House of Representatives Subcommittee on Oversight and Investigations, Committee on Energy and Commerce (chair, Democrat John D. Dingell, Michigan, longest-serving member of the House, since 1955), noted that high-containment biosafety laboratories, specifically biosafety levels 3 and 4 (BSL-3 and BSL-4), have been “proliferating” since the September 11, 2001 terrorist attacks. (1)

BSL-3 and especially BSL-4 often contain the most hazardous **biological agents**, i.e., “any microorganism (including, but not limited to, bacteria, viruses, fungi, rickettsiae, or protozoa) or infectious substance or any naturally occurring, bioengineered, or synthesized component of any such microorganism or infection substance, capable of causing death, disease, or other biological malfunction in a human, an animal, a plant, or another living organism; deterioration of food, water, equipment, supplies, or material of any kind; or deleterious alteration of the environment.” (2) Examples of biological agents handled in BSL-4 laboratories are the small pox virus (*Variola major*) and the plague virus (*Yersinia pestis*). Most hospital laboratories are BSL-2 laboratories.

The rationale for the House Committee tasking the GAO with the biosafety laboratory investigation was its “increasing concerns...raised about the safety, as well as operations” of high-containment laboratories. House committee members requested answers to three questions (3):

1. To what extent, and in what areas, has there been an expansion in the number of high-containment labs in the U.S?
2. Which federal agency is responsible for tracking the expansion of high-containment labs and determining the associated aggregate risks?
3. What lessons can be learned from recent incidents at high-containment laboratories?

Rhodes identified two U.S. examples of biosafety laboratory safety/operations issues at the Texas A&M University (TAMU) and Centers for Disease Control and Prevention (CDC) biosafety laboratories.



Some recent exposures in U.S. biodefense laboratories. Source: CDC, as per <http://www.sciencemag.org/cgi/content/full/317/584...>; accessed October 5, 2007.

Example One: TAMU, College Station, Texas, BSL-3 Laboratory Safety Issues

TAMU, Texas' first public institution of higher learning (opened Oct. 4, 1876) and one of a select few academic institutions in the nation to hold triple federal designation as a Land-Grant, Sea-Grant and Space-Grant university, initially received funding from the Department of Homeland Security in 2004 during the ramp up of *agro-security* programs beyond the Plum Island Animal Disease Center in Massachusetts. (4) TAMU's has several BSL-3 laboratories whose staff work extensively on animal diseases, including those caused by "select agents" *Brucella melitensis*, *Brucella abortus*, *Brucella suis*, and *Coxiella burnetii*. (5)

Select agents are a category of hazardous biological agents regulated by the Select Agent Program, whose origins date to the 1990s. (6) The CDC writes: "The CDC regulates the possession, use, and transfer of select agents and toxins that have the potential to pose a severe threat to public health and safety. The CDC Select Agent Program oversees these activities and registers all laboratories and other entities in the United States of America that possess, use, or transfer a select agent or toxin." (7) A list of regulated select agents is available elsewhere (7)

Because TAMU worked with select agents, it needed to comply with guidelines published by the Select Agent Program. TAMU belatedly reported a case of human

brucellosis that resulted from an accidental exposure when a BSL-3-authorized lab worker, accustomed only to *Mycobacterium tuberculosis* safety procedures, helped with the operating of the aerosolization chamber in a lab dealing with *Brucella* (i.e., she was not trained or authorized to be in that lab). (8) The afflicted laboratory worker was correctly diagnosed with brucellosis on April 16, 2006 via the Texas State Public Health Lab. (10) The incident was brought to light through public records requests by Edward Hammond of the Sunshine Project, a watchdog group in Austin Texas. (9) The CDC issued an order to TAMU on April 20, 2007 to “cease and desist all work with select agents and toxins,” as described elsewhere. (10) “In an August 2007 investigation, CDC inspectors found a dozen serious violations, including unapproved experiments, lost samples, improper safety training, and lab workers without select-agent authorization, as described elsewhere. (11)

Example Two: CDC Clifton Road, Atlanta, BSL-4 Safety Issues

On June 15, 2007, lightning struck in and around the CDC’s new \$214 million infectious disease building on Clifton Road, Atlanta, including the suite of six BSL-4 laboratories, causing a power surge that knocked out power. Remote backup generators never came on. The outage shut down negative air pressure systems, which keep select agents from escaping the containment areas. (12,13) The BSL-4 labs were uninhabited at the time of the lightning strike/power outage even though construction of the building, which had begun in 2001, had been completed in September 2005. (13) Thus, the public and CDC workers were not placed at any risk as a result of the power outage.



“The new Emerging Infectious Diseases Laboratory occupies a central space on the CDC’s Roybal Campus near Emory University in Atlanta. It consists of two wings: a high-rise lab and office tower (right) and a six-story high-containment lab, vivarium, and glasswash facility (left). (The curved-roofed building at the far right is Building 17, the Infectious Disease Laboratory; Building 15, a containment lab, is the white element



Necropsy suite at CDC’s new BSL-4 suite of laboratories. Source:

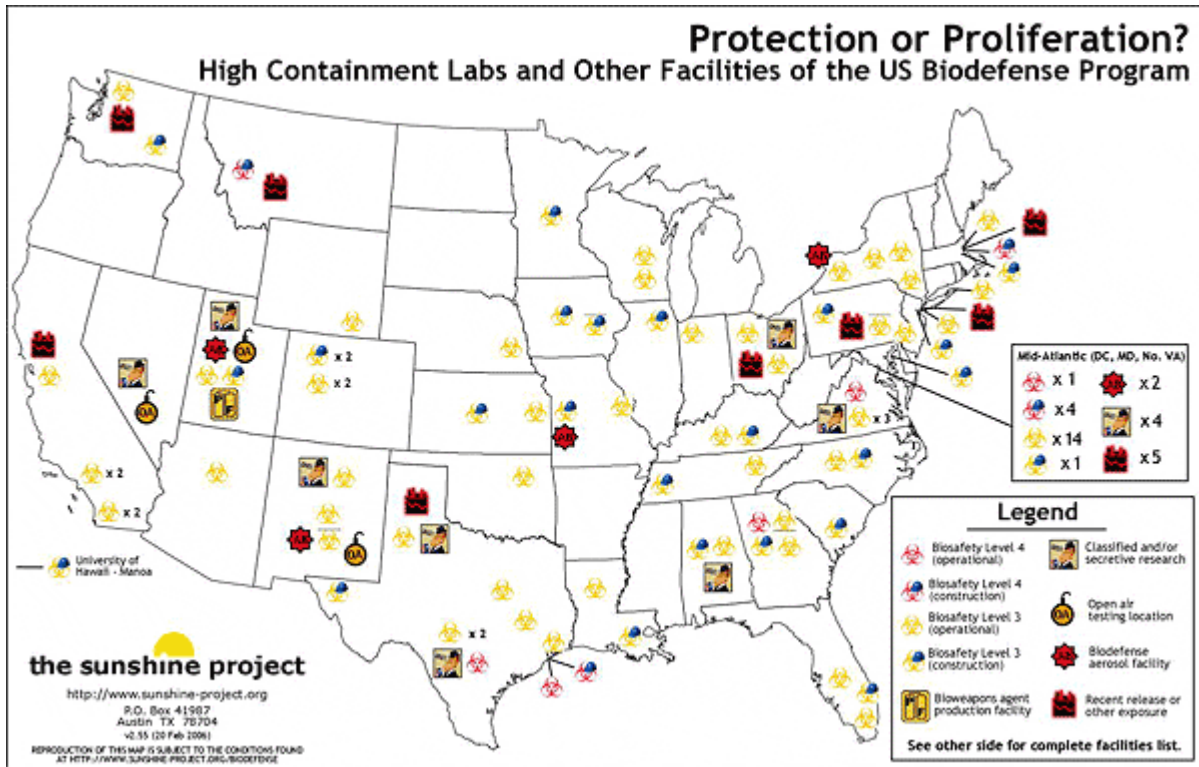
<http://www.labdesignnews.com/LaboratoryDesign/imag...>; accessed October 5, 2007.

behind the new containment wing at the far left.) All photos:
Balthazar Korab.” Source:
<http://www.labdesignnews.com/LaboratoryDesign/LD06...>;
accessed October 5, 2007.

Apparently, construction officials warned CDC since 2001 that its backup power system would not keep crucial lab systems from failing in an outage, according to internal documents obtained by *The Atlanta Journal-Constitution*.” (14) CDC determined that the cause of the failure of its power system servicing the BSL-4 laboratory suite was that “some time earlier, a critical grounding cable buried in the ground outside the building had been cut by construction workers digging at an adjacent site. The cutting of the grounding cable, which had gone unnoticed by CDC facility managers, compromised the electrical system of the facility that housed the BSL-4 lab.” (15) The irony of the situation is that it happened to CDC just as CDC was censuring TAMU for its BSL-3 safety violations.

U.S. Expansion of BSL-3 and BSL-4 Laboratories since 2001

GAO Keith Rhodes and his colleagues determined that the number of known BSL-4 laboratories in the U.S. has grown from 2 (before 1990) to 3 (1990-2000) to 10 (2001-present), which sum up to **15** known BSL-4 laboratories in U.S., as of 2007. (16) Multiple sectors own and operate these BSL-4 laboratories, i.e., federal government (9 labs), academic (4), state (1), and private (1). The two BSL-4 laboratories that existed in the U.S. in 1990 were the federal labs at the U.S. Army’s Research Institute for Infectious Diseases (USAMRIID) in Fort Detrick, Maryland, and at the CDC in Atlanta, Georgia. Between 1990 and 2000, three new BSL-4 laboratories were constructed at Georgia State University in Atlanta (first university BSL-4 lab), the National Institutes of Health campus in Bethesda, Maryland, and a privately-funded lab in San Antonio, Texas.



Map of some BSL-4 and BSL-3 laboratories compiled by the Sunshine Project, Austin Texas. Source: The Sunshine Project at <http://www.sunshine-project.org/>; accessed October 5, 2007.



the sunshine project

Key: High Containment Labs and Other Facilities of the US Biodefense Program

This map shows existing biosafety level three and four facilities used in US biodefense research, as well as planned biodefense labs. It also shows important aerosol facilities and open air testing locations used in biodefense. BSL-3/4 facilities not known to be heavily dedicated to biodefense are not indicated here.

Operational BSL-4 Facilities

USAMRIID Fort Detrick, Frederick, Maryland
DCLS "Biotech Six", Richmond, Virginia
Centers for Disease Control, Atlanta, Georgia (x2)
Univ. of Texas Medical Branch, Galveston
Southwest Fdn for Biomed. Res., San Antonio, TX

Planned / Under Construction BSL-4 Facilities

Boston University, Boston, Massachusetts
NIH Integrated Res. Fac., Frederick, Maryland
DHS NBACC (Phase 1), Frederick, Maryland
USAMRIID (Phase 1), Frederick, Maryland
USDA Planned Facility, Frederick, Maryland
Univ. of Texas Medical Branch, Galveston
Rocky Mountain Labs, Hamilton, Montana

Operational BSL-3 Facilities

Harvard University, Cambridge, MA
Cornell University, Ithaca, New York
DHS / USDA Plum Island, New York
CALSPAN-UB, Buffalo, New York
SUNY, Stony Brook, New York
PHRI, Newark, New Jersey
Wadsworth Center, Albany, New York
University of Pennsylvania, Philadelphia
Thomas Jefferson University, Philadelphia
University of Pittsburgh, Pittsburgh
Armed Forces Inst. of Pathology, Washington, DC
Naval Medical Research Ctr., Silver Spring, Maryland
University of Maryland CARB, Rockville
US Army SBRCCOMs, Aberdeen, Maryland
University of Maryland, Baltimore
Southern Research Institute, Frederick, Maryland
Versar, Gaithersburg, Maryland
The Pentagon, Northern Virginia
American Type Culture Collection, Manassas, VA
George Mason University, Manassas, Virginia
Naval Surface Weapons Center, Dahlgren, VA
Commonwealth Biotechnologies, Richmond, VA
Virginia Commonwealth University, Richmond
University of Kentucky, Lexington
Oak Ridge National Laboratory, Tennessee
Wake Forest University, Winston-Salem, NC
Emory University, Atlanta, Georgia
USDA FSIS / MOSPL, Athens, Georgia
Midwest Research Institute, Palm Bay, Florida
University of Miami, Florida
US EPA, Cincinnati, Ohio
Battelle Memorial Inst., West Jefferson, Ohio
IITRI, Chicago, Illinois
University of Wisconsin-Madison
St. Louis University, St. Louis, Missouri
Midwest Research Inst., Kansas City, Missouri
University of Nebraska, Lincoln
Southern Research Inst., Birmingham, Alabama
Louisiana State University, Baton Rouge
University of Texas Health Science Center, Houston
University of Texas Southwestern, Dallas
University of Texas Health Science Center, San Antonio
Lackland Air Force Base, San Antonio, TX
Texas Technological University, Lubbock
Texas A&M University, College Station
Oklahoma State University, Stillwater
Colorado State University, Ft. Collins, Colorado
Centers for Disease Control, Ft. Collins, Colorado
Los Alamos National Lab, Los Alamos, New Mexico
Lovelace Institute, Albuquerque, New Mexico
University of New Mexico, Albuquerque
US Army Dugway Proving Ground, Utah
Northern Arizona University, Flagstaff
University of California, Irvine
University of California, Los Angeles
San Diego State University, California
Scripps Research Inst., La Jolla, California
Lawrence Livermore Lab, Livermore, California
University of Washington, Seattle

(Major) Planned / Under Construction BSL-3 Facilities

Tufts University, Grafton, Massachusetts
UMD of New Jersey, Newark
University of Pittsburgh, Pennsylvania
University of Maryland, Baltimore
George Mason University, Fairfax, Virginia
University of Louisville, Kentucky
Duke University, Durham, North Carolina
Medical University Of South Carolina, Charleston
University of Georgia, Athens
Scripps Institute, Palm Beach County, Florida
University of Alabama at Birmingham
University of Tennessee at Memphis
Tulane Primate Center, Covington, Louisiana
University of Missouri, Columbia
University of Iowa, Iowa City (RCE planning)
USDA / Iowa State University, Ames, IA
Argonne National Lab, Argonne, Illinois
Agricultural Biosecurity Ctr., Manhattan, Kansas
Univ. of Minnesota, Minneapolis (RCE planning)
University of Texas at El Paso
US Army Dugway Proving Ground, Utah
Centers for Disease Control, Ft. Collins, Colorado
Colorado State University, Fort Collins
Pacific Northwest National Lab, Richland, Washington
University of Hawaii, Manoa

Bioweapons Agent Production Facilities

US Army Dugway Proving Ground, Utah

Biodefense Aerosol Facilities

CALSPAN-UB, Buffalo, New York
US Army Aberdeen Proving Ground, MD
George Mason University, Manassas, VA
Midwest Research Institute, Kansas City, MO
Lovelace Institute, Albuquerque, NM
US Army Dugway Proving Ground, Utah

Open-Air Testing Facilities

US Army Dugway Proving Ground, Utah
Nevada Test Site (proposed)
White Sands Missile Range, NM (probable)

Classified or Secretive Research

US Army Aberdeen Proving Ground, MD
USAMRIID Fort Detrick, Frederick, MD
Versar, Gaithersburg, MD
Commonwealth Biotechnologies, Richmond, VA
Southern Research Institute, Birmingham, AL
Battelle Institute, Columbus /W. Jefferson, OH
Southwest Fdn for Biomed. Res., San Antonio, TX
Texas Technological University, Lubbock
DTRA et. al., Kirtland / Albuquerque, NM
US Army Dugway Proving Ground, UT
DOE Nevada Test Site

Notable (Known) Recent US Accidents and Releases

Lab-acquired Tularemia (3x), Boston Univ, MA (2004)
Plague-infected mice "lost", UMDNJ, Newark, NJ (2005)
Lab-acquired E. coli O157:H7, USDA, Wyndmoor, PA (2002)
Anthrax in letters from Ft. Detrick (probable), MD (2001)
Anthrax-contaminated offices, Ft. Detrick, MD (2002)
Ebola needle stick, Ft. Detrick, MD (2004)
Lab-acquired E. coli O157:H7, USDA, Beltsville, MD (2003)
Live anthrax shipped as "dead", SRI, Frederick, MD (2004)
H2N2 flu in test kits, Meridian Biosci., Cincinnati, OH (2005)
Thomas Butler Case, Texas Tech Univ., Lubbock (2003)
Q Fever exposure, Rocky Mtn. Labs, Hamilton, MT (2005)
Faulty aerosol chamber infects 3, IDRI, Seattle, WA (2004)
Live anthrax mishandled, Oakland Children's Hosp, CA (2004)

Wants to Construct a BSL-4 Lab (not indicated on map)

Wadsworth Center, Albany, New York
Oak Ridge National Laboratory, Tennessee
University of Illinois, Chicago
Texas Technological University, Lubbock
University of Nebraska Medical Ctr, Omaha
University of New Mexico, Albuquerque
University of California, Davis
Oregon Health Sciences University, Portland

Dual-access gloveboxes between the BSL-3 and BSL-4 zones allow split handling of hazardous and unknown samples. The split-sample protocol prevents any material that's ever been in the BSL-4 zone from entering a BSL-3 area, even if it proves to be a BSL-3 agent. Source: <http://www.labdesignnews.com/LaboratoryDesign/LD06...>; accessed October 9, 2007.

Many more BSL-3 laboratories than BSL-4 laboratories are believed to exist, according to the research performed by Rhodes, et al. The only definitive data available on BSL-3 laboratories, such as the one at TAMU, exists in a federal database (more below) of laboratories handling select agents. This set of labs must register with the **CDC-USDA Select Agent Program**, as noted above. The number of BSL-3 laboratories currently registered with the Select Agent Program is 1356. Of the 1356, 1042 are registered with CDC and 314 are registered with USDA (United States Department of Agriculture). (17) Two thirds of the registered BSL-3 laboratories are outside of the federal sector.

According to a survey conducted by the **Association of Public Health Laboratories** (APHL) in August 2004, since 2001 state public health labs have used public health preparedness funding to build, expand, and enhance BSL-3 labs. In 1998, for example, APHL found that 12 of 38 responding states reported having a state public health laboratory at the BSL-3 level. Today, at least 46 states have at least one state public health BSL-3 lab. (17,18)

Federal Agency Responsibility for Tracking BSL-3/BSL-4 Expansion/Risks

“No single federal agency has the mission to track and determine the risk associated with the expansion of BSL-3 and BSL-4 laboratories in the United States, and no single federal agency knows how many such laboratories there are in the United States. Consequently, no one is responsible for determining the aggregate risks associated with the expansion of these high-containment labs,” notes GAO’s Rhodes. (19)

Lessons Learned about Study of Expansion of BSL-3/BSL-4 Laboratories in the U.S.

Rhodes’ group from GAO learned six lessons from their investigation of the expansion of high-containment laboratories in the U.S., as described elsewhere. (20) Four of the lessons are that barriers to reporting errors exist, clearer definition of what constitutes an “exposure” to a biologic agent is needed, laboratory workers need more safety training, and physical infrastructure of high-containment labs needs maintenance after being built.

Conclusion

The U.S. Congress awarded funding to organizations in many sectors to build high-containment laboratories following the terrorist attack on September 11, 2001 and the anthrax bioterrorism in October 2001. The goal was laudable: to expand the nation’s preparedness and response capabilities in the face of outbreaks of infectious disease. Insufficient thought, however, appears to have been invested in emplacing mechanisms

for measuring and improving the ongoing quality and safety of the new high-containment laboratories.

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