

**Centers for Disease Control and Prevention
Subcommittee on Oversight and Investigations
Hearing: “Continuing Concerns Over BioWatch and
the Surveillance of Bioterrorism” (June 18, 2013)
Questions for the Record**

The Honorable Tim Murphy

- 1. Do you agree that expanding BioWatch with Gen-3 would increase the financial strain of state and local health departments?**
- a. Do you agree that an additional financial strain could negatively impact the capability of these state and local departments to respond to an actual bioterrorism event?**

It is hard to predict the financial impact on state and local health departments since Generation 3 (Gen-3) is still in the acquisition phase and the performance, concept of operations, and cost of deployment has not yet been established.

Considering the impact a Gen-3 system could have on the operational capability of state and local health departments, CDC believes that the state and local health departments' capabilities should be a consideration in the final decision to deploy.

- 2. Given the reductions in the capacity of the state and local health departments to respond, do you think the country is worse off in this regard than we were five years ago in preparing against bioterrorism?**

Preparedness is a process of continual improvement of capabilities. The past five years have seen advances in preparedness planning and countermeasure development and stockpiling at a Federal level. However, reduced funding at all levels has led to staffing and other reductions at state and local public health agencies, which adversely impacts public health preparedness.

State and local health departments rely heavily on the CDC-administered Public Health Emergency Preparedness (PHEP) cooperative agreement to build and sustain preparedness capabilities and to develop and exercise their all-hazards preparedness and response plans. This funding to state and local health departments for public health preparedness has decreased 17 percent since 2008 and 42 percent since the terrorist attacks and anthrax letters in 2001.

- 3. Do you know what the sensitivity is for the current BioWatch technology?**

CDC does not have sensitivity information on the BioWatch assays. CDC previously provided to the Committee sensitivity information on the Laboratory Response Network (LRN) assays that are used as a single component in the Generation 2 system.

4. Do you agree with the Department of Homeland Security’s Assistant Secretary Alexander Garza that BioWatch has never had a false positive result?

There is common agreement on what a BioWatch Actionable Result (BAR) does and does not determine. However, the term “false positive” has been used in different ways. DHS’s use of the term “false positive” refers to a BAR being declared for a specific BioWatch agent, when in fact the DNA from that agent was not actually present. Other groups, including the CDC, consider a “false positive” to refer to a BAR being declared for a specific BioWatch agent, where the DNA is detected for the agent but the specific strain of agent is not a threat to public health. Both DHS and CDC are working to coordinate our use of scientific terminology when communicating with our stakeholders.

Since its inception in 2003, the BioWatch program has experienced a number of BARs. To date, none of these BARs represented the release of a biologic threat agent and thus would be considered “false positive” tests for a biologic agent in CDC's view. However, these are the type of infrequent results that can be expected in testing for any rare condition.

Although initial positive results do occur, it is important to note that BioWatch has implemented an overall detection resolution protocol to ensure these results do not inadvertently lead to a high-consequence action. Also, the BioWatch program has modified its sampling methods and equipment to reduce the number of these positive test results.

5. When the BioWatch has a BioWatch Actionable Result (BAR) and that BAR is not a detection of the threat agent but a detection of a near-neighbor bacteria that exists naturally in the environment, is the adjudication of a BAR a draft or burden on federal, state and local authorities?

The adjudication of a BAR does create work for the jurisdiction and for their Federal partners. If the adjudication of BARS is an infrequent occurrence, the process of adjudication could be a good exercise for all parties. If there are too many false positives, on the other hand, the adjudication takes too much time and people could lose faith in the sampling process.

6. Isn’t it true that there were some problems with the APDS (autonomous pathogen detection system) deployment regarding environmental cross reactivities?

a. What were some of the problems with the “previous experience with environmental cross reactivity and the problematic APDS [Gen 2.5] deployment?”

CDC has had no direct involvement with the APDS deployment and we have no data on its performance in the field.

7. The National Academies of Science, in its 2011 report on BioWatch, wrote: “From the wider perspective of public health authorities responsible for determining whether a confirmed positive laboratory test (a BAR) represents a plausible indication of a bioterrorist attack meriting initiation of mass dispensing of prophylaxis, the committee concluded that all BARs to date have

been ‘BAR false positives,’ meaning they have signaled the potential occurrence of a terrorist attack when none has occurred.” Do you agree with this statement?

CDC concurs with the language in the National Academies of Science 2011 report on BioWatch that all BARs to date have been BAR false positives. CDC and DHS believe that the BioWatch tests provide preliminary screening results that always require additional review and testing before a conclusion about the occurrence of a terrorist attack can be made.

a. And when a BAR is caused because the tests have detected near-neighbors or background organisms, rather than the targeted bioterrorism agent, in your professional judgment, is that a false-positive?

CDC believes the detection of a near neighbor organism, rather than the targeted bioterrorism agent, should be considered a false positive. DHS and CDC have worked to minimize the occurrence of BARS due to near neighbor organisms, and BioWatch has improved its analytical capability to rule out non-pathogenic sub-species of bioterrorism agents.

It is important to note that BioWatch has implemented an overall detection resolution protocol to ensure these results do not lead directly to a high-consequence action.

8. If BioWatch had been in place in 2001, would BioWatch have detected the anthrax letter attacks?

BioWatch was not designed or intended to detect that type of small scale release of biological agents.

9. How important is it to have a complete assay validation before deployment of Gen-3?

a. Is there a completely validated Gen-2 assay?

Assay validation before deployment of a Gen-3 system is critical. One must know the performance characteristics of the system, in order to make the correct decision about its deployment, to develop the appropriate concept of operations, and to interpret results. BioWatch current operations (a/k/a Gen-2) uses screening (initial testing) reagents from the Department of Defense Critical Reagents Program (CRP). Any sample that produces a screening positive result is subjected to a verification panel using the CDC LRN assays. As an element of the BioWatch Gen-3 assay characterization effort, DHS conducted validation of the CRP and LRN assays against the Stakeholder Panel on Agent Detection Assays. Standard Method Performance Requirements published in the *Journal of Association of Analytical Communities International*. The data from this validation was shared with us.

There has been substantial progress to improve BioWatch’s analytical capability, including a robust quality assurance program, launched in FY 2010. This program ensures, on a daily basis at every facility, the technical validity of field and laboratory operations and monitors the performance of reagents that are used for analysis in the laboratory.

10. What are some of the perceived limitations of the current Gen-2 system?

a. What would be some improvements?

In CDC's view, enhancements to the current Generation 2 system might include the following. Use of more specific nucleic acid signatures for some organisms to decrease the possibility of false positive results. The volume of air sampled could be increased to improve the sensitivity of detection. Improvement of the current filtering process with another method of particulate concentration could reduce collection of substances that interfere with the PCR testing. The frequency of PCR testing of a collected sample could be increased.

11. With respect to the Gen-3 autonomous "robot" system, do you believe that the public health laboratories will have confidence to take action on one test result from a Department of Homeland Security robot that does not use LRN assays?

Generation 3 is still in the acquisition phase, so it is difficult to tell how confident LRN laboratories, including those laboratories in the states, will be in the results from a Gen-3 system. To be confident in the results, the scientific community, including CDC and the LRN laboratories, will want the performance of the system to be adequately assessed, and they will want to see this performance data themselves. They will also want to see the system field tested, to ensure the accuracy of results.

12. What is the difference between the Public Safety Actionable Assay (PSAA) standard and the Public Health Actionable Assay (PHAA) testing standard?

a. Which testing standard would you support?

b. Why is the testing standard important?

Testing standards are important in order to understand how assays perform (e.g., sensitivity, specificity, robustness) and how this impacts the interpretation of the results. Both the PSAA standard and PHAA standard are sufficiently robust to support their respective intended uses. However, the two standards were developed for different purposes and are used in distinct ways.

The PSAA standard is intended to apply to technologies that would be used in the field by individuals with first responder training to accomplish the first detection of a biological threat agent. Results from these technologies under this standard are intended to support "immediate" Public Safety Actions that include closure and evaluation of a facility or area, and decontamination of individuals. An additional sample of the suspect material would then be sent to a CDC Laboratory Response Network (LRN) laboratory for confirmatory testing. The PSAA standard was developed by DHS S&T in collaboration with other Federal and private sector partners to support the commercial/private sector development of technologies and/or assays for use by First Responders and the private sector for screening of suspicious materials (environmental samples only) for biological threat agents.

The final verification test panel necessary for a BAR to be declared is done using CDC LRN assays, in affiliation with a CDC LRN Laboratory, which uses the PHAA standard. Also developed by DHS S&T in collaboration with other Federal partners, PHAAs are required to have the specificity, sensitivity, and robustness to provide critical information on agent-specific

detection to support public health actions and decisions such as initiating a national or local health alert warning, initiating a public health investigation, conducting risk assessments to support distribution of post exposure prophylaxis, and initiating public health risk communications.

CDC, DHS, and other Federal partners will continue to review and update standards that can be applied to improve and enhance the specificity of biosecurity technologies.

13. Why is it important to detect these agents as early as possible before citizens begin to develop symptoms?

a. Is it true that PHAA would give public health officials more information to base decisions for prescribing clinical remedies (e.g., vaccinations) in the event there was an attack.

Early detection allows public health to take measures to minimize further exposures, and earlier begin the processes of identifying persons at risk, and deploying and administering countermeasures. This could potentially save many lives.

The PSAA standard, as an initial indicator, is meant to provide a good screening assay to detect organisms that might constitute a threat to public health. The PHAA, as a verification of the initial results, would give public health officials more information. Specific panels of organisms have been developed and are used to validate assays intended for use with clinical specimens, and environmental (*e.g.*, BioWatch), food, and water samples positive results with tests that conform to the PHAA standard are more likely to be true positives and thus will provide better information to inform public health decisions, like the administration of vaccines.

14. In the event of a BAR, what additional information will the Centers for Disease Control and Prevention look for before taking public health actions with the distribution and dispensing of medical counter-measures?

The declaration of a BAR is just one step in a process of responding to a positive environmental test. The process includes subsequent steps that are used to determine if a high-consequence action (such as dispensing medical countermeasures) would be warranted. These steps include many local, states, and national partner agencies that would be involved in making decisions about what actions are needed and when they should be taken.

DHS has provided guidance to BioWatch jurisdictions on how to respond to a BAR. In the event of a BAR, a national conference call is convened by DHS and BioWatch representatives where CDC works with DHS and HHS/ASPR, the local jurisdiction, and other agencies to gather as much additional information as possible to determine whether the BAR represents an anomaly or a threat. During this call, CDC will ask the local jurisdiction to do additional testing on the sample that they have on hand. We may ask them to go out and perform environmental sampling in the area where the detector was located or other areas where the organism might be found. In addition, the national conference call will query intelligence agencies and law enforcement agencies to find out whether there is any indication that there might be a threat with this agent. Finally, the CDC will ask subject-matter experts in the field if there are other factors they think

might be causing this to be positive, and public health authorities will intensely scrutinize disease surveillance activities for evidence of unusual disease.