Chapter 4
Industrial Strength Expertise: The Views of Pharmaceutical and Biotechnology Industry Experts on BWC Monitoring

Representing an interesting cross-section of the pharmaceutical and biotechnology industries, a group of specialists graciously rose to the challenge of the Stimson Center's invitation to brainstorm the issues associated with monitoring the Biological and Toxin Weapons Convention (BWC). These industry experts had backgrounds in areas such as vaccine development and manufacturing, antibacterial research, and biotechnology product scale-up and development. Members of this group had vast experience in smaller, niche firms as well as in the large companies of the pharmaceutical and biotechnology industry such as Wyeth-Ayerst Research, DuPont Merck Pharmaceutical Company, Celgene Corp., and Cytec Industries. Cumulatively, the nine experts who composed this group possessed just under 200 years of experience in research and industry. The credentials of the industry brainstormers, four of whom chose to remain anonymous, are recounted in full in the appendix. Stimson facilitators marched the industry participants through the same mental exercise as the academic group, where they addressed the types of questions listed in box 1.1. The pages that follow document this group's pragmatic approach to the vexing questions of monitoring the BWC.

The views of the industry group on how to plan inspections for maximum effectiveness and receive them without compromising sensitive business data came from a deep reservoir of experience, for their facilities had all been involved in countless inspections. To illustrate the point, one participant estimated that his current plant fills out at least fifty reports per year just for state and federal environmental regulators. Also, manufacturing facilities get inspected by the Food and Drug Administration (FDA), the Commerce Department, the Occupational Safety and Health Administration, and state and federal environmental protection agencies. FDA inspectors show up on industry doorsteps without notice. FDA and environmental inspection teams can park on site for weeks, digging through records and examining operations that involve air, water, solids, waste, and emissions of any type. If one kind of inspector finds something wrong, they can call in sister regulatory inspection crews, so the phrase "crawling with inspectors" rang true to this group.[1] This kind of experience functions as a double-edged sword for how the industry approaches the prospect of monitoring under the BWC. "Well, the good news is that we're accustomed to inspections—we're set up for it, we have the people to handle these things.

[1] Dr. Steven Projan gave these examples and other group members agreed. Dr. Steven Projan, Director of Antibacterial Research at Wyeth-Ayerst Research, holds a PhD in molecular genetics and has over twenty years of experience in research and industry. Chemical surety inspectors also oversee some sites, noted one of the participants in the inspection 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 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.

The bad news is that the companies are extremely gun-shy. They don't want any more inspections than they are already getting."[2]

In addition to being concerned over the potential loss of confidential business data through inspections under the BWC, the industry group was understandably edgy about anything associated with the phrase "biological weapons."[3] The industry takes the reputation of these companies very seriously because the general public's trust in their products and their credibility with stockholders is at stake. Therefore, the industry group recommended that any possible BWC monitoring activity at corporate facilities be accomplished with the lowest possible profile. The inspectors should come and go in plain clothes without public announcement. This matter was so sensitive that the industry group did not even want the results of an inspection that gave a facility a clean bill of health to be disclosed publicly unless the host company specifically gave the inspectorate permission to do so.[4]

When it came to planning and executing an effective inspection, the industry group mentioned several things time and again. Their foremost mantra was the need for the inspectors to be wary of inconsistencies with the plant's stated purpose. No single incongruity is likely to be sufficient to label a facility "dirty," but an accumulation of them would certainly send up flares to that effect.[5] The industry group's other frequent refrains pertained to the need for the inspectors to be thorough, and to cross-check one thing with another with an eye toward consistency and whether activities at the site made good

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[2] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000. Dr. Robert Hamilton, holds a PhD in microbiology and cell biology and has over twenty-five years of experience in research and industry.

[3] 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. Defense Contractor 3, employed at a large nonprofit research organization, holds a PhD in physics. 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. Defense Contractor 2, a scientist at a medical research facility, is a veterinarian and a PhD microbiologist.

[4] Prior to its Chemical Weapons Convention (CWC) inspection in mid-2000, one US commercial facility engaged in defense research made a "no press" request, which the CWC inspectorate honored although it is under no specific treaty obligation to do so. No publicity resulted from this particular inspection. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. Defense Contractor 4 has a PhD in chemical engineering. For that matter, over 275 CWC inspections of industry facilities around the world had been concluded as mid-April 2001 without any press coverage. The general public has little or no idea when the CWC's inspectors are at a nearby chemical plant, the inspection reports are viewed only by corporate and host government officials, and the inspectorate maintains a confidential data system to safeguard all information associated with inspections. Senior official at the Technical Secretariat of the Organization for the Prohibition of Chemical Weapons, telephone interview with author, 19 April 2001.

[5] As one member described it, when inspectors came across something individually suspicious but not conclusive, "another flag goes up, and when there are a certain number of flags at one site, then more inspections would need to be done there and at other locations" to pin down the extent of the program. Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Dr. Robert Zagursky holds a PhD in biological science and has eighteen years of experience in industry.

business sense, both operationally and fiscally.[6] Since the inspectors would almost certainly encounter a constant stream of seeming contradictions on the job, the industry group repeatedly observed that fielding a cross-disciplinary team of inspectors would be integral to their ability to unravel these complexities and determine whether a facility was engaged in legitimate commercial work as opposed to illicit weapons research or production activities.

PRE-INSPECTION ACTIVITIES

Prior to an inspection, the industry group recommended that the inspectorate obtain certain information from the site itself and from open data sources. The group suggested keeping the data requested from the sites to the bare minimum, namely what product(s) a plant is making and how much is being manufactured. The industry brainstormers also wanted sites to provide a staff listing, including job titles.[7] Knowing the stated purpose and size of a facility would allow the inspectorate to deploy a team with the appropriate skill sets.[8] These who, what, and how much data points also create a certain set of expectations on the part of the inspectors about the sort of containment, waste treatment, and other operational set-ups they should anticipate seeing once on site, which would prepare them to discern departures from a normal operation.[9]

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[6] Defense contractors also viewed consistency of equipment scale, types, and set-up with a site's declared purpose as a very important point of the inspectors' evaluation. "I would be very shocked to go into a place and not see certain basic equipment around, and I'd be surprised to see other things." Defense Contractor 7, president and founder of a small sensor development company, 28 August 2000. Defense Contractor 7 has a PhD in microbiology. Also on this point: Defense Contractor 5, director of microbiology and special government projects, 28 August 2000. Defense Contractor 5, working at a defense contracting research company, has a PhD in microbiology.

[7] While it is true that this approach would minimize the paperwork burden on industry facilities, it would also avoid flooding the inspectorate with data that would have to be reviewed and, if misinterpreted or if an honest mistake were made, could send inspectors down the wrong path. Since a facility cannot be judged from afar, the purpose of declaration data should be to help set up a successful inspection. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. Allen I. Laskin, president, Laskin/Lawrence Associates, 23 August 2000. Industry Expert 2 has a PhD in biology and over twenty years of experience in research and industry. Dr. George Pierce has recently become professor of applied and environmental microbiology at Georgia State University where he draws not only on his academic credentials, a PhD in microbiology, but over twenty years of experience in research and industry. Dr. Allen I. Laskin has a PhD in microbiology and has over thirty years of experience in industry.

[8] Different kinds of expertise would be need to inspect a bacterial fermentation plant as opposed to one engaged in viral or cell-culture protein activities. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[9] Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Enthusiastically agreeing that the inspectors should do open-source homework in advance so that they can identify gaps during the opening presentation: Inspection Veteran 3, trial inspection observer and mock inspection participant, 27 April 2000.

Insights 4.1

The defense contracting group was also of the opinion that the inspectors would be well advised to "do a lot of work before they walk in the door," as they put it. The contractors suggested looking for press releases, federal grant and contract announcements, ISO 9000 laboratory qualification data, and records of regulatory violations. With the same phrase that the industry experts often employed, the defense contractors said that the inspectors should make good use of such publicly available sources to "uncover any kind of inconsistencies."

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[1] Continued this individual, "then they can see right off the bat how cooperative a company is going to be." 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. Also speaking out on the utility of careful research before inspecting a production facility, Defense Contractor 3, senior technical adviser; 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 7 has a PhD in microbiology. On the utility of regulatory violations (e.g., water standards, pollution) in getting a sense as to whether a facility had previously violated rules: Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company, 28 August 2000. Defense Contractor 6 has over fifteen years of experience in molecular genetics.

Working from the staff listing, the inspectorate should build a more complete picture of a facility from open source data. For instance, the inspectorate should search the scientific literature for publications, resumes that may be on file with professional associations, and other open source reports. Knowing the background of a plant's personnel would be important to understanding what those individuals could accomplish at the facility. Concerns would be raised, for example, if a concentration of personnel at a site had all published or worked on Q fever.[10] Other open source data that could be tapped to learn more about what has been happening at and around the facility include local newspaper stories and obituaries. That disease has broken out or that authorities have been called in to kill off livestock could indicate untoward activities at the facility.[11] The inspectorate should also attempt to assemble from open sources patent estate and intellectual property portfolios for the companies to be inspected.[12] In Insights 4.1, members of the defense contractors group provide additional suggestions for sources that inspectors should consult before heading into the field.

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[10] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Editor's note: Similar worries should arise if a site's personnel had no publication track record for an extended period of time. Scientists are normally eager share their work with colleagues.

[11] In fact, the inspectorate should monitor public news sources regularly, and reports of this type should precipitate an inspection. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Note that one defense contractor took the suggestion to examine such data a major step further, arguing that the inspectorate should sponsor widespread epidemiological studies around the globe to obtain the appropriate background information to enable detection of unusual outbreaks. Defense Contractor 7, president and founder of a small sensor development company, 28 August 2000.

[12] Such documents can be extremely sensitive because they often contain trade secrets. Also, in some areas of the world where intellectual property laws are weak, these documents may not exist and the plants may be making "knock-off" products. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. In the defense contracting group, some warned that patent estate and scientific literature searches would not be fruitful for their facilities, since the scientists they employ are often not permitted to publish the results of their research on the job, which is considered the property of their clients. Defense Contractor 7, president and founder of a small sensor development company; Defense Contractor 2, principal research scientist, 28 August 2000.

In addition to newspaper and other database searches, advance knowledge of the regulatory framework in which a plant is operating would be important for the inspectors to do their jobs well. Certainly, regulations differ from country to country, but even if the rules are weak, virtually every country has environmental, food and drug, commerce, and worker safety guidelines. These regulations would help the inspectors understand why processes are set up or done in a certain way.[13] As one brainstormer noted, the inspectorate would be short-sighted not to take advantage of the fact that "there's an amazing amount of information that's easily accessible."[14] Although the group emphasized the value of this data to the inspectors, they argued that the facilities should not be obligated to provide information from such outside sources.

Finally, before the inspectors leave headquarters, the industry group advocated looking at satellite images of the facility taken well in advance of any announced inspection. The operators of a facility can alter maps subtly to create certain impressions, but satellite photographs do not lie. Therefore, the inspectors will be able to get a bearing on the facility's layout and identify areas of interest. Also, it would be useful if the facility were monitored for signs of unusual activity after the inspection was announced .[15]

ON-SITE MONITORING ACTIVITIES: SITE TOUR

The industry brainstormers put a considerable amount of credence in the utility of simply observing what was going on at a facility.[16] Their instincts about the usefulness of a site tour were right on target, according to what an inspection veteran says in Insights 4.2. In a plant that was supposed to be making particular products, it would be noticeable if the facility were not configured and equipped accordingly. Also, the industry group reasoned, it would be conspicuous if the plant workers were ill at ease with or inept at performing tasks they were supposed to do daily.[17] So important was a plant tour in

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[13] In agreement on this point: Inspection Veteran 5, participant in two US trial inspections and a mock inspection; Inspection Veteran 3, trial inspection observer and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Inspection Veteran 5, a PhD scientist, 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 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. Even countries that are categorized as "developing" have waste water discharge permits, for instance. Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[14] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[15] Points made by Dr. Steven Projan, widely supported by the group.

[16] Jokingly, this was tagged the Yogi Berra method, as in "you can observe a lot just by watching." Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[17] "If they're doing what they normally do, they should be able to do it, but if they have to pretend they are doing something else, it's going to be hard." Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

Insights 4.2

One veteran of inspections at former Soviet biowarfare facilities gave support to the argument that just looking around could reveal a great deal. "There was plenty of physical evidence that we saw that showed it was obviously a biological weapons facility. They had removed lots of things, even explosive chambers. Their not admitting to it was what was so frustrating."[1] Seeing proof, in other words, did not necessarily mean that the other aspects of the inspection were a waltz.

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[1] 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.

their estimation that the industry group argued that the terms of on-site inspections should stipulate that the inspectors be taken on a site tour as soon as they walk through the door, preferably with the plant in operation.[18] Otherwise, the group worried that facility personnel might decrease the potency of this inspection tool by stalling for time with coffee and doughnuts, lengthy introductions, or special training.[19]

Of course, the industry group stated that the inspection ground rules should also specify that the inspectors wear whatever clothing the facility deems appropriate (e.g., gown, boots) and follow all of the facility's procedures to protect product integrity.[20] Inspectors would be accompanied at all times and would be prohibited from touching or picking up any items during the tour.[21] The inspection guidelines should also allow facility managers to see the equipment that the inspectors are carrying (e.g., pens, recorders, computers) and offer them comparable substitutes for use while in the controlled areas of the plant. This option would alleviate industry concerns about surreptitious listening, sampling, or photographic devices.[22] A final precondition for the tour and subsequent access to documents and

[18] Underscoring the importance of touring a facility, seeing cleanliness in a site claiming to make vaccines, as well as a scale and equipment that one would expect in the type of site declared. Defense Contractor 7, president and founder of a small sensor development company; Defense Contractor 3, senior technical adviser, 28 August 2000.

[19] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Assenting to the need to be wary of an unduly lengthy opening briefing, one inspection veteran said of a US full-scale BWC trial: "The introductory briefing seemed to delay the brass tacks of negotiating what we were going to see. We were pandered to in terms of safety and environmental issues. We wanted to know the boundaries of the inspection and when we were going to get there. I learned nothing, even though I was unfamiliar with the site." Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000. Inspection Veteran 9, 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. In the opposing corner, pointing out the utility from the host's perspective of consuming valuable inspection time in the conference room with briefings and coffee breaks, Inspection Veteran 3, trial inspection observer and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector, 27 April 2000. Finally, it must be noted that in the United States, Occupational Safety and Health Administration and state regulations, as well as legal considerations dictate that operators present appropriate "safety" information to visitors before they enter a plant. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[20] 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.

[21] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[22] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

personnel was that the inspectors sign a confidentiality agreement, just as all site visitors do. This requirement should exist regardless of any confidentiality oath that the inspectors may have taken upon being hired, and it would be needed to elicit anything other than the most begrudging cooperation on the part of industry sites.[23] The industry group also requested that the US government take steps to help protect their intellectual property rights by screening out any inspectors from countries that have not signed the Patent Cooperation Treaty.

Industry experts stated that the effectiveness of a site tour would be significantly affected if the inspectors were not able to conduct it with certain site maps and diagrams in hand. In that regard, they underlined the importance of requiring the plant to give the inspectors the floor layout, the architectural diagram, the as-built engineering diagram, and the piping and instrumentation diagram (PID). Having such diagrams would allow the inspectors to get a feeling for whether the facility made sense for its stated purpose, and whether it flowed meaningfully from place to place.[24] These blueprints would also let the inspectors know whether their hosts were steering them away from certain areas during the tour or taking them to the places they were supposed to see. Additionally, these diagrams would allow inspectors to determine whether equipment was missing and pipes were connected in the right sequence, welded appropriately, and headed where they should.[25] The as-built diagram would facilitate an evaluation of whether the buildings and equipment were constructed as stated or with materials that exceeded the requirements for the kind of production supposedly taking place.[26] Any modifications from the as-built

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[23] "Cooperation is simply not going to happen unless there is a real strong sense on our side that there's going to be strict confidentiality." Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. Even with such an agreement, industry representatives were skeptical that their companies would have any legal or fiscal recourse should international inspectors break their confidentiality pledges. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000. The inspectors would also be asked to sign a general indemnification waiver that holds the host facility harmless for whatever happens while they are on site. The experts from the defense contractor group also sought confidentiality assurances other than a generic pledge that might be made to a BWC inspectorate. Loss of confidential business data "would be a disaster. All we have is our intellectual property." Defense Contractor 7, president and founder of a small sensor development company, 28 August 2000.

[24] Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. The additional utility of these diagrams lies in the fact that making dummy sets of PIDs would be difficult. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[25] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000. "In Russia, there was no aerosolization equipment anywhere. It was a glaring omission. Pipes were still coming out of the wall, but there was no equipment." Inspection Veteran 8, trilateral and trial inspector, 27 April 2000.

[26] Like any industry, pharmaceutical manufacturers watch production costs. In other words, it would not make sense financially for a plant to employ glass-lined reactors for a cell production process. Top-of-the-line construction materials could be explained if a facility were used for multiple purposes or another type of product had previously been made there. Such explanations could be documented. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

diagram (e.g., walls around equipment, interior air locks, unusual devices), the group emphasized, should require an explanation.[27]

As they make their way around the facility, the PID and as-built diagrams would enable the inspectors to locate and account for key pieces of equipment (e.g., milling, autoclaves, spray and freeze driers, aerosolizers) ensuring that items were where they were supposed to be and that important pieces were not missing.[28] Some of these items would be out of place for the production of certain products, so the inspectors should question their presence, especially if there was no recovery process upstream.[29] Some industry experts thought that the inspectors should pin down the location of every autoclave in the facility, especially in the purification area.[30] Later, when they are reviewing documents, the inspectors should cross-match what they have seen with the equipment list as a double-check against hidden equipment.[31] With regard to the equipment and piping setup, the inspectors should be attentive to the mobility factor, whether mobile equipment is suitable for the plant's stated purposes and if pipe connections are hard or breakable.[32]

When inspectors come across freezers around the site, the industry brainstormers advised them not to over-react if they found a few unusual microorganisms among the freezer contents. Some strains might be there for research and development as opposed to production purposes, others might be forgotten from previous projects, and still others might have been left there by a staffer who forgot to tell colleagues.[33] Having said that, discovering a super virulent strain at a facility claiming to produce

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[27] Dr. Robert Hamilton and Industry Expert 2 provided the examples, and the group seconded the point.

[28] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[29] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[30] Concern should arise, they noted, if autoclaves in that area were being employed to purify recombinant protein. Industry Expert 4; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Industry Expert 4 is president and chief executive officer of a small US biotechnology company and holds a PhD in microbiology.

[31] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[32] Common wisdom holds that cheaters would stash possibly incriminating pieces of equipment off site during an inspection and re-insert them later. However, a mobile setup would not be unusual for a commercial facility making multiple products. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. The above-mentioned site diagrams and other documentation should help back up an explanation of legitimate mobile commercial plant. In a multipurpose facility, "everything is an open setup—the same piece of equipment might move around to ten different locations and do ten different things. We don't do anything dedicated anymore." Inspection Veteran 1, facility manager and US trial inspection host, 27 April 2000. Inspection Veteran 1 was a principal host of a US trial inspection held in late March 1996 at three facilities located in Albuquerque, New Mexico.

[33] Like their counterparts in other fields who have masses of outdated files, it would appear that pharmaceutical workers do not clean their freezers regularly. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Note that it may be difficult to cross-check explanations for all

vaccine should raise eyebrows.[34] The level of containment present may provide clues to a facility's intent for questionable strains.[35] Also, plant managers should be able to describe why they had such strains and provide supporting documentation, such as the grant information and batch records that show that the number and size of lots is consistent with that scope of work.[36]

After some discussion, the group concluded that inspectors should not be disturbed by large scale capacity, even if such capacity were in a high-level containment setting. Capacity per se was not the issue, but rather whether that capacity made sense for what the facility claimed to be doing.[37] Other matters that deserved to catch the attention of inspectors included the partitioning of reactors, air-handling systems, water cooling systems, and the like when the product(s) being made did not call for such measures.[38] Another sure-fire attention-grabber would be excessive containment.[39] Also in the look closely category would be a purification capability appropriate for the declared product(s). Missing tests

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questionable strains with outside organizations like the American Type Culture Collection or the National Collection of Type Cultures because personnel may have gotten a strain informally from a colleague. Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[34] In that setting, one would expect to find an attenuated strain, but one participant noted that something like an E-coli O1H5787 strain should be questioned. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[35] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[36] An example of an explanation might be that pandemic strains of influenza were present due to vaccine work for the World Health Organization. Documentation would be redacted to protect confidential business information. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Agreeing that records can be redacted and pointing out that many facilities are used to having their records reviewed, Inspection Veteran 5, participant in two US trial inspections and a mock inspection, 27 April 2000. According to Inspection Veteran 3, US regulatory inspectors retrieve "every piece of documentation they can possibly get at." On the need to redact carefully, lest a biodefense site reveal unthinkingly crucial national security information: Inspection Veteran 8, trilateral and trial inspector; Inspection Veteran 2, trial inspection observer 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.

[37] One participant called this "the Goldilocks phenomenon. It's got to be just right." Industry Expert 4, president and chief executive officer, small US biotechnology company, 23 August 2000. Industry Expert 2 made a similar statement and the group concurred.

[38] As one brainstormer put it, "If they start to partition too much stuff, they had better have a good story for that." Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Operators for a single-use manufacturing plant, for instance, would not ordinarily partition multiple reactors. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[39] Constructing high-level containment capacity is an expensive endeavor, so businesses would not do so unless product manufacturing requirements mandated it. Members of the industry group also observed that since some governments (e.g., Iraq) have conducted biowarfare research and production activities without the benefit of stringent containment, lack of high-level containment or a level of containment consistent with a facility's stated purposes would not automatically indicate an above-board operation. If the inspectors suspect that higher containment work is being done in a site that may appear to have that capability, one defense contractor recommended going to the roof to check for high efficiency particulate air (HEPA) filtration ducts. 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.

and purification steps would be peculiar, to say the least, for an industry facility supposedly concerned about product integrity and quality.[40] In the purification area, inspectors would want to check whether the containment setting was markedly out of step for the product(s)—unusually high containment for an animal vaccine or oddly low containment for a pharmaceutical for human consumption.[41]

Things to watch for in the warehouse and other storage areas would include unlabelled supplies, unusual supplies, or large inventories of certain supplies (e.g., antibiotics). Stocks of high efficiency particulate air (HEPA) filters, gowns, and disinfectant should be in line with the facility's declared activities and operational status.[42] With regard to media, the inspectors should be attuned not just to surplus quantities, but to the presence of media that was out of place, such as specialty media (e.g., oxide beef broth) not called for by the stated product(s).[43] The group explained that whereas the inspectors would probably see smaller inventories because of a just-in-time supply philosophy in Western, European, and Asian countries, in other parts of the globe they could see huge supply backlogs.

One of the areas not to be missed during the tour would be the waste handling system, the design, construction, and operation of which should fit with what was needed to inactivate and treat the organism(s) and other wastes supposedly generated at the facility. Inspectors should be puzzled if a plant that declared it was making nontoxic waste with no biologic activity had procedures, equipment, and chemicals in place to treat hazardous wastes.[44] Inspectors should also consider what wastes were being funneled into the treatment system. For instance, it would be odd if liquid waste from all phases of the production process were sent there, particularly from purification and formulation areas.[45]

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[40] Purification processes are costly and not needed for weapons manufacture, so some industry experts felt that cheaters could be tripped up in this area. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. Or, as another brainstormer noted, a smart proliferator could spend the extra money to purify a biological agent. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[41] Note that to safeguard against contamination, the downstream processing of some products is accomplished under high containment. The regulatory requirements can help inspectors determine whether the containment is excessive. In some countries, however, containment standards may not be uniformly maintained. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[42] Inventories would be larger for a three-shift operation than for a day-only operation. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[43] Specialty media is expensive, so a cost-conscious manufacturer would not use it unless necessary. Eggs were singled out as possibly of concern if they were being employed in a complete containment setting as opposed to clean, class 100 conditions. Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[44] To illustrate, a large inventory of an expensive chemical like sodium hydroxide would be superfluous under these circumstances and could betray an effort to mask trace waste. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[45] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Zagursky, distinguished

If present, another area that should receive close scrutiny would be an animal facility. The higher the species of animal and the more animals present, the harder the inspectors should look, especially if the animals are being kept isolated in individual, negative air flow chambers. Justification for a primate facility, the industry group agreed, would have to be crystal clear. "There's no reason why they should have a primate facility there unless they can prove that they're using it for some downstream testing of the product. And only then, the number of animals there would have to be consistent with the protocol."[46] Industry group members agreed that deciphering the real purpose of an animal facility might be difficult for inspectors because they would be highly unlikely to allow outsiders into that area, given the risk of contamination.[47] If this sector of the plant had video surveillance, inspectors may be able to view certain parts of it remotely. Or, one or two inspectors as opposed to the entire contingent might be allowed in some rooms. If these options were not acceptable, the inspectors could answer some questions through documentation (e.g., animal pathology records) and supplemental interviews with the personnel from the organizations that would certify the facility for animal work, the American Association for the Advancement of Laboratory Animal Care. Should such activities prove inconclusive, a complete tour of this area might be scheduled for a time when there is a break in the testing process.[48]

The industry group identified a few other types of activities that, if observed, would alert them to possible foul play. For instance, they would be wary if while on the premises they saw:

- an inordinately high number of paper shredders or controlled copy machines;[49]
- evidence of recent demolition activity;[50]

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research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

[46] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Also, Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Note that commercial plants would try to keep the number of primates involved to a minimum because they are very expensive. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000. Large animal facilities are more frequently located near production facilities overseas than they are in the United States. Also, the quality of animals may vary significantly from country to country.

[47] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[48] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Industry group members were willing to release some animal modeling data, of course redacted to protect trade secrets, to answer inspectors general questions about their animal facilities. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Industry Expert 4, president and chief executive officer, small US biotechnology company, 23 August 2000.

[49] While it is normal for a commercial facility to have a few shredders and controlled copiers around to safeguard its proprietary data, a swarm of such machines would be out of place and perhaps indicative of very strong precautions in place to prevent people from sneaking data out of a covert military site. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[50] Recently destroyed buildings or bulldozed ground could indicate an effort to bury contaminated evidence. Plant

- on-site housing and a preponderance of unmarried workers;[51]
- strange or excessive food and waste handling procedures in the cafeteria; [52]or,
- a medical facility that was unusually large, had isolation capacity, was stocked with certain medications (e.g., a specific immunoglobulin), or had a morgue attached to it.[53]

Such capabilities or activities would appear even more suspect if security measures were being taken that seemed excessive for a commercial enterprise.[54] Heightened security is one of the hallmarks of military facilities.

Facility layout, capabilities, and equipment should not be the only matters to come under the watchful eye of inspectors during the tour. According to the industry group, it would be very telling to view the plant's staff performing their daily activities. Were they to see personnel use stringent precautions while working with a nonpathogenic, bacterial agent, it could indicate that they were more accustomed to tissue culture or other high-level containment work. Another telltale sign of personnel quickly pulled from high-level containment to lower precaution work would be dermatitis on the hands, a skin condition that can be caused by wearing protective gloves. Observing the staff go through their degowning procedures could also reveal some peculiarities for the type of product supposedly being

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managers should be able to explain any demolition activity and back that up with documentation that it was planned. Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[51] Note that in some countries, on-site housing could be a benefit of employment. However, pharmaceutical and biotechnology workers are usually very well paid and could afford off-site housing. Therefore, such arrangements could be precautions against the spread of infectious disease to spouses or children or others outside of the compound. Industry Expert 2, senior vice president, US biopharmaceutical company; Industry Expert 4, president and chief executive officer, small US biotechnology company, 23 August 2000.

[52] Note that an examination of operational documents might also uncover such procedures if the cafeteria were not in operation. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[53] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[54] Aside from an unusually high number or guards, extra security around product or ingredient materials should be noted. Such measures would exceed normal security at a site manufacturing ethical pharmaceuticals or at a containment or animal facility. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Prior to the inspection, satellite imagery could also reveal unusual external security measures, such as double fences and clear zones. Such imagery would also show whether a military installation was located nearby, which might also raise suspicion. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. Security for many Western plants is handled by third party contractors, so facility managers may have to forward some inspectors' inquiries about these matters to their contractors.

made.[55] In all sectors of the plant, personnel would be executing their tasks and standard operating procedures (SOPs) smoothly if they are doing what they are accustomed to instead of putting on some type of masquerade. Should the inspectors note awkwardness, they might ask later to see staff perform certain SOPs. As one industry brainstormer stated, "it can become very apparent very fast that these people are not trained, that they are not used to doing this operation."[56] For this reason, the industry group widely endorsed the idea of just observing the staff go through their paces.

As for their reaction were they on the receiving end of this type of inspection, members of the industry group stated that they would willingly show inspectors practically all of their facilities. However, they could think of a few justifiable reasons not to take inspectors into each and every building or room.[57] For instance, a room may contain proprietary processes or a dilapidated building may be closed for safety reasons, prior to demolition. In some areas, they would opt to shroud sensitive equipment and the attached piping but leave the rest of the room open to view.[58] Defense contractors would take similar steps, as Insights 4.3 describes. For areas where they would not be able to provide visual access, the industry group

Insights 4.3

Although edgy about having international inspectors in their midst, defense contractors said they would shroud extensively to shield equipment under development and that for proprietary reasons would deny any access at all to certain areas of their sites.[1] One of the contractors had hosted a Chemical Weapons Convention inspection and stated that the inspectors accepted it when his company declined to let them to look in certain biosafety hoods because proprietary items were inside. He doubted, however, that denial of access to an entire building would fly with inspectors.[2]

NOTES

[1] Defense Contractor 1, staff scientist in biotechnology; Defense Contractor 7, president and founder of a small sensor development company; Defense Contractor 2, principal research scientist, 28 August 2000. Defense Contractor 1, a scientist at a large research contractor, has an MA in cellular and molecular biology. Defense Contractor 7 has a PhD in microbiology. Defense Contractor 2, a scientist at a medical research facility, is a veterinarian and a PhD microbiologist. For one defense contractor, however, the thought of taking inspectors anywhere other than a conference room was very unsettling. Defense Contractor 6, senior vice president and co-founder of a biotechnology research contracting company, 28 August 2000. Defense Contractor 6 has over fifteen years of experience in molecular genetics.

[2] Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. Defense Contractor 4 has a PhD in chemical engineering.

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[55] For example, the disinfectants used might be incongruous for the declared setting. A large number of workers sporting bleached hair might also indicate something was amiss. Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

[56] Continued this individual, running through SOPs is "just like any other physical thing. The more someone does it, the better they get at it," so lack of skills would be evident. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. A defense contractor was also of the opinion that a laboratory technician should be comfortable answering a question about why, for example, a huge jar of cystine is sitting over there. "They're the ones who should know, and if they prevaricate," then it should be noted. Defense Contractor 1, staff scientist in biotechnology, 28 August 2000.

[57] In the same vein, on showing the inspectors what they came to see, but not everything: Inspection Veteran 5, participant in two US trial inspections and a mock inspection, 27 April 2000.

[58] Industry Expert 2 made this statement, and the group nodded in agreement. During a Chemical Weapons Convention inspection of an industry site that performs defense research under contract, the laboratory's managers shrouded proprietary and sensitive equipment, a practice that the inspectors did not challenge. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. The Chemical Weapons Convention specifically permits inspected facilities to

members were confident that they could explain the reasons and give sufficient documentation to allay suspicions. Following the tour or any other entrances into controlled areas of the plant, the industry group sought the right for the facility managers to inspect the inspectors to ensure they had not unintentionally or purposefully acquired proprietary data, including testing residues on shoes and clothing.[59]

While the industry group advocated visual observation as an effective inspection tool, they also pointed out its limitations. Grates could lead to an air drop instead of HEPA filters and pipes through the ceiling could be channeled to a hidden filter. While inspectors can take certain steps to visually ascertain what is going on—going to the roof and counting exhaust stacks in this instance—that would only take them so far.[60] Therefore, the inspectors would have to bolster their visual observations with document reviews and interviews with facility personnel.

ON-SITE MONITORING ACTIVITY: REVIEW OF DOCUMENTS AND RECORDS

One of the fundamental activities that inspectors should undertake to investigate what they saw during the site tour is to review documents and records. The reason that the industry group had strong faith in the utility of a thorough document review was summed up by one participant in the following way: "I personally have believed all along that one of the best things the inspectors can do is detailed auditing of paperwork because if someone's dirty and trying to hide, they can't. No one's that good."[61] When it comes to paperwork, the military and legitimate pharmaceutical companies both document their activities voluminously. Inspectors can take advantage of that fact. Everyone agreed that somewhere along the line, the inconsistencies in paperwork would belie a cheater. Conversely, a paperwork trail that cross-checks well would buttress a legitimate plant's case for a clean bill of health.[62] In box 4.1, the inspection veterans draw upon their experience reviewing records to show why the industry group's faith in this monitoring tool was well placed.

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shroud.

[59] Dr. Robert Hamilton articulated this point to a chorus of agreement from the group.

[60] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[61] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Agreeing that it is "harder to hide inconsistencies" in documents and records: Defense Contractor 1, staff scientist in biotechnology, 28 August 2000.

[62] Concurring that a complete absence of records flags a problem, a veteran of visits to former Soviet biowarfare institutes said that there were virtually "no records" there, nothing. Inspection Veteran 8, trilateral and trial inspector; Inspection Veteran 2, trilateral and mock inspection participant, 27 April 2000.

Box 4.1: Veteran Voices on the Examination of Site Records

As one inspection veteran put it, "Records are a very important part of the archaeological dig. They provide an audit trail for people, material, and equipment. Sometimes there will clearly be a mass balance problem."[1] In addition, records can substantiate explanations, as was the case during a 1991 Russian inspection of a US defense facility under the trilateral agreement.[2] At the same time, cautioned another inspection veteran, "records can also be very disorienting" because different facilities and inspectors, depending on their discipline, ascribe different meanings to the terminology in the records.[3] Moreover, a large, multipurpose facility will order all types of supplies for different purposes, so inspectors could come to erroneous conclusions about whether those supplies are being channeled to a covert program or used in legitimate, separate projects.[4] Even though it may take a while to sort them out, one veteran advocated going after the records—especially the shipping and receiving documents—up front during an inspection, instead of at a later point as the United Nations did during the series of inspections at Iraqi biological facilities.[5] Finally, given the increasing tendency of records to be placed in electronic databases, the veterans group urged that the pluses and minuses of that reality be taken into account.[6]

NOTES

[1] 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.

[2] Sometimes cultural and regulatory differences in the way countries conduct research, development, and testing can be the source of suspicions. The Russians, for example, had a different approach to laboratory animal medicine. "The Russians were convinced that the large number of veterinarians [at this site] indicated a hidden command and control for the institution and that everything else was a front. We used records to prove that regulations require US facilities to have lots of vets." Also on this inspection, host officials were able to use construction and regulatory records to explain why a room at the facility was constructed in a certain manner and salvage and demolition records to document the destruction of a capability shown in an old facility brochure. Inspection Veteran 5, participant in two US trial inspections and a mock inspection, 27 April 2000. Inspection Veteran 5, a PhD scientist, 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.

[3] 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.

[4] 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.

[5] Inspection Veteran 7, United Nations Special Commission on Iraq 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. Shipping and receiving documents enabled the inspectors to piece together the fact that Iraq had imported media far beyond the stated needs of the facilities inspected. United Nations, *Report of the Executive Chairman on the Activities of the Special Commission Established by the Secretary-General Pursuant to Paragraph 9(b)(i) of Resolution 687 (1991*), S/1998/920 (New York: United Nations, 6 October 1998); United Nations, *Report of the Executive Chairman on the Activities of the Special Commission Established by the Secretary-General Pursuant to Paragraph 9(b)(i) of Resolution 687 (1991*), S/1998/920 (New York: United Nations, 16 April 1998); Barton Gellman, "A Futile Game of Hide and Seek; Ritter, UNSCOM Foiled by Saddam's Concealment Strategy," *Washington Post*, 11 October 1998; William Broad and Judith Miller, "The Hunt for the Germs of War—Iraq's Deadliest Arms: Puzzles Breed Fears," *New York Times*, 26 February 1998.

[6] For example, a word search could possibly enable inspectors to locate desired data within seconds. Site managers, however, will have to make careful decisions about how and if to provide inspectors access to such databases, which are likely to contain sensitive information. Host officials could perform the search themselves, providing thereafter appropriately redacted records. Inspection Veteran 3, Inspection Veteran 6, and Inspection Veteran 9 raised these points during discussion. 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. Inspection Veteran 6, a PhD scientist, was on the host team during the mock inspection at the Dugway Proving Ground, Utah, and on the inspection team during the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

Accustomed as they were to having inspectors pore over their records, the industry group did not have much of a problem with handling this aspect of a possible BWC inspection, provided facility-specific confidentiality agreements were in effect. The industry group members said they would adopt a strategy of trying to predict the main questions that the inspectors would ask and have the supporting documentation pulled and ready for review. If the inspectors chose other lines of inquiry, they would do their best to satisfy the requests and in most instances their regulatory affairs staffs could do so quickly. However, some documents may take time to locate and prepare for review. To protect proprietary data, they would redact some documents, heavily if need be.[63] Also, the industry group would show the inspectors just the information that answered their specific questions, putting the onus on the inspectors to ask for additional documentation. Finally, documents given to inspectors should be read only. Unless facility managers gave explicit permission for a specific document to be copied, no plant records should leave the site.[64]

Retrieving documents would be one of the more expensive aspects of hosting an inspection. The industry group members stated that when a trio of Food and Drug Administration inspectors show up, escorting them, finding requested documents, and otherwise answering their inquiries can swallow the time of eight to ten staffers. They estimated that the price tag for preparing for a BWC inspection would be roughly $500,000. They put the manpower costs to host a five-day inspection at $125,000. Therefore, hosting a larger inspection team would be difficult for smaller firms to handle. The industry group would want the US government to cover companies' costs to host BWC inspections.

A genuine manufacturing facility will have a paperwork trail that stretches from beginning to end, with several types of overlapping records. The industry group devised a lengthy roster of documents that inspectors should consult, as shown in table 4.1. All inspectors, it was observed, work from some type of a checklist. The savvy ones keep facility managers guessing to a certain extent, however, by mixing it up, varying the emphasis of their inquiry each time they come through the door.[65]

At the outset, inspectors can survey the ingredients coming into a facility via documents such as purchasing requisitions, receiving documents, disposition and warehousing records, and the bill of materials, which lists every ingredient used to manufacture product(s) at the facility. Comparing these documents, the inspectors can tell what kinds and amounts of materials the facility is regularly receiving

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[63] At defense facilities, one of the true difficulties about parsing the records is the classification level. Inspection Veteran 8, trilateral and trial inspector, 27 April 2000.

[64] Dr. Steven Projan, Dr. Robert Zagursky, and Industry Expert 2 voiced this strategy and the group as a whole concurred.

[65] The group chuckled at the common practice of telephoning each other to find out what inspectors had been focusing on in the last go-around. With so much to examine, the inspectors could keep them on their toes just by shifting their focus from one area to another.

and whether items are being ordered in types and quantities other than what is needed to make the stated product(s).[66] The inspectors might want to look especially closely at the numbers of personal protective equipment and other biosafety items that the site is consuming.[67] More detailed paperwork on the media, namely the material safety data sheets and the paperwork that certifies the media being used, should also be available in plants operating in many countries.[68]

Table 4.1: Documents for Inspectors to Review

bills of materials	billing documents
purchasing requisitions	sales/shipping records
receiving documents	site map
disposition information	piping and instrumentation diagrams
patents	as-built diagrams
strain list	airflow diagrams
material safety data sheets or equivalent	visitor logs
media qualification paperwork	equipment list
logs (equipment, activity, cleaning)	equipment calibration records
quality control paperwork (material lists/SOPs)	staff list with job titles/organizational chart
batch records	product release tests
timesheets	gate records

Another set of records that the industry group believed would be very important for the inspectors to look into would be the logbooks that record who is coming and going from the site. A legitimate business would receive a certain number of outsiders. Visitor logs, however, might reveal oddly low levels of traffic at the site, callers from the military or who had expertise that might be of concern, or more routine traffic from maintenance contractors, business partners, and regulatory inspectors. Such data points could be quite helpful in facilitating inspectors' efforts to determine what is happening at a site.[69] For instance, a site engaged in covert activity would probably do its maintenance work in-house, but

[66] Indeed, these records can reveal a lot, such as "what kind of reagents they're ordering, how much. So if they are a small facility that is ordering thousands of trypticase soy agar plates and huge quantities of growth media, then what is that all about?" Defense Contractor 2 to widespread agreement from the other contractors.

[67] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Note that some participants had no problem revealing the ingredients that they use for their product, of course leaving formulas and specific amounts off limits. Since their processes were not patent protected, others would have to redact the bill of materials and receiving documents to hide the identity of the companies that ship them goods as well as the type of media used. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[68] This point was brought up by Dr. Steven Projan and agreed by the whole group.

[69] Dr. George Pierce, Dr. Robert Hamilton, and Industry Expert 2 articulated these points, which the whole group then acknowledged as important. A couple of the participants observed that a few log entries might need to be redacted to mask the identities of possible joint venture partners. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Also, it was noted that some contractors did not make routine visits because they worked on an as-needed basis. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

many commercial plants employ outside contractors for all manner of maintenance and other tasks (e.g., site security).[70]

The pace of the facility's manufacturing activities can be traced through activity, equipment, and cleaning logs. Batch records, for instance, will show how much product was processed within certain time periods, which can be checked against ingredient inventory levels and the list of products that a facility manufactures at every step.[71] Since normal plants do not operate perfectly, inspectors should see records of deviations as well as investigations at the plant.[72] In a similar vein, inspectors can learn about the tempo of plant operations by looking through the engineering control records for biosafety cabinets, high efficiency particulate air filters, autoclaves, and decontamination operations as well as the hazards operations evaluation documents.[73] Moreover, equipment in certain areas of the facility will generate pressure and temperature data, which inspectors should review to see that trends correspond to the manufacture of the stated product(s).[74] A site's operations can also be explored through equipment validation and calibration records. For instance, equipment is routinely calibrated, but inspectors should be sensitive to the possibility that plant managers trying to rig an inspection would recalibrate equipment to give false readings just before the arrival of the inspection team.[75]

Another area of documentation rich with helpful data would be the records related to personnel management. A review of the organizational charts would show whether staff ratios in different departments were reasonable for a facility's stated activity. To see one quality control staffer for every thirty individuals in manufacturing would be a peculiar ratio in the West.[76] Training records should

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[70] Although reliance on contractors is quite prevalent in the West, this may not necessarily be the case in the developing world. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[71] Also, note that overseas, some companies generate extensive analyses of their processes to compare them with manufacturers in other countries using different raw materials. Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[72] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[73] Note that documentation related to HEPA filter changes would help the inspectors understand some things they may not be able to observe. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Allen I. Laskin, president, Laskin/Lawrence Associates; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[74] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[75] If records showed recent calibration, inspectors should examine the nature of the changes carefully. The group as a whole emphasized the importance of calibration records. Standards requiring equipment validation would differ from country to country, but normally some type of document would indicate whether equipment had passed negative pressure tests, which would be strange if there was no apparent need for negative pressure operation. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[76] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Note that organizational charts can be highly confidential because job titles and organizational set ups and titles can tell outsiders a lot about what a

conform with the facility's stated activities, and personnel turnover rates should be within the expected range for the industry in that country.[77]

A manufacturing plant will have a raft of SOPs that inspectors can peruse for consistency or lack thereof with a plant's stated activities. A facility purportedly working with innocuous microorganisms would need to explain why it was employing SOPs that would require seed cultures to be handled under high-containment conditions.[78] Looking through the SOPs for a manufacturing process that ordinarily requires a "kill step" after fermentation (e.g., bacterial vaccines), inspectors should wonder if those SOPs do not show one. In the biosafety arena, SOPs for emergency response should match the kind of microorganisms the plant has declared.

The industry group underscored that SOPs for quality control testing should be examined to see whether the tests being run make sense for the product(s) the plant is supposed to manufacture. Products using bacteria, for example, should be tested for endotoxins (i.e., lipopolysaccharide) and pyrogens. If something appears out of order to the inspectors, these SOPs should be cross-matched against the list of quality control supplies and raw test data, which in and of itself constitutes a huge paper trail. The lot release test records would also contain lot numbers that can be put side by side with batch records as well as product specifications. Faking this cross-cutting documentation would be no easy task.[79] Should the inspectors have reason to believe commercial goods are not normally coming off the line, they can study the product billing, sales, and shipping records.[80]

Again, the beauty of having a wealth of documentation is that inspectors worried that something may be awry can compare various items against each other. Should the inspectors sense that a plant is really working around the clock instead of fielding just a day shift, they can pull gate records and timesheets.[81] These items can be checked against utility expenditure documents (e.g., energy, water),

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facility is doing. Therefore, industry group members indicated they would alter these documents would to only contain generalized titles and redact them in some areas. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Dr. George Pierce, former manager, technology development and engineering, Cytech Industries; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[77] A controlled workforce would have abnormally low or no turnover. The first point was made by Industry Expert 2, the second by Dr. Steven Projan.

[78] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[79] Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

[80] Sales and shipping records are highly sensitive, so the industry group suggested the inspectors not ask for them unless necessary. If they were requested, plant managers would respond best to a specific inquiry that would enable them to provide a slice of data. Industry Expert 2, senior vice president, US biopharmaceutical company; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[81] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

airflow diagrams, and heating, ventilation and air conditioning maintenance records, among other things. Utility bills and filter changes would need to be in line with the number of shifts the plant says it is running.[82] Inspectors could cross-check visitor logs with service contracts, and if need be, subsequently interview contract personnel to confirm the nature of their activity on site. Inspectors that believe they have been fed a cover story can request project proposals and reports, service contracts, Institutional Animal Care and Use Committee documents, and records from internal review committees that govern project approval, biosafety, and waste management.

ON-SITE MONITORING ACTIVITIES: INTERVIEWS

Following a site tour and a thorough review of documents, inspectors should have a good idea of what questions, if any, they would like to pose to the facility's personnel. Ideally, key people in each division would be made available for interviews, and the industry group noted that it would be a bad omen if all of the key people at a site were conveniently out of town on vacation or "business" when the inspectors arrived.[83] Aside from senior personnel, the industry group strongly encouraged the inspectors to speak with the rank and file. The thrust of those interviews would be to find out whether the worker bees really know how to operate the facility, to have them run through their own SOPs if inspectors believe something is amiss. Personnel at a *bona fide* facility would have a solid understanding of their own processes and SOPs. If not, that knowledge gap should be patently clear to inspectors experienced in commercial operations.[84] Or, as another industry group member said, "It always helps an inspector if basically the person convicts themselves" by contradicting during an interview what is in a plant's SOPs, historical production records, or open source data about the facility.[85] Nervousness could account for a fumble or two during interviews, but if individuals in the waste management, post-production, biosafety, and other divisions cannot confidently and comfortably relay information about the tasks they are supposed to perform regularly, then the inspectors would have sound grounds to believe something suspect was happening. For this reason, the industry group as a whole stated that staff interviews would allow the inspectors to gain significant insight into a facility's true status.

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[82] "If they're pumping a lot of air and have a lot of water flow, that will tell you something." Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. Note that inspectors would also need to calculate what effect local climatic conditions would have on energy usage. Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000. Seconding the idea that looking at power consumption would be a sound investigative course, but warning that the inspectors would need to be well-versed in the energy use requirements of industry versus weapons production sites: Defense Contractor 3, senior technical adviser, 28 August 2000.

[83] Dr. George Pierce made this comment, which the group followed with a chorus of groans and assents.

[84] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[85] Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

When it came to the prospect of having BWC inspectors interview their personnel, aside from the time sink involved, members of the industry group were quite nonplussed. Some companies have formal training to teach staffers how to respond to inspectors' questions. If that were not the case, a facility's managers would probably talk to staff beforehand to acquaint them with the context of the inspection and let them know the types of questions that they should and should not answer. In the latter category, personnel would be instructed to follow standard house rules not to reveal propriety data.[86] The major guideline that the industry group wanted in place for interviews was that a senior plant manager be present during all interviews to guard against improper fishing expeditions on the part of the inspectors. The inspectors would be welcome to ask about SOPs and other operational issues pertinent to plant operations, but pressing for confidential business data would be out of bounds and the manager would have the right to intervene should inspectors do so.[87]

If the inspectors are getting mixed signals from interviews, documents, and visual observation, they could opt to pursue matters further by seeking out and interviewing ex-employees, contractors, neighbors, and other entities that supposedly work with the facility in question (e.g., Institutional Animal Care and Use Committees, American Type Culture Collection). Unless they volunteer to locate such individuals, the facility's managers should be under no obligation to help the inspectors with outside interviews. Also, the inspectors should be conscious of the possibility that ex-employees might hold a grudge and neighbors might simply speculate about activities behind the fence. Inspectors would need to consider such factors when they evaluate what outsiders and ex-employees had to say about the site.[88] Although seeking out such outside interviews would be a logistical burden and some interviews could be tainted, the industry group believed that inspectors grappling with ambiguities about a site's status should not pass up opportunities to gain additional perspective on a questionable facility.

ON-SITE MONITORING ACTIVITIES: SAMPLING AND IDENTIFICATION

Sampling is often thought of as an ace in the inspector's toolkit.[89] This viewpoint certainly came out in the course of the industry group's discussion. To that effect, one industry brainstormer simply said: "If the inspectors can get a sample—any kind—they should take it."[90] Theoretically, all manner of

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[86] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[87] Industry Expert 2 stated this ground rule, to which the rest of the group heartily agreed.

[88] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[89] "Data can still be picked up after a room is decontaminated. Studies have been done to that effect." Inspection Veteran 6, member of host and inspection teams during two mock inspections, 27 April 2000. Inspection Veteran 6, a PhD scientist, was on the host team during the mock inspection at the Dugway Proving Ground, Utah, and on the inspection team during the mock inspection at the Edgewood Arsenal, Aberdeen Proving Ground, Maryland.

[90] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

samples could be taken at a site to enable inspectors to pinpoint whether microorganisms of concern are present.[91] In practice, however, the industry brainstormers expected commercial firms to give only one type of sample without much, if any, hesitation, namely a final product sample. As one participant said, "every ethical company will happily give inspectors a sample of their final product that can be tested to specifications to verify" legitimacy in an appropriate laboratory.[92] A final product sample would be the only type of sample that does not raise the specter of losing proprietary, extremely valuable business data. Understandably, therefore, the industry group approached the prospect of other types of sampling with considerable trepidation. Despite their concerns, their discussion of this topic also showed creativity and willingness to craft sampling and analysis ground rules that would satisfy the needs of inspectors and host facilities alike.

As a matter of fact, the industry brainstormers proposed a set of ground rules for sampling and analysis that they believed was feasible and should be acceptable to their colleagues in industry. Their ground rules and rationale are summarized below, and the meat of their discussion on this tough topic is presented verbatim in box 4.2 at the end of this chapter. The first governing principle would be that due to its intrusiveness, sampling should be a tool of challenge inspections unless the industry facility volunteered a sample under other circumstances. Second, the inspectors should have the right to request samples, and the host facility the right to refuse that request. Members of the group differed on what factors would influence a company's decision to accept or reject a sample request.[93] Insights 4.4 relates the factors that one of the inspection veterans considered when faced with this decision. Third, if samples were in order, they should be taken by facility staff or a third party with proven skills on the first day of the inspection.[94] The sampling techniques would be pre-stated with protocols that are based on accepted practice for different sample types (e.g., air, water, wipe, other medium).[95] The sample should be split

[91] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[92] Quote from Industry Expert 2, and the group agreed to this principle.

[93] During the 23 August 2000 meeting, Dr. Robert Hamilton thought that a company's decision would "probably depend on how serious they thought the allegations were and whether they thought the inspectors had the wrong image [about their plant] for some reason." Industry Expert 2 believed that large companies with decades of ethical behavior would reject a sample request because they would bet that their company's stock would not plummet due to an unsubstantiated allegation concerning bioweapons work. Such an allegation would torpedo the stock of a small biotech firm, however, so a smaller company would take the risk to try to clear its name. Dr. Robert Zagursky stated that the size of the company involved would not matter because even the big companies are sensitive to bad press.

[94] Otherwise, as Dr. Steven Projan stated, the industry group believed that a weapons producer would flush their system and get rid of evidence. Though defense contractors viewed sampling as being of particularly low utility on their sites, one contractor said that if samples were taken he would also want to conduct their own analysis. Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000.

[95] "Appropriate steps have to be taken to preserve the samples. Part of the puzzle has been solved, such as how to provide a sterile environment and temperature guidelines, but there is still work to be done. Refrigeration would help maximize the sample. More research and testing is definitely needed, confirmed in various field conditions." Inspection Veteran 6, member of host and inspection teams during two mock inspections, 27 April 2000. The industry group suggested that several accepted sampling practices might be the basis for these protocols, including the Environmental Protection Agency's certified

into blind or double blind sets for the inspectors and the host site and subsequently held in a lock box on site.

If the inspectors were able to conclude their work and resolve their concerns without analysis of the samples, then the host facility would have the right to destroy the samples. In the event that the investigation needed to proceed to analysis to resolve ambiguities, the analytical test(s) performed on the sample(s) would have to be prevalidated, with false positive rates articulated.[96] One industry group member noted that the inspectors might be able to employ a portable riboprinter that can speciate bacterial strains within eight hours.[97] Preparing the assays for other samples would be a lengthy process, but the industry group reasoned that running unvalidated assays would not be scientifically credible and might not even catch a cheater. Once validated assays were available, the samples would be taken from the dual key lock box and preferably analyzed on site under the watchful eye of inspectors.[98] Another, less desirable option would be to ship the samples under pre-agreed chain of custody procedures to certified third-party laboratories that are routinely tested for competency. In that case, the plant would have the right to have its personnel observe the analytical work from start to finish.[99]

Insights 4.4

The decision to allow samples to be taken is not easily made. One individual who hosted a US BWC trial described his deliberations in the following terms: "I was torn because sampling was the only way I could prove I was clean and wasn't using all of that [equipment] for biowarfare purposes. In theory, it might give me a clean bill of health. I weighed that against the possibility of them finding one little organism, in which case I'm probably worse off than before they sampled. In the best of all worlds, sampling would prove guilt or innocence."[1]

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[1] 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.

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samples for environmental chemicals, US Pharmacopoeia, the Association of Official Analytical Chemists, the American Society for Testing Materials, and Standard Methods for Water and Wastewater Analysis.

[96] The industry group estimated that four or five years would be needed to develop, test, and validate the assays to be used. The assay could probably be 75 percent validated based on laboratory studies, with the remaining 25 percent of the validation pertaining to ruggedness and reproducibility. Both the inspectorate and the host company should accept the data, which would be subsequently tested. If the BWC protocol was activated prior to the validation of assays, samples would be stored according to a pre-stated storage protocol until the validated tests were available.

[97] Dupont makes a riboprinter, which performs automated southern blotting to break down and identify a sample. Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

[98] In the interim until the assays were ready, the industry group also considered the possibility that an agreed third party could store the samples, using the appropriate chain of custody and storage protocols.

[99] "Without a doubt, whether it is done on site or at a contract laboratory, I'm going to have one of my technical experts in that lab watching exactly how the samples are handled, making sure that all the necessary positive and negative controls are run, and that the tests are being run appropriately because it's too sensitive of an issue." Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Also, the group stated that a set of samples should always be archived at an agreed central repository in case a re-test was needed. The company could request another test if the wrong assay was used. Also, the company could generate its own test in an effort to clear itself of any allegations.

Aside from a final product sample, the other types of samples that might be taken at a manufacturing plant include samples from points along the production process, from the waste treatment system, from personnel or test animals, and from the other general surface locations inside or outside the fence. Ordinarily, many of the pieces of equipment along the production cycle are equipped with sampling ports.[100] Indeed, a plant that claims to be making vaccine or biopharmaceuticals but does not have multiple sampling access points within its production process should automatically provoke questions from the inspectors.[101]

Unanimously, the industry group agreed that the waste treatment system would be an ideal location if samples were needed to unscramble a facility's true nature. A sample of waste, as one industry brainstormer observed, "tells all lies right there. Just because something doesn't grow doesn't mean that the telltale signs of that organism are not still present, and the best way to figure that out is to sample the waste."[102] The filters in the waste handling system, everyone agreed, would be truly revealing, and taking a sample from those filters would be an extremely sensitive matter for that very reason.[103] As for whether companies would grant permission for such samples, one industry group participant did not think that his facility would have a problem providing a waste sample. Even before doing so, however, this individual would still try to answer the inspectors' questions by showing them documentation that outside organizations had certified the waste to be clean.[104] Other industry group members objected to any sample other than from a final product unless validated tests and other guidelines discussed above were in force. Their concerns stemmed from the possible damage to their company's public image if a false positive indicating bioweapons manufacture resulted from an unvalidated test.

Even though the group considered sampling as a possibly definitive inspection strategy, the prospect of taking blood or other fluid samples from animals or personnel at a facility was truly unsettling for the industry group. Prevailing opinion held that commercial firms would flatly refuse animal samples because of the potential to compromise proprietary data.[105] Samples from personnel run up against the same dilemma—powerful investigation tool versus powerful potential to reveal proprietary data. Because of the latter circumstance, they argued that such samples be considered a tool of "last resort," to be

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[100] In some plants, some of these sampling processes are automated. Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm, 23 August 2000.

[101] Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[102] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

[103] Aside from waste treatment and high efficiency particulate air filters, the industry group identified drains, sewage, garbage, and gloves as possible sampling locations.

[104] Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines, 23 August 2000.

[105] In addition to blood samples, the industry group discussed sampling fecal matter and concluded such sampling for antibodies there would be similarly problematic.

employed only when there were really serious concerns of illegal activity.[106] Members of the industry group suggested that as an alternative some medical records might be made available to inspectors, but that would depend on company policy and whether the individual(s) involved viewed the release of such data as infringing on their civil and legal rights.[107] The same provisos applied to permitting blood samples, where some complications might be avoided by masking the identity of the employees giving the samples.

As for the possibility that inspectors would request samples from various surfaces around the plant or from garbage, the industry group stated that even with the precautions that manufacturers use to control the environment, the fact of the matter is that workers or visitors can track or bring anything inside a building. Therefore, such environmental samples could hardly be considered conclusive. General samples from outside of buildings or the fence line would be a similarly unattractive basis for any assessment of a facility's nature.[108]

ON-SITE MONITORING ACTIVITIES: PHOTOGRAPHS, VIDEOTAPES, AND REPORT PREPARATION

The industry experts recognized that inspectors would find it quite useful to document certain things with photographs or videotapes.[109] Not only would photographs and videos provide a record of the inspection that would be difficult to refute, it would allow inspectors to tap into additional expertise within the inspectorate to help determine what a certain setup might represent.[110] The industry group argued that it would be far preferable to host a larger team that incorporated the needed expertise than to permit the inspectors to take photos or videos. The industry group was adamantly opposed to the idea that treaty ground rules would stipulate that inspectors automatically be allowed to take visual records from the premises. The inspection team should have the right to ask if they could take photographs or

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[106] Industry Expert 4 stated this point, and the rest of the group readily agreed. Note that if such blood samples were necessary, the group recommended that they be taken from operational and maintenance workers as opposed to the managers whose duties would make them less likely to have developed antibodies. These samples could also be analyzed to determine if workers had been vaccinated against a disease of concern. Dr. Robert Zagursky, distinguished research scientist, Wyeth-Lederle Vaccines; Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Industry Expert 2, senior vice president, US biopharmaceutical company; Industry Expert 4, president and chief executive officer, small US biotechnology company, 23 August 2000.

[107] Dr. Robert Hamilton, senior scientist and group leader, US biotechnology firm; Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000. Stating that providing medical records would definitely not be allowed at his facility: Inspection Veteran 2, trilateral and mock inspection participant, 27 April 2000.

[108] Dr. George Pierce laid out this reasoning, to the agreement of the rest of the group.

[109] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research; Industry Expert 4, president and chief executive officer, small US biotechnology company, 23 August 2000.

[110] If the needed expertise was not on the inspection team, transmittal of such data and subsequent discussion could be very helpful to the team on site. Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000.

Insights 4.5

An inspector who had been inside former Soviet biowarfare facilities agreed that "photos are a very important piece of the documentary evidence, especially for such things as scale. Two rows of eight three-story fermenters—that says it all right there."[1] Regular photographs and videotapes were a standard part of trilateral inspections in the United States and Russia, United Nations inspections in Iraq, and US trial and mock inspections, [2] but the inspection veterans were leery of digital photographs that could be manipulated. This group advised that site operators always be the ones looking through the viewfinder and pushing the shutter button. Copies of any visual records, they said, should be made for host and inspectors alike.

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[1] 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.

[2] For instance, the Russians walked through two US defense facilities with videos in hand. No photographs were allowed en route to any US sites, and at other locations host officials took photographs for the Russians on a case by case basis. In Russia, some items were shrouded, but otherwise photographs were allowed. Photographs were allowed inside Iraqi sites, but not outside, where the cameras might capture security. Two sites involved in a US BWC trial refused all photographs fearing bad publicity and subsequent protests from animal rights activists, but another site allowed photos in all but a few locations. Inspection Veteran 1, facility manager and US trial inspection host; Inspection Veteran 3, trial inspection observer and mock inspection participant; Inspection Veteran 5, participant in two US trial inspections and a mock inspection; Inspection Veteran 6, member of host and inspection teams during two mock inspections; Inspection Veteran 7, United Nations Special Commission on Iraq inspector and mock inspection participant; Inspection Veteran 8, trilateral and trial inspector; Inspection Veteran 9, participant in trial and one mock inspection, 27 April 2000.

videos, but the host facility should have an equal right to decline such requests. Industry brainstormers projected that few, if any, commercial plants would give permission for photographs and videos. As Insights 4.5 relates, the inspection veterans group recalled that in the past inspectors have often pulled out cameras.

At the conclusion of the inspection, the industry group expected commercial companies to have certain rights pertaining to the preparation of draft and final inspection reports. The experience of a defense contractor whose firm had been inspected under the CWC, described in Insights 4.6, indicates that perseverance would serve industry officials well during the drafting of an actual inspection report, as would ironing out in the protocol text host site rights vis-à-vis the report drafting process. First, the industry would want to obviate the chances that an arms control inspection could place them in double jeopardy with US regulatory agencies. Therefore, draft and final reports should not contain any information that could get a commercial facility in trouble with US regulators.[111] Also, the industry group stated that companies would want a right of response or rebuttal to the draft and final reports in the event that company representatives believed that they had been misquoted or data had been misinterpreted. Ideally, the company's response would be incorporated as a formal part of the inspection record.[112] A copy of the final report and any other

[111] In fact, the entire group asked that the official US escorts for the inspectors come from a non-regulatory organization, such as the State Department or Commerce Department. "This is an arms control inspection, and when all is said and done, there is no reason for cooperation with that type of inspection to bring any US regulators through the door." Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

[112] The company should be allowed sufficient time to prepare this response. Dr. Robert Hamilton, senior scientist and

associated documentation should remain with the inspected company.[113] Finally, the industry group suggested that the facilities hosting inspections should have the right to file their own reports about the competency of the inspectors.

INDUSTRY GROUP ASSESSMENT OF MONITORING TECHNIQUES

Since a treaty monitoring regime is often judged primarily by its effectiveness, the Stimson facilitators asked the industry group to flesh out what effectiveness meant in the context of their proposed BWC inspection tools and strategies. They defined effectiveness as the ability of monitoring techniques to help determine whether a facility was intentionally violating or was compliant with the BWC's provisions. Having said that, the industry group stated that no single monitoring tool in and of itself would necessarily get to the "truth." They stressed that the monitoring tools would only be as good as the inspectors and that intentional violations would be difficult to prove. Still, if the BWC inspections were focused on inconsistencies with expected legitimate practice, then the industry group believed that visual observation, document review, interviews, and, as a last resort, sampling and analysis would lend clarity and confirm compliance or noncompliance. In some cases, they expected that the results of using these tools would have to be somewhat qualified or graded. Their predictions for the effectiveness of their monitoring approaches to evaluate the status of a manufacturing facility can be found in table 4.2. They projected that monitoring effectiveness would be very high in one area, high in five areas, medium in four areas, and low in one. In two other areas, their assessment differed depending upon whether samples were involved.

Insights 4.6

According to a defense contractor who had hosted a Chemical Weapons Convention inspection, settling the details of the report was one of the most tedious parts of the inspection. While the inspectors tabled a draft report that was factual in nature and eschewed subjective judgments, the facility's managers still had to pay careful attention to the report's wording. This facility, which had government and commercial clients, wanted to ensure that the report did not compromise its customers and thereby its business. Part of the problem encountered was that the various individuals drafting the report were from a variety of organizations and backgrounds and ascribed different meanings to the same words. After "long hours" of haggling over the wording, this defense facility "got a positive report from the inspectors. They didn't really find anything that they were concerned about in terms of production of offensive chemicals, activities, or anything like that."

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[1] Defense Contractor 4, president of a defense and commercial contracting firm, 28 August 2000. Defense Contractor 4 has a PhD in chemical engineering.

group leader, US biotechnology firm, 23 August 2000.

[113] Industry group members explained that such reports would possibly be needed for patent application.

Table 4.2: Expected Effectiveness of BWC Monitoring Techniques

Area of Inconsistency with Site's Stated Purpose	Expected Level of Effectiveness of Monitoring Techniques Used in Combination
Level of Containment	High
Supplies	High
Equipment and Materials of Construction	Medium
Medical Facilities	High
Facilities (e.g., air filtration, cooling)	High
Waste Handling and Treatment Systems	Low to Medium without Sample High with Sample
Procedures	Low
Management Program	Medium to High
Downstream Processing	Very High
Degree of Concern with Product Integrity/Quality	High for Human Products Medium to High for Animal Products
Microorganisms on Site	Medium with Sample Low without Sample
Animal Facilities and Numbers	Medium to High

The industry group characterized their overall expectation of how these monitoring techniques would perform in the field by stating that good inspectors employing them would find careless bioweapons makers and very large offensive programs. In other words, these techniques would unmask the type of bioweapons program run by the former Soviet Union. Therefore, the industry experts reasoned that initiating such inspections would make it more difficult for proliferators to hide their activities at industry facilities and would certainly increase the risk that cheaters would be caught.

Even though they estimated that these monitoring tools would be reasonably effective in identifying and parsing the nature of inconsistencies, the industry group pointed out that their inconsistency inspection strategy is one that could cut both ways. The inspectors will find inconsistencies at real commercial plants for the simple reasons that humans make mistakes. "An erroneous assumption that is sometimes made is that a credible operation will always do a very good job," but genuine commercial sites do not run perfectly, explained one industry expert.[114] Picking up that same train of thought, another industry group member turned it the other way:

> For many of processes that we've developed, we never get it right the first time. There's trial and error that goes into these things and it takes a long time to work out all the kinks. If they're trying

[114] Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Another industry participant also voiced this sentiment: "I think it's going to be almost impossible for even an ethical manufacturer to have one of these inspections, and not have a couple of flags." Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

> to cloak a weapons facility inside a legitimate manufacturing plant, to do a phony process at the same time as doing a valid process, it's going to be very tough to get it all working right. It's going to smell to high heaven unless they practice it *ad infinitum*.[115]

Sorting through the inconsistencies at some facilities could be a monumental challenge, however. To wit, a couple of the group's members described an animal or poultry vaccine manufacturing facility as optimal cover for a bioweapons facility because they operate at scale, produce in bulk, have a sound rational for having aerosol chambers and other key equipment.[116] In short, should a protocol be concluded and BWC inspections become a reality, the industry group believed that the inspectors would have their work cut out for them. They hoped that negotiators of the protocol would give those inspectors a fighting chance by adopting their recommendations for the design of such a monitoring regime.

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[115] Dr. Steven Projan, director of antibacterial research, Wyeth-Ayerst Research, 23 August 2000. Another industry expert made a similar remark: A cheating facility "is probably going to try to cover it up, but that is going to be very, very hard for someone to do across all the bases. All that is needed is to have them slip up on one or two things—they don't even have to be major slip-ups—and that can be enough to get the inspectors started on the track." Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000.

[116] In the West, animal vaccine facilities are almost as heavily regulated as those that produce human medications, but in other countries, that may not be the case. Dr. George Pierce, former manager, technology development and engineering, Cytech Industries, 23 August 2000. Seconded by Industry Expert 2, senior vice president, US biopharmaceutical company, 23 August 2000.

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.