UCRL-JRNL-204034

LAWRENCE
LIVERMORE
NATIONAL
LABORATORY

Science and Technology for Bioterrorism Defense

J. Patrick Fitch

May 7, 2004

Encyclopedia of Bioterrorism

Science and Technology for Bioterrorism Defense

J. Patrick Fitch, Ph.D.
Lawrence Livermore National Laboratory

The Lawrence Livermore National Laboratory (LLNL) Chemical & Biological National Security Program (CBNP) provides science, technology, and integrated systems for chemical and biological security. Our approach is to develop and field systems that dramatically improve the nation's capabilities to prevent, prepare for, detect, and respond to terrorist use of chemical or biological weapons.

Background

History underscores the importance of preparing to defend against terrorism. A well-documented example of a terrorist organization is the Aum Shinrikyo cult [1]. After several flawed attempts at terrorism using botulinum toxin, *Bacillus anthracis* spores, and other biological agents, the cult released sarin nerve gas in Tokyo's subway in March 1995, injuring more than 3,000 people. These terrorist acts served to catalyze and focus the early LLNL program on civilian counterterrorism. In 1995, LLNL began the CBNP using Laboratory-Directed R&D investments and a focus on biodetection. The 1996 Nunn-Lugar-Domenici Defense Against Weapons of Mass Destruction Act initiated several U.S. nonproliferation and counterterrorism programs, including the Department of Energy (DOE) Chemical and Biological Nonproliferation Program (also known as the CBNP). In 2002, the Department of Homeland Security (DHS) was formed. The DOE CBNP and many of the LLNL CBNP activities have been transferred to the new Department as part of the Science and Technology Directorate's Biological and Chemical Countermeasures Program. The LLNL activities represented about half of the program that was transferred to DHS from DOE.

LLNL has a long history in national security, including nonproliferation of weapons of mass destruction. In biology, LLNL had a key role in starting and implementing the Human Genome Project and, more recently, the Microbial Genome Program. In addition, a medical device program at LLNL began in the early 1990s. The collective culture of the CBNP program at LLNL blends a national security mission focus, the competitive spirit of the human genome "race," and strong partnerships with industry and end users developed in medical programs so that our systems would be both useful and commercially viable. Commercial viability is the catalyst for change and for the investment required to meet the safety and efficacy standards for health-associated systems. Blending these three cultures supports our strategy of identifying new, high-impact systems and taking the systems from concept to operational proof-of-principle.

In addition to the CBNP-specific expertise, LLNL has more than 1,000 scientists and engineers with relevant expertise in biology, chemistry, decontamination, instrumentation, microtechnologies, atmospheric modeling, and field experimentation. More than 100 LLNL scientists and engineers work full time on chemical and biological national security projects. The program also leverages special facilities that are part of the LLNL infrastructure, including the National Atmospheric Release Advisory Capability (NARAC), the Forensic Science Center (FSC), the Biosecurity and

Nanoscience Support Laboratory (BSNL), Fermentation Laboratory, Pathogen Laboratories, the Micro Technology Center (MTC), and the Center for Accelerator Mass Spectrometry (CAMS). **Demonstration Programs**

Critical shortcomings remain in the ability to prevent, prepare for, detect, and respond to chemical or biological terrorism. Thus, the LLNL CBNP emphasizes collaborative demonstration programs with end users as part of a spiral development strategy. These programs provide near-term capabilities, opportunities for dialogue among scientists and end users, focus for R&D investments, and paths for pilot-to-regional-to-national systems. Our development strategy is strengthened by involvement in both operational systems and basic research in pathogen biology, material science, computer algorithms, and instrument development.

Current and emerging collaborative demonstration programs include:

- Biological Aerosol Sentry and Information System (BASIS) is an environmental monitoring system originally designed for the Salt Lake City 2002 Winter Olympics. BASIS is a joint project of LLNL and Los Alamos National Laboratory (LANL) with significant participation by law enforcement and public health organizations. BASIS was successfully deployed at the Olympics, and the LLNL team has been deployed to several other sites. In the past two years, several hundred thousand assays have been performed by LLNL in support of counterbioterrorism using a BASIS-like architecture with no false alarms. The BASIS team won an R&D100 award in 2003.
- Environmental testing cannot identify low-level releases and can only detect known pathogens. Laboratory testing of sentinel populations for early detection of bioterrorism (SENTINEL) is a strategy that complements BASIS-type environmental monitoring by performing surveillance of the population through direct, high-throughput testing of clinical samples of opportunity. LLNL has demonstrated 1,000 samples (10,000 assays) performed in an 8-hour shift with only two technicians. SENTINEL is an emerging program in collaboration with health providers to directly detect pathogens and toxins in samples. Preliminary data by LLNL and an industrial collaborator indicates that the strategy might also be applied to presymptomatic detection of host response biomarkers. LLNL is pursuing a basic science program known as Pathomics to establish the links between pathogenicity and host response [2]. In addition to possibly addressing the genetically modified threat, a SENTINEL strategy is useful in public health applications (e.g., influenza) even in the absence of bioterrorism.
- Local Integration of NARAC in Cities (LINC) provides responders in local government with modeling and prediction tools for decision support. Composite views of aerosol plume prediction with important local features, including schools and fire and police stations, are available to the users. Both local and reach-back capabilities are provided. The first pilot city for LINC evaluation, which began in September 2002, is Seattle, Washington. At present, there are five LINC cities.
- Bio-Forensics is a joint LLNL, Northern Arizona University, and LANL project to make specific forensic tools and data available to the broader community. The focus

is on supporting law enforcement and the Centers for Disease Control and Prevention (CDC) PulseNet Laboratories for food-borne illnesses. Round-robin comparisons of different methods and assays will precede the principle deliverables of (1) a database for a variety of end users focused on law enforcement and (2) strain-sensitive markers and validated assays for *Salmonella* and *E. coli* for CDC PulseNet.

- PROTECT is an Argonne National Laboratory, Sandia National Laboratories (SNL), and LLNL program for protection of key facilities, focused mostly on chemical attacks. LLNL is supporting PROTECT through NARAC and biodetection. NARAC is doing modeling and predictions for outside-facility and scenario studies, including operational support of deployed systems.
- LLNL was selected by the U.S. State Department as the second U.S.-designated laboratory for the Office for the Prohibition of Chemical Weapons (OPCW). We have implemented all the technical, safety, and procedural systems required and have been ISO-17025 approved. OPCW designation was received in 2003. The first U.S. OPCW-Certified Laboratory is at ECBC in Edgewood, Maryland. The ECBC group provided substantial assistance to LLNL in this process.
- Restoration of Operations is demonstrating strategies for decontamination and restoration of operations for major transportation facilities [3]. The activity builds on LLNL restoration planning for chemical warfare agent attacks on transportation facilities, decontamination reagents including L-Gel, sampling strategies to support decontamination, high-throughput sample processing, accelerated viability testing, and published studies to establish “How clean is clean enough?” LLNL and SNL jointly execute the project with a focus on airports and establishing templates for restoration strategies.
- Model Cities is a LLNL, SNL and LANL project to better understand geographic and other local or regional factors that influence prevention, preparation, and response. The goal is to create common “templates” that can be applied in many locations and in combination to create more comprehensive regional plans. The initial testbeds for the concept have been the other demonstration projects (e.g., BASIS and LINC) and a tri-lab demonstration in Albuquerque, New Mexico, in December 2002. Integration and evaluation of multiple detection schemes for wide-area, special-facility, and epidemiological surveillance were accomplished.

Science and Technology Areas

Demonstration programs help focus our science and technology (S&T) investments. The S&T is managed in four areas: (1) decontamination and restoration, (2) modeling and prediction, (3) instrumentation, and (4) applied science. Some of the current S&T activities include:

- **Decontamination and restoration.** The goal is to provide the S&T and systems approach to quickly restore civilian facilities to operation [4]. Decontamination in a civilian setting requires fundamentally different technology from that for most military applications. Rapid and effective means of decontamination are needed for equipment, facilities, and large urban areas. LLNL developed and is licensing the L-

Gel decontamination technology. Several new decontamination chemistries are in development and testing, including vaporous hydrogen peroxide. In addition, appropriate protocols for efficient restoration are being investigated [5].

- **Modeling and Prediction.** The goal is to develop predictive urban-environment modeling tools for local and other users for response, planning, and vulnerability assessments. Advances in computing algorithms and hardware now make it possible to model air flows over very complex terrain. LLNL is developing tools for modeling such flows in urban environments, including around buildings and in subways, to determine in advance how to best respond and to permit real-time prediction of agent dispersal during an actual event.
- **Instrumentation for Biological Detection.** The goal is to provide highly sensitive and accurate instruments for early warning, treatment triage, and detection of contaminated areas**.** LLNL is developing and integrating instruments with substantial increases in detection performance [6]. LLNL technology for rapid DNA detection was licensed to industry and enabled a successful product that has been applied to counterterrorism. LLNL has developed prototypes for a new instrument that is capable of 100 simultaneous assays; detecting viruses, toxins, spores, and vegetative bacteria; and autonomous operation for several days at a time. Prototypes of this instrument have been tested with aerosolized live agents and were deployed in a limited capacity in 2002. Several next-generation instruments that are part of our R&D portfolio address major current shortcomings, including cost per assay, operational complexity, and real-time response.
- **Applied science.** The goal is to provide biological and chemical support for detection and other countermeasures. The availability of DNA and RNA sequence information has enabled rapid development of biological signatures that are highly specific and sensitive [7]. Techniques are also being developed for ligand signature discovery as well as subspecies-level bioforensics. LLNL has invented several high-throughput approaches for vetting signatures (both nucleic acid and ligand) including computational screening of potential signatures, automated strain-panel testing, complex environmental sample testing and, more recently, pathogen-associated function and host-associated response using genomic and proteomic tools (pathomics).

Summary

The LLNL program is developing new systems to improve the ability to prepare for, detect, and respond to a terrorist event. Improvements come from a blend of new technologies and operational concepts that are vetted in experiments in the field with public health, law enforcement, and other collaborators. Several of the LLNL systems are already operational and deployed, specifically NARAC, BASIS, and the Forensics Science Center. The next technology development focuses on cost reduction and shortening response times. As we look to the future, the most promising systems are dual-use in that they are valuable in the absence of terrorist events and invaluable during one.

Biography

J. Patrick Fitch, Ph.D., leads the Chemical and Biological National Security Program (CBNP) at Lawrence Livermore National Laboratory (LLNL). This was a $54M and 150-person activity in FY02. Before the CBNP, Dr. Fitch led R&D teams in genomics, bioengineering, medical devices, miniaturized systems, and imaging systems. Recent presentations and publications include pathogen genomics, proteomics, and modeling and the book, *An Engineering Introduction to Biotechnology* (SPIE Press, 2002).

Acknowledgements

This work was performed under the auspices of the U.S. Department of Energy by UC, Lawrence Livermore National Laboratory under Contract W-7405-ENG-48. The work would not have been possible without the interest and support of our sponsors at DHS (J. Vitko, G. Parker, E. George, et al.), DARPA (A. Alving, R. Gibbs, S. Buchsbaum, et al.), and other organizations. We have numerous collaborations at other laboratories, especially Sandia and Los Alamos, and with industry, academia and other government agencies, especially the CDC and DoD. Our team at LLNL is both talented and dedicated. We are organized by discipline with P. McCready, A. Burnham, B. Colston, and D. Imbro leading the biological, chemical, instrumentation, and systems and deployments areas, respectively. LLNL discipline organizations provide their best talent in computations, biology, physics, engineering, chemistry and environmental sciences and we acknowledge their generous support. V. Hambrick provides outstanding coordination and administrative support for the program, and we would be lost without her.

---

[1] K.B. Olson, "Aum Shinrikyo: Once and future threat?" *Emerging Infectious Diseases* **5**(4), July–Aug., 1999, pp. 513–516. [online www.cdc.gov/ncidod/EID/vol5no4/pdf/olson.pdf]

[2] J.P. Fitch, B.A. Chromy, C.E. Forde, E. Garcia, S.N. Gardner, P. Gu, T.A. Kuczmarksi, C. Melius, S.L. McCutchen-Maloney, F.M. Milanovich, V.L. Motin, L.L. Ott, A. Quong, J. Quong, J.M. Rocco, T.R. Slezak, B.A. Sokhansanj, E.A. Vitalis, A.T. Zemla, and P.M. McCready, "Biosignatures of pathogen and host," *Proc. IEEE Workshop on Genomic Signal Processing and Statistics (GENSIPS)*, Raleigh, NC, Oct. 12–13, 2002.

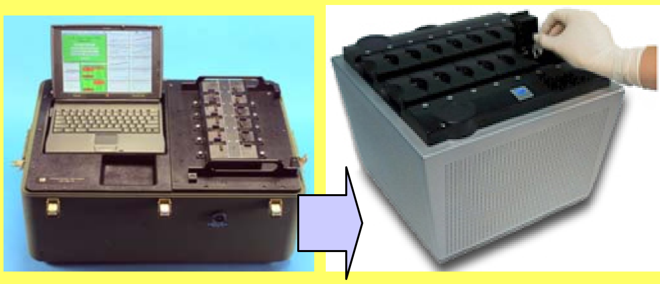
[3] D.R. Imbro *et al*., paper presented at the Chemical and Biological National Security Program Summer Meeting, Washington, D.C., 3–5 June 2003.

[4] E. Raber, J.M. Hirabayashi, S.P. Mancieri, A.L. Jin, K.J. Folks, T.M. Carlsen, and P. Estacio, "Chemical and biological agent incident response and decision process for civilian and public sector facilities," *Risk Analysis* **22**(2), pp. 195–202, April 2002.

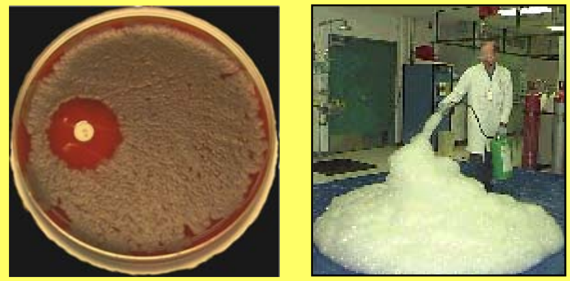
[5] E. Raber, A. Jin, K. Noonan, R. McGuire, and R. Kirvel, "Decontamination issues for chemical and biological warfare agents: how clean is clean enough?" *Int. J. Env. Health Res*. **11**(2), pp. 128–148, June 2001.

[6] M.T. McBride, S. Gammon, M. Pitesky, T.W. O'Brien, T. Smith, J. Aldrich, R.G. Langlois, B. Colston, and K.S. Venkateeswaran, "Multiplexed liquid arrays for simultaneous detection of simulants of biological warfare agents," *Anal. Chem*. **75**(8), pp. 1924–1930, April 15, 2003.

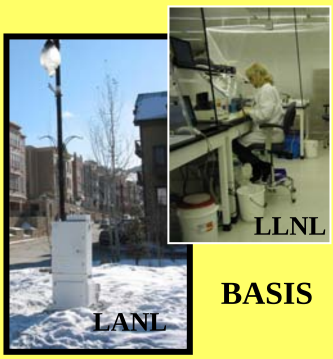
[7] J.P. Fitch, S.N. Gardner, T.A. Kuczmarski, S. Kurtz, R. Myers, L.L. Ott, T.R. Slezak, E.A. Vitalis, A.T. Zemla, and P.M. McCready, "Rapid development of nucleic acid diagnostics," *Proc. IEEE* **90**(11), pp. 1708–1721, Nov. 2002.



The LLNL Advanced Nucleic Acid Analyzer demonstrated 7 minute PCR detection in April 1999. LLNL technology licensed to Cepheid helped create the Smartcycler product that is now used in LLNL field labs.



LLNL restoration R&D ranges from development of new decontamination agents, to room-size demonstrations, to evaluation of large-scale restoration for special facilities like transportation hubs.



BASIS

Future

The BASIS biodetection system is based on a aerosol collector network with a central deployable field laboratory. The field lab can also support decontamination/restoration activities and clinical sentinels for early detection. In December 2002, over 10,000 assays were performed in an 8 hour shift by two technicians. A next generation instrument (APDS) is in development by LLNL and includes the collector and laboratory in one unit with unattended operation for several days. Miniaturization of various components improve performance and reduce costs.

Atmospheric modeling and experiments are being used to assess sensor placements and to provide feedback to first responders in urban environments. Photograph of August 7, 1998 tire fire in Tracy, CA with LLNL/NARAC-simulated particle positions in red (top) and city-wide simulations of a plume.