Stuck on the Same Refrain

By Lynn C. Klotz

A very brief history

In early 2003 during the application process to fund construction of a high biocontainment biodefense research facility, Boston University wrote a letter to the National Institute of Allergy and Infectious Diseases stating that the facility "would be devoted exclusively to biodefense research and other NIAID-defined research programs… " The biodefense focus of the facility is reflected in its original name as well, National Center for Emerging Infectious Diseases and Biodefense. NIAID approved the Boston University application in September 2003, contributing $128 million toward building the facility.

Growing concern over the biodefense focus and a letter titled "No Place to Hide" signed by 165 Boston area scientists may have contributed to the lab's name being changed to the current one, National Emerging Infectious Disease Laboratories, eliminating all reference to biodefense. Boston University may have hoped the new name would make the lab acceptable to its Boston and suburban neighbors. It didn't, because its biodefense focus hadn't changed, just the name.

The present

Now, a decade later, Boston University emphasizes the emerging infectious disease focus. In their own words "The facility is dedicated to the development of diagnostics, vaccines and therapeutics to combat emerging and re-emerging infectious diseases."

Roxbury Safety Net has long opposed the NEIDL. In its 2010 document *An Alternative Vision for the Boston University National Emerging Infectious Diseases Laboratory,* Roxbury Safety Net argued that NEIDL's BSL4 pathogens are not emerging diseases:

> "The term 'emerging infectious diseases' has been applied by Boston University to BSL4 bioweapons agents such as the hemorrhagic fever viruses Ebola, Marburg and Lassa. The term is misleading as it implies a public health urgency that these pathogens do not deserve. They, in fact, present no public health threat in the United States and only a minor health threat anywhere else…In fact, the rare BSL4 pathogens should be rightfully classified as "exotic," not emerging."

Roxbury Safety Net's argument has gotten implicit support from two sources. One source is an unlikely one indeed, Anthony Fauci the Director of NIAID whose agency supplied much of the funding to build the facility. In the December 2012 article that Fauci co-authored "*Emerging Infectious Diseases in 2012: 20 Years after the Institute of Medicine Report*," his list of important emerging and reemerging infectious diseases and their causative pathogens are highlighted.

> "As predicted in 1992, previously unrecognized infectious diseases have continued to emerge, including variable Creutzfeldt-Jakob disease/bovine spongiform encephalopathy (vCJD/BSE), severe acute respiratory syndrome (SARS), and 2009 pandemic H1N1 influenza, and others have reemerged, e.g., disease caused by multiple-drug-resistant *Staphylococcus aureus* (MRSA), multiple-drug-resistant and extensively drug-resistant (MDR and XDR) tuberculosis, cholera, and dengue."

Fauci's list does not include the BSL4 "likely research areas of interest at NEIDL" as listed in Table 3-2 of the 2012 Final Risk Assessment for the NEIDL. Fauci's agency has also led the ongoing attempts to produce an acceptable risk assessment necessary to allow research in the high biocontainment BSL3 and

BSL4 labs of the NEIDL. From the final risk assessment, the likely NEIDL research areas requiring a BSL4 laboratory are Ebola, Marburg and Lassa viruses. A perusal of the NEIDL website identifies two other BSL4 viruses, Hendra and Nipah, that NEIDL will research, somehow missed in the risk assessment. We call these five deadly viruses the "NEIDL-five."

The second source of support is another 2012 article, *Emerging Disease or Diagnosis?* It was published in the prestigious journal Science. Among the twelve authors of the article are two high profile MIT scientists Eric Lander and Pardis Sabeti. Here is what the article says:

> "Recent epidemiologic and genetic studies of Lassa and Ebola fevers suggest that these diseases may have widespread prevalence and ancient origins. They raise the possibility that some viral infections may reflect "emerging diagnoses" of diseases that are circulating more widely than thought, with an emerging character primarily a matter of improved detection of the culprit pathogens."

"Ancient origins" means they did not emerge 50 years ago as was widely believed. They may have infected humans hundreds of years before. This finding further supports the Alternative Vision claim the viruses are not "emerging."

In nature, the NEIDL-five are restricted to narrow geographical areas defined by their animal reservoirs (a species of rodent for Lassa and monkeys for Ebola.) confined mostly to tropical countries where they are only minor fatality threats. They cause a few dozen to perhaps a few thousand fatalities per year where they are endemic. Compare this to the fatalities from the major public health threats such as malaria, AIDS, tuberculosis and the many respiratory and diarrheal diseases that kill millions worldwide each year. The NEIDL -five do not display the characteristics of emerging infectious diseases either, as the number of yearly fatalities has not increased over the years and the geographic range has not widened.

Supporting "widespread prevalence," the Science article authors found that 50% of people in some endemic areas have been exposed to Lassa and 5% to 20% exposed to Ebola. These large exposure percentages may be because their animal reservoirs have very high infection rates. But the viruses still are absent from the US and other developed countries where their animal reservoirs don't live. Most exposures are clearly not fatal. Although annual deaths may be considerably more than the dozens to hundreds confirmed each year, they are nowhere near the fatalities of the major threats.

What defines BSL4 pathogens?

How then, does a virus earn the BSL4 designation?

> "Biosafety Level 4 is required for work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments, or a related agent with unknown risk of transmission."

Only a small number of pathogens meet this CDC definition (all told, perhaps less than 25), and all are exotic viruses not present if the U.S. [For a list of fifteen BSL4 pathogens, see Table 6 in Biosafety in Microbiological and Biomedical Laboratories. The NEIDL-five are on this small list.

Conclusions

So why is the NEIDL focusing on these five viruses? Three of them (Ebola, Marburg and Lassa) are Category A bioweapons agents, the highest priority agents.. The CDC describes the Category A agents as "agents…that pose a risk to national security."

Considerable progress on developing countermeasures for Category A agents has been made by hundreds of BSL2 and BSL3 laboratories working with non-infectious parts of the viruses. Worldwide over 30 BSL4 labs are working with the live agents. Boston University is too late in the game to contribute to this large effort.

Looking at the reverse side of the coin, many pathogens on Fauci's list of emerging and reemerging pathogens, such as "multiple-drug-resistant Staphylococcus aureus (MRSA), multiple-drug-resistant and extensively drug-resistant (MDR and XDR) tuberculosis, cholera, and dengue" are not BSL4 pathogens, and except for tuberculosis are not on the NEIDL list of pathogens to be researched.

So how did Boston University get itself into the position where it plans to focus its National Emerging Infectious Disease Laboratories BSL4 research on non-emerging diseases that are no public health threat in the U.S. and ignores many important emerging diseases that do not even require BSL4? I submit it is because Boston University wants to have a BSL4 laboratory at any cost mainly to fulfill its unpopular biodefense mission.

This is folly in my opinion. BSL4 labs are very expensive to operate and maintain. The seemingly small amount of BSL4 research at the NEIDL on these exotic live pathogens does not justify the risk or the expense. The research should be carried out instead in already operating BSL4 laboratories.

What to do about the already built and equipped, expensive NEIDL BSL4 laboratory? Here is a suggestion. Open the doors and utilize it as a BSL2 laboratory. The expensive air handling, air filtration equipment, etc. needed for BSL4 can be "mothballed," to employ the term the Navy uses for ships not now in use but to be used potentially. When would such a mothballed BSL4 lab be resurrected? Perhaps never.

The Bush era biodefense strategy seemed ill-conceived to many of us. The original NEIDL strategy was a poster child for what was wrong with Bush-era biodefense. The shift to non-BSL4 basic research in infectious disease that I am beginning to see at the NEIDL is welcome. But the risky and unneeded biodefense focused BSL4 research remains, as is apparent in the final risk assessment.