

PUBLIC HEALTH LABORATORY ISSUES IN BRIEF: BIOTERRORISM CAPACITY

Association of Public Health Laboratories

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State Public Health Laboratory Bioterrorism Capacity

Since the events of September 11, 2001 and subsequent anthrax and ricin attacks, bioterrorism preparedness has been a high priority for the nation. Federal funding for state and local bioterrorism preparedness increased from \$67 million in FY 2001 to \$934 million in FY 2004. These funds have improved public health infrastructure and enhanced the capacity of public health laboratories (PHLs) to detect and respond to acts of bioterrorism and infectious disease outbreaks. To assess the impact of this public health preparedness funding on PHL capacity, the Association of Public Health Laboratories (APHL) has periodically surveyed these laboratories. This issue brief provides an update on the status of the state public health laboratories (SPHLs) based on survey data collected in the fall of 2004. It describes SPHL bioterrorism preparedness in terms of advances in laboratory capacity, unmet needs and emerging issues.

State Public Health Laboratories: The Backbone of National Response to Terrorism

Public health laboratories are the backbone of the Laboratory Response Network (LRN), the nation's system for identifying, testing and characterizing potential agents of biologic and chemical terrorism.¹ (See Figure 1.) High quality laboratory testing is an essential component to initiating a public health response and for effective decision-making to close buildings, to treat exposed persons and to deploy the Strategic National Stockpile.



Public Health Laboratory Issues in Brief

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The concept of the LRN as a state-federal partnership with assets available in all states was developed in 1999 and articulated in the Centers for Disease Control and Prevention's (CDC) Bioterrorism Strategic Plan.² While initially structured to test only human clinical samples for biological agents of terrorism, in 2001, more than one million anthrax tests were performed by the LRN on a wide variety of samples that were both clinical and environmental.³ Since then, the LRN has continued to evolve and expand. In 2003, the capability to detect chemical terrorism agents in human samples was added. The LRN now provides essential support for several surveillance

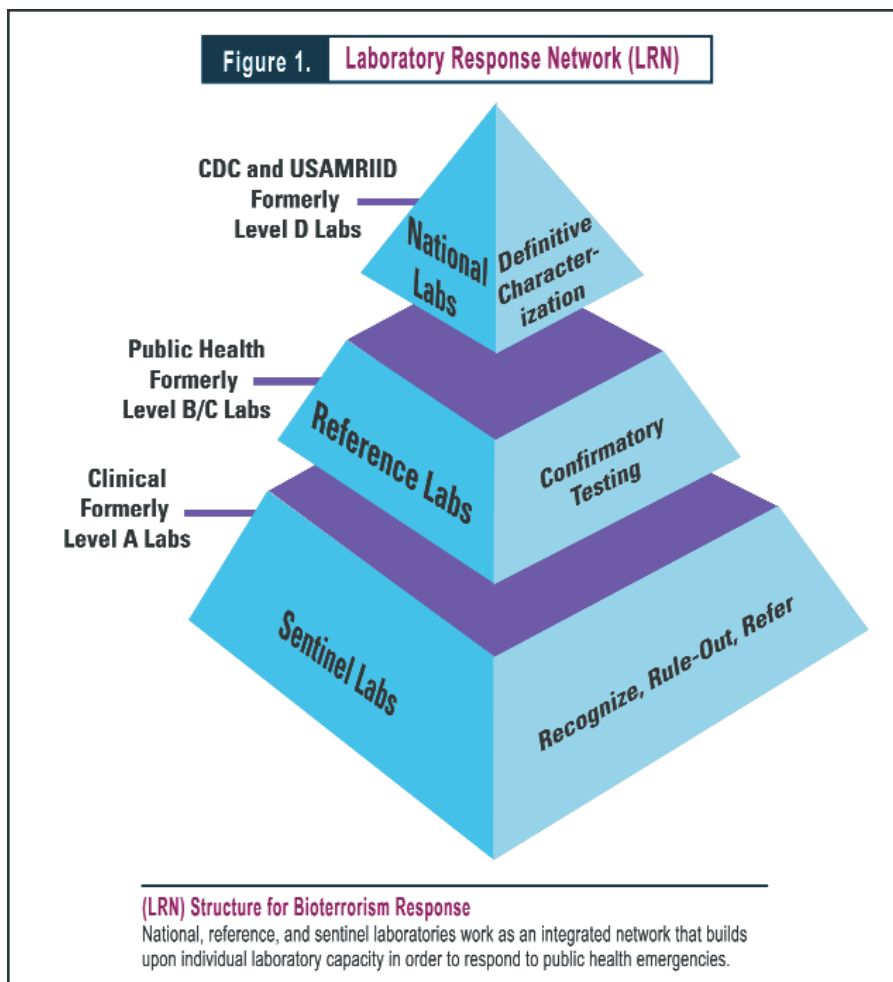
activities, which include the nation's Biowatch program and the United States Postal Service's (USPS) Biohazard Detection System (BDS). With expectations to implement new technologies, support early warning surveillance systems, and add more tests for additional agents of bioterrorism and other infectious disease threats, the current resources available for the LRN are being stretched.

Nationwide, public health laboratories have been working closely with traditional and non-traditional partners. Over the past few years, PHLs have been very successful in developing stronger linkages with the clinical laboratory community as well as with local and federal law enforcement

agencies and emergency response entities. Similar enhancement of coordination with veterinary, food, environmental agencies and laboratories is still being developed. While all of these initiatives to expand the role of the LRN are intended to markedly improve local, state, and national public health preparedness, there is an ongoing need for appropriate resources to ensure continued development and success.

Methods

Data for this issue brief were collected in August 2004 by APHL when it conducted its third survey of state public health laboratory readiness for bioterrorism. This brief is a follow-up to previous surveys that collected 2001 data used to establish a baseline of SPHL capability and capacity prior to the availability of emergency supplemental funds



for terrorism preparedness,⁴ and 2002 data used to measure what progress had been made after one year of federal funding for bioterrorism.⁵ Summarized data from these former surveys are available online at the APHL Web site, www.aphl.org.

For the current survey, participants were asked to report on bioterrorism capability and capacity as of August 31, 2004. Unless otherwise noted, data were collected for a period of 20 months, covering activities from January 1, 2003 to August 31, 2004. APHL decided to evaluate this expanded time period in order to better align the data with CDC's cycle of Cooperative Agreement funding for state and local preparedness.

The survey was sent to all 50 states, the District of Columbia (DC), and four territories. Fifty-two responses were received, representing all states, the District of Columbia, and Puerto Rico. Unless otherwise noted, 52 responses were given to each question. For the purposes of this report, the term "states" or "state public health laboratories" will be used to refer to all respondents, including DC and Puerto Rico.

The survey was administered via APHL's LabNet, a Web-based repository and survey tool designed for APHL members. Descriptive statistics were gathered for all of the variables. Results are reported for the following categories:

- **Testing**
- **Funding and Benchmarks**
- **Laboratory Connectivity and Training**
- **Workforce**
- **Facilities and Biosecurity**

- **Reagents and Equipment**
- **Smallpox Preparedness**
- **Transportation and Courier Service**
- **BioWatch**

APHL members are able to review aggregate data on APHL's LabNet, www.aphl.org/labnet. APHL will continue to survey state public health laboratories at regular intervals to assess their readiness to respond to bioterrorism and to identify challenges that might persist.

Testing

Policymakers may be unaware that the LRN confirmatory laboratories respond to various threats and emergencies on a routine basis in support of law enforcement and partner public health agencies.

- **States reported that they received over 25,000 unknown samples for testing to rule out or confirm potential agents of terrorism in the period January 2003 through August 2004. Ninety percent of these unknowns were environmental samples of various types, including threat letters, powders, unknown packages, food and samples from the USPS.**

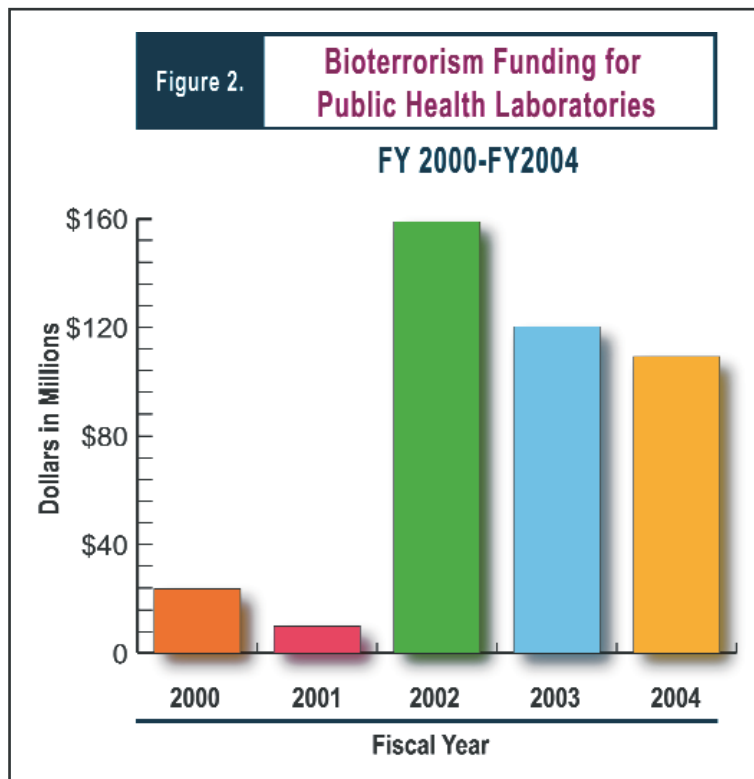
Funding and Benchmarks

State public health laboratories receive funding for bioterrorism preparedness through the CDC Cooperative Agreement on Public Health Preparedness and Response for Bioterrorism. Following the anthrax attacks of 2001, there was an influx of money to strengthen the public health laboratory infrastructure and to develop and

improve laboratory bioterrorism response and detection capabilities.

In FY 2002, states received a total of \$940 million for public health preparedness activities from the

This funding has supported numerous elements of capacity building in public health laboratories as shown in Figure 3. The majority of funds have been used to support personnel and equipment. Further reductions in this funding threaten existing progress and the ability of LRN laboratories to maintain newly established infrastructure.



CDC, of which laboratories received \$153 million to build and enhance capacity to detect agents of bioterrorism. One year later, in FY 2003, laboratories received \$116 million of \$940 million, a \$37 million decrease, for bioterrorism preparedness activities.

There was a further reduction in FY 2004 to support capacity for detecting biologic agents, when laboratories received only \$104 million of the \$934 million, a \$49 million decrease from FY 2002. (See Figure 2.)

- Federal funding for bioterrorism preparedness has become even more critical as reductions in state funding create additional strains on resources. In FY 2003, twenty-two states reported an average reduction of 12% in state funding. Only 10% (5/51) of state public health laboratories received funding from the Department of Justice for terrorism preparedness activities.

- Forty-three (83%) state public health laboratories indicated that they have some type of funding specifically for testing of food as part of investigating outbreaks of human illness. However, only 25 (48%) of the state public health laboratories

indicated that they have funding for the testing of food after a recognized intentional contamination. Funding for food protection is necessary if states are expected to address testing of food triggered by intentional contamination.

- State public health laboratories continue to engage other partners in expanding the Laboratory Response Network. Since December 2002, an additional 9 public health laboratories were added to the confirmatory level of the LRN, and 23 more are in the final stages toward meeting

entry requirements to provide support to state public health laboratories in a potential bioterrorism event. **Twenty-five (48%) respondents shared federal funding with other LRN confirmatory laboratories in their state.** LRN confirmatory laboratories receiving bioterrorism funding include branch state public health laboratories, city and county public health laboratories, as well as clinical research, veterinary diagnostic, agriculture and food laboratories.

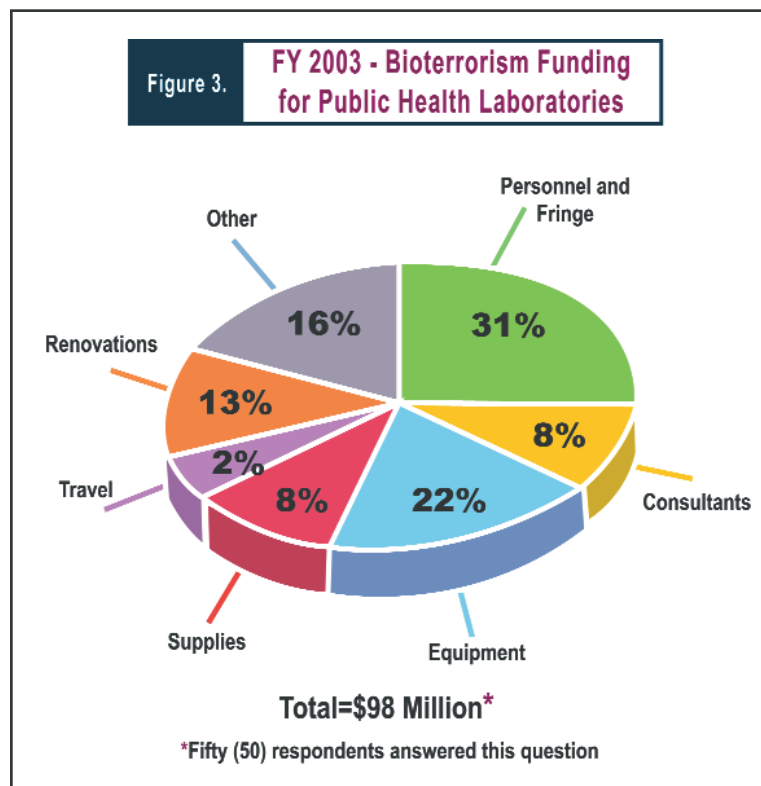
Laboratory Connectivity and Training

A critical benchmark in the Preparedness Cooperative Agreement funding from both the CDC and the Health Resources and Services Administration (HRSA) requires PHLs to identify and enhance coordination with the local clinical laboratory community. Great strides have been made in reaching this benchmark. **As of August 31, 2004, forty-nine (94%) states sponsored sentinel (clinical) laboratory training and offered a total of 717 courses to over 9,000 laboratorians.** On average, 15 (range 1 -189) training courses were offered in each jurisdiction. The training covered rule-out testing, packaging and shipping, and biosafety guidelines.

- Forty-two states (81%) employ a staff person responsible for coordinating training and other activities with the sentinel laboratories. This represents an improvement from 2002, when only 32 states had a

liaison to the clinical laboratory community. However, only twenty-nine respondents report that the staff person is dedicated full time to this activity.

- Fifty-one (98%) of the respondents maintain a database of demographic and contact information for all sentinel laboratories in their state. This is a significant improvement from the last assessment when only 44 states had established a sentinel laboratory database.
- Forty-four (85%) states now have access to current information on the capabilities of all sentinel laboratories in their state, an improvement over 34 states in 2002.
- Forty-five (87%) states have a means to communicate rapidly (blast fax and e-mail) with sentinel laboratories. In 2002, only 38



states reported having this capability. Of the 45 states with rapid communications systems, 39 states utilized this system during the 20-month period (January 2003 – August 2004) to communicate health alerts, provide infectious diseases updates, notify the clinical community of training courses and provide information on bioterrorism exercises.

- **Only twenty-nine states (56%) indicated that they have a Bioterrorism Advisory Committee in place that includes representatives from the clinical community.** Most of these states held at least one meeting in the past 20 months to discuss state specific plans and coordination efforts.
- **Twenty-four (46%) states have a formal or informal proficiency testing system in place to assess the competency of sentinel laboratories to rule out bioterrorism agents.**
- **Thirty-nine (75%) states indicated that they are developing working relationships with their veterinary laboratories.**

To assure standardized testing, the CDC provides training to state public health laboratories as resources permit. Respondents indicated that more training on confirmatory assays for bioterrorism agents is needed.

- **Of the fifty-two respondents, 50 (96%) indicated they would participate in future LRN confirmatory laboratory training courses.** Resources are needed to support ongoing CDC and state public health laboratory training efforts.

Workforce

Sustained funding for public health laboratories to hire, train and maintain a highly-skilled laboratory workforce is essential for national security. However, even after four years of additional funding, many states still do not have a full complement of trained staff. The lack of highly-skilled personnel to perform molecular testing in public health laboratories remains problematic. Consequently, in the event of an emergency, many states would be unable to sustain surge capacity testing for an indefinite period. While some federal funding exists for the hiring of a skilled workforce, there is a national shortage of trained laboratorians and recruitment in some areas is nearing impossible.

Policymakers need to recognize that delays in state draw-downs of emergency preparedness funds may be due to intractable vacancy rates rather than excess workforce funding. Public health organizations are calling for the federal government to invest more in the education and training of a skilled public health laboratory workforce. The nationwide shortage of skilled laboratorians requires ongoing funding and a long-term national strategy.

- **States reported that they were able to use FY 2003 CDC cooperative agreement funds to hire 132 new full time employees.** Some states also lost highly skilled personnel and the recruiting pool of qualified applicants is dimly inadequate.
- Survey results show that 31 (60%) state public health laboratories have a full-time doctoral

molecular bioterrorism scientist. **Twenty-one (40%) state public health laboratories still lack a full-time doctoral-level molecular bioterrorism scientist.** This number has increased since APHL's last assessment of the state public health laboratories, indicating that states have been unable to retain some of their highly-skilled personnel. Currently, only 12 states have more than one doctoral-level molecular scientist.

- Fifty-one (98%) states have at least one laboratorian trained to perform real-time polymerase chain reactions (PCR) assays for agents of bioterrorism. **On average, states indicated that at least two additional laboratorians trained in real-time PCR assays are needed to assure adequate capacity in an emergency.**
- Forty-nine (94%) states have at least one laboratorian trained to perform time-resolved fluorescence (TRF) assays for bioterrorism agents. **On average, states indicated that two additional laboratorians trained in TRF are needed to assure adequate capacity in an emergency.**
- Fifty-one (98%) states have at least two laboratorians trained to perform confirmatory testing for *Bacillus anthracis* (anthrax) and *Yersinia pestis* (plague). However, **thirty-two states indicated that additional trained personnel are needed to perform confirmatory testing for anthrax and plague to meet anticipated surge needs during an event.**
- Fifty-one (98%) states have at least one laboratorian trained to perform confirmatory testing for *Francisella tularensis* (tularemia). Thirty-one (60%) states need additional trained personnel to perform confirmatory testing for tularemia.
- Forty-seven (90%) states have at least one laboratorian trained to perform confirmatory testing for *Brucella* species (brucellosis). Thirty-four (65%) states need additional trained personnel to perform confirmatory testing for brucellosis.
- **Only 20 (38%) states have at least one laboratorian trained to perform testing for botulism (*Clostridium botulinum*) toxin.** It is important to note that biosafety level 2 (BSL-2) animal facilities are required in order to perform the confirmatory assay for this agent and many public health laboratories do not have such animal facilities. In an effort to provide additional methods to public health laboratories, the CDC along with the Food and Drug Administration (FDA) developed a screening assay, the DIG-ELISA, for the detection of *Clostridium botulinum* toxin. Currently, only sixteen states have at least one laboratorian trained to perform the screening assay. The CDC needs additional resources to provide training and reagents to all states to perform this new screening assay.
- Only forty (77%) states have at least one laboratorian trained to perform confirmatory testing for *Burkholderia* species (glanders). Thirty-eight (73%) states indicate a need for additional trained personnel to perform confirmatory testing for *Burkholderia* sp.
- Thirty-eight (73%) states have at least one laboratorian trained to perform confirmatory testing for Staphylococcal enterotoxin B. Thirty-nine (75%) states need additional trained personnel to perform confirmatory testing for this agent.

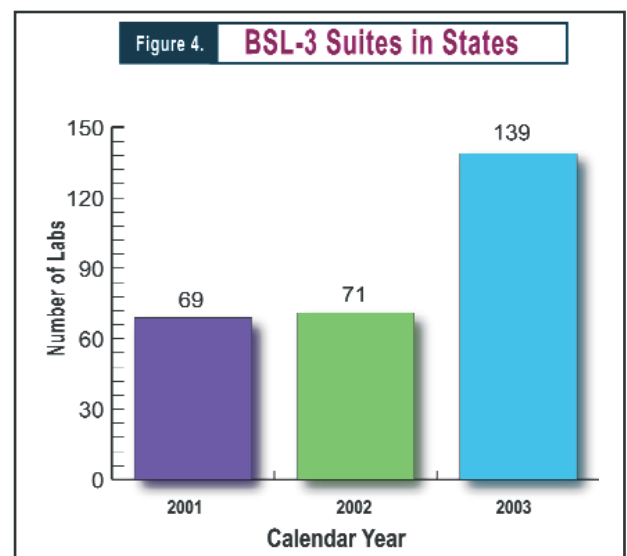
Facilities and Biosecurity

As LRN laboratories are increasingly called upon to provide testing to rule-out biological, chemical, radiological and even explosive hazards for unknown samples and packages, their capability to safely screen (“triage”) such unknowns has become a high priority. The current lack of standardized screening protocols for all-hazards environmental sample collection and analysis represents a risk for first responders, HazMat personnel, law enforcement, and laboratory personnel. The federal government has not provided any standardized guidelines for facilities or procedures to safely conduct all-hazards screening of unknown suspicious samples. APHL continues to request that the federal government provide guidance regarding this critical gap.

- Only twenty-seven (52%) states indicated that they have a designated triage area for receiving and screening unknown samples.
- Twenty-two (42%) states have purchased new technologies, such as SensIR™, to assist in the screening of unknown samples for chemical agents and other substances suggestive of terrorism agents.
- Thirty-nine (75%) states indicated that they require law enforcement/first responders to perform field screening of unknown samples for chemical, radiological, nuclear and explosive materials prior to bringing these samples to the public health laboratory. Many states report

that even with field screening, additional testing is often needed to confirm the field results after the material arrives at the LRN confirmatory laboratory.

Since 2001, SPHLs have used Public Health Preparedness funding to build, expand and enhance biosafety level 3 (BSL-3) suites* and improve security within their facilities. (See Figure



4.) While the number of BSL-3 suites has grown, the effort is not yet complete.

- Forty-six (88%) of states have at least one BSL-3 suite within their laboratory. However, **six state public health laboratories still lack a BSL-**

*A BSL-3 suite is a contained area within a laboratory that must meet stringent requirements for biosafety. BSL-3 suites must include biosafety cabinets, controlled double door access, and engineering controls, including maintaining negative air pressure relative to the surrounding rooms (so that all air flow is directed into the BSL-3 suite, not out into the surrounding rooms), microfiltration of air; and air-lock buffer zones.

3 suite, compared with eight from the last assessment and at least 10 prior to the influx of funding. Additional BSL-3 suites have been added in many states to enhance surge response capacity.

- **More than 50 percent of states report needing at least one additional BSL-3 facility in the SPHL system.** According to the survey results, an additional 70 such facilities are needed nationwide. Justifications for this expanded capacity include providing geographic coverage, surge capacity, the burden of additional mandates and the replacement of existing aged facilities.
- **Forty-four (85%) states upgraded their security systems.** States also reported upgrading their specimen and mail receiving areas, air handling systems, redundant fan systems, dedicated power/generator, biohazard disposal, freezer capacity and reagent storage facilities. However, additional upgrades are still needed for many of these laboratory components, most notably specimen and mail receiving areas and air handling systems.
- All but one of the respondents indicated that they are registered with the Select Agent Program at the CDC or the United States Department of Agriculture (USDA).

Reagents and Equipment

Since the anthrax attacks of 2001, the LRN confirmatory laboratories have become the trusted entity for confirmation of test results regardless of the source of the initial testing. The LRN reagents[♦] provide high confidence test capability for clinical, environmental and food testing methods. The demand for and use of LRN validated tests and reagents have grown rapidly and will continue to grow as more surveillance and early warning systems are implemented, and as the number of tests for more biologic agents is increased.

State LRN laboratories do not have adequate stocks of reagents on site. A rapidly deployable repository of these LRN reagents sufficient to meet current needs and potential emergency surge needs does not exist. This lack of a robust reagent supply threatens the continued success of the LRN. In a 2004 letter to the White House Homeland Security Council, the Department of Health and Human Services (HHS), the CDC, and the Department of Homeland Security (DHS), APHL stated that a national reagent stockpile was critical to maintaining preparedness and response capabilities of our public health laboratories.⁶

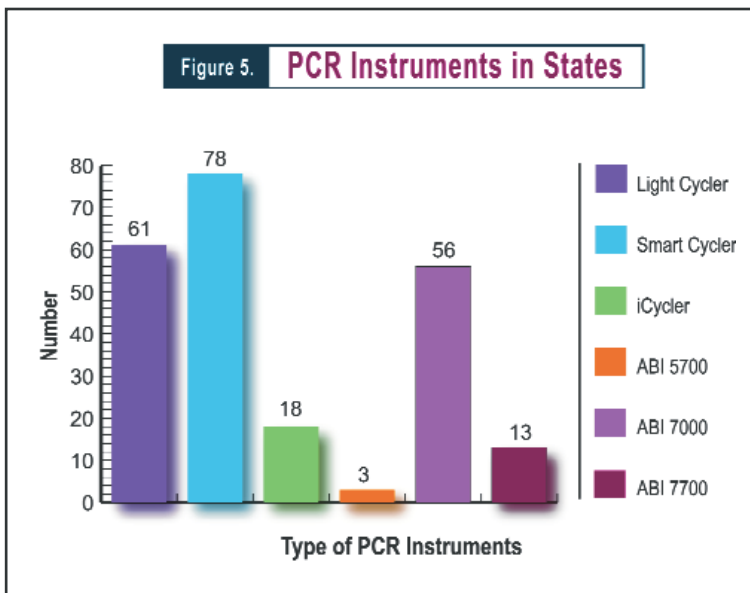
- Twenty-two (42%) states reported experiencing delays in receiving CDC-supplied LRN reagents. **States cited several reasons for this**

[♦] Reagents are special materials used in laboratory tests that result in the development of measurable reactions with specific target agents. The CDC produces these specialized, standardized reagents for use by the LRN confirmatory laboratories to detect and confirm biologic threat agents. These reagents are proprietary and are not available commercially.

delay, including the rationing of certain LRN reagents and the lack of required USDA/APHIS/VS permits.*

- Despite delays in receiving reagents, 47 (90%) states reported that they would prefer to continue to receive reagents through the CDC instead of a commercial supplier.

The LRN's rapid response capabilities are based on the use of various real-time molecular detection and antigen detection systems. As new technologies are developed, new instrumentation will be required.



- All states have at least one real-time PCR instrument for rapid detection of agents of bioterrorism. Figure 5 illustrates the number and types of PCR instruments available in

*This is the Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services permit to import or transport controlled material or organisms or vectors. As described in 9 CFR part 122, controlled material includes any organism that may cause infection in animals. This very broad definition, which lacks any list of specific biologic agents covered by the regulation, along with the

SPHLs as of August 31, 2004. Twenty-three states indicated that additional PCR instruments are needed to meet surge capacity needs and to provide redundancy in platforms.

- Eighteen (35%) states have a Luminex® instrument. Thirty-four states reported that they did not have a Luminex® instrument. This instrument enables laboratories to multiplex (simultaneously measure) multiple analytes quickly. This is an example of new technology, currently under evaluation by the CDC's Rapid Response and Advanced Technology Laboratory, which will be required to enhance the capacity of the LRN confirmatory laboratories.
- All but one state reported that they have a Victor time-resolved fluorescence (TRF) instrument. This instrument is used to analyze samples for ricin and Staphylococcal enterotoxin B.

To provide results of sample analyses rapidly to key decision makers, laboratory scientists are developing faster, more cost-effective assays. Consequently, public health laboratories need continued funding to acquire these new technologies, equipment and reagents for the detection of bioterrorism agents.

Smallpox Preparedness

The CDC and other federal agencies remain concerned that smallpox virus could be used by terrorists as a bioweapon.⁷ All LRN confirmatory

implementation of the Select Agent program requirements, which also cover import of certain high consequence pathogens, has created confusion, added burden and caused delays in preparedness for LRN laboratories. The USDA has determined that LRN laboratories must have BOTH Select Agent registration and a VS Form 16-3 permit to work with controlled material.

laboratories have access to standardized assays for varicella (chickenpox/shingles virus) and an orthopox (various pox viruses) screening assay. APHL has worked with the CDC to establish additional security and biosafety criteria for LRN laboratories that wish to perform testing to detect and differentiate smallpox from other orthopox viruses.

- All but two state public health laboratories have implemented at least one rapid method for detection of varicella zoster virus (VZV), the causative agent of chickenpox, which is the disease most likely to be confused with smallpox.
- **Nineteen labs (37%) have a validated PCR assay for smallpox.** An additional 26 labs are interested in establishing smallpox-specific testing capability. Decisions regarding further expansion of smallpox testing capability depend on further evaluation of test performance and laboratory proficiency by the CDC, as well as the ability of LRN laboratories to meet special biosafety and facility requirements.
- **The greatest gaps in smallpox preparedness are in electron microscopy (EM) facilities and PCR assays for smallpox look-alike diseases caused by herpesviruses and enteroviruses.** Forty-three state public health laboratories do not have electron microscopes, and only 27 of these laboratories have located a nearby site with EM to provide assistance. In-house validated (homebrew), non-FDA-cleared PCR assays for herpesviruses and enteroviruses are available in the private sector and could be used to assist in rule-out diagnostic testing for smallpox; however, none of these assays have been evaluated or standardized for use in the LRN.

Transportation and Courier Service

A reliable state-wide courier service offers an effective method for rapidly moving samples on both a routine and emergency basis. However, such courier systems are vulnerable to budgetary cuts because they are unlikely to be supported by federal funds.

- **Only twenty-eight (54%) states have an intra-state courier system, and of these, only 16 provided full-state coverage for all types of specimens.** This is, however, an improvement from 2002 when only 7 states provided full coverage.
- Since our last assessment, 15 (29%) states have added or expanded state laboratory courier service.

BioWatch

BioWatch is a surveillance system that continuously samples the air in select metropolitan areas for biological terrorism agents. Special filters located at air-quality monitoring stations in select cities are used to collect the samples.⁸ Filters are routinely collected each day and transported to confirmatory public health laboratories in the LRN for testing. **States reported that in a 20-month period, BioWatch laboratories processed over 75,000 filters.**

The BioWatch program is administered by the DHS in partnership with the Environmental Protection Agency (EPA) and HHS. The CDC provides technical expertise on laboratory analyses and oversees the federal BioWatch laboratory workforce currently deployed in the LRN laboratories. In response to criticisms from many public health officials that the program lacked conse-

quence management plans for response in the event of a positive result, the federal agencies responsible for the coordination of this program have begun to address the consequence management issue. However, more guidance from the federal government is needed at the state and local level. **The majority of responding LRN laboratories indicated that they prefer to work with the CDC and do not want to this program administered by a private contractor.**

Conclusion

Since APHL's first assessment in 2002, state public health laboratories have made substantial progress in preparing for bioterrorism and building response capacity. Examples of this success include outreach to sentinel laboratories, training of laboratorians at the sentinel and confirmatory levels and improvements in the security of facilities. These combined efforts have resulted in a stronger public health system and a nation with enhanced emergency preparedness capacity.

Despite these improvements, notable gaps in laboratory preparedness remain. These include work-

force shortages, inadequate stocks of LRN reagents and lack of federal standardized guidelines for facilities and procedures to safely conduct all-hazards screening of unknown samples. Proposed reductions in federal laboratory preparedness funding threaten the ability of public health labs to successfully address these gaps and maintain the progress that has been made.

APHL calls for a continued commitment by the federal government to improve and modernize our nation's public health system, which has been under-funded for decades. Short-term funding cannot adequately address the results of many years of neglect. To maintain and enhance vital laboratory bioterrorism preparedness programs, sustained funding for public health laboratories is essential.

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