

Concerned about new or reemerging pathogens, many virologists are dreaming of their own high-containment labs. But worried neighbors may derail their plans

The Boom in Biosafety Labs

PLUM ISLAND, NEW YORK, AND GALVESTON, TEXAS—When safety officer Thomas Sawicki starts explaining the rules, you realize that this is no ordinary lab visit. Before entering, Sawicki instructed a small band of reporters last month, you'll have to take off all your clothes and jewelry. Then, you'll walk naked through a narrow hallway and open a door, after which you'll find a locker room where you can grab some underwear and don a disposable lab suit. Now you're ready to enter the innards of the facility—where the viruses are.

Later, before you exit, drop your entire outfit in a laundry bin, blow your nose, clear your throat and spit, scrub under your nails, and dip your glasses in disinfectant. Then step under the shower and wash your entire body and your hair for at least three minutes. Oh, and forget about bringing any notes you took. They'll be faxed to the outside world; the originals will be incinerated.

This press tour is part of a new public relations campaign at Plum Island Animal Disease Center, designed to assuage the fears of the surrounding community. The laboratory, sitting in isolation on a tiny island in the Atlantic off Long Island, is the only place in the United States where scientists are allowed to study several deadly pathogens that infect animals—a sort of Alcatraz of microbiology. Despite the evident safeguards, local critics have long worried that the bugs might somehow escape and make their way across 2 kilometers of ocean, setting off an Ebola-like epidemic in an upscale New York suburb. For decades, the lab was shrouded in secrecy; now, as part of the new *glasnost*, lab officials routinely shepherd through hordes of reporters and residents of nearby towns so they can see for themselves what scientists are doing here—and how seriously they

take safety. The PR is essential, they concede, because the U.S. Department of Agriculture (USDA), which operates Plum Island, wants to upgrade the facility so that it can handle the most dangerous pathogens in the world—those that infect humans as well as animals—and it can't do so without the public's blessing.

USDA is not alone in its ambitions. For decades, the United States had only two major high-containment laboratories, known as biosafety level 4 (BSL-4) facilities, both of them run by the government—one at the U.S. Army Medical Research Institute of Infec-

tious Diseases (USAMRIID) in Fort Detrick, Maryland, the other at the Centers for Disease Control and Prevention (CDC) in Atlanta. (The National Institutes of Health also has one but currently doesn't use it for viruses.) But over the last 2 years, two small BSL-4 facilities have been built, and plans are afoot to build three more—with universities, not the government, paying the hefty bill.

Researchers claim they urgently need these facilities if they are to prepare for future outbreaks of deadly scourges and build defenses against bioterrorism. "There are so many threats out there," says pathologist David Walker of the University of Texas Medical Branch (UTMB) in Galveston, which is angling for its own level 4 facility. "And CDC and USAMRIID really don't have time for every one of these viruses."

For the universities, these labs provide other perks as well. Having a BSL-4 lab is a way to put themselves on the map in the hot field of emerging infectious diseases. They can also be a powerful bargaining chip in recruiting topflight faculty and a way to get a head start in the grant game.

A few skeptics wonder whether the country actually needs nine (see map) of these high-tech, multimillion-dollar labs—

in addition to over a dozen that exist overseas. But one thing is clear: For any of the plans to succeed, courting the public will be at least as important as fund raising. "If you haven't thought about the public concern before getting the funding, you have the cart before the horse," says UTMB's vice president, Adrian Perachio.

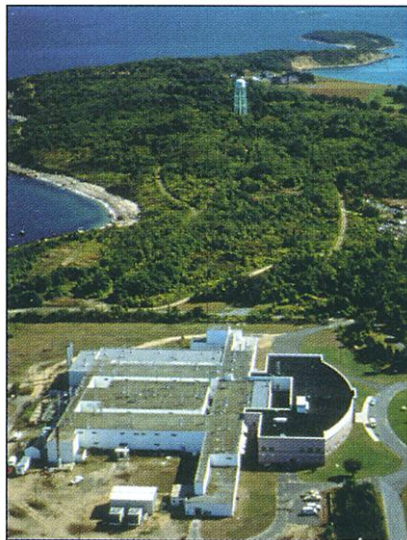
The hot zone

Biosafety level 4 is reserved for highly infectious viruses (no bacterium or parasite is considered this dangerous) that are often lethal and for which there is no cure, let alone a vaccine. Federal guidelines currently list about 16 viruses that must always be handled in BSL-4 facilities; some notorious, like Ebola, others, like Omsk hemorrhagic fever and Hypr, rather obscure. In addition, hundreds of viruses have been assigned to slightly more relaxed level 3 conditions—like those now at Plum Island—unless researchers intend to grow the viruses in large quantities or infect certain animal hosts, in which case level 4 is required. The "strictly BSL-4" list is expected to grow, however; some 120 viruses discovered over the past century have been temporarily assigned to level 3 because nobody knows whether they infect humans and pose a threat at all; some could easily be promoted should a deadly outbreak occur.

Everything in BSL-4 labs is aimed at containment: Researchers work in space suits that shield them from the viruses, air pressure is kept low so that nothing can accidentally waft out, and nothing leaves the lab without being thoroughly sterilized.

Until recently, most researchers have been content to work in level 3 labs—or, for riskier work, to beg and borrow time at CDC or USAMRIID. But now, with a few dozen new viruses and revved-up interest in the field, space is tight, and everyone wants one at home. "We're all dressed up but we have nowhere to go," says hantavirus expert Brian Hjelle of the University of New Mexico, Albuquerque.

The Southwest Foundation for Biomedical Research (SFBR) in San Antonio, Texas, was the first nongovernment lab to "go hot" to meet this growing demand. Since the late 1970s the foundation has operated a small, simple type of BSL-4 lab, known as a "glove box," enabling its researchers to study her-



Splendid isolation. USDA wants to upgrade its lab on tiny Plum Island, off the New York coast, to study the most deadly viruses around.

CREDIT: PLUM ISLAND ANIMAL DISEASE CENTER

pes-B virus, which occurs naturally in monkeys but occasionally infects scientists and zoo personnel working with the animals—with potentially fatal consequences. Researchers don't need to wear space suits; instead they keep their samples inside a sealed cabinet and manipulate them through arm-sized rubber gloves. Last year, however, SFBR joined the big league, replacing its glove-box facility with a full-fledged "suit lab"—similar to, if smaller than, those at CDC and USAMRIID. Now its 30 virologists are able to work with lethal South American arenaviruses, such as Guanarito and Sabia, which can cause hemorrhagic fevers.

Other universities in Texas are eager to join the club. Indeed, three more institutions are clamoring to set up level 4 facilities in the Lone Star state.

Texas "just happens to be where a lot of the brainpower is for doing BSL-4 work," explains virologist Julia Hilliard of Georgia State University in Atlanta. It also just happens to be a place where funds are relatively flush. UTMB, for instance, is building up a world-class research center for infectious diseases—and that makes a BSL-4 facility de rigueur (*Science*, 28 April, p. 598). The university hopes to break ground early next year for a 180-m² level 4 lab that will enable its scientists to work with arenaviruses and hantaviruses without having to fly to Atlanta and work at CDC. A private foundation has pledged to cover the estimated \$7.5 million bill.

In Lubbock, 1000 kilometers to the northwest, Texas Tech University is thinking of adding a BSL-4 lab to its new Institute of Environmental and Human Health. Last year Congress approved a Department of Defense plan to appropriate \$5 million to Texas Tech to develop countermeasures to chemical weapons and bioterrorism. If the university becomes a major player in this field, it will have to work with several agents on the BSL-4-mandatory list. Texas Tech vice president David Schmidly says that money should be no problem. The university can provide at least half of the expected \$8 million tab, and Schmidly expects both the city and state to kick in some additional funds.

Finally, Texas A&M University in College Station wants a BSL-4 lab to study animal

viruses—much like the proposed upgrade at Plum Island. The plan is ambitious, as it requires facilities to house animals inside the airlock lab, and for now it is on hold because A&M hasn't been able to find funds.

EXISTING BSL-4 LABS

National Institutes of Health (NIH)—
Bethesda, Maryland

Centers for Disease Control and Prevention—
Atlanta, Georgia

U.S. Army Medical Research Institute of Infectious Diseases—Fort Detrick, Maryland

Southwest Foundation for Biomedical Research—San Antonio, Texas

Georgia State University—Atlanta, Georgia

Canadian Science Centre for Human and Animal Health—Winnipeg, Canada

PROPOSED BSL-4 LABS

University of Texas Medical Branch—
Galveston, Texas

Texas Tech University—Lubbock, Texas

Plum Island Animal Disease Center—
Plum Island, New York

Texas A&M University—College Station, Texas

Overkill?

Although most researchers agree that more BSL-4 labs are needed, some question whether the country actually needs

virus, which wiped out the Malaysian pig industry last year and killed 105 people. (See p. 1432 of this issue.) If the virus should ever reach U.S. soil, either by accident or as a result of bioterrorism, the country would be powerless to study it, as none of the existing BSL-4 labs can house pigs. "That's really a national embarrassment," says Murphy.

But does the country really need two—one at Plum Island, and one at Texas A&M? Some scientists don't think so. And if only one lab gets built, perhaps it shouldn't be at Plum, says well-known virus hunter C. J. Pe-

Building boom.

The U.S. now has five BSL-4 labs, and four more are planned.

nine, with four in one state alone. Frederick Murphy, dean of veterinary medicine at the University of California, Davis, says it may be hard for universities to attract and properly train skilled staff. If BSL-4 personnel—from scientists to cleaners—don't get training at the same level as at the federal labs, cautions Murphy, then they may be at risk.

Cost—both construction and maintenance—is another issue. UTMB virologist Charles Fulhorst thinks it would make more sense for Texas Tech researchers to do their research at Galveston's new lab. "Texas is a big state," counters Texas Tech's Schmidly; "I don't think Galveston can meet everybody's needs." The Texas Higher Education Coordinating Board may ultimately decide, as it has to approve university construction plans whose cost exceeds \$1 million. Last month UTMB received the board's blessing; Texas Tech's plans could well be vetoed if the board finds them duplicative.

Almost no one questions the need for a BSL-4 animal lab in the United States. Plum Island's level 3 facility sufficed until recently, as most livestock diseases weren't thought to pose a serious health threat to humans. That changed with the discovery of several new viruses, including the Nipah



ters of CDC. Construction is expensive, there's no other academic center or lab nearby to collaborate with, and it's hard to attract young scientists because of staggering real estate prices, he says. Atlanta, or the USDA's



Dressed for danger. "Space suits" protect workers in BSL-4 labs from exposure to viruses.

veterinary lab in Ames, Iowa, would be better places, says Peters: "You can't do science in a vacuum anymore. You need synergy."

But USDA is in a bind: The law currently demands that research on foot-and-mouth disease and rinderpest, which are level 3

Learning the Hard Way

Until its festive dedication in June, the Canadian Science Centre for Human and Animal Health had not run into major opposition. Researchers—some of them trained by professional consultants—had spoken at dozens of meetings, thousands of people had toured the lab, and all seemed fine. But barely a week later, the lab accidentally released a batch of wastewater into the city's sewage system without properly sterilizing it. At first, lab officials didn't report the incident, says director Norm Willis, because they were positive the water didn't contain any virus and thus posed no risk.

But when news about the leak reached the press, opponents claimed there had been a cover-up—just as they had predicted would happen in case of mishap—and public opinion soured. As a result, the two agencies responsible for the lab decided to delay the permits needed to import biosafety level 4 (BSL-4) viruses. For a while, it seemed like the lab might go the path of its failed predecessor in Toronto, which has never operated as a BSL-4 facility because of opposition from its neighbors (see main text).

To win back the squandered trust, the center installed a "public liaison committee," a diverse group of 16 Winnipeg citizens, to serve as a go-between. For several months, the group—which comprised conservationists and health workers as well as the editor of the local Filipino journal—studied the 10-cm-thick safety handbooks, inspected the lab, and asked countless questions. "We've made it quite clear that we intend to blow the whistle if we have concerns that aren't being looked at," says Bob Douglas, a former city council member who co-chairs the committee. In the end, the group became convinced that all was in order, and in March, it endorsed the level 4 operations. One month later, Health Canada finally issued the coveted permit. Ultimately, the group became the lab's best advocate; members even wrote to Ottawa to urge speedier delivery of the permits.

—M.E.

agents because they're harmless to humans, take place on an island that's not connected to the mainland by bridges or tunnels. So unless Congress gets involved, at least that part of Plum Island's work has to remain where it is.

Winning hearts and minds

But even if money and people were no problem, public resistance may imperil some of the plans. In 1996, for instance, Ontario's provincial government completed a brand-new BSL-4 lab in Toronto that had been in the works for 10 years—almost unnoticed, initially. But as the opening date came close, opponents whipped up a media frenzy, which gained even more force when the hit movie *Outbreak* was released. Ultimately, the government backed off, and the lab never opened as a BSL-4 facility. (Instead, it works with less dangerous level 2 organisms.) The same happened to a lab in Tokyo in 1981. And neighbors' worries—in this case, about radioactive pollution rather than bugs—also led to the permanent shutdown of the High Flux Beam Reactor at Brookhaven National Laboratory on Long Island. Some say the closure could have been prevented if scientists hadn't shrugged off the public's concerns for so long (*Science*, 25 February, p. 1382).

Plum Island is barely 50 kilometers east of Brookhaven—which is one reason why USDA is going out of its way to persuade its neighbors. Even so, fierce opposition may have derailed the planned upgrade. Debbie O'Kane, for one, is not convinced there's nothing to worry about. O'Kane, who directs the North Fork Environmental Council on Long Island, recently did Plum's

lab tour, nail-scrubbing and all, but rather than reassure her, the visit made her think twice. Nobody was there to watch whether she actually went through all the prescribed steps, she says—she could have walked right out without doing them. Nor was O'Kane impressed by several town meetings. "USDA came across as incredibly patronizing," she says.

O'Kane and other activists subsequently barraged their congressman, Michael Forbes (D-NY), with hundreds of petitions to kill the project. He, in turn, lobbied the White House, which had originally supported the project; as a result, USDA's request for



Windy city. Galveston is prone to hurricanes, like the 1900 storm that heavily damaged the medical school. But worries about escaping bugs are unfounded, say university officials.

\$75 million in funding for the new facility in fiscal year 2001 was denied. USDA officials hope that funding will come next year, but Forbes has vowed to fight the upgrade.

From the start, Galveston officials were determined to avoid such setbacks. "When I proposed this plan to the [University of Texas] Board of Regents," says UTMB's Perachio, "their first question was: How does your community feel about this?" There are understandable reasons for concern, because Galveston is prone to hurricanes. A giant storm whipped up a surge in 1900 that killed thousands and partly destroyed the city. Many worry that a repeat might damage the lab, spewing pathogens all over the place. "Why would you want to build it here, of all places?" asks Jackie Cole, a Galveston veterinarian.

The university's answer, conveyed in countless meetings, on a Web site, and through other channels, is that Galveston now has a 5-meter-high sea wall and that hurricanes come with ample warning nowadays. If landfall is predicted with some degree of certainty, an emergency plan would be activated to shut down the facility in 90 minutes and sterilize it; all viruses would be put in secure freezers. Besides, the building will be solid as a rock, and even if the freezers were torn apart, the viruses would be in almost unbreakable containers and vials.

Perachio didn't enjoy the extensive public scrutiny of the plans. "When I see a TV camera aimed at me, it's like looking down the barrel of a howitzer," he says. But the exercise seems to have paid off: Although some people still oppose the plan, resistance here isn't as organized or active as on Long Island. "UTMB's approach has been honest and open," says Harris Kempner, a local businessman from an influential Galveston family who has been won over. "There's no surprises here." Perachio says that the university will keep up the effort as construction proceeds: "It ain't over till it's over." Indeed, he may follow the example of colleagues in Winnipeg, who almost lost their new BSL-4 facility and then set up a permanent community liaison committee to deal with issues as they arise (see sidebar).

In the long run, the best way for labs to strengthen confidence is simply to show that they can work safely year after year, says Tony Della-Porta, head of technical services of a BSL-4 lab in Geelong, Australia, that opened in 1986. "You have to develop a track record of safety, and that takes time," says Della-Porta. "But if you succeed, you can actually get the community to take pride in what you achieve."

—MARTIN ENSERINK

CREDIT: ROSENBERG LIBRARY, UTMB