Chapter 3
By the Book: Academic and Research Institute Perspectives on BWC Monitoring

The academic and research institute experts who accepted the Stimson Center's invitation to brainstorm the technical feasibility of monitoring the Biological and Toxin Weapons Convention (BWC) covered a wide spectrum of expertise and brought ample years of experience to the table. Among the participants were Dr. Robert Shope, an infectious disease epidemiologist of world renown, Dr. Barry Kreiswirth, the director of the Public Health Research Institute's tuberculosis research laboratories, Dr. Corrie Brown, a veterinary pathologist specializing in the diagnosis and pathogenesis of foreign animal diseases, and Dr. Anne Vidaver, a plant pathologist who alone has more than thirty years of teaching experience. This group's credentials included degrees in microbiology, zoology, bacterial genetics, virology, and veterinary medicine, as well as extensive experience in high containment laboratories handling dangerous pathogens. As the full resumes in the appendix attest, the attendees hold several patents and have authored literally hundreds of peer reviewed journal articles. Two of the ten participants in this group opted to remain anonymous.

Stimson facilitators walked this group of technical experts through a progressive mental exercise that required them to consider a broad list of monitoring issues, thinking alternately as BWC inspectors and as hosts of BWC inspections. Box 1.1 shows the type of questions that Stimson facilitators posed iteratively to the brainstormers. The group's concerns, work-arounds, and overall reflections are the basis of this chapter.

The academic and research institute experts were no strangers to the concepts and realities of inspections. Activities at their facilities are overseen by an assortment of internal and external entities, any one of which could put the brakes on their work. Within their organizations, internal research, animal care, fire safety, and biosafety committees review projects. At various times, outside regulatory entities such as the Food and Drug Administration, the Occupational Health and Safety Administration, state and federal environmental protection agencies, fire inspectors, the US Department of Agriculture, and the Nuclear Regulatory Commission troop through their laboratories and wade through their records.[1] If an

[1] Chemical surety inspectors also oversee some sites, noted one individual from the veterans group, who said that the Food and Drug Administration was at his facility for thirty days in 1999. Inspection Veteran 3, trial inspection observer and mock inspection participant, 27 April 2001. Inspection Veteran 3, who holds a DVM and a PhD, observed the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and participated in the mock trilateral inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland. If a laboratory is affiliated with a hospital, the Joint Commission on Accreditation of Healthcare Organizations would also have an oversight role. These inspections can be quite harrowing for the recipients. One academic participant cited a case where supplementary records were not readily available when Nuclear Regulatory Commission inspectors came through a facility. The inspectors began to press site personnel very hard. "They asked and asked and asked and made the staff feel horrible." The laboratory in question was almost fined $5,000 for momentarily leaving a freezer containing radioactive material unlocked. Dr. Nancy Connell recounted the Nuclear Regulatory Commission inspection. Dr. Nancy Connell, PhD in bacterial genetics, works in the Department of Microbiology and Molecular Genetics at the New Jersey Medical School, where she also serves as the director of molecular mycobacteriology at the National Tuberculosis Center. Note that commercial organizations that sponsor research also have an oversight role. On other oversight

accident occurs in a research laboratory, the Centers for Disease Control and Prevention enters the picture to investigate the problem, which one participant described as "your worst nightmare. They will stay until they are done. They are asked to come in because there is an outbreak problem. . . . They are trying to figure out what happened as opposed to did it happen or not. They have almost full carte blanche."[2]

While the presence of inspectors site can be unnerving and inconvenient, members of this group explained that inspections can also prompt beneficial changes in the way a laboratory is run (e.g., safety, operational practices).[3] Having inspectors in their midst can, in other words, be a positive learning experience. Such was the case for the two brainstormers who hosted an inspection that the Stimson Center mounted to test this group's monitoring concepts, an exercise described at length in box 3.1 at the end of this chapter.

Encounters with inspectors aside, the participants had all spent considerable time in laboratories replete with the very equipment and skilled personnel that they believed would be of concern to an inspectorate charged with monitoring the BWC. Research laboratories are inherently fungible places. Scientists could be studying innocuous strains one moment, but in the next they could place a super virulent strain under the microscope. Given that reality, one participant simply stated that "an overarching aspect of this is that it is going to be very easy to hide" improper activity at research institutes.[4] Consequently, the group concluded that it would be extremely hard to uncover prohibited activity in research laboratories. The difficulty of the task did not dissuade their efforts, however, to pull

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and inspections: Dr. Corrie Brown, DVM and PhD in comparative pathology; Dr. Barry Kreiswirth, PhD in microbiology; Academic Expert 1, PhD in microbiology; and Academic Expert 2, MD, 6 January 2000 and 16 August 2000. Dr. Corrie Brown, DVM and PhD in comparative pathology, heads the Department of Veterinary Pathology at the University of Georgia College of Veterinary Medicine. Dr. Barry Kreiswirth, PhD in microbiology, is the director of the Tuberculosis Center at the Public Health Research Institute. Academic Expert 1 is a virologist with a PhD in microbiology currently working in a microbiology and immunology department at a large US university. Academic Expert 2, MD, is a pathology professor at a major US medical school and the director of a tissue typing laboratory.

[2] Dr. Barry Kreiswirth described the Centers for Disease Control and Prevention's approach to inspections. Next in the nightmare category might be the Internal Revenue Service, which one participant recalled roosting at a university for three years. Academic Expert 1, PhD in microbiology, 16 August 2000.

[3] Dr. Robert Shope noted on 16 August 2000 that inspectors from the Centers for Disease Control were very helpful when they came to a laboratory at Yale University, including their efforts to explain matters to the media. Dr. Robert Shope, MD and epidemiologist, is a professor of pathology in the Center for Tropical Diseases at the University of Texas Medical Branch at Galveston. In the 6 January 2000 meeting, Dr. Corrie Brown noted another possible upside to hosting inspections in that they would broaden the horizons of workers and therefore possibly increase their productivity.

[4] Dr. Robert Shope, MD and epidemiologist, 16 August 2000. Some in the group pondered the likelihood that a chain of research laboratories would communally engage in bioweapons development, with each laboratory specializing in different areas. They surmised that such an approach would be even harder for inspectors to detect. Theodore Myatt, doctoral candidate, former biosafety officer; Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Theodore Myatt was previously a biosafety officer and currently serves in the Division of Epidemiology and Immunization at the Massachusetts Department of Public Health. Editor's note: The former Soviet Union took exactly that approach, nesting weapons research activities in a web of research laboratories. For more on the history of this vast weapons program, see Ken Alibek with Stephen Handleman, *Biohazard* (New York: Random House, 1999). On efforts to transform these bioweapons research institutes into peaceful research centers: Amy E. Smithson, *Toxic Archipelago: Preventing Proliferation from the Former Soviet Chemical and Biological Weapons Complexes* (Washington, DC: Henry L. Stimson Center, December 1999).

together a monitoring approach that they believed would be fair to legitimate research institutes and instill the fear of discovery in those involved in weapons research.

Early in their discussions, the academic and research institute experts differentiated between two kinds of monitoring concerns. The first category encompassed matters that the inspectors would know about ahead of time due to some sort of declaration process or information gathered from other outside sources; the second, matters that the inspectors found once on site. The group came to consensus that the essential features that should qualify research laboratories automatically for BWC monitoring were the presence of: 1) bioweapons agents, and 2) biosafety level 3 or 4 capabilities. Any defensive research activities in these settings, they presumed, would be declared. Other capabilities with weaponization potential (e.g., aerosolization, milling, encapsulation), they observed, would elevate a facility up the inspectors' target list. Such capabilities should be declared but should not in and of themselves automatically draw an inspection because of their ubiquitous use for legitimate research purposes.[5] Based on these criteria alone, it was noted with a mixture of apprehension and irony, that most collegiate laboratories would not be subject to BWC monitoring. Some in the group worried that not casting the inspection net wider would make it easier for cheaters, but others said that catching a violator red-handed in the laboratory setting would be a tremendous feat. Violations, they reasoned, would be more readily detected at the other sites involved in a full-scale bioweapons program (e.g., manufacturing plants, large test facilities).[6]

Other tenets that the group adopted early and reconfirmed continually included the need for inspections at academic and research institutes to proceed from a presumption of legitimacy and for inspectors to evaluate the big picture at a facility as opposed to a single item or capability located there. Essentially, few, if any, of the matters that concerned them could alone clearly signal to inspectors that something unsavory was taking place at a given research site. Simply having a primate facility or fermentation and aerosolization capabilities could not be viewed as conclusive of involvement in offensive weapons work, since these very capacities are also essential to vindicable research.[7] Certainly, such features would constitute a "flag" of possible concern, but the inspectors would need to assess such features in combination and in context to determine whether a laboratory's work constituted a genuine

[5] "Labs working with these agents by definition are going to be under some suspicion, so I think that monitoring comes with the territory." Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Dr. Nancy Connell, PhD in bacterial genetics; Dr. Corrie Brown, DVM and PhD in comparative pathology; Dr. Robert Shope, MD and epidemiologist; and Academic Expert 1, PhD in microbiology, expressed similar views about the importance of agents as well as biosafety levels and key equipment, to which the group concurred.

[6] Dr. Barry Kreiswirth, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist; Dr. Nancy Connell, PhD in bacterial genetics; and Academic Expert 1, PhD in microbiology, expressed such sentiments.

[7] For example, some may consider aerosolization capabilities indicative of possible offensive work, but it is not uncommon for university laboratories to have some aerosol capacity, for instance those working on plant diseases. Dr. Anne Vidaver, PhD in bacteriology, 6 January 2000. Dr. Anne Vidaver heads the Department of Plant Pathology at the University of Nebraska-Lincoln. Also on this point, Theodore Myatt, doctoral candidate, former biosafety officer.

BWC violation.[8] Thus, the group designed a "dig deeper and deeper" monitoring approach, but only if necessary given the presumption of legitimacy. They concocted a tri-level inspection scheme, with an inspection team getting increasingly intrusive if inspectors unearthed signs of possible foul play.

PRE-INSPECTION ACTIVITIES

Working from declarations, the academic and research institute experts believed that the inspectorate could perform several literature searches to help prepare inspectors for their work on site. This group advised pulling up the publication records and presentation activities of a laboratory's staff. Universities in most countries operate under a time-honored "publish-or-perish" rule, and there is considerable pressure at research institutes to air research results as well. One would expect laboratory personnel to leave a wake of scientific publications and presentations commensurate with their tenure in the field.[9] Therefore, scanning publications and conference presentations offers the inspectors a quick gauge of legitimacy. "They have all this money, all this equipment, all these people, and they haven't published in a decade. That's a tipoff."[10] These data searches would also give inspectors an idea of what organizations have been funding a laboratory's work and who has been interacting with its scientists.[11] Rarely are research institutes islands. Their work is very collaborative, so a facility with few or no outside ties would definitely be atypical. Finally, a review of newspaper and other media sources might reveal if there had been any unusual disease outbreaks among humans, livestock, or crops in the vicinity of the laboratory. News to that effect should certainly forewarn inspectors to be on their toes. While helpful for a quick assessment and for the assignment of suitably skilled individuals to the inspection

[8] As one participant put it, "There are various flags, but it takes several flags to turn them red." Academic Expert 1, PhD in microbiology, 6 January 2000. Another brainstormer labeled this approach "multiple variant analysis." Academic Expert 2, MD, 6 January 2000.

[9] The group noted that such data may be hard to come by in some countries, such as Iran and North Korea. However, scientific journals exist in virtually all of the world's languages, and professional conferences are routinely held on a national, regional, and international basis. Total lack of publications and presentations would therefore be most unusual. To the group's agreement, Dr. Jerry Goldstein voiced these observations about the importance of looking into the publication track record of facility scientists. Dr. Jerry Goldstein, PhD in microbiology, is a professor of microbiology and chairman of the Botany/Microbiology Department at Ohio Wesleyan University.

[10] Academic Expert 1, PhD in microbiology, 16 August 2000. Dr. Barry Kreiswirth also noted the utility of a literature search to reveal gaps in time where scientists did not publish, which would necessitate an explanation. Dr. Corrie Brown added that literature searches would be "especially important in those countries that only publish in-country" because their scientists are therefore unlikely to have much of a profile internationally. Some in the defense contractors group also agreed that it would be somewhat useful to examine resumes, papers published, membership in professional societies, attendance at professional meetings, and whatever data was available about a site's activities. Defense Contractor 3, senior technical adviser; Defense Contractor 5, director of microbiology and special government projects; Defense Contractor 7, president and founder of a small sensor development company, 28 August 2000. Defense Contractor 3, employed at a large, nonprofit research organization, holds a PhD in physics. Defense Contractor 5, working at a small defense contracting research company, has a PhD in microbiology. Defense Contractor 7 has a PhD in microbiology.

[11] Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000.

team, these off-site data searches, the academic and research institute group decided, were of low utility in comparison to on-site monitoring activities.[12]

ON-SITE MONITORING ACTIVITIES: LEVEL 1 INSPECTION

Once on site, the inspectors must contend with the daunting task of trying to determine whether laboratories that have declared possession of biological agents of concern and/or have a biosafety level 3 or 4 capability are engaging in illicit offensive research and development activities. Should a laboratory have a scale of capabilities that could contribute to weaponization work (e.g., media, serum, concentrators, fermenters, milling and aerosolization equipment) and that surpassed the laboratory's needs, academic and research institute experts argued that the excess scale should quickly elicit concern on the part of the inspectors.[13] A facility also engaged in studies targeting increased virulence, resistance to therapeutics, stability, and human or animal toxic dosage should make the inspectors chafe even more.[14] With regard to biosafety matters, this group advised inspectors to be alerted by a physically isolated facility, one that employed unusual clean-up protocols or waste treatment procedures, one that had non-standard biosafety oversight arrangements, or one that experienced an inordinately high level of infectious illness among its staff.[15] Another oddity that should heighten inspectors' suspicions would be if the facility's staff were not open to inquiry. Personnel in universities and research institutes normally thrive on interaction with other scientists. To encounter individuals who were closed, who refused to reveal how many people worked in their laboratory, to explain their work, or to show their working environment would be an unlikely occurrence in the scientific research community. Aside from inappropriate reactions to questions and requests, the inspectors could be tipped off by personnel telling conflicting stories.

Inspectors, they instructed, should also look askance at a facility that had few or no records, or that had overly organized records. While universities and research institutes certainly adhere to regulations and scientific standards, the atmosphere in a research facility is not the same as in the

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[12] Theodore Myatt made a statement about the low monitoring utility of the data searches, which elicited nods of agreement from other participants. The need to send appropriately skilled inspectors is discussed subsequently. Since the inspectors would track down such data on their own, the institutes being monitored would not be inconvenienced at all. Dr. Nancy Connell, PhD in bacterial genetics, 16 August 2000.

[13] Dr. Jennie Hunter-Cevera, PhD in microbiology; Dr. Nancy Connell, PhD in bacterial genetics; Academic Expert 2, MD, 6 January 2000. Dr. Jennie Hunter-Cevera, PhD in microbiology, is president of the University of Maryland Biotechnology Institute.

[14] Dr. Corrie Brown, DVM and PhD in comparative pathology; Dr. Anne Vidaver, PhD in bacteriology; Academic Expert 2, MD, 6 January 2000.

[15] The group reasoned that a proliferator might want to take the extra precaution of isolating a bioweapons research facility, although that might not always be the case. Odd cleanup or waste treatment procedures might indicate that personnel were working with more dangerous microorganisms than the one(s) declared. A research institute that lacked a biosafety oversight committee or biosafety officer(s) would be quite uncommon, as would overkill in the biosafety department. Biosafety oversight should fit the stated research work. Finally, sick leave due to infectious illness would warrant investigation.

manufacturing sector, where every "i" must be dotted, every "t" crossed. In an academic setting, logbooks devoid of erasures or mistakes and other perfectly lined-up records could be a giveaway to cooked books. Summing up the group's views on this point, one participant stated: "Lab books are supposed to be messy."[16] That same too-good-to-be-true principle could apply to the appearance of the laboratory as a whole. Some of the brainstormers asserted that a laboratory that was too tidy, too organized, or otherwise presented as if "tied up in a bow" would stand out sorely from the normal university or research laboratory. However, an immaculate high-containment laboratory could also simply be a matter of good biosafety practices.[17]

As for other matters that this group thought might be worrisome, no sooner had one participant identified why something might warrant concern than did another give a reason why it should not. For instance, a large number of sub-types in a culture collection could be consistent with vaccine research or it might indicate that the laboratory was performing comparative research on disease strains, a step on the road to improving a disease strain for weapons purposes.[18] Whereas one school of thought held that large animal handling capabilities in a high-level containment infectious disease laboratory should raise hackles, particularly if primates were involved, another held that such capabilities could be found in most agricultural and veterinary colleges.[19] Similarly, the group batted back and forth whether the inspectors should fret about research on diseases not endemic to a region.[20] For some, military funding or affiliation with other entities conducting defense research would be troublesome, but eventually the group coalesced on the view that monies for offensive research could be channeled through any number of other government departments. The inspectors' evaluation of funding and affiliations, they decided, should be guided by whether a facility tried to hide its funders or stated the nature of their affiliations openly and subsequently explained and documented them.[21] Finally, the group was of the opinion that the inspectors

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[16] Academic Expert 1, PhD in microbiology, 16 August 2000.

[17] Dr. Jennie Hunter-Cevera verbalized this point, to the agreement of other participants. Also noting that a real laboratory would have a "lived-in" look: Defense Contractor 5, director of microbiology and special government projects, 28 August 2000. In the same academic session, Dr. Robert Shope argued the dissenting view that a tidy laboratory should not prompt automatic concern.

[18] Academic Expert 1, PhD in microbiology; Dr. Jennie Hunter-Cevera, PhD in microbiology, 6 January 2000.

[19] In addition to primates, the animals specified were dogs, pigs, sheep, and cattle. Dr. Corrie Brown, DVM and PhD in comparative pathology; Dr. Jennie Hunter-Cevera, PhD in microbiology; and Academic Expert 2, MD, primarily waged this debate.

[20] "Doing rinderpest work in the US would seem more questionable than if it were being done in Africa. The same with foot and mouth." Academic Expert 2, MD, 6 January 2000. Academic Expert 1 provided the counterpoint that "We do foot and mouth work here, yet we don't have a foot and mouth problem." Academic Expert 1, PhD in microbiology, 6 January 2000. Dr. Corrie Brown noted that the research into particular diseases is indeed relevant if their introduction would unleash economic havoc. For example, US research into foot and mouth is based on the reality that the appearance of this disease could lay waste to livestock and wreak economic havoc. Research into the properties, behavior, and treatments for human, plant, and animal diseases is done as a safety measure against natural transmission of the disease into the country, as well as to guard against possible deliberate use in hostilities.

[21] Academic Expert 1 debated this matter with several other participants, eventually leading to agreement that military funding in and of itself should not be a concern.

should take note if the laboratory were heavily populated with post-doctoral or graduate students from countries thought to harbor bioweapons programs.

On this litany of possibly ambiguous matters, some of which the inspectors would have little or no way of knowing beforehand, the group suggested that by employing a variety of investigative tools, the inspectors should be able to figure out whether a facility was part of an offensive weapons program. According to the group, the inspectors' first pass at the facility should include a facility tour, a review of select records, and interviews with certain staff members. Upon arrival, laboratory managers or key project leaders would be expected to acquaint the inspectors with the work being done there, as well as with the house safety rules. No particular time limit was specified for this introductory briefing because such overviews can provide a useful basis for the subsequent tour, review of records, and interviews. The academic and research institute group noted, however, that the inspectors should object if they thought the briefers were droning on to avoid giving the inspectors access. Also, the inspectors should ask about the laboratory's level of funding, sources of funding, and affiliations if such information is not volunteered during the briefing. In Box 3.2, the inspection veterans group culled its collective experience to guide facility managers through this first step of an inspection.

A guided tour of the premises should follow the briefing, with inspectors observing requisite safety precautions (e.g., wearing laboratory coats, booties, racal hoods).[22] Along the way, the inspectors should take careful notes on the general setup of the facility; the inventory of key supplies (e.g., media, personal protective equipment); the number and species of animals, if present; and the types and numbers of equipment (e.g., milling, aerosolizers, autoclaves).[23] They should also view key laboratory features, such as waste treatment and air handling systems. In small, cramped, or highly regulated areas, host officials should have the right to request that one or two inspectors be given access instead of the entire entourage. The site being inspected may also want to consider restricting the number of host government escorts that enter tight quarters, as Insights 3.1 explains. The appropriate vaccinations should be a pre-requisite for inspectors' entry into some high-level containment areas.[24] Ideally, the tour would be

[22] If house biosafety rules are not followed, laboratories working with dangerous pathogens would have to undergo weeks of decontamination and biosafety checks, essentially shutting the facility down prior to the inspections. Such an interruption would not only be burdensome, touring a sanitized laboratory would disadvantage inspectors, who could learn more from seeing the normal work setting. Academic Expert 1, PhD in microbiology, 16 August 2000. Also Dr. Nancy Connell, PhD in bacterial genetics; Dr. Barry Kreiswirth, PhD in microbiology; Dr. Corrie Brown, DVM and PhD in comparative pathology. Agreeing that inspectors must abide by all host facility safety rules: Defense Contractor 2, principal research scientist; Defense Contractor 5, director of microbiology and special government projects, 28 August 2000. Defense Contractor 2, a scientist at a medical research facility, is a veterinarian and a PhD microbiologist.

[23] A facility tour would include the relevant laboratories, all equipment therein, growth chambers, associated storage areas, animal holding pens, greenhouses, and administrative areas, as applicable depending on the type of site inspected. While this group specified that the inspectors take notes, they did not mention that the inspectors should use any other methods, such as photographs or videos, to record what they saw.

[24] Agreeing that inspectors would have to be vaccinated for the agents that the facilities declare, or, as a much less desirable alternative, sign a liability waiver for the host facility: Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company; Defense Contractor 7, president and founder of a small sensor development

Box 3.2: Cliffs Notes on the Opening Moves as the Host of an Inspection

The inspection veterans could not emphasize enough the need to prepare carefully for an inspection.[1] They sought to dispel the impression that there was "such a thing as a collegial visit" since the host site would be trying to protect its equities and government escorts might have agendas of their own.[2] Government bureaucrats and sometimes a company's own senior managers do not have an adequate understanding of the technical issues underpinning a site's operation and the inspection.[3] They counseled site managers to agree from the outset on their strategy to host an inspection, beginning with the contents of the introductory briefing.[4] Some inspection veterans said that from the host's viewpoint, the less said in the opening briefing, the better. Inspectors, however, should be expected to probe deeper after a perfunctory briefing. Also, taking the opposite tack and giving a briefing that reasonably reviews the activities known to be of interest to the inspectors could "de-fang" them.[5] The trick is to find common ground between hosts and inspectors who are somewhat at cross purposes. "Typically, one assumes that the task is to rattle off a list of facts about the facility—square footage, number of light bulbs, number of class 3 hoods. Really, however, the inspection team wants something very different from that or in addition to that. A least common denominator approach to the introductory briefing is almost destined to result in disappointment."[6] The straightest route to finding that common ground, according to one participant who spoke from the added experience of regulatory inspections, was to let the inspectors brief the host officials *first* on what they want so that facility managers can figure out how to address their agenda and requirements.[7] Moreover, facility managers should decide from the start what records, equipment, or areas of the site are proprietary so that an overeager, inexperienced, or nervous briefer does not inadvertently blurt out such information. Designating a chief spokesperson ahead of time who will call the shots for the host facility is crucial.[8]

NOTES

[1] During one BWC trial, "the team walked into the first lab and, despite months of preparation, there was a glaring declaratory malfeasance." When it came to interviews, "the inspection team picked a random person, and it was like hogs looking at wristwatches—absolutely no understanding of what the team was doing there." Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, who has an MD and a PhD, took part in the trial inspection at US vaccine production plant in late October 1995, the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland. *(continued, next page)*

accomplished with as little disruption as possible to ongoing work.[25] Also, site personnel should accompany inspectors every step of the way.[26]

The inspectors should walk through with an eye toward whether containment precautions, equipment, and supplies are in line with the demands of the research described. "If they went into a laboratory that said it was working with a harmless bug and yet they had an inordinate number of

company; Defense Contractor 5, director of microbiology and special government projects, 28 August 2000. Defense Contractor 6 has over fifteen years of experience in molecular genetics.

[25] Academic Expert 1 argued that a tour would be disruptive, but Dr. Nancy Connell and Dr. Barry Kreiswirth stated that a walk-through would not be much of a bother. Everyone agreed that the inspectors should try to minimize their burden on the host facility while still accomplishing their mission.

[26] The group's stress on the perils of unescorted inspectors was expressed by Dr. Barry Kreiswirth, who said: "I don't think you'd want anyone just going around grabbing things willy nilly in your lab. You would want to be with the person and you would want to make sure *you* know what they are looking at and that *they* know what they're looking at."

Box 3.2: Cliffs Notes (continued)

[2] On this point, "Call it a confidence-building measure or whatever you want, but we had trouble with collegial visits with some of our allies." Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Inspection Veteran 8, a PhD scientist, went on several trilateral visits to former Soviet biowarfare facilities and was an inspector during the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico.

[3] Inspection Veteran 2, trilateral and mock inspection participant, 27 April 2000. Inspection Veteran 2 participated in inspections under the 1992 trilateral agreement, took part in a series of round robin mock inspections at military facilities in the western United States, and engaged in background planning for the mock visit to the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

[4] For some sites, just putting together the introductory briefing can be quite complex because the facility's direct management and headquarters personnel may differ on what can be said. Negotiating what can be said should not be left until the last minute because those talks can be quite time consuming. Inspection Veteran 2, trilateral and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Some sites are accustomed to inspections (e.g., military and commercial facilities), but others may be unprepared for anything that goes beyond the superficial introductory briefing and tour one would give international visitors or high school students. Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000.

[5] Advocating a name-rank-and-serial-number philosophy for the opening briefing: Inspection Veteran 3, trial inspection observer and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Pointing out that inspectors would "chew up" someone who took a perfunctory approach and that sometimes they come in with a certain piece of information to "nail" the site: Inspection Veteran 2, trilateral and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Recalling an opening briefing that included a discussion of such sensitive data as particle sizes: Inspection Veteran 7, United Nations Inspection Commission inspector and mock inspection participant, 27 April 2000. Inspection Veteran 7, a PhD scientist, served on several United Nations Special Commission on Iraq missions, was on the host team during the mock inspection at Dugway Proving Ground, Utah, and took part in a follow-on round robin exercise. Editor's note: During one of the early trial inspections held at a US commercial chemical plant to explore the effectiveness and feasibility of Chemical Weapons Convention monitoring techniques, the introductory briefer showed a viewgraph that contained the single piece of information—a chemical formula—that the site's managers had determined must not be revealed.

[6] Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000.

[7] "Hardly a month goes by that I don't have some US organization inspecting my facility. . . . They come in with a target, so I usually have them give the opening presentation so they can say why they are there and what I can do to help them." Inspection Veteran 3, trial inspection observer and mock inspection participant, 27 April 2000. Inspection Veteran 3, who holds a DVM and a PhD, observed the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and participated in the mock trilateral inspection at the Edgewood Arsenal, Aberdeen Proving Ground. Agreeing that it is crucial to find out right away what is important to the inspectors: Inspection Veteran 8, trilateral and trial inspector, 27 April 2000.

[8] Inspection Veteran 3, trial inspection observer and mock inspection participant, 27 April 2000. Having just one spokesman or point of contact may be difficult unless that individual is intimately familiar with the entirety of a site's operations. Otherwise, detailed questions about certain programs will have to be referred to site experts who can answer them. Inspection Veteran 1, facility manager and US trial inspection host, 27 April 2000. Inspection Veteran 1, a facility manager, was a principal host of a US trial inspection held in late March 1996 at three facilities located in Albuquerque, New Mexico.

biosafety cabinets, the inspectors should be concerned."[27] Moreover, they should be alert to whether the laboratory is outfitted more richly than its visible funding level. Evaluating a facility's status, it was noted, would be even more complicated if the laboratory were not operating at its full biosafety level. Moreover, if excess equipment were sitting about, the inspectors should be wary of explanations that such equipment is no longer used, particularly if its condition does not indicate that to be the case.[28] In general, the inspectors should get a feel during the tour for whether they are in a working laboratory and what they see fits with the facility's declaration, other data gathered prior to the inspection, and the introductory briefing.

[27] Theodore Myatt, doctoral candidate, former biosafety officer, 16 August 2000.

[28] On housing lower level research in a high-level biosafety laboratory: Dr. Corrie Brown, DVM and PhD in comparative pathology, 6 January 2000. On the quick and dirty way to determine equipment use status: "We have old steel hoods that have crusty old lab tape over them. It's pretty obvious that we don't use them anymore." Theodore Myatt, doctoral candidate, former biosafety officer, 16 August 2000.

Insights 3.1

The issue here is not just the size of the inspection team, but the number of US government "minders" sent to accompany it. One defense contractor remembered that when his site received a Chemical Weapons Convention inspection, there were only four international inspectors, but the size of the group ballooned with at least eight additional US government escorts. Someone from the facility had to accompany each of the outsiders, which was quite a drain on personnel resources. The facility had difficulty accommodating a group of this size in some areas and in providing sufficient office space.[1]

NOTES

[1] The US government sent personnel from the Commerce Department, the Defense Security Service, the Federal Bureau of Investigation, and the Defense Threat Reduction Agency. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. The president of a company that provides consultant, technical, and materials evaluation support to government agencies and commercial clients, this individual received a PhD in chemical engineering but is also trained in physics and previously worked for almost a decade in the aerospace industry.

Next, the inspectors would undertake a first-level review of a site's records, requesting documents from the Institutional Animal Care and Use Committee, the institutional review board, and the biosafety committee.[29] These documents would provide a basis from which the inspectors can judge variance from what they have already heard and seen. Also, these records give the exact numbers for the items (e.g., animals and species, agents, recombinant deoxyribonucleic acid work) that are supposed to be in the laboratory. Biosafety documents compose a second important series of records that should correlate back to the baseline explanation of research activities. Here, the inspectors should examine the engineering control records for biosafety cabinets, autoclaves, high efficiency particulate air (HEPA) filters, and decontamination activities. They should also see biosafety protocols and records pertaining to personal protective equipment (e.g., suits, respirators) and administrative controls, such as those on personnel training and vaccinations.[30] Again, the inspectors' assignment is to consider whether these documents validate or refute the explanations provided about the facility's work. Other than the personnel costs to retrieve these documents, the academic and research institute experts did not describe this type of inspection activity as a burden to their facilities.[31]

Also in this first-level monitoring pass, the research institute and academic group experts recommended that inspectors interview biosafety officers and bench scientists, including graduate students. According to what the inspection veterans described in Insights 3.2, interviews can turn out to be a monitoring bonanza or a bust. The academic group perceived interviews with the biosafety officer(s) as being particularly useful since these individuals are outside of the laboratory and their outlook on its activities would be somewhat different. Biosafety officers would not only have a "big picture" perspective on the laboratory, they should certainly know what work was being done with dangerous

[29] In the 6 January 2000 meeting, Theodore Myatt noted that such oversight committees and documentation may not exist in other countries.

[30] Biosafety officers normally categorize things in terms of engineering, administration, and personal protective equipment. Ibid.

[31] Academic Expert 1 stated that these salary costs would accrue with personnel in other departments outside of this person's laboratory. Other participants noted personnel costs as well, but did not portray them as being heavy.

Insights 3.2

The inspection veterans group confirmed that interviewing scientists and technicians could be a goldmine, especially if done without supervision and in a social setting.[1] At a former Soviet biowarfare facility, said one inspection veteran, "I interviewed a junior person on video as he was explaining an aerosol capability, and we nailed him."[2] Thereafter, the Russians did not allow unsupervised interviews. If their bosses are present, technical staffers can find the experience petrifying.[3] Supervised interviews produced much less of monitoring value.

Inspectors should also be sensitive that to the likelihood that different strata of personnel—bosses versus technicians—could construe and possibly answer the same question differently. In some cases, the different answers result from varying perspectives and language barriers. In others, the variance could be much more meaningful, with one of the interviewees having revealed something they were not supposed to discuss. The inspectors' efforts to make this judgment call may be handicapped by poor interpretation and by disciplinary differences between the inspector and the interviewee. Such problems surfaced in Russia and Iraq, as well as during US BWC trial inspections.[4]

Despite the difficulties entailed in interviewing, one veteran inspector described interviews as "the only real place to mine for intent. Inspectors won't read or measure the smoking gun, but they can get at it through interviews. This is the eye of the tiger for success, it's where the vulnerabilities lie" because people do slip up in interviews.[5]

NOTES

[1] "The scientists wanted to blurt out everything they were doing." Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, who has an MD and a PhD, took part in the trial inspection at US vaccine production plant in late October 1995, the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland. Inspection Veteran 1 made a virtually identical statement. Inspection Veteran 1, a facility manager, was a principal host of a US trial inspection held in late March 1996 at three facilities located in Albuquerque, New Mexico.

[2] Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Inspection Veteran 8, a PhD scientist, went on several trilateral visits to former Soviet biowarfare facilities and was an inspector during the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico.

[3] For instance, when the Russians interviewed a US woman at an American biodefense facility, she started to cry. The situation was so stressful for another US staffer that the individual did not want to be interviewed at all. Inspection Veteran 2, trilateral and mock inspection participant, 27 April 2000. Inspection Veteran 2 participated in inspections under the 1992 trilateral agreement, took part in a series of round robin mock inspections at military facilities in the western United States, and engaged in background planning for the mock visit to the Edgewood Arsenal, Aberdeen Proving Ground, Maryland. Also on this point, Inspection Veteran 8, trilateral and trial inspector, 27 April 2000.

[4] Inspection Veteran 9, participant in trial and one mock, 27 April 2000. Note that interpreters do not tend to be scientists, so they can inadvertently distort technical aspects of a conversation. An inspector who is a microbiologist would use terminology differently than an administrator trained in management.

[5] Inspection Veteran 8, trilateral and trial inspector, PhD microbiologist, 27 April 2000.

pathogens. Inspectors could query them about equipment, procedures, or other operational matters, probing for variance with what they had been told already.[32] What the biosafety officers have to say can also be checked against documentation and other interviews. By chatting with the scientists, inspectors who are experts in their own rights would know fairly quickly whether these individuals were really

[32] Note that the biosafety officers were seen as individuals who would really know what was going on in a laboratory but also as a possible source of both negative and positive information. In an academic setting, it would be unusual for the biosafety officer to be in cahoots with an individual principal investigator who was doing something wrong. Academic Expert 1, PhD in microbiology; Theodore Myatt, doctoral candidate, former biosafety officer; Dr. Barry Kreiswirth, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist, 16 August 2000.

proficient at their work or might have been planted there, instructed to provide a cover story.[33] The main costs of interviewing to the host laboratory would include lost productivity and salaries for those being interviewed.[34]

When it came to costs to the host facility, group participants adamantly and unanimously stated their participation in BWC monitoring activities should not cost them anything. Cooperation with inspectors was one thing, lost productivity another entirely. The US government, they posited, should reimburse them for preparation costs (e.g., advance retrieval of supporting documents), salaries of employees called upon for interviews, recall of additional documents, escort functions, and any other costs associated with the inspection.[35] Indeed, as a defense contractor recounts in Insights 3.3, the tab for hosting an inspection can be high. If the cost issue was resolved, the academic and research institute group was quite amenable to occasional inspections, say on the order of every five years or so.[36] When the BWC inspectorate did want to send in a team, the academic and research institute scientists requested advance notice of up to two weeks and the leeway to negotiate when the inspectors would arrive to ensure that key personnel would be there to assist with the inspection.[37] Another guideline that would make the inspections more palatable is if they were held during normal business hours.[38] Finally, the commitment

[33] The group expected that the inspectors might find it easier to draw the scientists out in an informal setting, although how the inspectors should go about arranging such informal conversations over the course of a few days was left unspecified.

[34] Academic Expert 1, PhD in microbiology; Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Dr. Kreiswirth also had concerns that biosafety officers or scientists who had a gripe with one of their colleagues might provide the inspectors false information. "I guarantee that if there is one person there who's out to get you, they can make it really ugly," he stated. In addition, Dr. Kreiswirth worried about negative effects on the quality of the work environment and difficulty recruiting personnel if word got out that a facility's personnel were going to be routinely grilled about possible bioweapons research. Dr. Robert Shope cautioned against overplaying these and other concerns about interviews possibly creating dissension within the laboratory.

[35] The group heartily backed statements of Academic Expert 1 to this effect.

[36] Participants debated how frequently inspections should take place given the presumption of innocence and the need to deter ready use of supposedly legitimate research laboratories as fronts for offensive work. According to one view, sites should be selected randomly and an individual laboratory should not be inspected more frequently than every five years. Others held that given the need to check treaty compliance, the inspection rate ought to be not less than five years. Several agreed that the inspectorate would probably not employ enough inspectors to allow them to inspect laboratories so frequently, estimating that twenty-five years would pass between BWC inspections. Dr. Nancy Connell, PhD in bacterial genetics; Dr. Robert Shope, MD and epidemiologist; Dr. Barry Kreiswirth, PhD in microbiology; Academic Expert 1, PhD in microbiology, 16 August 2000.

[37] On this latter point, professional commitments are often made far in advance, and scientists slated to attend a conference elsewhere should not have to cancel their plans because of an incoming BWC inspection. A delay of one or a few days might allow everyone's schedules to be accommodated. Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Flexibility on the part of the inspectorate can be helpful, pointed out an expert from a defense contractor facility that had received a Chemical Weapons Convention (CWC) inspection, but it can also be frustrating when schedules slip. The date for their CWC inspection was apparently moved several times, which made it difficult to plan and execute regular laboratory activities. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. Defense Contractor 4 has a PhD in chemical engineering. On the need for advance notice: Academic Expert 1, PhD in microbiology; and Dr. Nancy Connell, PhD in bacterial genetics, 16 August 2000. The main reason given for wanting a week or more advance notice was the need to have other departments within the institution pull personnel, occupational health, and other supporting documents.

[38] This point of view was represented by Academic Expert 1, who said: "My concern is that I have people sitting around till 8 or 9 o'clock at night waiting to be interviewed. Although it could be advantageous to the host to just get it over with."

to accept BWC inspections would be much easier to make if the inspectors were obliged to go about their business quietly, with no blaring signs of their presence and no public announcements. A low-profile approach to the inspections would counteract the potential for the mere fact that this type of inspection was taking place to be misconstrued and equated to a facility's involvement in bioweapons research, which would deal a serious blow to a lawful laboratory.[39]

Insights 3.3

One commercial facility engaged in contract defense research that was inspected under the CWC estimated its costs at $100,000, including the time the inspectors were on site and the preparation requirements. Senior personnel devoted a considerable amount of time to preparing for the inspectors in the four days prior to their arrival, which meant that for all intents and purposes, laboratory operations were hampered, at times shut down, during this preparatory phase as well during the inspection itself.[1]

NOTES

[1] Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. The president of a company that provides consultant, technical, and materials evaluation support to government agencies and commercial clients, this individual received a PhD in chemical engineering but is also trained in physics and previously worked for almost a decade in the aerospace industry.

The academic and research institute experts expected this first level of monitoring activity to be quite effective in identifying inconsistencies with a site's declaration, other background information, and what the inspectors saw, heard, or read once on site. They defined effectiveness as "being capable of distinguishing between legitimate and illegitimate activity as defined in the BWC."[40] As shown in table 3.1, the group quickly and universally rated a facility tour as having a high level of monitoring effectiveness, particularly given the ability to play off what was observed against paperwork and interviews. On the utility of reviewing project and biosafety documents, some in the group thought this activity would be highly effective, others were at the opposite end of the spectrum. Therefore, the group settled on a moderate rank for document reviews, but returned to rate what inspectors could determine from interviewing biosafety officers and bench scientists as high.[41]

[39] Academic Expert 1 was particularly worried about the "collateral" damage (e.g., student pickets, waning university support or outright cancellation of legitimate research programs underway) that could result from faulty media coverage of an inspection. Several other brainstormers agreed that a low profile would be helpful. However, others noted that the inspections would be conducted at many laboratories, just like other types of inspections, and that in time there would be few, if any, negative connotations to being on the BWC inspection list. Dr. Barry Kreiswirth, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist, 16 August 2000. One participant in the defense contractor group was also terribly worried about adverse publicity. "Just the association . . . . We cannot tolerate that type of notoriety." Defense Contractor 3, senior technical adviser, 28 August 2000. Another remarked that the cat was already out of the bag, so to speak, due to the inspections they underwent to gain their licenses to work with these agents. Because their community was already aware that they "use these agents, I don't perceive that as a problem." Defense Contractor 2, principal research scientist, 28 August 2000.

[40] The group mulled over stipulating how to factor in size of capacities and ultimately decided that size was intrinsic to legitimate or illegitimate. Dr. Barry Kreiswirth, Dr. Robert Shope, and Academic Expert 1 also gave examples of how these monitoring techniques would not be effective against an individual terrorist. The goal was to detect fairly large-scale cheating, and the group believed the three-level approach could function effectively in that regard.

[41] Since the Institutional Animal Care and Use Committee and the institutional review board are outside of the laboratory itself, they offer some assurance that activities therein are being watched by other organizations. Put differently, were the laboratory involved in offensive research activities, it would indicate a more widespread conspiracy within the institution as a

Table 3.1: Anticipated Effectiveness of Level 1 Inspection Activities

Type of Inspection Activity	Expected Level of Effectiveness
Facility Tour	High
Review of Project Paperwork	Moderate
Review of Biosafety Documentation	Moderate
Interviews	High

The group decided three days, perhaps less depending on the size of the laboratory, would be needed to conduct a level 1 inspection.[42] At the conclusion of these initial monitoring activities, if the inspectors have found nothing suspicious or otherwise have no reason to believe that the laboratory is engaged in clandestine offensive bioweapons research, the academic group recommended that the inspection be curtailed, with legitimacy presumed. This approach would not impose an unreasonable burden on peaceful research facilities. Also, given the wafer-thinness of the dual-use line in the laboratory setting, this approach would go a long way toward calming the misgivings that legitimate research facilities have about false accusations resulting from a BWC inspection.[43]

ON-SITE MONITORING ACTIVITIES: LEVEL 2 INSPECTION

If, on the other hand, inspectors have heard conflicting stories, have seen records that do not match up, or otherwise have reason to believe that something is wrong, the inspection should proceed to a second level wherein mostly the same tools would be plied, but in a more intensive fashion. The objective of second-level monitoring would be to confirm or dispel suspicions raised earlier. Accomplishing this task would require an inspection of longer duration. Although the academic and research institute specialists did not agree on a time limit for this phase of the inspection, they obviously did not want the inspectors to camp out indefinitely in their midst. The situation would be serious enough that they believed the inspectors should nonetheless be allowed several additional days to conclude their work. [44]

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whole. The detail inherent in biosafety documents would offer reassurance that the facility was operating as stated or perhaps subtle signs that operations were not as portrayed.

[42] A one to three day time range was discussed, with Dr. Jerry Goldstein in particular expressing strong views that one day would not be sufficient time to tour, interview, and review paperwork. The job might be accomplished in two days in a smaller laboratory, and three days should be enough time for a large laboratory. Dr. Nancy Connell, PhD in bacterial genetics; Dr. Robert Shope, MD and epidemiologist, 16 August 2000.

[43] "That's actually really good, because that helps my feeling of being able to come out of one of these things with my skin on me." Academic Expert 1, PhD in microbiology, 16 August 2000. Dr. Barry Kreiswirth expressed similar thoughts.

[44] Academic Expert 1's comments about not wanting a "camp out" but still wanting to give the inspectors leeway to do their jobs was characteristic of the group's views on the time allotted for a phase two inspection. Some experts mentioned three days to a week of additional time on site as being reasonable, but others wanted to leave the timeframe open-ended.

The academic and research institute brainstormers recommended opening the second phase of an inspection with a monitoring tool commensurate with the gravity of having determined that a second level was necessary: sampling. Analysis of samples can cut straight through cover stories by identifying microorganisms. Because of its ability to provide definitive information about a facility's activities, some in the group advocated sampling in the first level of inspection. Weighing both the intrusiveness and cost of this tool against the presumption of innocence, however, the brainstormers ultimately decided that the appropriate placement of sampling and analysis was at the beginning of the second level of inspection.[45] After taking samples, the inspectors would go through another, deeper round of document reviews and interviews, which might prove sufficient.[46] The following paragraphs describe the group's rationale for this monitoring strategy as well as the qualms they would have if it were implemented in their laboratories.

Sampling, the academic and research institute group decided, was not a tool to be used sparingly or with hesitation. If a second phase of inspection has been triggered, a laboratory is out to clear its name and the inspectors would be hot on the trail of a possible cheater. Thus, at the outset of the second phase the inspectors should head straight toward the laboratory's HEPA filters. Historical data about what has occurred in a laboratory would most likely be distilled from HEPA filters in biosafety cabinets, racal hoods, and animal facilities, making these filters especially important sampling targets. The inspectors should also collect samples from freezer filters, gloves, drains, sewage, and animal feces. In addition, air and background environmental samples should be secured. These baseline samples are important because something could come out of the HEPA that does not reflect the work being done in the laboratory.[47]

The crux of sampling is to take a sample that would capture historical data, and the group acknowledged several of their recommended sampling locations would provide data only about activities that took place just before the inspection. They also conceded that a laboratory could rig or discard

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[45] Outside maintenance personnel might have to be called in to assist with taking some of the desired samples (e.g., HEPA filters). Theodore Myatt, doctoral candidate, former biosafety officer; Academic Expert 1, PhD in microbiology; Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000.

[46] During a CWC inspection of a commercial site conducting defense contract research, the inspectors did request samples, but did not push for them since the facility's records were clear and comprehensive. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000.

[47] Academic Expert 1 brought up this last point, to widespread agreement among the group. Recommendations for sampling locations came from Dr. Robert Shope, MD and epidemiologist; Dr. Corrie Brown, DVM and PhD in comparative pathology; Theodore Myatt, doctoral candidate, former biosafety officer; Dr. Barry Kreiswirth, PhD in microbiology; Dr. Jennie Hunter-Cevera, PhD in microbiology; Dr. Nancy Connell, PhD in bacterial genetics; Academic Expert 1, PhD in microbiology, 6 January and 16 August 2000. As one of the participants in the inspection veterans group noted, "Absent characterization of collections taken from all over the world, it's hard to know what the sampling data from an individual inspection shows. Think of sampling in the BWC context as discovering fingerprinting, but not having the FBI's fingerprint database. Sure, we can fingerprint, but what does it mean? We could become less wise as a result of having more data." Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, who has an MD and a PhD, took part in the trial inspection at US vaccine production plant in late October 1995, the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

evidence from some of these sample areas.[48] While sampling from less obvious locations (e.g., air conditioning compressor fans, compressor radiators on freezers) might trip up a less adept cheater, the group favored establishing a guideline prohibiting laboratories from changing their HEPA filters upon receiving notice of an inspection. Filter change-outs would therefore be accomplished under the watchful eye of inspectors, with samples taken from the area(s) of the filter(s) most likely to provide the desired historical data.[49] The group debated the wisdom of getting on with sample analysis versus holding the samples to see if other inspection activities resolved suspicions. In the end, they sided with the former option. "If a sample is taken, it should always be analyzed. It seems to me, why take it if you aren't going to analyze it?"[50]

Sampling from some locations would not be that complicated of an exercise, but the group stated that taking HEPA samples would be an unprecedented act for most university or research laboratories. Therefore, they recommended that this aspect of the protocol be grounded in rigorous studies to pin down sampling and analysis strategies and techniques that would furnish optimum results. Among the factors to be clarified, for example, are the utility of sampling from the intake side versus other areas of the filter, the ideal size of the filter samples, and how many and which biosafety cabinets should be sampled in a multi-cabinet laboratory to gain confidence that the results accurately represent the laboratory's activities.[51] While the academic and research institute brainstormers identified several analytical techniques that could be employed (e.g., biochemical and biophysical assays, nucleic acid-based and immunologically-based assays, and classic clinical laboratory identification), studies should also rank the various techniques according to their ability to culture, separate, and identify background data from more unique data points on the filter.[52] The group's strong view that the accuracy of the results would be

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[48] Dr. Robert Shope, MD and epidemiologist; Theodore Myatt, doctoral candidate, former biosafety officer; and Academic Expert 1, PhD in microbiology, sustained this part of the discussion.

[49] Academic Expert 1 first expressed this concept, which the group later refined, when he said: "What you do is call three weeks ahead of time and say 'do not change out your HEPA filter. We will change it for you.'" On the advisability of having facility or regular contract maintenance personnel—who are very familiar with the site's safety protocols—pull the filter while the inspectors watch: Theodore Myatt, doctoral candidate, former biosafety officer; Dr. Barry Kreiswirth, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist, 16 August 2000.

[50] Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. The group agreed with this sentiment, and one participant—Academic Expert 1—commented that he would even be annoyed if samples were taken but not analyzed.

[51] Theodore Myatt, doctoral candidate, former biosafety officer, thought there would be so many problems with sampling that it would never be employed. Others voted for studies to resolve those problems. The tradeoffs between analytical results and safety factors such as whether decontamination of the HEPA filter precedes sampling should also be studied. In addition, the appropriate procedures to prevent contamination or compromise of the samples should be identified. Dr. Robert Shope, MD and epidemiologist; Academic Expert 1, PhD in microbiology; Dr. Barry Kreiswirth, PhD in microbiology; and Dr. Nancy Connell, PhD in bacterial genetics, discussed these points. On size of samples: Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Mr. Myatt, Dr. Connell, Dr. Shope, and Dr. Kreiswirth debated whether inspectors should by default sample all filters, only those that can be more easily accessed (e.g., racal filters) as opposed to other filter locations, or leave this matter to the judgment call of the inspectors. On the best sample location(s) on the filter surface: Academic Expert 1, PhD in microbiology, 16 August 2000.

[52] Such studies would define, for instance, the number and type of culture tests to be used to detect various microorganisms, as well as the polymerase chain reaction or other types of assays to be employed. Note that any declaration of

"absolutely critical" and that these activities were also costly underscored the need for sampling and analysis to be undertaken with deliberation.[53] The academic and research institute experts were willing to have the inspectors oversee analysis conducted on site or to send the samples to outside laboratories, as long as they were certified and appropriate precautions were taken to protect the integrity of the samples. What was most important was that the process yield accurate results.[54]

A second principal way to sort out uncertainties would be for inspectors to return to the paper chase. They should investigate their suspicions via project log books; computer records; additional project paperwork; purchasing, supply, and shipping records; and animal and plant pathology records. Logs in the laboratory would provide historical data on air pressure readings, temperatures, and use of key pieces of equipment (e.g., freeze driers). Extensive use of the autoclave(s) just prior to the inspection, for example, would be noteworthy. Facility personnel are normally required to initial their notations in these logs, which would enable inspectors to trace the working patterns of different individuals and identify personnel for further interviews. Computer records of laboratory activities are also kept, and while they can be edited, someone with computer expertise could track down the timing and pattern of such edits to determine whether a cover-up had been attempted. These log books and computer records can help straighten out or confirm inconsistencies and are usually at the fingertips of laboratory personnel.[55]

Additional project paperwork that the inspectors should seek would include project proposals, contracts, and reports—all of which should corroborate a site's described activities. This category of documents should also help answer questions about a laboratory's funding sources.[56] The complications in accessing these materials stem from confidentiality. Some data therein might be controlled by a laboratory's contractual arrangements with outside sponsors (e.g., commercial firms, government agencies). The defense contracting group shared this problem, as Insights 3.4 conveys. In addition, the

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infectious agents present in the laboratory would serve as a control for the analysis. The prospect of engineering around publicly announced analytical techniques was broached, which led to a suggestion that the inspectorate could rely on random primers and therefore make it more difficult for a laboratory to foil sampling and analysis. Dr. Barry Kreiswirth, PhD in microbiology; Academic Expert 1, PhD in microbiology; Dr. Jennie Hunter-Cevera, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist, 16 August 2000.

[53] The group agreed with Academic Expert 1's statement that the analysis results must be accurate. Dr. Barry Kreiswirth stated that an emergency filter change in his laboratory would cost $1,800, but others estimated their costs at closer to $500.

[54] If an outside laboratory were employed, the group agreed that the results should be verified at a second certified laboratory. Academic Expert 1, PhD in microbiology; Dr. Barry Kreiswirth, PhD in microbiology; Dr. Nancy Connell, PhD in bacterial genetics; and Theodore Myatt, doctoral candidate, former biosafety officer, were the mainstays of this discussion.

[55] "It's right there in the top drawer because people are always asking for it." Dr. Nancy Connell, PhD in bacterial genetics, 6 January 2000. Seconding this point, Academic Expert 1, PhD in microbiology. On the importance of accessing such records to understand patterns of autoclave use and other inconsistencies observed: Dr. Jennie Hunter-Cevera, PhD in microbiology; Dr. Jerry Goldstein, PhD in microbiology, 6 January 2000.

[56] If these documents do not clarify funding sources, then the inspectors should request documents to provide a historical record of funding. Dr. Anne Vidaver and Dr. Jennie Hunter-Cevera emphasized the importance of gaining an overall understanding of funding sources, and the group agreed.

Insights 3.4

Defense contractors, it should be noted, faced similar quandaries about the need to protect the confidentiality of research being conducted for other government and commercial entities. They feared losing credibility with their clients if they were compelled to reveal contract data without the specific permission of clients. "We have an obligation to the clients not to tell and we just can't do that or we'd lose our credibility."[1]

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[1] Defense Contractor 5, director of microbiology and special government projects, 28 August 2000. Defense Contractor 5, works at a small defense contracting research company and has a PhD in microbiology. Defense Contractor 3 expressed a virtually identical opinion, noting that they were at liberty neither to describe their work nor name their clients. Defense Contractor 3, a senior technical adviser at a large, nonprofit research organization, holds a PhD in physics. For that matter, projects may be so tightly secured that people in the same building may be unaware of the work being done in the adjacent room. Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Inspection Veteran 8, a PhD scientist, went on several trilateral visits to former Soviet biowarfare facilities and was an inspector during the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico.

research world can be highly competitive, so some laboratories also enforce policies to prevent others from getting an unwarranted glimpse of a laboratory's work. Both the laboratories and the outside sponsors are likely to require the inspectors to sign a confidentiality agreement to see these documents.[57]

A review of purchasing, supply, and shipping records should also prove useful to understanding the scale of a laboratory's activities and its interactions with outside entities. Paperwork for media, serum, animal supplies, and personal protective equipment would verify that a laboratory's purchases were qualitatively and quantitatively in line with the research supposedly underway.[58] Unusual types or quantities of media purchased might indicate a different type of research was actually being performed.[59] Shipping data would tell inspectors more about the pace and nature of the laboratory's work with outside organizations (e.g., routine culture supplier versus infrequent exchanges). Pathology records would validate or refute facility staffers' explanations for studies in increased virulence or other work that teeters on the fine line between offensive and legitimate research. Normally, such records would be maintained by individuals outside of the laboratory itself (e.g., purchasing, administrative, or pathology departments), so pulling this set of records would begin to spread the burden of the inspection outside of the laboratory's immediate staff. In Insights 3.5, members of the inspection veterans group explain the difficulties a facility can have in tracking down some documents. Also, turning

[57] The laboratories themselves are subject to penalties if they breech the confidentiality arrangements in their contracts with outside sponsors. At the very least, the laboratory would have to get permission from outside sponsors to show inspectors these documents. Dr. Barry Kreiswirth, PhD in microbiology; Dr. Nancy Connell, PhD in bacterial genetics; Academic Expert 1, PhD in microbiology, 16 August 2000.

[58] Defense contractors agreed that inspectors should question unusual quantities or combinations of supplies, agent, or other materials that appear out of kilter with a facility's stated purpose. "Well, if this solution is made and added on top of that one, they they've got a great media for those type of organisms." Defense Contractor 1, staff scientist in biotechnology, 28 August 2000. Defense Contractor 1, a scientist at a large research contractor, has an MA in cellular and molecular biology. Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company, made a similar comment.

[59] Dr. Barry Kreiswirth, PhD in microbiology, made this comment, which the group thought was sound.

over pathology records brought up concerns among the academic experts about compromising intellectual property.[60]

A final aspect of a second-level paper chase would be for the inspectors to cross-check the information in all of the previously accessed documents with two additional key sources of data. In this regard, laboratory notebooks can function somewhat like a polygraph. Scientists record each step of their work, the problems encountered, and the results in these notebooks. Their authenticity should be readily apparent to an experienced inspector who should recognize whether the blow-by-blow notes back up or contradict the research that has been described.[61] Laboratories also maintain inventories of the contents of their freezers, and these inventory lists can be compared against the media supplies and laboratory setup. Culture collection items, equipment, other physical laboratory features, and laboratory biosafety protocols should all correspond to the stated research program(s).

Insights 3.5

During one US BWC trial and a trilateral inspection of a US defense facility, locating some of the supporting documentation was described an "onerous" task because the items of interest were intermingled with so many other records. Also, some documents were not necessarily centrally filed, others had been destroyed long ago or placed who knows where by a staffer long since retired, and some ancient activities were not even documented.[1] Most sites have no cultural experience with international inspections and do not have their record keeping system set up to support quick document retrieval.[2]

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[1] Inspection Veteran 1, facility manager and US trial inspection host; Inspection Veteran 2, trilateral and mock inspection participant, 27 April 2000. Inspection Veteran 1, a facility manager, was a principal host of a US trial inspection held in late March 1996 at three facilities located in Albuquerque, New Mexico. Inspection Veteran 2 participated in inspections under the 1992 trilateral agreement, took part in a series of round robin mock inspections at military facilities in the western United States, and engaged in background planning for the mock visit to the Edgewood Arsenal, Aberdeen Proving Ground, Maryland. Agreeing that trying to round up the records for any type of inspection is the "biggest headache," Inspection Veteran 3, trial inspection observer and mock inspection participant, 27 April 2000. Inspection Veteran 3, who holds a DVM and a PhD, observed the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and participated in the mock trilateral inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

[2] Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, who has an MD and a PhD, took part in the trial inspection at US vaccine production plant in late October 1995, the late March 1996 trial inspection at three facilities located in Albuquerque, New Mexico, and the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

While examining documents, the inspectors may turn up additional scientists that they should interview. Even if that is not so, the academic and research institute experts suggested that the inspectors broaden the scope of their interviews to include personnel who support the laboratory's operation. Unless well coached, animal caretakers, janitors, administrators, and bookkeepers would all have difficulty

[60] On negatively affecting the productivity of other personnel at the institution: Dr. Barry Kreiswirth, PhD in microbiology; Academic Expert 1, PhD in microbiology; Dr. Nancy Connell, PhD in bacterial genetics, 16 August 2000. The group would provide pathology records, but preferred that the inspectors sign a confidentiality agreement beforehand.

[61] Dr. Robert Shope, MD and epidemiologist; Academic Expert 1, PhD in microbiology, 16 August 2000. Should log books or other documents of interest be in a high containment facility, inspectors can suit up and examine them there, scan documents out, or tape desired records to the window for review.

Table 3.2: Anticipated Effectiveness of Level 2 Monitoring Activities

Type of Inspection Activity	Expected Level of Effectiveness
Sampling and Analysis	High
Review of Additional Project Paperwork	Moderate
Review of Purchasing, Supply Records	Moderate
Review of Project Log Books, Computer Records	Moderate
Review of Animal, Plant Pathology Records	Moderate
Additional Interviews	High
Correlating Laboratory Notebooks, Freezer Inventories with Other Documentation	High

sustaining a cover story convincingly.[62] Consequently, the group ranked interviews as one of a trio of second-tier inspection activities that should be highly effective. Other monitoring activities that rated highly were correlation of documents and sampling and analysis. The latter was described as being able to provide the proverbial smoking gun or clean bill of health. As table 3.2 shows, the group expected the four other monitoring activities that delve into laboratory paperwork to be moderately effective in determining a facility's true status.

ON-SITE MONITORING ACTIVITIES: LEVEL 3 INSPECTION

Should suspicions of illegitimate activity persist throughout the second phase of an inspection, the group concurred that a third level of inspection should be initiated to try to determine the specific violation. The objective in level three would be, in the words of one participant, "to finger point," and the time needed to complete this phase of the investigation should be left "to the discretion of the inspectors."[63] The group concluded that in addition to the results of the analysis from samples taken previously, finger pointing was most likely to be accomplished through examining freezer contents and taking additional samples.[64]

Investigating the contents of facility freezers is an activity with possible high inspection payoffs and high costs to the inspected site, which is why the group placed this monitoring tool in the third level. The academic brainstormers believed that the freezers would be where evidence of illegitimate activity could be found. Cultures might be marked accurately, ambiguously, or with some type of code. In the first instance, laboratory scientists would have erred on the side of safety and any undeclared biowarfare

[62] While a covert facility might rehearse its laboratory scientists and managers with mock interviews, thorough preparations might not occur with support personnel. Inspectors might also catch some of these people off guard. Conversely, inspectors would notice if all of these individuals gave the same rote answers to questions.

[63] "If they get to level three, then I think it should be up to the discretion of the inspectors, because then they're obviously on to something. At that point it's an investigation." Academic Expert 1, PhD in microbiology, 16 August 2000.

[64] Note that the results of sample analysis would probably not be available prior to the onset of level three inspection activities. Running the appropriate tests could take four weeks or longer, a time lag that did not bother the group.

agents could be identified. By observing the distribution of freezer crystals on the surfaces of items, inspectors would also note if certain cultures had been handled just prior to the inspection. The Stimson inspectors who conducted a trial of a biosafety level 3 laboratory to facilitate this group's discussion scrutinized the freezer crystals on the vials in this laboratory's culture collection, as box 3.1 describes at the end of this chapter. Should more recently handled cultures have strange labels that host officials cannot reasonably explain, then those cultures should be examined.[65]

From the host facility's perspective, rummaging through the freezer presents potential biosafety problems and could damage invaluable culture collections. "Your catalogue is priceless. Without that, I can just go home."[66] Therefore, the group agreed that guidelines should be stipulated for searches of freezer contents.[67] After taking inventory of the freezer contents, the group recommended returning to the documentation to match inventory results with associated documents (e.g., inventory list). Throughout this process, the inspectors would be asking the host officials to explain anomalies. However, if the hosts juggle for answers and the contents and documentation do not jibe, then the academic experts recommended that some strains be pulled randomly for sampling as another cross-check.[68]

Finally, another type of sample could be taken to ferret out what is really happening at a laboratory, namely collecting blood samples from laboratory personnel or animals. The group viewed blood samples as another smoking gun tool because they would reveal antibodies in the donors.[69] Not surprisingly, members of the group were concerned about confidentiality and the aftershocks that could

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[65] Some organisms can be seen readily under the microscope, but others need tissue culture and specialzed techniques for viewing. An electron microscope might also be needed for certain organisms. Even then, a simple visual examination might not tell the inspectors what they need to know because many rod-shaped bacteria look alike. Genetic or serological techniques would be required for specific identification, perhaps even animal or plant tests. Dr. Anne Vidaver, PhD in bacteriology, 6 January 2000.

[66] Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Academic Expert 1 chimed in on the possible harm to culture collections, noting that some microorganisms are quite delicate. "Some things are sensitive to warming up even if they don't thaw. The temperature goes up and down even though they remain frozen." Academic Expert 1, PhD in microbiology. A biosafety hazard could occur if a freezer located in a biosafety level 2 area actually had dangerous pathogens. Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000. Other participants agreed with both points.

[67] Among the guidelines advocated were the necessity of having host personnel present during a freezer search, of limiting the time that freezer doors could remain open, and of establishing who should be allowed to retrieve items from freezers for further examination. When inventorying freezer contents, the participants were flexible about whether inspectors followed host facility rules or inspectors directed host personnel to accomplish tasks. Dr. Nancy Connell, PhD in bacterial genetics; Dr. Barry Kreiswirth, PhD in microbiology; Academic Expert 1, PhD in microbiology, 16 August 2000.

[68] Dr. Barry Kreiswirth articulated this strategy, which struck the rest of the group as a good idea.

[69] "Blood samples could identify agents that have been worked with, what they have been immunized against and exposed to." Dr. Robert Shope, MD and epidemiologist, 16 August 2000. Also on this point: Dr. Nancy Connell, PhD in bacterial genetics; Dr. Corrie Brown, DVM and PhD in comparative pathology. Tests could be prioritized according to the type of research the laboratory was conducting (e.g., viral versus bacterial). Heartily agreeing on the informative nature of blood samples from employees and animals, "that really is great information, especially if they are zero-positive for anthrax and their declaration is saying otherwise. That's a red flag right there, that could be the one determinant thing that put them out of compliance with the treaty: everybody here has been exposed to anthrax." Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company, 28 August 2000.

reverberate through a laboratory if inspectors used this tool.[70] Some laboratories have archived blood samples that might be accessed for this purpose, but in other cases hurdles might have to be cleared prior to sampling.[71] Because of its exculpatory power, several brainstormers also noted that a laboratory ought to be allowed to volunteer blood samples during the first phase of an inspection as a means to avoid the more extensive activities outlined for the second- and third-tier monitoring.[72]

At the conclusion of an inspection, the academic group was extremely wary that the reports prepared at this juncture might be worded to the effect that the inspectors did not see, hear, or detect anything untoward while they were there, but the capability and expertise were present to do bad things nonetheless. The implication of such wording was that the moment the inspectors left, the site reverted to being a weapons facility.[73] For this reason, the group wanted not only the right to review the report, but to have their rebuttals of any of its factual or subjective statements included in the body of the report. The reports should be confidential. In addition, the academic and research institute participants wanted a copy of the report sent to them directly, not just to some point of contact in the government.[74]

As table 3.3 indicates, the group graded all three monitoring activities in the third level as being equally potent. Throughout their discussions, various academic and research institute brainstormers worried that given the dual-use nature of their working environments, the inspectors would never be able to discern what a facility's researchers were really doing. Yet, they gave the preponderance of their recommended inspection techniques moderate or high effectiveness ratings. This seeming contradiction was explained by the group's fundamental belief that with the appropriate expertise, techniques, and care, inspectors could conduct a successful investigation with palpable results. The group's agreed statement was as follows: "The likelihood of these on-site techniques uncovering violations of the BWC by a state in an academic research setting is reasonably high and may deter states from using the academic community to violate the treaty."[75] Moreover, laboratories conducting peaceful research have a vested

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[70] Some staffers are upset about taking a purified protein derivative skin test for tuberculosis, much less one related to exposure to biowarfare agents. Some staffers might object on Constitutional grounds. Dr. Barry Kreiswirth, PhD in microbiology; Dr. Robert Shope, MD and epidemiologist; Dr. Nancy Connell, PhD in bacterial genetics, 16 August 2000.

[71] For example, the institutional review board would have to approve such activity. Moreover, the blood would have to be drawn by a physician, a nurse, or a certified phlebotomist. Academic Expert 1, PhD in microbiology; Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000.

[72] For instance, Academic Expert 1 and Dr. Robert Shope stated they would hand over blood samples early to verify the accuracy of their declarations and the legitimacy of their laboratories.

[73] As in "everything looks okay, but we think he could have hidden everything in the steam tunnel." Such an approach would be a "disaster," "uncalled for and slanderous in some ways." Academic Expert 1 and Dr. Barry Kreiswirth made these statements.

[74] Furthermore, the group wanted the US government to notify an inspected facility formally that it has received a "clean bill of health."

[75] The group's agreed statement continued with: "However, these techniques may not be successful in detecting terrorist activity." Dr. Robert Shope initially made the observation, to roundhouse assent, that regardless of their tangible effectiveness, the inspections would be worthwhile because they might deter laboratories from engaging in offensive research.

Table 3.3: Anticipated Effectiveness of Level 3 Monitoring Activities

Type of Inspection Activity	**Expected Level of Effectiveness**
Inventory, Examine, Sample Freezer Contents	High
Correlate Freezer Contents with Documentation	High
Take Blood Samples from Staff, Animals	High

interest in participating in some sort of regular BWC inspection process, namely to confirm their legitimacy and strengthen the ability of international monitors to pursue suspected cheaters.[76]

[76] "The purpose of the treaty, from an American point of view, is to establish that we have our house in order, that what is being done here is perfectly legitimate. The purpose of the regular inspections is to validate inspections on a challenge basis to look at a lab that *is* suspect. The legitimacy of inspections needs to be established." Dr. Nancy Connell, PhD in bacterial genetics, 16 August 2000. Just as the academic and research institute experts saw reason for some sort of non-challenge inspections in addition to challenge inspections, several defense contractors were adamantly opposed to a protocol built only upon challenge inspections. "That's worse, a worse connotation even if you're found innocent, regardless of the outcome." Defense Contractor 2, principal research scientist, 28 August 2000. Other contractor participants concurred. Still several defense contractors were very anxious about non-challenge inspections as well, underscoring the importance of the screening criteria used to prompt them. They took a strong position that the inspectors would need a reason—a probable cause—to inspect one of their sites. Defense Contractor 5, director of microbiology and special government projects; Defense Contractor 7, president and founder of a small sensor development company; Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company; Defense Contractor 3, senior technical adviser, 28 August 2000. On the benefit of getting a clean bill of health out of this inspection process: Academic Expert 1, PhD in microbiology, 16 August 2000. Also on the reasons for non-challenge inspections: "You want to have a baseline that says, 'this is what should be done, and in some places people are abiding by the treaty, in other places they aren't.'" Dr. Barry Kreiswirth, PhD in microbiology, 16 August 2000.

Box 3.1: Trial Inspection of a Biosafety Level 3 Research Laboratory

On 7 July 2000, the Public Health Research Institute (PHRI) in the heart of New York City hosted a duo of seasoned inspectors whose mission that day was to give the monitoring techniques suggested in the initial meeting of the academic and research institute group a trial run in a high-containment research laboratory setting.[1] The inspectors were Lt.Col. Karen Jansen (USA, ret.) and Dr. David Franz, a team with hard-earned inspection experience in Iraq and the former Soviet Union.[2] As Dr. Barry Kreiswirth, the head of one of the biosafety level 3 laboratories at PHRI, explained during the introductory briefing, PHRI has a venerable history, dating back to the early 1940s. PHRI is home to twenty-two research laboratories working in such fields as microbiology, genomics, virology, immunology, biochemistry, genetics, and cell and structural biology. At the time of the inspection, PHRI was funded by twenty-three National Institutes of Health grants as well as the Centers for Disease Control and Prevention, pharmaceutical and biotechnology companies, private foundations, and other government sources, including the Defense Advanced Research Projects Agency. PHRI also housed a separate biosafety level 3 facility and other laboratory areas that were not the focus of the trial inspection. [3] Collocated in the same multi-story building were the New York City Health Department Bureau of Laboratories, a poison control center, a local university ophthalmology department, a common library, the Diamond AIDS research laboratory, and other clinical and hospital laboratories.

A local epidemic of tuberculosis in 1991 prompted the establishment of Kreiswirth's laboratory. The rise in the number of drug-resistant cases made it apparent to PHRI's management that tuberculosis again represented a public health problem, and money was raised to construct two biosafety level 3 laboratories, which opened in 1992.[4] The larger biosafety level 3 laboratory overseen by Kreiswirth was used mainly by the researchers whose primary task is to genotype or characterize the strains of

[1] The Henry L. Stimson Center is grateful to PHRI for its generous cooperation with this inspection.

[2] Briefly, Lt. Col. Jansen (USA, ret.), a microbiologist and twenty-year veteran of the Army's Chemical Corps, led four United Nations Special Commission on Iraq inspections of biological facilities following the Persian Gulf War. Dr. Franz, who holds a DVM and a PhD, was formerly the commander of the US Army Medical Research Institute of Infectious Diseases and has been to numerous institutes involved in the former Soviet Union's massive biowarfare program. Lengthier resumes for both individuals, who also facilitated each of the brainstorming meetings, can be found in the appendix. In addition, the inspection team included Amy E. Smithson, PhD and senior associate at the Stimson Center, as an observer and note taker.

[3] At the outset, the laboratory was funded locally and conducted research on influenza, hemoglobin, and basic research and development applied to public health until the early 1970s. Among PHRI's long-standing research efforts are programs that explore fundamental aspects of gene expression, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) replication and recombination, genetic competence, enzyme structure and function, and viral assembly and structure. The other biosafety level 3 laboratory was concentrating on two Centers for Disease Control and Prevention-funded human immunodeficiency virus (HIV) research projects. For more information on PHRI, see http://www.phri.nyu.edu/.

[4] More details about this tuberculosis laboratory can be found at: http://www.phri.nyu.edu/tb.htm/. In keeping with its status as a world-class research institute, the media frequently consults PHRI staff on a variety of topics. See, for example, Constance Holden, "Stalking a Killer in Russia's Prisons," *Science*, 26 November 1999, 1670; Susan Okie, "The Frontiers of Medicine: Science Races to Stem TB's Threat," *Washington Post*, 10 August 1999; Ian Fisher, "Hospitals Uniting to Fight Drug-Resistant Bacteria," *New York Times*, 23 June 1998; Richard Saltus, "Antibiotics: Overused and Misunderstood," *American Health* 14 (October 1995): 50.

tuberculosis. During the briefing, Kreiswirth mentioned that his scientists had developed drug resistant strains of the disease, and his colleague Dr. Nancy Connell, who helped to host the inspection, noted that crossing a gene into tuberculosis strains would be possible. As part of the general characterization of their work, Kreiswirth readily listed several of his laboratory's outside collaborators, naming a few biotechnology companies, nongovernmental and governmental research laboratories in the United States, and other research institutes around the globe (e.g., Russia, Egypt, the Czech Republic). Kreiswirth mentioned that some of the laboratory's collaborators conducted animal research. He said that he had met with Defense Department scientists (e.g., Walter Reed) to discuss collaborative work, but no such relationship had been established. Kreiswirth also volunteered that they had sent control strains to Russia and had received over 1,600 tuberculosis strains from Russia. The Russian aspect of the research was funded by a grant from the Soros Foundation. Aside from the project's scientists, Kreiswirth pointed out that several other PHRI researchers and scientists from collaborating organizations also had access to both biosafety level 3 facilities.[5]

The tour that followed was casual and informative, beginning with an introduction to PHRI's president, Mr. Lewis Weinstein. As the entourage made its way around the building's floors, Kreiswirth explained the general purpose of various laboratories, introducing the inspectors to numerous scientists, including one Chinese and a few Russian researchers.[6] To a person, these widely published scientists were easy to engage in conversation, with a number of them lapsing enthusiastically into lengthy descriptions of their research. They readily discussed their funding sources, their collaborators domestic and foreign, and their travel to places near and far (e.g., Vietnam, Russia, Cuba).[7] After an overall site tour that lasted one and a half hours, the inspectors honed in on the portion of PHRI that was the target of the inspection, namely two biosafety level 3 laboratories, one approximately 250 square feet and another 650 square feet in size.[8] At this point, Kreiswirth handed the inspectors over to his chief laboratory technician, who described procedures for recording the receipt of samples, media preparation, culturing, and moving samples to the fingerprinting laboratories. The chief technician also reviewed the lab's safety protocols and showed them paperwork for various procedures, as well as the computer database used to

[5] The introductory briefing lasted an hour. In a more confrontational setting, Franz and Jansen said that they would have curtailed the briefing earlier, but in this case they allowed a lengthy briefing because in an abbreviated inspection format it gave them a sound basis for where to focus subsequently. In the spring of 2001, PHRI was to move to a new, state-of-the-art facility in Newark, New Jersey, with over twenty biosafety hoods in a biosafety level 3 capacity for pathogen studies, where mice and perhaps pigs will be exposed to aerosols and then moved into biosafety level 3 animal rooms. Kreiswirth also described the features and biosafety protocols for the tuberculosis laboratories.

[6] Not only were several Russians working in the lab, the laboratory chief and several other scientists employed there had traveled to Russia, Cuba, and elsewhere. According to the laboratory chief, most of the Russian contingent in the lab, which was focusing on virulence, preferred to work at night. This information was voluntarily disclosed.

[7] Annually, PHRI's scientists publish in over fifty peer reviewed journals.

[8] Initially, they were testing polymerase chain reaction (PCR) diagnostic kits in the smaller laboratory, but work switched over to macrophage research. The smaller laboratory is still dedicated to tuberculosis work. Inspectors viewed the smaller facility through the observation window.

track samples. The inspectors found that the records for outgoing shipments were not as well organized as those tracking incoming samples, and the chief technician explained that the laboratory was not required to keep such documentation.[9]

Moving to the anteroom of the larger biosafety level 3 laboratory, which doubled as a supply storeroom, the inspectors, following host facility protocols, suited up and entered the laboratory. Coded entry pads safeguard the entrance of both laboratories.[10] The larger facility was equipped with three biosafety cabinets, four double standing incubators, a smaller incubator, a bac-tech machine to detect and diagnose *Mycobacterium tuberculosis* in clinical settings, an electric autoclave, a tabletop centrifuge, a large sink area, two refrigerators, shelving, and a large, low-temperature chest freezer that contained approximately 11,000 frozen strains of tuberculosis.[11] Unbeknownst to Franz and Jansen, Kreiswirth and Connell had planted a few clues that, if noticed, should have cued the inspectors that something wrong was afoot. They put on the shelves inside the laboratory two containers of media used not for tuberculosis (e.g., brain-heart infusion) but rather for *Bacillus subtilis*; placed a strain in the freezer labeled "BA" with a corresponding titillating entry penciled into the logbook; set a blood plate streaked with *Bacillus subtilis* in one of the incubators; and instructed the chief technician to behave nervously.[12] Deliberately making their way around the laboratory, the inspectors looked into the incubators, refrigerators, and the freezer. They asked whether the color of the slant marked "0/19/00" inside the freezer was typical of tuberculosis because the bright yellow color looked unusual to them.[13] Otherwise, it did not appear to Franz and Jansen that anything was out of the ordinary in the freezer because the ice

[9] Logs for incoming samples, the inspectors observed, were kept meticulously. Compared to the number of samples the laboratory received, not that many samples were shipped elsewhere. However, the laboratory had a general policy of sending what was requested.

[10] Note that the other security precautions at PHRI were inconsistent with an expectation that high security would be a signature of a covert military facility. At the main entry, signs said that everyone must wear badges, but such badges were not always visible on personnel entering the building. Two or three security guards were present, but did not check the inspectors' identification. The inspectors were asked to sign in, and Kreiswirth and Connell met the inspection team as they stepped off of the elevator.

[11] Two databases—one written in a logbook, the other computerized—are kept of these isolates. Incoming samples are split, with half going to frozen stock and the other half going to DNA preparation. The freezer has a built-in alarm system that alerts the laboratory chief or a designee of an unauthorized entry and a 24-hour backup carbon-dioxide supply. The larger biosafety level 3 laboratory has twenty-three air exchanges. An outside contractor maintains and certifies the high efficiency particulate air (HEPA) filters every six months. The laboratory is outfitted with ultraviolet lights and HEPA filters at the entrance and above each of the biosafety cabinets. These latter HEPAs are ducted together and feed into a fan, which draws to the rooftop.

[12] *Bacillus subtilis* was selected for the blood plate because its colony morphology is similar to that of *Bacillus anthracis*. The strain record entries in the logbook and the electronic access database are sequentially numbered. The planted strain was number 9717. On that line in the logbook, Kreiswirth wrote "control strain" with "BA" beside it, for *Bacillus anthracis*. In the corresponding empty slot in the freezer, his chief technician placed a normal isolate from Cairo. The planted blood plate in the incubator was marked number 26.

[13] Aside from the chief technician, Kreiswirth did not give any particular instructions to any of his staff members about how to interact with the inspectors. The chief technician's response that she was uncertain of what she should tell them struck Franz and Jansen as somewhat odd. The slant they had identified was not the one planted in the freezer, and since its bright yellow color was indeed typical, a straightforward answer would have sufficed.

crystal dust was evenly distributed across the thousands of vials. They also queried the chief technician about one of the cultures inside an incubator, one that was marked "RIFMIC."[14] Franz saw the different media on the shelf.[15]

Another thing that Franz and Jansen observed was that the exterior filter padding on the ducts leading to the high efficiency particulate air (HEPA) filter was brand new. To hedge against the possibility that the filter had been changed just prior to the inspection in an effort to hide something, they took a notional sample of the filter.[16] When asked about the filter status, the chief technician said there had been some water leaks into the laboratory recently, and they had just replaced and autoclaved the filters on the preceding Friday, 30 June. The day before, the facility had also been repainted. Looking behind equipment, the inspectors noticed only two paint chips, but no other signs of recent repair work.[17] Since the walls did not look freshly painted, this explanation did not sound right to Franz and Jansen, who also saw an atypical entry in the anteroom logbook for 30 June.[18] Upon exiting the laboratory, the inspectors asked to spend more time with the shipping records.

As they would explain to Kreiswirth and Connell during the post-inspection discussion that followed, the inspectors returned to the shipping records instead of other paperwork to try to rule out the possibility that the facility might have been a source of virulent strains for proliferators. Given the laboratory's international connections, its collaboration with institutions that conduct animal studies, its strain manipulation capabilities, and its stellar scientific staff, Franz and Jansen sought and received assurance of their concern through the shipping records and the staff's behavior during interviews.[19] The duo of inspectors also articulated their plans for chasing down other oddities that they had noticed, had time allowed. To sort out the suspicious timing of the maintenance activities just before the inspection, they would have interviewed the biosafety officer(s), maintenance personnel who had repaired the broken freezer compressor, the contractor(s) who changed the filters, and the painter(s). They would have also

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[14] Later, Jansen and Franz said they asked about this culture because they thought that RIFMIC might have stood for Rift Valley Fever, an idea they subsequently dismissed. They also checked the latest entry date for that incubator and noted it as "6/28/00."

[15] Franz thought it was unusual for the media to be inside the laboratory because they had been told that all media preparation was done outside of the laboratory. Franz and Jansen even discussed the utility of various media types for research, but decided not to make an issue of it since preparing media inside the laboratory was not that big of a deal.

[16] The protocol for PCR analysis of the sample was to be negotiated later.

[17] A ledge that ran around the entire laboratory had black sooty dirt, but no paint chips, dust, or other signs of leakage.

[18] This entry was outside of the normal lines and marked with an asterisk, but other standard notations (e.g., name, time) were absent. As for the behavior of the chief technician, Franz and Jansen did not detect anything out of the ordinary other than this one statement. This capable individual was no surrogate, clearly demonstrating during the course of the inspection extensive knowledge of the facility's operations, biosafety protocols, and science.

[19] Earlier, they had pulled at random sample receiving logbooks, biosafety protocol notebooks, and laboratory notebooks inside the larger biosafety level 3 facility. Examining these records, they found nothing out of the ordinary. Ideally, the team would have been larger, including at least one technician assigned to do nothing but review records.

sought documentation of this work.[20] Time permitting, they would have interviewed additional scientists to alleviate their concerns about the laboratory's connections with institutions in countries that the US government publicly names as being of proliferation concern. Both Franz and Jansen explained that while it may be unfair that nationality alone would trigger suspicion, their training was such that inevitably nationality tripped that wire. Interviews can quiet such qualms.

Finally, Jansen and Franz conceded their handicap in carrying out a trial inspection in a facility specializing in tuberculosis research.[21] Neither had the specific expertise necessary to identify the brain-heart infusion media as inappropriate for the laboratory's applications and thus could not pursue the matter further. Having a tuberculosis expert on the inspection team could have made for quite a different inspection outcome. Had they been allotted time to investigate the other ambiguities, both Jansen and Franz agreed that they would have given the facility a clean bill of health, according to the guideline set by the academic and research institute brainstormers: a facility is presumed legitimate unless evidence indicates otherwise. For their part, Kreiswirth and Connell described the inspection as a valuable learning experience, despite its cost.[22]

[20] Kreiswirth and Connell said that it never occurred to them that maintenance work would raise the inspectors' suspicions. Something broke, it needed to be fixed, and the repairs were made without a second thought. They explained that the paint did not look fresh because they had employed several base coats topped by a special, high-sheen epoxy paint to make sure, given the building's porous, cinderblock construction, that the facility was airtight.

[21] Note that both individuals said they would have been more aggressive in a genuine inspection, but they gauged their behavior to the cooperation extended by PHRI for the exercise.

[22] The cost of shutting down the laboratory, Kreiswirth and Connell stated, was offset by the insight they gained into how inspectors do their jobs. Kreiswirth estimated the cost of the exercise to be approximately $5,000. The figure constitutes the cost for temporarily closing the larger biosafety laboratory to PHRI's scientists. Had a real sample been taken of the HEPA filter, he estimated that it would have cost about $2,000 to bring their outside contractor to do that work over the course of two days, including decontamination, sampling, and filter change. Added Connell: "Because we hand nothing to hide, we had a great time. For a whole day, we talked about how cool [PHRI] was. The scientists waxed poetic."

Appendix: Participant Biographies

Corrie Brown has worked at the University of Georgia College of Veterinary Medicine as professor and head of the department of veterinary pathology since 1996. She received her DVM from Ontario Veterinary College at the University of Guelph. After practicing for a short period in western New York, she did a combined residency/PhD in comparative pathology at the University of California at Davis. Board certification (ACVP) and PhD were both attained in 1986. She was an assistant professor of pathology at Louisiana State University briefly before joining the US Department of Agriculture at Plum Island, where, as head of the pathology section, she specialized in the diagnosis and pathogenesis of foreign animal diseases. Her professional interests are in infectious diseases of food-producing animals, emerging diseases, agroterror and international veterinary medicine. She has over 250 scientific publications and presentations. She currently serves as coordinator of international veterinary medicine for the College of Veterinary Medicine.

Nancy Connell earned her PhD in bacterial genetics from Harvard Medical School, where she studied gene expression during the stationary phase of growth in *Eschrichia coli*. She then held a postdoctoral position at Albert Einstein College of Medicine where she developed live recombinant vaccines. In 1992 Dr. Connell joined the Department of Microbiology and Molecular Genetics in the medical school at the University of Medicine and Dentistry of New Jersey. Using genetic and cell biological approaches, her laboratory focuses on intracellular metabolism of *Mycobacterium tuberculosis*, a bacterium that infects and replicates in macrophages. She has a joint appointment in the department of medicine and is the director of molecular mycobacteriology at the New Jersey Medical School National Tuberculosis Center. In addition to mycobacterial metabolism, her laboratory has been examining the molecular basis of resistance in multidrug-resistant clinical strains of *M. tuberculosis*. Finally, Dr. Connell has been working for many years in the area of the control of proliferation of biological weapons.

David R. Franz has been the vice president of the Chemical and Biological Defense Division of Southern Research Institute since 1998. He retired from the US Army at the rank of colonel, having served as commander of the US Army Medical Research Institute of Infectious Diseases. During over twenty years on active duty, Franz was a group veterinarian for the 10th Special Forces Group before going on to assignments at four of the Medical Research and Development Command's laboratories. Armed with a DVM from Kansas State University and a PhD in physiology from Baylor College of Medicine, Franz conducted research and published in the areas of frostbite pathogenesis, organophosphate chemical warfare agent effects on pulmonary and upper airways function, the role of cell-mediated small vessel dysfunction in cerebral malaria, and most recently, medical countermeasures to the biological toxins. Franz was the chief inspector on two United Nations Special Commission on Iraq biological warfare inspection missions to Iraq and was technical advisor on long-term monitoring. He was also a member of the first two US/British teams to visit Russia in support of the Trilateral Joint Statement on Biological Weapons.

Jerry Goldstein is a professor of microbiology and chairman of the Botany/Microbiology Department at Ohio Wesleyan University. Dr. Goldstein earned a PhD in microbiology from the University of Wisconsin-Milwaukee where he began research on the effectiveness of antiviral drugs on polio, vaccinia, herpes and adenovirus-infected cells. Currently his laboratory is involved with cloning, sequencing, and expressing a variety of bacterial protease genes in various expression vectors.

Robert Hamilton is a senior scientist and group leader at a large biotechnology company that has sales approaching $2 billion annually. A PhD microbiologist with more than seventeen years of experience in industrial biotechnology including yeast, E. coli, and mammalian cell culture process development and manufacturing process improvement. Among his proficiencies are troubleshooting at large scale, project management, directing research and development laboratories, Good Manufacturing Process regulations, regulatory filings for chemistry, manufacturing, and control sections at the IND and NDA (BLA) stages as well as validation and regulatory aspects involved in process change implementation. Prior to joining industry, Hamilton spent five years as a postdoctoral research fellow at the Department of Biological Chemistry at the Pennsylvania State University College of Medicine. He holds a US patent and has had a dozen articles published in key peer-reviewed journals.

Jennie Hunter-Cevera is president of the University of Maryland Biotechnology Institute. Hunter-Cevera received her doctoral degree in microbiology from Rutgers University in New Jersey in 1978. Dr. Hunter-Cevera began her career at E.R. Squibb in Princeton, NJ as a researcher and later moved to Cetus Corporation. In 1990, she started a consulting company specializing in biotechnology, agricultural and industrial microbiology, bioremediation and pharmaceuticals. Hunter-Cevera then went on to direct the Department of Environmental Biology and Biochemistry for the Lawrence Berkeley National Laboratory, which is operated by the University of California as part of the Department of Energy's national laboratory system. There she started the Center for Environmental Biotechnology where she remained until becoming president of the University of Maryland Biotechnology Institute in 1999. Hunter-Cevera is also a principal investigator of two cooperative programs sponsored by the Department of Energy with Ukrainian institutes to screen rare botanical and microbial extracts throughout the former Soviet Union. She has also worked on *Bacillus anthracis* biomarkers, specifically saspB which is now a classified assay.

Karen Jansen (Lt.Col., ret.) served as a US Army Chemical Corps officer from 1978 in a variety of command and staff positions that included assignments in Germany, Saudi Arabia, and South Korea. With a background in microbiology and immunology, she made contributions to US chemical and biological weapons defenses. From 1991 to 1992, Jansen was a chemical and biological weapons inspection operations officer for the United Nations Special Commission on Iraq (1991-1992), having participated in six and led four inspection missions. She was subsequently posted as a chemical inspection team chief to the US On-Site Inspection Agency. Jansen has an MS in microbiology from North Carolina State University.

Barry Kreiswirth has more than twenty years of microbiology research experience. For nearly ten years, Kreiswirth has directed the Tuberculosis Center at the Public Health Research Institute (PHRI) in New York City. With the burgeoning tuberculosis epidemic in Russia, the program's most recent work has focused on efforts to develop demonstration tuberculosis control projects that could form a model for replication throughout Russia. Prior to his current role, Kreiswirth headed the New York City Department of Health Phage Typing and Antibiotic Susceptibility Testing Laboratory. He had previously spent four years as a research scientist and postdoctoral fellow at PHRI. A PhD in microbiology, he has had dozens of articles published in such journals as *Emerging Infectious Diseases*, *Journal of the American Medical Association*, *Clinical Microbiology*, and *Journal of Infectious Diseases*, and is a member of the American Association for the Advancement of Science, American Society for Microbiology, and the New York Academy of Sciences.

Allen I. Laskin is president of Laskin/Lawrence Associates and serves as an independent consultant in microbiology and biotechnology. For fourteen years, Laskin was assistant director of microbiology at the Squibb Institute for Medical Research. He subsequently spent fifteen years as head of biosciences research at Exxon Research and Engineering Company. Later, he was instrumental in developing the New Jersey Center for Advanced Biotechnology and Medicine and became its first associate director. He then spent three years as president of Matrix Laboratories, a small start-up biotechnology company, before starting his current consulting activities. Laskin, who holds a PhD in microbiology, has received several awards and honors. He is a fellow of the American Academy of Microbiology, the American Association for the Advancement of Sciences, the Society for Industrial Microbiology, and the New York Academy of Sciences. He has authored numerous scientific papers and US patents, is the editor or co-editor of many books and book series, and is a senior editor of the *Journal of Industrial Microbiology and Biotechnology*.

Theodore Myatt is a doctoral candidate at the Harvard School of Public Health in the where he is studying the airborne transmission of common cold pathogens and their relation to building management. Mr. Myatt earned his master's degree in environmental management from Duke University and interned at the Centers for Disease Control and Prevention in Atlanta. Subsequently, he was a biological safety officer at UCLA's Office of Environment, Health, and Safety. In addition, Mr. Myatt now serves in the Division of Epidemiology and Immunization at the Massachusetts Department of Public Health.

George Pierce became a professor of applied and environmental microbiology at Georgia State University in late 2000. Prior to his transition to academia, Pierce worked for nearly ten years at Cytec Industries, formerly American Cynamid, where his last position was manager of technology development and engineering. He has also held senior research posts with Battelle Memorial Institute and at Celgene Corp., where he was the director of research and development. His research interests include development and scale-up of microbial processes for pollution prevention, site remediation and restoration at Superfund and Resource Conservation and Recovery Act sites, scale-up and development of

commercial biotechnology products, development of enzyme based and fermentation based products, and regulatory affairs and compliance in the area of environmental and industrial microbiology. A PhD in microbiology, Pierce has also been an adjunct profession at Ohio State University and at the Rensselaer Polytechnic Institute. He has numerous publications and patents in biotechnology and has served in several professional organizations, including a stint as the director of the Society for Industrial Microbiology.

Steven J. Projan is the director of antibacterial research at Wyeth-Ayerst Research, which is the research and development division of American Home Products Corporation. He has a PhD in molecular genetics and over twenty years of experience in research and industry, having begun his career as a postdoctoral fellow at the Public Health Research Institute in New York City, where he studied plasmid replication and virulence in *Staphylococcus aureus*. After becoming an associate at the Public Health Research Institute, Projan continued his work on plasmid replication, antibiotic resistance and staphylococcal virulence though 1994. In 1987 Projan became a senior scientist and then group leader at Applied Microbiology, Inc.—then an in-house biotechnology company at the Public Health Research Institute—working on antimicrobial peptides and bacteriocins. In 1993, Projan moved to Lederle Laboratories, which Wyeth-Ayerst Research absorbed, as a group leader in anti-infectives research. Four years later, Projan became an associate director in bacterial genetics and subsequently moved to his current position. The author of over fifty papers and book chapters, Dr. Projan is a past chair of the Gordon Research Conference on Staphylococcal Diseases, a member of the Bacteriology and Mycology I National Institutes of Health Study Section, and serves on four editorial boards.

Robert Shope is a professor of pathology in the Center for Tropical Diseases at the University of Texas Medical Branch at Galveston. He graduated with a BA in zoology and went on to earn an MD from Cornell University Medical College. Before joining the University of Texas he was a professor of epidemiology and head of the Division of Infectious Disease Epidemiology at Yale University's Department of Epidemiology and Public Health. Dr. Shope's research activities are mainly in the epidemiology of arboviruses and rodent-associated viruses, anti-viral compounds, vaccines and emerging infectious diseases. His career also includes a stint as a Captain in the US Army Medical Research Corps during which he was stationed at the US Army Medical Research Institute for Infectious Diseases. Dr. Shope is a member of numerous committees and programs including the International Committee on Taxonomy of Viruses, the Defense Department's Biomedical Technology Area Review and Assessment, and the Institute of Medicine's Committee on Research and Development Needs for Improving Civilian Medical Response to Chemical and Biological Terrorism Incidents.

Amy E. Smithson has been a senior associate at the Henry L. Stimson Center since 1990. In January 1993, she initiated the Chemical and Biological Weapons Nonproliferation Project, which conducts analytical research across the spectrum of complex topics associated with the control and elimination of chemical and biological weapons. She has published widely in journals, testified before Congress, and is

frequently consulted by the media. Before her tenure at the Stimson Center, she worked at Pacific-Sierra Research Corporation and the Center for Naval Analyses. She holds a PhD in political science from George Washington University.

Anne Vidaver is head of the Department of Plant Pathology at the University of Nebraska-Lincoln. She received her PhD in bacteriology with a minor in plant physiology from Indiana University in Bloomington. Vidaver has more than thirty-five years of teaching experience, as well as research in phytopathogenic bacteria and bacteria associated with plants. Her work has included systematics, epidemiology and control, plasmid, bacteriophage and bacteriocin characterization and genetics. She has served as an advisor or consultant to several companies and federal agencies. She has authored or co-authored over 180 scientific articles and a book. In collaboration with colleagues, she also holds two patents.

Robert Zagursky is a distinguished research scientist for research and development at Wyeth-Lederle Vaccines, a business unit of Wyeth-Ayerst Research, which is a division of American Home Products Corporation. Zagursky has eighteen years of experience in industry: seven years in research and development of bacterial vaccines at Wyeth-Lederle Vaccines; three years in research and development of eukaryotic expression and HIV research at DuPont Merck Pharmaceutical Company; and nine years in corporate research and development studying fluorescent DNA detection and PseudoRabies viral recombination at E.I. DuPont de Nemours & Co. Zagursky, who holds a PhD in biological science, also has two years postdoctoral experience in bacterial research at the US Army Medical Research Institute for Infectious Diseases. He is a recent recipient of American Home Products' Exceptional Achievement Award and Team of the Year Award, a member of the American Society for Microbiology, and a member of the editorial board for *BioTechniques*.

Academic Expert 1 is a PhD microbiologist and a virology professor in a major US university's microbiology and immunology department. This expert's research has focused on the molecular genetics of alphavirus pathogenesis, the design of molecularly cloned vaccines, and the development of alphaviruses as in vivo and in vitro expression systems. This individual is also a founding scientist of a commercial enterprise for applications of an innovative vaccine delivery technology.

Academic Expert 2 is a pathology professor at a top-ten US medical school. The director of a tissue typing laboratory, this physician's research is in the area of autoimmune endocrine disease, having helped define the basis of the autoimmune response to thyroid autoantigens. In particular, this person's recent work has focused on epitope mapping of thyroid peroxidase, a major autoantigen in autoimmune thyroid disease. His laboratory has used molecular biologic techniques to identify the specific epitopes recognized in thyroid peroxidase and shown that the recognition of this autoantigen is heterogeneous in different individuals. This expert, who has published numerous articles, has also served on the editorial boards and as a review for several professional journals.

Defense Contractor 1 is a staff scientist in the biotechnology sector of a large contract research organization that handles both governmental and private clients. This individual holds an MA in cellular and molecular biology and concentrates on method development and validation in molecular biology.

Defense Contractor 2 is a principal research scientist at a medical research facility that works primarily under government contracts and is part of a large global technology development company. A PhD microbiologist and veterinarian, this individual is an anatomic pathologist with in-depth experience in veterinary medicine and research.

Defense Contractor 3 is a senior technical adviser at a large a nonprofit organization focusing on basic and applied research, product development and policy studies in a range of fields of science. A PhD in physics, this individual has over thirty-five years of instrumentation development experience, over twenty years of direct experience working on several government and industry committees concerning weapons of mass destruction.

Defense Contractor 4 is president of a company that provides consultant, technical, and materials evaluation support to government agencies and commercial clients. This individual received a PhD in chemical engineering but is also trained in physics and previously worked for almost a decade in the aerospace industry.

Defense Contractor 5 is the director of microbiology and special government projects for a small defense contracting research firm. The recipient of a PhD in microbiology and an MS in human genetics, this individual is a board-certified medical technologist who has co-authored numerous peer-reviewed journal articles. Previously, this person served in the US Air Force as chief of molecular biology in a clinical investigation facility.

Defense Contractor 6 is senior vice president, director, and co-founder of a biotechnology research contracting firm. Previously, this individual managed a research laboratory in a cancer center in the microbiology, biology, and immunology department of a university. With over fifteen years in molecular genetics, this individual is the co-inventor of US patents and co-author of over peer-reviewed journal articles and book chapters.

Industry Expert 1 is the associate director for fermentation development at a US vaccine company that specializes in the development and manufacture of bacterial and viral vaccines and is a division of a Fortune 100 pharmaceutical firm. He holds a PhD in microbiology and has thirteen years experience in process development and scale up for the production of new and licensed vaccines for infants and adults. He also has extensive background working with biosafety level 2 and 3 microorganisms and designing facilities for large scale biosafety level 2 and 3 operation.

Industry Expert 2 is a senior vice president at a US biopharmaceutical company overseeing operations, product development and manufacturing. Prior to joining this firm, this expert served as vice president of manufacturing operations and process development at a US vaccine manufacturer, where he was responsible for all phases of vaccine manufacturing, including bulk manufacturing, filling, and packaging. Previously, this expert, who holds a PhD in biology, was the senior director for biological manufacturing at a US pharmaceutical company with roughly $40 billion in annual sales. In this capacity, he was responsible for manufacturing licensed bulk biologicals, including several vaccines. Earlier, this individual served as the director of the department of gene expression sciences and as the associate director of the biological process sciences department in one of the largest drug companies globally. This expert was previously the president of the Society for Industrial Microbiology and is a member of other professional organizations.

Industry Expert 3 is a senior research scientist at a small US biotechnology company that is a subsidiary of a larger firm that specializes in the discovery, analysis, and manufacture of proteins to be used in new applications. After receiving a PhD in biochemistry, this individual began a career in industry and research that has stretched over twenty-five years. This expert has worked in several research positions at a large US chemical corporation with well over a billion dollars in annual sales where his research concentrated in the field of polymers for biomedical applications. Prior to joining industry, he held research positions in two different research institutes of the National Institutes of Health. His bibliography contains more than eighty published pieces, he holds over ten patents, and he is a member of several professional associations.

Industry Expert 4 is president and chief executive officer of a small US biotechnology company focusing on novel therapeutics for the pharmaceutical and dietary supplement industry. The firm is a wholly-owned subsidiary of a privately held international company that sells cosmetics and supplements overseas. This individual holds a PhD in microbiology.