Council for Responsible Genetics

Biological Laboratories: Risks and Regulations

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Table of Contents

Introduction

Recent high profile incidents at the Centers for Disease Control and the National Institutes have brought the discussion of biosafety back to the forefront of the public conscious. In June 2014, the CDC reported that eighty-four personnel were exposed to live anthrax spores that were supposed to have been killed. The sample had left the lab twenty four hours after it went though a killing procedure, instead of the forty eight-hour window that is recommended.[1] While no one was infected, the incident set off a major scare at the CDC and renewed concerns about biosafety. Later in July 2014, it was reported that freeze dried vials of smallpox were found in an unused storage room at the NIH.[2] Prior to this discovery it was assumed that all remaining vials of smallpox were kept either at the CDC or at VECTOR, the State Research Center of Virology and Biotechnology in Russia. These two incidents illustrate the relevancy and risks associated with biosafety in today's world. As biosafety expert Michael Osterholm states in regards to the vials of smallpox and biosafety accidents, "I'm not convinced this will be the last of these potential situations. I wouldn't be surprised if somewhere else in the world this same type of thing happens again." [3]

Health biotechnology and biological research has led to incredible advances in our understanding of the human body and healthcare. The growing importance of such research resulted in a rapid expansion of both public and private labs doing biological research, particularly in the San Francisco Bay Area. These labs conduct research ranging from drug discovery, genetic engineering, biofuels to infectious diseases. Biological

[1] Steenhuysen, Julie, and Sharon Begley. "Anthrax Scare: CDC Lab Didn't Heed Its Own Lessons." *NBC News*. NBC, 29 June 2014. Web.
[2] Szabo, Liz. "Forgotten Vials of Smallpox Found near D.C." *USA Today*. Gannet Company, 9 July 2014. Web
[3] Szabo, Liz. "Forgotten Vials of Smallpox Found near D.C."

research is conducted at 4 levels, with biosafety level (BSL) 1 being the least secure and biosafety level 4 being the most secure. The issue of the expansion of the labs is the lack of oversight, at both the local and federal level and the risk of an accidents occurring because of the lack of oversight.

The San Francisco Bay Area has seen a rapid growth in biotechnology companies and research in the past twenty-five years. This has been attributed to the combination of strong academic research institutions in the Bay Area (University of California (UC) Berkeley, University of California San Francisco (UCSF) and Stanford University being the largest), two federal labs (The Lawrence Livermore National Laboratory (LLNL) and the Lawrence Berkeley National Laboratory (LBNL) and the startup culture of the Silicon Valley. As stated earlier, the types of research being done varies widely, but a fair amount involves biological materials, including pathogens. Accompanying this rapid growth in biotech has been biological lab accidents, including laboratory-acquired infections, explosions and accidental releases of biological material. These have mainly occurred in high security labs. There are currently no BSL 4 labs in California, but there are several BSL 3 labs in the Bay Area at academic institutions and LLNL, with an unknown number at private corporations. In some cases, a BSL 2 lab can be modified to perform BSL 3 experiments, meaning that BSL -3 research may have been or currently be carried out in a non-dedicated BSL 3 facility. This is referred to as BSL 2 plus. Additionally, LBNL is building a second campus in Richmond Bay, CA, which will be a new research center covering a wide range of fields including work on synthetic biology. Since both the federal government and the cities that comprise the Bay Area do not require laboratories to register themselves, there is no way of knowing exactly how

many biological labs there are in the Bay Area, though we have attempted to create a current list (appendix 3) The gaps in oversight and the potential risks of these gaps are an alarming problem for the Bay Area, and one that will only lead to more risk if it is not addressed. In light of the recent accidents with two deadly pathogens, where severe and deadly outbreaks were just barely avoided, the urgency of biosafety reform is all the more apparent.

The Problem

Biological research is carried out in labs that have differing biosafety levels (BSL). BSL describes the level of biocontaiment appropriate for the type of research done in a lab. There are four biosafety levels, ranging from 1 (the least secure) to 4 (the most secure). (SEE APPENDIX 2) Biosafety level 1 is for work with agents that are not known to cause disease in healthy adult humans. Some examples of agents studied at this level include non-pathogenic e-coli and other non-infectious bacteria and viruses. Biosafety level 2 is for agents that have the potential to pose a moderate hazard to people and the environment. Examples of pathogens that require this level of biocontaiment include Hepatitis A, B and C, Salmonella and mumps.[4] BSL 2 requires that research personnel had specific training in handling pathogenic agents, access to the laboratory is limited while work is being conducted, extreme precautions are taken with contaminated sharp items and procedures that could create infectious splashes and aerosols are conducted in biosafety cabinets.[5] Biosafety level 3 is for pathogens that can cause serious and lethal disease after inhalation, but for which treatment is available, including *Yersinia*

[4] United States of America. The Centers for Disease Control. Safety, Health and Enviroment. *Biosafety in Microbiological and Biomedical Laboratories*. 5th ed. Atlanta: CDC, 2009. Print

[5] The Centers for Disease Control. Safety, Health and Enviroment. *Biosafety in Microbiological and Biomedical Laboratories*

pestis, SARS and rabies. Work is conducted in a laboratory facility that has all of the air filtered before being discharged outdoors, ventilation that is balanced to provide directional airflow into the room, restricted access while research is in progress, work is conducted in biosafety cabinets and appropriate protective gear like masks and faceplates are worn.[6] Biosafety level 4 is the most secure level and is for work with exotic and dangerous pathogens for which there is no cure or vaccine available like Ebola, Marburg and other hemorrhagic fevers. Defining features of this level of biocontaiment are the use of a positive pressure suit with a segregated air supply, decontamination showers, and other decontamination processes.[7] The laboratory is in an isolated part of the building, has tightly controlled access and is usually negatively pressurized to prevent any chance of the pathogen escaping. There are currently only fifteen BSL-4 labs in the United Sates.

Depending the type of research conducted within the lab, it may be required to register with the Centers for Disease Control's (CDC) Division of Select Agents and Toxins (DSAT). DSAT regulates a list of select agents and toxins that "could pose a severe threat to public health and safety."[8] DSAT- co-maintains the list, called the National Select Agent Registry (NSAR) with The Animal and Plant Health Inspection Services (APHIS). Included on the list are pathogens such as *Yersinia pestis* (plague), Variola major virus (smallpox) and Ebola. Labs that work with agents on the list are required to be registered with DSAT and APHIS so that they can inspect the facilities

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[6] The Centers for Disease Control. Safety, Health and Enviroment. *Biosafety in Microbiological and Biomedical Laboratories*

[7] The Centers for Disease Control. Safety, Health and Enviroment. *Biosafety in Microbiological and Biomedical Laboratories*

[8] "Regulation of Select Agents and Toxins." *Centers for Disease Control and Prevention*. Centers for Disease Control and Prevention, 26 July 2013. Web. 23 July 2014.

where the agents are worked on, run security risk assessments on people working with the agents and investigating lab accidents that occur with select agents. Notably not included on the list are other virulent pathogens such as *influenza* and *neisseria meningitides*, which can spread easily, and have the potential for a high mortality rate.

BSL 1, 2 and 3 labs are widespread throughout the world. BSL 1 labs generally do not pose at risk to the community, but BSL 2 and BSL 3 labs can potentially harbor dangerous pathogens that could cause harm. BSL 2 labs are quite common and while they work with pathogens that have less potential to start an outbreak, this does not mean that the pathogens are harmless. In fact, quite the opposite is true where many of pathogens can kill quickly and easily, such as certain strains of influenza or *n. meningitides* (which causes meningitis). While pathogens that require this level of biosecurity do not have a combination of factors that would require a higher level of biocontainment (such as either high virulence and transmissibility, but not both), they can still easily kill. BSL 3 labs on the other hand work with pathogens that can are quite virulent and infectious. Currently there is no United States federal government organization that is in charge of registering and inspecting all BSL 3 labs. The CDC's DSAT and APHIS do require that they inspect labs using the select agents list. However, this only covers a subset of BSL-3 labs, and there are labs that conduct BSL 3 and BSl 2 research with pathogens that can cause a lot of harm and destruction if accidently released into the population, such as influenza. Furthermore, the lack of federal oversight raises concerns about the proliferation of biological research for use in homegrown bioterrorism.

While bioterrorism is a rare event, two recent events, the 2001 Anthrax mailing and the 2013 ricin letters illustrate the growing risk and ease of bioterrorism. This is

even more concerning with the growth of the DIY bio and "biohacking" movements, which support amateur biological research and experimentation. There are even biohacking facilities, like New York City's Genspace and Sunnyvale CA's Biocurious, that are shared lab facilities where individuals can rent lab bench space on a monthly basis, though the work done in these facilities is basic in nature. More concerning are bio incubators, which operate as spaces for startup biotechnology companies and are becoming increasingly common. Some examples of bio incubators include the California Institute for Quantitative Biosciences and Berkley Bio Labs, both in San Francisco Bay Area. The varying nature of the research conducted within the facilities, and the lack of a central reviewing board, like an Institutional Biosafety Committee that would be found at an academic institution or large biotechnology company, results in gaps of oversight. This in turn breeds risk of bioterrorism, as it creates an opportunity for the cultivation and modification of an agent used for such an event free from the preventive safeguards normally found in private companies, federal labs, and academic institutions.

Much more worrisome is the greater risk of a pathogen escaping a lab. Prior studies have shown that lab workers tend to have a higher incidence and risk of becoming infected with certain pathogens relative to the general population.[9] There is a risk of a lab worker bringing home a dangerous pathogen that could start in an outbreak with disastrous consequences. Compounding this risk is the growth of genetic engineering and synthetic biology in research projects. These techniques can be used to make pathogens safer to handle or more virulent to study the effects of vaccines on it. A notable example of this is the recent work of Dr. Yoshihiro Kawaoka and his creation of an H1N1 strain

[9] Singh, Kamaljit. "Laboratory-Acquired Infections." *Clinical Infectious Diseases* 49.1 (2009): 142-47. Web.

that can avoid human antibodies. The risk is that this kind of research, called gain of function research where the researcher tries to induce new characteristics in a pathogen, can occur in a lower biosafety level than in probably should be conducted at. Dr. Kawaoka's work occurred in a BSL-2 lab, even though the resulting strain was an incredibly deadly pathogen that was designed to evade the immune system. This incident highlights the need for more stringent regulations of the products that result from genetic engineering and biosafety.

Up until recently, the majority of the government's focus was on BSL 4 labs because of the virulence of the pathogens that they work with. However, with the recent events at the CDC and NIH, the attention is now justifiably focused on BSL 3 and BSL 2 labs. While certainly BSL 4 labs get the most press because of their high security and the exotic nature of their research, it is the lower level labs that pose the greater risk. At BSL 4 facilities, there are redundancies upon redundancies with security, and while one layer may be breached, as of now there has not been a major collapse of all the layers of security. But BSL 3 and BSL 2 labs do not have the same amount if amount redundancies, if they have them at all, and as a result are at much greater risk of being the site of a biosafety accident. While the pathogens that require BSL 2 and BSL 3 containment have the same virulence and transmissibility as pathogens that require BSL4, they can still kill and spread throughout the population with ease. Coupled with genetic engineering and gain of function research and lower biosafety standards, the potential of creating a new strain at a lower biocontainment level is quite high and is a major cause of concern. A potential outbreak of a genetically modified pathogen would be a catastrophe that would likely become the worst biosafety accident in history.

Issue 1: The non-regulation of bio labs

Lack of Federal Regulation

There is currently no one US government agency that is in charge of monitoring all high containment (BSL 3 and 4) labs in the US, and no monitoring at all for BSL 1 and 2 labs. Even more concerning, there are no national standards for building high containment labs (HCLs).[10] This means that while generally there may be proper containment measures in place, subtle changes in design could lead to an increased risk of accidental release of a pathogen if that change undermines the containment measures.[11] Additionally, the lack of federal oversight means that there is no way to tell exactly how many HCL's there are in the US and no means of enforcing safety and design regulations.

While the NSAR keeps monitors all labs that do experiments with select agents, the scope of agents of registry does not cover all pathogens that require BSL 3 containment. The CDC's DSAT is in charge of inspecting labs that use select agents and toxins. Yet, while the number of BS 3 labs has grown, the budget of DSAT has decreased. In 2004 DSATs budget was $14.2 million and had a total of twenty-five inspectors for "150 entities with 415 BSL-3 labs according to a 2009 Government Accountability Office report. [12] Yet in 2008, the most recent data available, DSAT's budget decreased to $12.1 million and had twenty-eight inspectors for "242 entities with

[10] The United States of America. Government Accountability Office. *High-Containment Laboratories: Assessment of the Nation's Need Is Missing*. By Nancy Kingsbury, Sushil Sharma, Amy Bowser, Penny Pickett, Laurel Rabin, and Elaine Vaurio. 1st ed. Vol. 1. Washington DC: GAO, 2013. Print.
[11] The United States of America. Government Accountability Office. *High-Containment Laboratories: Assessment of the Nation's Need Is Missing*
[12] The United States of America. Government Accountability Office. *High-Containment Laboratories National Strategy for Oversight Is Needed*. By Nancy Kingsbury, Sushil Sharma, Amy Bowser, George Depaoli, Terrell Dorn, Jeff McDermott, Jean McSween, Jack Melling, Corey Scherrer, Linda Sellevaag, and Elaine Vaurio. 1st ed. Vol. 1. Washington DC: Government Accountability Office, 2009. Print.

415 BSL-3 labs."[13] Despite a more than 3-fold increase in labs to inspect and only slight increase in inspectors, DSATs budget went down by more than two million dollars. This is concerning as both private biotech ventures and academic biological research has expanded in recent years. While it is unknown at this time how exactly the decreased budget has affected the ability of DSAT to inspect labs working with select agents, the inverse relationship of the number of labs and DSAT's budget is troubling.

Additionally, the GAO released a report in February 2013 saying that very little action had been taken on their recommendations in their 2009 report, including a continued lack of standards for building HCLs and no assessment as to the US's need for HCL's.[14] They did note that the Biosafety in Microbiological and Biomedical Laboratories (BMBL), a manual that provides biosafety guidance, did have many recommendations about design, conduction and working habits for proper biosafety. However the GAO report also stated, "that guidance does not equate to standards that should be adhered to or ways to determine if such standards have been achieved."[15] Furthermore, the NIH, which co publishes the BMBL with the CDC and the US Public Health Service, has very little enforcement powers in the event of a violation is found. While they can threaten to pull funding, there is little they can do in the way of legal action.[16] The lack of a single agency that is responsible for monitoring all biological labs is the reason why proper building and safety standards are difficult to enforce.

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[13] The United States of America. Government Accountability Office. *High-Containment Laboratories National Strategy for Oversight Is Needed*.
[14] The United States of America. Government Accountability Office. *High-Containment Laboratories: Assessment of the Nation's Need Is Missing*
[15] The United States of America. Government Accountability Office. *High-Containment Laboratories: Assessment of the Nation's Need Is Missing*
[16] "Biosafety, NIH Guidelines." *NIH Guidelines*. Office of Science Policy, National Institutes of Health, 2014. Web. 23 July 2014.

Institutional Biosafety Committees

Beyond the federal level, there are very few laws that concern the oversight of HCL's. Within academic institutions an institutional biosafety committee (IBC) is mandated by NIH guidelines, but not by law (unlike Institutional Review Boards and Institutional Animal Care and Use Committees), for institutions that receive NIH funding for research involving recombinant DNA (rDNA). IBC's make sure that a research project complies with the NIH's guidelines for research involving recombinant and synthetic molecules.[17] Many institutions do have biosafety officer who review proposals. The NIH launched a registration database for IBC's but registration is not mandatory. Additionally, the NIH has guidelines on rDNA and synthetic biology that institutions are supposed to follow. Agents are divided into four subgroups based on potential harm. Varying levels of approval are needed in order to conduct an experiment, ranging from creating transgenic mice that require simply notifying the IBC to experiments that involve making pathogens more deadly and virulent (e.g. transferring resistance or making a strain airborne) that require the approval of the IBC, the NIH director and the recovery audit contractor.[18] Risk group classification depends on where the majority of the genetic code originated (e.g the BSL required for a transgenic influenza strain would be based off of where most of the genetic information came from)[19] There are many levels of notification that broadly fall under three categories: no IBC notification needed, simultaneous IBC notification with initiation of the experiment, and prior IBC and NIH notification to the stat of the experiment. Experiments that require no notification

[17] *Investigator Responsibilities under the NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. Bethesda: National Institutes of Health/ Office of Biotechnology Activities, 2014. Print.

[18] "Biosafety, NIH Guidelines." *NIH Guidelines*. Office of Science Policy, National Institutes of Health,

[19] "Biosafety, NIH Guidelines." *NIH Guidelines*. Office of Science Policy, National Institutes of Health,

generally do not take place in cells, organisms or viruses or the pathogens have been modified so that they cannot penetrate cell walls. There are also experiments that require IBC notice simultaneously with initiation. Some examples of these types of experiments involve whole plants, transgenic rodents or the formation of recombinant synthetic nucleic acid molecules containing no more than two-thirds of the genome of any eukaryotic virus.[20] Lastly there are experiments that require approval of the IBC, NIH or RAC before initiation, including experiments involving transferring of resistance, cloning toxins and human gene transfer. [21]

A major issue with IBC's is how limited they are in that they only review experiments involving recombinant DNA. Many experiments involving virulent pathogens do not involve rDNA and thus do not fall under the criteria that would be covered by an IBC. There is also a shocking lack of transparency with IBC's and reporting, where a survey done by the American Biological Safety Association showed that slightly more than half (54%) IBC's in 2007 make a formal report to an institutional official and just 15% reported from 2002-2007 incidents to the NIH.[22] While this number rose in 2010 to 31% of IBC's reporting incidents, the math reveals a startling figure. From the survey, that means that likely for the same number of incidents, 54% were reported within institutions and 15% where reported to the NIH. That means that only 28% of incidents reported to anyone at all were reported to the NIH and conversely 72% of incidents were not reported to the NIH. This illustrates a trend of the lack of transparency of IBCs. The same survey also noted that when the NIH conducted on-site

[20] "Biosafety, NIH Guidelines." *NIH Guidelines*. Office of Science Policy, National Institutes of Health,
[21] "Biosafety, NIH Guidelines." *NIH Guidelines*. Office of Science Policy, National Institutes of Health,
[22] Hackney, Raymond W., Jr., Theodore A. Myatt, Kathleen M. Gilbert, Rebecca E. Caruso, and Susanne L. Simon. "Current Trends in Institutional Biosafety Committee Practices." *Applied Biosafety* 17.1 (2012): 11-18. Web

visits incident reported was generally higher. The survey reported that of institutions that had site visits, 46% reported incidents, while those that were not visited by the NIH, 20% reported incidents. [23] Even more striking was the difference in academic institutions, where 85% of those that received NIH visits reported incidents compared to 25% that did not receive NIH visits that reported incidents.[24].

Additionally, a conflict of interest may arise, especially in private companies, where the need and desire to generate profit may overrule safety concerns. Since there is no real oversight above an IBC, there is no way to know for certain how if the NIH regulations are being followed. Most schools have IBC's, including the Bay Area's largest schools; Stanford, UC Berkley and UCSF. Stanford does not have a permanent BSL 3 facility, but allows work with BSl 3 agents with permission.[25] UC Berkley and UCSF both have dedicated BSL 3 facilities, but similarly to Stanford, both institutions allow BSL 3 research to be carried out in a BSL 2 lab with modifications to the lab.[26] [27] [28] San Francisco State University and Touro University, located in San Francisco and Vallejo respectively, also have biosafety requirements that require approval of BSL 2 and 3 agents, and BSL 3 work can be carried out in modified BSL 2 labs.[29] [30] The author of this report could not find any biosafety information for the remaining academic

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[23] Hackney, Raymond W., Jr. et al.

[24] Hackney, Raymond W., Jr. et al.

[25] "Biohazardous Agents and Recombinant DNA." *Stanford University, DoResearch*. Stanford University, 2014. Web. 23 July 2014.

[26] "University of California, San Francisco." *Genentech Hall*. SmithGroup JJR, 2014. Web. 23 July 2014.

[27] http://or.ucsf.edu/ehs/8192-DSY/version/default/part/4/data/

[28] "UC Berkeley BSL3 Facility." *UC Berkeley BSL3 Facility*. University of California Berkeley, 2014. Web. 23 July 2014.

[29] *Institutional Biosafety Committee Approved with Contingency(ies) INITIAL REVIEW FORM*. Touro University, 17 Jan. 2012. Web.

[30]"A. C.O.S.E. Biosafety Program." *A. C.O.S.E. Biosafety Program*. San Francisco State University, Dec. 2008. Web. 24 July 2014. <http://www.sfsu.edu/~safety/Web_documents/files_biosafety/BiosafetyPlan_Dec2008.pdf>.

institutions in the Bay Area that conduct biological research, which include The College of San Mateo, Mills College, Saint Mary's College of California, University of the Pacific, and Sonoma State University.

While many academic institutions have internal biosafety guidelines, it is not a universal practice. Without federal regulation to require at least registration for HCL's, there is no way of knowing the exact risk of the research conducted in these institutions. Coupled with the exponential growth of biotechnology companies in the Bay Area, many of which lack the same internal controls that are found at academic institutions, results in a frightening risk. A survey of biotech companies found in the Bay Area for this report found that there at least two hundred and nineteen biotech companies (a number which could very likely be higher).[31] While for the most part the work done by these companies does not involve infectious agents, seven work with infectious agents ranging form influenza to HIV, and nine work with recombinant DNA technologies. Additionally, there is an HCL at LLNL as well as work with both infectious agents and rDNA. Perhaps the lack of oversight has given rise to the other major issue covered in this report, laboratory accidents.

Lax Culture of Safety

In recent investigations and hearing on the CDC's anthrax incident have shed light on cultural issues at the CDC and other biological research institutions that contributed lapses in biosafety. Dr. Michael Bell, who was appointed by the Director of the CDC Dr. Thomas Frieden to investigate the incident, was "most concerned about the

[31] Appendix 3

"potential for hubris" among researchers who grow so inured to the daily grind of working with deadly microbes that they cease to follow safety protocols."[32] Researchers become so accustomed to working with dangerous pathogens that they starting to take shortcuts in biosafety. With no current threat of inspection or subsequent punishment, researches grow lax in regards to biosafety. Contributing to this lax safety culture is a "lack of managerial control" in responses to biosafety breaches and "delays in decontamination and lockdown of affected areas, unclear objectives for mid-level managers and their subordinates, and general confusion amongst responders and personnel potentially exposed to the agent (In the CDC anthrax incident)."[33] This suggests that managers were not as concerned with biosafety protocol as they should be, and that this, in the case of the CDC anthrax incident, resulted in a delay of response. Had the incident involved a more infectious agent, such a delay could have been quite deadly. The lackadaisical attitude towards biosafety resulted in a lack of action during a crisis, which is frightening considering that the CDC is supposed to be the United States' highest defense against public health threats. This complacence leads to risks and accidents, as was so dramatically demonstrated in the CDC anthrax incident. In order for this culture to change, there needs to be harsher penalties and enforcement to give negative consequences for not following biosafety protocol.

A recent survey published in Nature revealed some startling statistics about the culture of laboratory safety. About 30% of lab workers had witnessed a major lab injury (that required attention from a medical professional) and only 60% said that had received

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[32] Fausset, Richard, and Donald G. McNeil, Jr. "After Lapses, C.D.C. Admits a Lax Culture at Labs." *The New York Times* 14 July 2014: A1. Print.

[33] The United States of America. Animal and Plant Health Inspection Service. United States Department of Agriculture. By Unknown. 1st ed. Vol. 1. Washington DC: USDA, 2014. Print.http://apps.washingtonpost.com/g/page/national/usdas-anthrax-inspection-report/

safety training on the specific hazards that they worked with.[34] Additionally the survey found that "the biggest barriers to improving safety in the lab were 'time and hassle' and 'apathy" and two-fifths (of lab workers) felt that safety training "focused on training compliance regulations rather than on improving laboratory safety."[35] These results provide further evidence to the relaxed culture of biosafety and the commonness of serious incidents occurring. Additionally, the survey suggests that one reason for this culture is the current regulations and safety training sessions because of their focus on "compliance" with federal regulations rather than actual safety.[36] While "time and hassle" are unfortunate byproducts of regulation, they are necessary to get such regulation in place. That researchers become inured to the dangers of laboratory research is a simple result of the repetitive nature of work and comfort with the workplace feedback. But without a system of negative feedback, there is no reason why these behaviors would naturally be rectified. Because of the way the current system is structured; there is no standard set of punishments or ways of holding labs with relaxed safety standards accountable, this attitude is allowed to fester and grow.

Genetic Engineering

Lastly it is important to note the risk associated with genetic engineering, synthetic biology and biosafety. An important takeaway from the aforementioned Dr. Kawoka's experiment, where he created a strain of H1N1 (swine) flu that could evade the body's immune system, is that is was conducted at a BSL 2 level facility. In regards to

[34] Van Noorden, Richard. "Safety Survey Reveals Lab Risks." *Nature.com*. Nature Publishing Group, 2 Jan. 2012. Web. 30 July 2014. <http://www.nature.com/news/safety-survey-reveals-lab-risks-1.12121>.
[35] Van Noorden, Richard. "Safety Survey Reveals Lab Risks."
[36] Van Noorden, Richard. "Safety Survey Reveals Lab Risks."

genetic engineering, biosafety level is determined by the danger of the initial pathogen, not the new one created by the experiment. The disturbing fact is that a new pathogen could be created, one that may require a biosafety level far above the original strain, in a facility that is equated to handles its virulence. This kind of research is called "gain of function research" where scientists try and induce mutations into pathogens to see the potential results these mutations could have on the pathogens' function.[37] However, current NIH guidelines stipulate that biosafety level is determined by where the majority of the genetic information of the strain originated, which does not take into account that only a small mutation or gene insertion may be required to dramatically increase the virulence of the pathogen.[38] As such the facility may not be equipped to handle as dangerous a pathogen as the one they created.

Issue 2: Laboratory Accidents

Despite the best efforts of researchers in academic, private and federal settings, laboratory accidents occur. Lab accidents can include chemical explosions and exposure, equipment malfunction, and most worrisome, a breakdown in biosafety protocol that results in a laboratory acquired infection (LAI) or accidental release of a pathogen.[39] A survey conducted for this report found nineteen lab accidents that have occurred in the bay area since 1977. Eleven of these incidents involved mishandling of pathogenic agents; including risky biowarefare agents' anthrax and Q fever.

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[37]Garret, Laurie. "It's 10 O'Clock -- Do You Know Where Your Bubonic Plague Is?" *Foreign Policy*. Foreign Policy, 10 July 2014. Web. 24 July 2014.
[38] Lipkin, W. I. "Biocontainment in Gain-of-Function Infectious Disease Research." *MBio* 3.5 (2012): E00290-12. Web.
[39] Singh, Kamaljit. "Laboratory-Acquired Infections." *Clinical Infectious Diseases* 49.1 (2009): 142-47. Web.

Laboratory acquired infections occur when a researcher working a biological lab becomes infected with a pathogen that they are working with. Common LAI's include *n. meningitides, f. tularensis, bacillus anthracis*. and hepatitis B.[40] While generally these pathogens are secured in labs, accidents do occur. Once a person has become infected, they could easily spread the infection to others, starting an outbreak. Even more troubling is if the person is infected with a pathogen, like Ebola, that not commonly found in an area like the Bay Area or a pathogen that has been genetically modified to become deadlier. This is would lead to the deadly spread of a pathogen in a population that is susceptible to it due to either never been exposed to said pathogen and thus little to no naturally occurring immunity or a pathogen that was designed to kill. Luckily such an outbreak has never occurred, but could very well happen.

Worldwide several biosafety accidents illustrate the danger in lapses of biosafety. One of the more dangerous LAI's occurred in 1994 when a Yale research was infected with the Sabia virus, also known as Brazilian hemorrhagic fever, after a test tube containing the virus shattered. This incident was similar to a number of other LAI's involving similar hemorrhagic fevers at Yale, which raised questions about the safety of research at the university.[41] The researcher ultimately recovered, but his infection with a pathogen as deadly as Sabia was disturbing. In 2004, a Russian research scientist at Vector, Russia's State Research Center of Virology and Biotechnology accidentally pricked herself with a needle laced with the Ebola Virus and died.[42] Troublingly, the lower level officials at Vector did not notify its own lab directors or the WHO of the

[40] Singh, Kamaljit. "Laboratory-Acquired Infections."
[41] Altman, Lawerence K. "The Doctors World; Researcher's Infection Raises Concerns for Laboratory Safety." *The New York Times* 23 Aug. 1994: n. pag. Print.
[42] Miller, Juith. "Russian Scientist Dies in Ebola Accident at Former Weapons Lab." *The New York Times* 25 May 2004: n. pag. Print

accident until weeks after it had occurred.[43] While the infection was not transmitted to anyone else, the lack of transparency and accountability could have led to disastrous consequences. More recently, a laboratory-acquired infection at Texas Agriculture & Mining University (TAMU) went unreported in 2006.[44] The significant factor was that the lab worker was infected with a selected agent, *Brucella,* a select agent for which she was not trained to work with, and the CDC was not notified until weeks after the infection.[45] While the infection was not transmitted to anyone else, the egregious biosafety lapse of the lab worker being allowed to work on a pathogen for which she did not have proper training for is disturbing. Lastly, in 2007, an outbreak of foot and mouth disease in the United Kingdom was traced back to the Pirbirght Lab Site, which was home to the United Kingdom's Institute for Animal Health and Merial Animal Health ltd. Poorly kept facilities and drainage were attributed to the outbreak. [46] Ultimately about 2,600 animals were infected, causing ultimately two hundred million dollars in damage from lost trade and response. [47] These three incidents demonstrate the severe consequences of biosafety lapses worldwide and the Bay Area is no exception. The survey of Bay Area biological accidents revealed a history of near misses and deaths.

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[43] Miller, Juith. "Russian Scientist Dies in Ebola Accident at Former Weapons Lab." .
[44] United States of America. Government Accountability Office. *High- Containment Biosafety Laboratories; Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*. By Keith Rhodes. 1st ed. Vol. 1. Washington D.C.: GAO, 2007. Print.
[45] United States of America. Government Accountability Office. *High- Containment Biosafety Laboratories; Preliminary Observations on the Oversight of the Proliferation of BSL-3 and BSL-4 Laboratories in the United States*.
[46] "Pirbright: Labs at Centre of Outbreak." *BBC*. BBC, 14 Sept. 2007. Web. <http://news.bbc.co.uk/2/hi/uk_news/6931830.stm>.
[47] "At What Cost? 2001 and 2007 Foot and Mouth Disease Outbreak United Kingdom." *Oklahoma Department of Agriculture Food and Forestry*. State of Oklahoma, n.d. Web. <http://www.oda.state.ok.us/ais/atwhatcost.pdf>.

A Brief Review of Biological Lab Accidents in the Bay Area

Our review of lab accidents went back forty years. The first incident in this time frame was a 1977 lab explosion at Oread Inc, a now defunct pharmaceutical company. The period from 1986-1988 was a particular bad period with 4 serious accidents occurring, which ranged from lab explosions[48], a near accidental release of plague (*Yersinia pestis*)[49] and a laboratory worker infected by meningitis.[50] The most egregious violation of biosafety during these years was the US Army's plan to mail pathogens that could be used as biowarfare agents.[51] The obvious risk was that a leak, while unlikely, would easily spread the pathogen throughout the country while it was being mailed. Additionally there was the risk that groups working against the United States could intercept the package. While the packages had many safeguards, even Fort Detrick scientists felt that the risk was too great.[52]

In the 1990's there were two lab explosions, one of which in 1996 resulted in exposure to a harmless bacterium *bacillus stearothermophilus* when a vial being heated with the organism exploded and injured six people.[53] While thankfully there was not a harmful pathogen in the vial when it exploded, the potential of what could have happened illustrates how risky sometimes bio labs can be to work in. In 1999 there was a controversy over a GlaxoSmithKline employee who was reusing needles to draw blood

[48] Two injured in accident at lab at S.F. General: [FOURTH Edition] San Francisco Examiner [San Francisco, Calif] 12 Sep 1998: A-3
[49] Bubonic Plague Bacteria Spilled in S.F. State Lab Diane Curtis, Michael Harris. San Francisco Chronicle
[50] "Epidemiologic Notes and Reports Laboratory-Acquired Meningococcemia -- California and Massachusetts." *Morbidity and Mortality Weekly Report*40 (25 Jan. 1991): 46-47. Print.
[51] Pollack, Andrew. "Army Plan to Mail Warfare Toxins Draws Protest." *The New York Times* 13 June 1988: n. pag. Print.
[52] Pollack, Andrew. "Army Plan to Mail Warfare Toxins Draws Protest."
[53] "Vial With Germ Explodes in Lab -- 6 Injured, Clinic Evacuated." *San Francisco Gate Chronicle* 16 July 1996: n. pag. Print.

for testing, putting many at risk for infection by bloodborne pathogens like HIV.[54] This was a gross violation of biosafety that led to a class action lawsuit against GSK.

In the early 2000's there were two widely published security breaches at LLNL. In 2003 a pair of security keys went missing. While they would not have necessarily allowed access to sensitive parts of the lab due to redundancies in security, was a concerning lapse in security for a lab that works with dangerous pathogens for biodefense and nuclear research.[55] Then in 2005, a shipment of anthrax was packed by LLNL workers improperly and leaked.[56] Luckily no anthrax leaked out of the package, but as with similar cases, the ultimate damage could have been significantly greater.

Lastly, three recent lab accidents highlight the continued danger that lapses in biosafety can pose to lab workers and the surrounding community. In 2004 Oakland Children's Research Hospital worked with live Anthrax spores, thinking that they were killed. In actuality, the company they ordered from had not fully killed them, which resulted in eight workers being forced to take a regimen of antibiotics in case of exposure.[57] A similar accidental exposure to anthrax, where the spores where not properly killed, occurred this year in Atlanta, where 84 CDC personnel were exposed to anthrax spores that had gone though the killing process for the requisite amount of time.[58] The Sunshine Project, a now defunct NGO that focused on uncovering bio lab accidents and lapses in biosecurity, discovered that in 2005 researchers at UC Berkeley has accidentally

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[54] Chase, Marilyn. "A Safer Medical Needle Shouldn't Be Quite so Hard to Find." *The Wall Street Journal* [New York CIty] 26 Apr. 1999: n. pag. Print.
[55] Livermore lab security keys disappear FROM STAFF AND WIRE REPORTS. Oakland Tribune [Oakland, Calif] 15 May 2003: 1.
[56] Mason, Besty, Jia-Rui Chong, and Carol Eisenberg. "UC Fined for Livermore Lab's '05 Anthrax Leak." *San Jose Mercury News* 10 May 2007: n. pag. Print.
[57] Kunkle, Fredrick. "Md. Lab Ships Live Anthrax In Error U.S. Investigating; Calif. Workers Given Antibiotics." *Washington Post* 12 June 2005: B05. Print.
[58] Steenhuysen, Julie, and Sharon Begley. "Anthrax Scare: CDC Lab Didn't Heed Its Own Lessons."

left a container of Rocky Mountain Spotted Fever out in the lab with no containment because it has been mislabeled as harmless.[59] This bacterium is airborne and can cause an extremely life threatening condition in humans. Then in 2012 a lab assistant at the San Francisco VA medical center became infected with n. meningitides, serotype B, for which there is no vaccine, and died.[60] These three incidents illustrate how even in recent years, with advances in technology and biosafety practice, dangerous and fatal accidents can still occur.

Why Do Accidents Matter?

While nineteen accidents in forty years may not seem like an exorbitant amount, there are a couple of important issues to consider. First, despite the low chance of biosafety accidents occurring, more than half of the ones found in the survey involved infectious agents. In all the incidents except those involving anthrax, which is deadly to individuals but cannot be transmitted form person to person, an outbreak could have resulted if the disease had by chance managed to infect others the lab worker came in contact with. Just because this did not happen does not mean that it will not in the future. Secondly, only labs that received NIH funding are required to report lab accidents, but there are no penalties not doing so.[61] This means that there are likely many more lab accidents that have occurred and gone unreported. The combination of these two things is worrying, as in the future it could result in an incident going unreported, and leading to

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[59] Mackenzie, Debora. "Plague of Bioweapons Accidents Afflicts the US." *New Scientist* 5 July 2007: n. pag. Print.
[60] Standen, Amy. "Lab Accident at San Francisco VA Leaves Man Dead of Bacterial Meningitis." *KQED News Fix*. Public Media for Northern California, 2 May 2012. Web. 24 July 2014. <http://blogs.kqed.org/newsfix/2012/05/02/lab-accident-at-san-francisco-va-leaves-man-dead-of-bacterial-meningitis/>.
[61] Miller, John. "Biosafety Labs Urged to Report Accidents and near Misses."*News@nature* (2007): n. pag. Web.

an outbreak stemming from a laboratory acquired infection that could have been stopped earlier if the infected lab worker had been quarantined. The aforementioned issue of the lack of oversight of biological labs means that there is still no mechanism in place to make sure that A) biosafety protocols and design are properly being implemented and B) lab accidents that could potentially threaten the surrounding community are reported.

Two recent high profile incidents illustrate how pressing of an issue biosecurity is. In June 2014, eighty four CDC employees were exposed to live Anthrax spores that were supposedly killed. Then, in July 2014, vials of freeze-dried smallpox were found in a little used storage room at the NIH. While luckily in both incidents no one was infected, the potential for what could have happened is frightening. Additionally, a subsequent investigation of the CDC anthrax incident by APHIS revealed shocking lapses in biosecurity. Some of these included inadequate inactivation protocols in the lab, the use of expired disinfectant, inadequate training of lab personnel for handling select agents, the use Ziploc bags to transport infectious materials "which do not meet the 'durable' requirement for secondary containment," storage of anthrax in unlocked fridges with unrestricted hallways and unrestricted access to the lab.[62] The APHIS report demonstrates that even at a supposedly highly secured federal facility, significant and severe accidents still occurred. It is even more worrisome to consider that if an accident this egregious could occur at a highly reregulated facility, what could happen at an much more lightly regulated private facility or academic institution. A major catastrophe was

[62] The United States of America. Animal and Plant Health Inspection Service. United States Department of Agriculture. By Unknown. 1st ed. Vol. 1. Washington DC: USDA, 2014. Print.http://apps.washingtonpost.com/g/page/national/usdas-anthrax-inspection-report/1179/

averted when no one became infected, but if someone had, particularly with smallpox, a major public health crisis would have occurred.

Potential Solutions

Expanding oversight could likely solve both issues with biological lab safety. This would address both the lack of regulation, which in turn would likely lead to a decreased risk of lab accidents occurring. There are two types of regulation, the local level, and the federal level.

Federal Level Solutions

One method of increasing federal oversight would be to expand DSAT's power to enforce bio labs by lengthening the select agent list, which would give DSAT the ability to inspect more labs. Expanding the list to include diseases like influenza and tuberculosis would give DSAT broader authority to inspect labs. DSAT currently has the ability to revoke the use of select agents, levy fines in the form of civil money penalties and imprison people who are not registered to possess select agents but do so any way, or a registered person who transfers a select agent to a unregistered person.[63] If DSAT is allowed to use its regulatory powers on a wider variety of labs, then it can cover new areas where it could not before.

While expanding the select agent list could alleviate some of the gaps in regulation, it would be difficult to expand the list to such an extent that would cover all possible pathogens and allow DSAT to work effectively. Another way around this would be to make IBC registration mandatory with the NIH and give the NIH's Office of Science Policy (OSP) regulatory powers with inspections, the ability to levy fines and

[63] "General FAQ's about Select Agents and Toxins." *National Select Agent Registry*. Centers for Disease Control and APHIS, 23 May 2014. Web. 24 July 2014. <http://www.selectagents.gov/FAQ_General.html>.

possibly stipulate prison time for individuals These results from the aforementioned ABSA survey where of institutions that had site visits, 46% reported incidents, while those that were not visited by the NIH, 20% reported incidents suggest that site visits could help with reporting incidents to an extent and perhaps if more NIH site visits were scheduled, than better regulation and oversight could be achieved. Doing so would likely require an expansion of the OSP's role and funding so that so that more visits could be scheduled.

Alternatively, a new agency could be created, or regulatory power could be assigned to another agency, in order to provide oversight. The reasoning behind this, as biosafety expert Richard Elbright noted in a recent hearing on the CDC Anthrax biosafety lapse, that there is a conflict of interest with the CDC and NIH both monitoring select agents and using them for research.[64] Thus, it is a possibility, such as one that is being explored in the current CDC Anthrax investigation, that in labs that are part of the same organizations that monitor select agents or regulate experiments with rDNA, could be subject to less oversight than outside labs in an effort to maximize productively at the expense of safety. An outside agency that is solely devoted to monitoring HCLs would be free of this conflict of interest, and could also help keep track of all HCL's not just ones that use select agents. In fact it was the recommendation of Dr. Nancy Kingsbury, Managing Director for Applied Research and Methods at the Government Accountability Office, to create an independent HCL monitoring agency. This new agency could both establish federal biosafety standards, investigate and inspect HCL's to make sure that

[64] *Review of CDC Anthrax Lab Incident: Hearing before the House Committee on Energy and Commerce*, 113th Cong. (2014) (testimony of Richard Elbright).

they are complying with said standards, and meter out punishments and fines as necessary.

Another way to ensure more federal oversight is to require IBC's to create both an accreditation organization for IBC's and an accrediting process, similar to the Association for Assessment and Accreditation of Laboratory Animal Care for IACUC's and the Association for the Accreditation of Human Research Programs for IRBs.[65] Both of these organizations require site visits and program reviews form peers outside the institution.[66] An accreditation process would help make IBCs more accountable by ensuring proper training for IBCs, having site visits to labs to make sure they have the proper biosafety conditions and a more formal reporting process. Approaching the issue of regulation of biological labs from the perspective of IBCs has an advantage in that it utilizes an existing mechanism of reporting and guidelines and makes them more enforceable and accountable. This would mostly avoid the need to create new bureaucracy outside of an accreditation organization.

Lastly there should be a consideration at least to revise, if not completely redefine the existing classification levels. The levels were first defined in the 1970's and while there are now NIH guidelines for rDNA research, there still is some confusion over proper biosafety protocols.[67] As explored earlier, current NIH protocols states that biosafety level is determined by the IBC, and in part by the genetic material used in the experiment. Yet, the recent work of Dr. Kawoka and the creation of an undetectable H1N1 strain in a BSL 2 lab illustrate how the current system of classification may be

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[65] Hackney, Raymond W., Jr. et al.
[66] Hackney, Raymond W., Jr. et al.
[67] Connell, Nancy. *BRIEF HISTORY OF BIOSAFETY*. Rep. 1st ed. Vol. 1. Washington DC: Federation of American Scientists, 2011. Print.

flawed. Some similar pathogens also recommended for BSl 2 containment include N. meningitides, which causes bacterial meningitis, Helicobacter pylori, which causes gastritis and stomach ulcers, and Herpes viruses. While these agents can cause relatively high morbidity or mortality, they generally do not present a high risk of infection and transmissibility from person to person. By contrast, Dr. Kawoka's H1N1 strain is both highly infections, and lethal, in that it avoids immune system detection. This genetically engineered pathogen is much more virulent and infectious then other pathogens stored at this level, suggesting that in the age of genetic engineering the current biosafety levels are not detailed enough. In this report we have seen examples of both BSL 2 plus and BSl 3 plus, where existing BSl 2 and 3 facilities were modified to perform experiments at biosafety level higher than for which it was originally designed. A new system of biosafety levels could allow for reduced risk when attempting to create new strains, while also negating the need to resort to performing all research in ultra high containment BSL 4 labs. For example, Dr. W Ian Lipkin Writes "In lieu of a shift to BSL-4, it may be feasible to introduce specific requirements for research at BSL-3-Ag for agents with pandemic potential, particularly research concerned with a gain of function that enhances virulence or transmissibility."[68] He suggests that perhaps there should be a new biosafety level between 3 and 4 that takes precautions against increased virulence while also acknowledge the fact that said research does not need to be limited to expensive and are BSL 4 labs. Similarly, a new level between BSL 2 and BSl 3 would operate on the same principle. A revision of the biosafety levels would both help ensure proper

[68] Lipkin, W. I. "Biocontainment in Gain-of-Function Infectious Disease Research." *MBio* 3.5 (2012): E00290-12. Web.

biocontainment methods, while simultaneously preventing an over restriction for research to ultra high containment labs.

Local Level Solutions

Local level solutions involve city governments and community partnerships. One possible solution would be to be for cities in the Bay Area to require that labs become registered with them, similarly to the city of Boston. Boston defines a laboratory as a "building, room, or workplace designed and/or used for the development, conduct, or observation of scientific, including but not limited to the medical, chemical, physical, or biological disciplines, experimentation or research, including non-routine testing, analysis, experimentation, or other similar activities that involve the use or storage of hazardous materials."[69] The city requires that all labs are registered and have licenses for the storage of flammable liquids and gases. Additionally, it requires that chemical waste, chemical storage, BSL 3 and 4 agents and other equipment is located on architectural plans. [70] The purpose of registration is to help first responders accurately prepare in case of an emergency at a laboratory facility and to allow of the inspection of labs to enforce biosafety requirements. [71] The registration also gives the city a record of the type and extent of research being done within its boundaries. A similar piece of legislation enacted in Bay Area Cities would allow first responders to be better prepared for emergencies, create a growing record of labs and research in the area and help enforce biosafety regulations though the use of inspections and fines by the cities. This approach would

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[69] "Laboratory Registration." *The City of Boston*. The City of Boston Government, 2014. Web. <http%253A%252F%252Fwww.cityofboston.gov%252Ffire%252Fprevention%252Flab.asp>.
[70] "Laboratory Registration." *The City of Boston*.
[71] Lok, Corie. "Boston to Require Labs to Register with Fire Department."*Boston Blog*. Nature, 10 June 2006. Web. 24 July 2014. <http://blogs.nature.com/boston/2006/06/10/boston-to-require-labs-to-register-with-fire-department>.

partially negate the need for a larger federal presence because of the inspections by the city, though NIH oversight would be needed for assessments of the dangers of the research, particularly if it involves rDNA.

A second approach involves encouraging labs to form partnerships with the community. An example of this is Ft. Detrick in Maryland, which formed an affiliation with the city of Fredrick, Maryland's, Containment Lab Community Advisory Committee (CLCAC). [72] CLCAC helps foster communication between the City of Fredrick and Fort Detrick. It is charged with answering questions from the general public about safety concerns with the activities in Ft. Detrick, gathering safety performance data and is attempting to compile a list of all BSL 3 labs in Fredrick County, MD. The CLCAC helps increase transparency with Fort Detrick and other HCLs in Fredrick County by providing a process for the public to submit questions about work being done in HCL's and to become more informed about the research.[73] This model may be a good one for organizations like LLNL, LBNL and academic institutions in the Bay Area to follow in order to foster a good transparent relationship with the surrounding community. Yet this approach is not a comprehensive as the previous two and it would not make sense to form a committee for every single biotech or biological research institution. Additionally, there the CLCAC noted in its 2013 review that it still had some difficulties with communicating with the public and HCL's.[74] They are still determining the best methods of doing both, and thus other communities that want to follow this model should bear in

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[72] "Containment Lab Community Advisory Committee." *The City of Fredrick, MD*. The City of Fredrick, MD, 2014. Web. <https%3A%2F%2Fwww.cityoffrederick.com%2Findex.aspx%3FNID%3D564>.
[73] *The Containment Laboratory Community Advisory Committee (CLCAC) Second Annual Report*. Rep. 1st ed. Vol. 2. Fredrick MD: City Of Fredrick MD, 2012. Print.
[74] *The Containment Laboratory Community Advisory Committee (CLCAC) Third Annual Report*. Rep. 1st ed. Vol. 3. Fredrick MD: City Of Fredrick MD, 2013. Print.

mind that it is still a work in progress. Perhaps a solution would be for each town and city or county to form a committee that is in charge of this transparency effort. This would be a good measure to implement in tandem with the others since it easy to implement and helps improve relationships with HCL's and their surrounding communities.

Conclusion

Biotechnology has a lot of promise to solve many pressing issues in society today. But that potential should not outweigh the need to conduct research in a safe manner. The lack of both federal and state oversight for HCL's and the risks stemming form the non-existence of a biosafety standard are unacceptable. While lab accidents are rare events, it only takes one case of an LAI being transferred from person to person to stark an outbreak. Until there is more federal oversight and enforcement of biosafety procedures that risk will still remain. This risk has increased exponentially in the San Francisco Bay Area where the biotech industry, academic research institutions and federal labs have grown in number in recent years. The rapid growth has made it difficult to pin down the exact number of labs and the type of research they are doing.

Some of the solutions to this problem included expanding the select agent list to give DSAT more authority to inspect more labs. Another way to expand federal oversight would be to require that IBC's are both mandatory at institutions doing research with rDNA, forming an accrediting organization to hold IBC's to a standard to enforce that started, and lastly to require at all IBC"s are registered with the NIH. This would help ensure that IBC's are going their job properly and there is a way of enforcing this. A third suggestion is to follow the model set forth by the city of Boston and require that all labs are registered with the city so that first responders will have accurate information to

prepare in the event of an emergency. Boston also carries out inspections of labs to make sure that proper biosafety practices are being followed. Lastly, a fourth option could be to form city or county level committees that are tasked with fostering transparent communication with the HCL and the surrounding community in order to help the community hold the lab accountable.

It is likely that a successful solution will use a combination of these suggestions in order to truly provide a comprehensive resolution to the problem. No single suggestion will result in ensuring that the proper oversight is in place, and it is likely that some combination of state and federal regulation is put into place. Regardless of whatever method or methods is chosen, the recent biosafety lapses at the CDC with anthrax and at the NIH with smallpox underscore the need for new regulations of high containment labs and the ongoing risk of a lack of oversight. Perhaps these new high profile incidents will spurn the government into action to address this issue before a more serious one arises.

Appendix
1. List of Bay Area Lab Accidents

Table of Lab Accidents in the San Francisco Bay Area		
Date	Description	Location
1983	Q fever infection found in lab workers	UCSF medical Center
3/7/86	Plague Spill	SFSU
6/1/88	Army to mail toxins to CA labs	
8/3/88	Lab Worker Infected with Meningitis and later died	Northern California
9/12/88	2 injured in Lab Explosion at SF General	SF General Hospital
3/10/95	Explosion in a pharmaceutical lab injures professor	UCSF
7/16/96	Lab Explosion / germ exposure	Drew Clinic, East Palo Alto
1/21/97	Chemical explosion, 0 injured	Oread Inc
4/26/99	Reusing of Needles at GSK	GlaxoSmithKline Palo Alto
5/1/03	Lapse in Security at LLNL	LLNL
2004	Accidental experiments with live anthrax,	Oakland Children's Hospital
6/17/05	Meningitis sample accidentally mailed to family	San Francisco (San MateoHealth Dept mailed to Berkley
10/5/05	Improper Anthrax Handling	Lawrence Livermore National Lab
2005	RM spotted fever mishandled at UC berkley	UC Berkely
6/1/06	Lapse in Security at LLNL	LLNL
2008	Allergan found to not have IBC	Allergan
4/26/11	Chemical Explosion, 2 injured	Agilent Technologies
5/2/12	Death by bacterial Meningitis	SF VA hospital
1/9/14	Lab Explosion	Amgen

2. Explanation of Biosafety Levels

Biosafety Level (BSL)	Requirements
BSL 1	• Suited for work with agents not known to cause human disease • Minimal protection (generally just gloves) • Decontamination procedures relatively minimal (hand washing, autoclaved glassware etc) • Lab not separated form general traffic pattern of the facility
BSL 2	• Suited for work involving agents that pose a moderate hazard to the environment and personnel • Lab personnel have training in handling pathogenic agents • Access to lab is limited while work is being conducted • extreme precautions are taken with sharp items • procedures that could result in aerosols and splashes are conducted in a biosafety cabinet
BSL 3	• BSL 2 requirements + • Recommended double zone access doors and sealed penetrations • All proceeds involving infectious materials are done in biosafety hoods • Filtered air exhaust from lab is discharged into the room • Access to the lab is more restricted • Protective suits, face masks/guards may be needed
BSL 4	• BSL 2 and 3 requirements + • positive pressure suits with separate oxygen supply • work is confined to class III biosafety cabinets • the room has directional airflow and negatively pressurized facilities

3. List of Biotech Companies, Academic institutions and Federal and State Labs doing Biological Research

means Genetic Engineering | means works with infectious disease

Name	Website	Status	Research and Products	Address	BSL
Amyris	http://www.amyris.com/		biofene based products	5885 Hollis Street, Ste.100 Emeryville CA 94608	
DynaVax	http://www.dynavax.com/	Public	TLR based drug candiates	2929 Seventh Street, Suite 100 Berkeley, CA 94	Unknown (UK)
XOMA corp	http://www.xoma.com/	Public	thepeudic antibodies	2910 Seventh Street Berkeley, CA 94710	BSL 2
Kiverdi Inc	http://www.kiverdi.com/	Private	sustianaible chemicals	2929 Seventh Street, Suite 120 Berkeley, CA 94	UK
Molecular Sciences Institute	http://www.molsci.org/	Non Profit	algae fuels	2168 Shattuck Ave 2nd Floor, Berkeley, CA 9470	UK
Caribou Life Sciences	http://www.cariboubiosciences.com/	Private	bioengineering	2929 7th Street, Suite 120 Berkeley, CA 94710	UK
Lygos Inc	http://lygos.com/	Private	GMOs that produce chemicals, fuels etc	636 San Pablo Ave. Albany, CA 94706	UK
Pivot Bio	http://www.pivotbio.com/	Private	genome scale programming of microbes	1700 4th Byers Hill 214 San Francisco, CA 9415	UK
Universal Bio mining	http://universalbiomining.com/?page_id=5	Private	bioengineering to reduce envriomental ir	665 3rd Street Suite 250 San Francisco, Californ	UK
Siluria Technologies	http://www.siluria.com/	Private	biofuels	409 Illinois St, San Francisco, CA 94158	UK
Solazyme	http://solazyme.com/	Public	biofuels	225 Gateway Blvd. South San Francisco, Califor	UK
Institute for One World Health	http://www.path.org/		health tech for devleoping world		UK
Sutro Biopharma	http://www.sutrobio.com/	Private	biochemical protein synthesis	310 Utah Ave, S San Francisco, CA 94080	UK
REG Life Sciences (Renewable	http://www.reglifesciences.com/	Public	renewable fuels	600 Gateway Blvd South San Francisco, CA 940	UK
Genelabs technologies	http://www.genelabs.com/	Public	Drug Discovery, HCV	505 Penobscot Drive Redwood City, CA 94063-4	UK
Codexis	http://www.codexis.com/	Public	Enzymes and Screening tools	200 Penobscot Drive Redwood City, CA 94063	UK
SRI International	http://www.sri.com/	Non-Proift	Drug Discovery, Biosynthesis	333 Ravenswood Avenue Menlo Park, CA 9402	BSL 2 and 3
Pacific Biosciences	http://www.pacificbiosciences.com/	Public	DNA sequencing	1380 Willow Rd, Menlo Park, CA 94025	UK
Affymax	http://www.affymax.com/	Public	drug discovery	19200 Stevens Creek Blvd., Suite 240 Cupertino	UK
Celera	https://www.celera.com/	Public	Genetics	1401 Harbor Bay Parkway Alameda, CA 94502-7	UK
Bayer HealthCare	http://healthcare.bayer.com/scripts/pages/	Public	drug discovery and development	800 Dwight Way Berkeley, CA	UK
Plexxikon Inc	http://www.plexxikon.com/	Private	drug discovery and development		UK
InterMune Inc.	http://www.intermune.com/	Private	Pulmonary and fribrotic dsiease treatmer	91 Bolivar Drive Berkeley, CA 94710	UK
SuperGen (also known as Aste	http://astx.com/about/mission-values/	Public	Oncology Drugs	4140 Dublin Blvd.Suite 200 Dublin, CA 94568, U	UK
KineMed Inc	http://www.kinemed.com/	Private	biomarker discovery and testing	5980 Horton St Suite #470 Emeryville CA 94608	UK
NovaBay Pharmaceuticals	http://novabay.com/company/corporate-pr	Private	Aganocide drug development	5980 Horton Street, Suite 550 Emeryville, CA 94	UK
Novartis Vaccines and Diagnos	http://www.novartis.com/	Public	Broad Drug Discovery	4560 Horton St Emeryville, CA	UK
Onyx Pharmaceuticals Inc.	http://www.onyx.com/	Private	Cancer Drugs	249 E. Grand Avenue South San Francisco, CA	UK
Gilead Sciences Inc.	http://www.gilead.com/	Private	Broad Drug Discovery	333 Lakeside Drive Foster City, CA 94404	UK
SciClone Pharmaceuticals Inc.	http://sciclone.com/	public	drug discovery	50 Tower Lane, Suite 900 Foster City, California	UK
Cymabay	http://www.cymabay.com/	Public	metabolic disease drugs	7999 Gateway Blvd., Suite 130 Newark, CA 945	UK
DepoMed Inc.	http://www.depomed.com/about	Public	CNS and neurology drugs	7999 Gateway Blvd., Suite 300 Newark, CA 945	UK
Alexza Pharmaceuticals Inc.	http://www.alexza.com/about/company_o	Public	Drug Discovery and Delivery	2091 Stierlin Court Mountain View, CA 94043	UK
ChemoCentryx Inc.	http://www.chemocentryx.com/index.html	Public	Oral Drugs for autoimmune diseases,	850 W Maude Ave, Mountain View, CA 940	UK
MAP Pharmaceuticals Inc. (now	owned by Allergen)	Public	Neurology and Migrane Drugs	2525 Dupont Drive Irvine, CA 92612	UK
Vivus Inc.	http://www.vivus.com/home	Public	Drug Development	351 E. Evelyn Avenue Mountain View, CA 94041	UK
BioMarin Pharmaceutical Inc	http://www.bmrn.com/index.php	Public	Drugs for Inherited Disorders	770 Lindaro Street San Rafael, CA 94901	UK
Jazz Pharmaceuticals Inc.	http://www.jazzpharma.com/about-us/	Public	Drugs for narcolepsy, oncology, pain anc	3180 Porter Dr, Palo Alto, CA 94304	UK
Abbot Labs (formerly Facet Bio	http://www.abbott.com/index.htm	Public	Cancer and Autoimmune drugs	4900 Hopyard Rd, Pleasanton, CA 94588	UK
Nektar Therapeutics	http://www.nektar.com/	Public	Broad Drug Discovery	455 Mission Bay Boulevard South San Francisc	UK
Oncomed Pharmaceuticals Inc.	http://www.oncomed.com/	Private	Cancer Drugs	800 Chesapeake Drive Redwood City, CA 94063	UK
Sangamo Biosciences Inc	http://www.sangamo.com/index.html	Public	Drug Discovery	501 Canal Blvd. Richmond, CA 94804	UK
Xenoport	http://www.xenoport.com/	Public	Neurology Drugs	3410 Central Expressway Santa Clara, CA 9505	UK
Amgen	http://www.amgen.com/about/overview.ht	Public	Drug Development	One Amgen Center DriveThousand Oaks, CA	UK
Cytokinetics Inc.	http://www.cytokinetics.com/	Public	Drugs for muscle function and cytoskele	280 E Grand Ave, S San Francisco, CA 94080	UK
Exelis	http://www.exelixis.com/	public	Cancer Drugs	210 East Grand Avenue So. San Francisco, CA	UK
FibroGen Inc.	http://www.fibrogen.com/	Private	CTGF and HIF based drugs	409 Illinois St, San Francisco, CA 94158	UK

Genentech Inc.	http://www.gene.com/	Private (di	Braod Drug Discovery	1 DNA Way South San Francisco, CA 94080	UK
Pain Therapeutics Inc.	http://www.paintrials.com/index.html	Private	Analgesics	2211 Bridgepointe Parkway Suite 500, San Mate	UK
Rigel Pharmaceuticals Inc.	http://www.rigel.com/indexnoflash.php	Public	Drug Discovery	1180 Veterans Boulevard South San Francisco, (	UK
Theravance Inc	http://www.theravance.com/Theravance_I	Public	Multivalent Drugs	01 Gateway Blvd, S San Francisco, CA 94080	UK
Questcor Pharmaceuticals Inc.	http://www.questcor.com/	public	Autoimmune and Anti-Inflammatory drug	1300 Kellogg Dr, Anaheim, CA 92807	UK
Arcadia Biosciences, Davis Lab	http://www.arcadiabio.com/	Private	GMO's	202 Cousteau Pl #200, Davis, CA 95618	UK
Davis Sequencing Inc.	http://www.davissequencing.com/	Private	DNA sequencing	1450 Drew Ave, Suite 100 Davis, CA 95618	UK
Harris Moran Seed Company	http://www.harrismoran.com/index.htm	Private	Agriculture products	555 Codoni Ave, Modesto, CA 95357	UK
Kiff Analytical	http://www.kiffanalytical.com/	Private	Testing	2795 2nd St # 300, Davis, CA 95618	UK
Marrone Bio Innovations	http://www.marronebioinnovations.com/	Private	Biopesticides	2121 Second St., Suite 107B Davis, CA 95618	BSL 1
MMI Genomics Inc.	http://www.metamorphixinc.com/	Private	testing	1756 Picasso Ave, Davis, CA 95618	UK
Monsanto/ Calgene, Inc.	http://www.monsanto.com/pages/default.a	Public	GMO's	1910 5th St Davis, CA	UK
Novozymes Inc.	http://www.novozymes.com/en/Pages/def	Public	Enzymes	1445 Drew Ave, Davis, CA 95618	BSL 1
Ventria Bioscience	http://www.ventria.com/about-us	Private	Drugs and Vaccines	702 Drake Dr, Davis, CA 95616	UK
Vitalea Science	http://www.vitaleascience.com/	Private	Drug Canidate Testing	2121 Second Street Suite B101 Davis, CA 9561	UK
Vista Analytical Laboratory	http://www.vista-analytical.com/	Private	Enviromental Testing	1104 Windfield Way, El Dorado Hills, CA 95762	UK
California Seed and Plant Lab I	http://csplabs.com/index.php	Private	Plant Testing	7877 Pleasant Grove Rd, Elverta, CA 95626	UK
Air Toxics Limited	http://www.eurofins.com/en/about-us/labo	Private	Testing	180 Blue Ravine Road Ste. B Folsom, CA 9563	UK
Cell Marque	http://www.cellmarque.com/cmc/home.ph	Private	Diagnostic Antibodies	6600 Sierra College Blvd. Rocklin, California 95	UK
IDEXX Labs	https://www.idexx.com/corporate/home.ht	Public	Animal Health and Testing	6300 Jimmy Carter Blvd, Norcross, GA 30071	UK
Immuno Concepts	http://www.immunoconcepts.com/	Private	Diagnostic Tests	9825 Goethe Rd #350, Sacramento, CA 95827	UK
The Jackson Laboratory— Wes	http://jaxmice.jax.org/jaxwest/	Private	Genetic seaeuncing and modeling	1650 Santa Ana Avenue Sacramento, CA 95838	UK
DesigneRx Pharmaceuticals	http://www.polarispharma.com/	Private	Cancer Dugs	4941 Allison Pkwy, Vacaville, CA 95688	UK
Hygieia Biological Laboratories	http://www.hygieialabs.com/index.html	Private	Treatments for Animals	1785 E Main St # 4, Davis, CA 9561	UK
Act Biotech	http://www.actbiotech.com/	Private	Cancer drugs	717 Market St #650, San Francisco, CA 94103	UK
CS Bio	http://www.csbio.com/	Private	Peptides	20 Kelly Ct. Menlo Park, California 94025	UK
Mendel Biotechnology, Inc.	http://www.mendel.com/index.php	Private	Agriculture	3935 Point Eden Way, Hayward, CA 94545	UK
CureLine	http://www.cureline.com/	Private	Human Tissue Research	290 Utah Ave #300, South San Francisco, CA 94	UK
Bavarian Nordic	http://www.bavarian-nordic.com/	Public	Cancer drugs	2450 Bayshore Parkway Mountain View, CA 940	UK
23andMe	https://www.23andme.com/	Private	Genetic Testing and Sequencing	2606 Bayshore Parkway Mountain View, CA 940	UK
Achaogen	http://www.achaogen.com/	Public	Antibacterials	7000 Shoreline Ct, S San Francisco, CA 94080	UK
Actelio	http://www1.actelion.us/us/index.page	Public	Small Molecules	5000 Shoreline Court, Suite 200 South San Fran	UK
ActiveSite Pharmaceuticals	http://www.activesitepharma.com/	Private	Small Molecules	1456 4th St # C, Berkeley, CA 94710	UK
Acumen Pharmaceuticals	http://www.acumenpharm.com/	Private	Alzheimer's treatment	4435 North First Street, # 360 Livermore, Califor	UK
Adams Pharma	http://adamaspharma.com/	Private	CNS treatments	2200 Powell St #220, Emeryville, CA 94608	UK
Aduro Bitotech	http://www.adurobiotech.com/	Private	Drug Development	626 Bancroft Way, #3C Berkeley, CA 94710-222	UK
Adynxx	http://www.adynxx.com/	Private	Analgesics	31 Market Street #420, San Francisco, CA 9410	UK
Aegea medical	http://aegeamedical.com/	Private	Treatments	686 Middlefield Rd, Redwood City, CA 940	UK
Aeolus Pharmaceuticals	http://investor.aeoluspharma.com/release	Private	Oncology and Biodefense	26361 Crown Valley Pkwy, Mission Viejo, CA 92	UK
Alector	http://alector.com/	Private	Alzeimer's Antibody Treatments	953 Indiana Street San Francisco, CA 94107	UK
Alexza Pharmaceuticals	http://www.alexza.com/	Public	Drug Delivery, Small Molecule	2091 Stierlin Court Mountain View, CA 94043	UK
Alios Biopharma	http://www.aliosbiopharma.com/	Private	Small Molecules, Biologics	260 East Grand Ave, 2nd Floor South San Franc	UK
Alvine Pharmaceuticals	http://www.alvinepharma.com/	Private	Autoimmune disease drugs	75 Shoreway Rd, San Carlos, CA 94070	UK
Amarantus Therapeutics	http://www.amarantus.com/	Public	Therapeutic Proteins	953 Indiana Street San Francisco, CA 94107	UK
Amedica Biotech	http://www.amedicabiotech.com/	Private	In-Vitro Diagnostics	28301 Industrial Blvd, Hayward, CA 94545	UK
Anthera	http://www.anthera.com/about_overview.h	Public	Auttoimmune treatments	25801 Industrial Blvd, Suite B Hayward, CA 945	UK
Antibody Solutions	http://www.antibody.com/	Private	Antibody Developemnt	1130 Mountain View -Alviso Rd, Sunnyvale, CA	UK
Antigen Discovery	http://www.antigendiscovery.com/	Private	Diagnostic Techniques and Assays	1 Technology Dr. Suite E309 Irvine, CA 92618	UK
Antipodean Pharmaceuticals	http://www.antipodeanpharma.com/	Private	Anti-Oxidative treatments	3000 Sand Hill Road Building 4 Suite 210 Menlo	UK
Apexigen	http://www.apexigen.com/company.shtml	Private	Drug Development	863A Mitten Road, Suite 100C Burlingame, CA 9	UK
Applied StemCell	http://www.appliedstemcell.com/	Private	Stem Cell Treatments	1165 O'Brien Dr, Menlo Park, CA 94025	BSL 1

Aptiv Solutions	http://www.aptivsolutions.com/lung-cancer	Private	Clinical Trials Support	1925 Isaac Newton Square E, Reston, VA 20190	UK
Aradigm	http://www.aradigm.com/	Public	Pulmonary Disease treatments	3929 Point Eden Way Hayward, CA 94545	UK
Aragen Bioscience	http://www.aragenbioscience.com/about/	Private	Lab Services	380 Woodview Avenue Morgan Hill, CA 95037	UK
Arbor Vita	http://www.arborvita.com/	Private	Diagnostic Tests	48371 Fremont Blvd, Suite 101 Fremont, 94538	UK
Ardelyx	http://www.ardelyx.com/	Private	Small molecule Therapies	34175 Ardenwood Blvd, Fremont, CA 94555	UK
Aridis Pharmaceuticals	http://www.aridispharma.com/	Private	Drug Treatments	5941 Optical Court San Jose, CA 95138	UK
Ariosa Diagnostics	http://www.ariosadx.com/	Private	Diagnostic Testing	5945 Optical Court, San Jose, CA 95138	UK
Ark Diagnostics	http://www.ark-tdm.com/	Private	Diagnostic Testing	48089 Fremont Blvd, Fremont, CA 9453	UK
Atara Biotherapeutics	http://www.atarabio.com/	Private	Drug Development	2659 Townsgate Road, Suite 236 Thousand Oak	UK
Audentes Therapeutics	http://www.audentestx.com/	Private	Gene Threrapy	101 Montgomery Street, Suite 2650 San Francis	UK
Audeo Oncology (Alchemia)	http://www.audeooncology.com/	Public (ow	Cancer Drugs	100 Pine Street Suite 2040 San Francisco, Calif	UK
Amunix	http://www.amunix.com/	Private	Life Extension	500 Ellis St, Mountain View, CA 94043	UK
Anacor Pharmaceuticals	http://www.anacor.com/	Public	Small Molecules	1020 East Meadow Circle Palo Alto, CA 94303-4	UK
AvidBiotics	http://www.avidbiotics.com/	Private	proteins	100 Kimball Way South San Francisco, CA 9408	BSL 3
Baxter	http://www.baxter.com/index.html	Public	Broad Drug Discovery		UK
Bell Biosystems	http://www.bellbiosystems.com/Home	Private	Synthetic Bio	530 Lytton Ave, Palo Alto, CA 94301	UK
BetaStem Therapeutics	http://betastemtherapy.com/	Private	Stem Cell Treatments	300 Brannan St, San Francisco, CA 94107	UK
Biomarker Pharmaceuticals	http://www.biomarkerinc.com/	Private	Life Extenson	5941 Optical Court San Jose, CA 95138	UK
BioTime	http://www.biotimeinc.com/	Public	Stem Cell and Aging Treatments	1301 Harbor Bay Parkway Alameda, CA 94502	BSL 2
Boehringer Ingelheim	http://www.boehringer-ingelheim.com/	Private	Broad Drug Discovey	6701 Kaiser Drive Fremont, CA 94555	UK
Bristol-Myers Squibb	http://www.bms.com/pages/default.aspx	Public	Broad Drug Discovery	700 Bay Rd Ste A, Redwood City, CA 94063	UK
Catalyst Biosciences	http://www.catalystbiosciences.com/	Private	Eyzmes to fight disease	260 Littlefield Ave, S San Francisco, CA 94080	UK
Cellecta	http://www.cellecta.com/index.php	Private	Drug Screening	320 Logue Ave, Mountain View, CA 94043	UK
Cellerant Therapeutics	http://www.cellerant.com/	Private	Stem Cells	1561 Industrial Rd, San Carlos, CA 94070	UK
Centrillion Biosciences	http://www.centrillionbio.com/	Private	Gemonic Screening	2438 Embarcadero Way Palo Alto, CA 94303	UK
Chronix Biomedical	http://www.chronixbiomedical.com/connec	Private	Biomarker discovery and testing	5941 Optical Court Suite 203E San Jose, CA 95	UK
Clovis Oncology	http://www.clovisoncology.com/	Public	Cancer treatments	1700 Owens Street Suite 205 San Francisco, CA	UK
Colby Pharmaceuticals	http://www.colbypharma.com/	Private	Cancer treatments	1095 Colby Ave, Menlo Park, CA 94025	UK
CoMentis	http://comentis.com/	Private	Cancer Treatments	280 Utah Avenue, Suite 275 South San Francisc	UK
Complete Genomics	http://www.completegenomics.com/	Public	Genomic Sequencing	Complete Genomics, Inc. 2071 Stierlin Court Mo	UK
Corcept Therapeutics	http://www.corcept.com/	Public	metabolic disease drugs	149 Commonwealth Drive Menlo Park, CA 9402	UK
Coronado Biosciences	http://www.coronadobiosciences.com/	Public	Immunotherapy	4365 Executive Drive Suite 1500 San Diego Cal	UK
Crescendo Bioscience	http://www.crescendobio.com/	Private (ow	Diagnostics	341 Oyster Point Blvd South San Francisco, CA	UK
Crown Bioscience	http://www.crownbio.com/	Private	Drug and Biomarker Discovery	3375 Scott Blvd., Suite 108 Santa Clara, CA 950	UK
Cyterix Pharmaceuticals	http://www.cyterix.com/	Private	Cancer Treatments	75 Shoreway Road Suite D San Carlos, CA 9407	UK
Dance Pharmaceuticals	http://dancebiopharm.com/	Private bu	Diabetes Treatments	150 North Hill Drive, Suite 24 Brisbane, Californi	UK
Del Mar Pharmaceuticals	http://www.delmarpharma.com/	Public	Cancer Treatments	3475 Edison Way, Suite R Menlo Park, Californi	UK
DNA2.0	https://www.dna20.com/	private	Gene Synthesis	1140 O'Brien Drive, Suite A Menlo Park, CA 940	UK
Eiger Biopharmaceuticals	http://www.eigerbio.com/	Private	Antivrial Treatments	San Carlos, CA 94070	UK
Epiphany Biosciences	http://www.epiphanybio.com/contact/direc	Private	Infectious Disease Treatments	One California Street Suite 2800 San Francisco,	UK
EpitoGenesis	http://www.epitogenesis.com/	Private	Immune adjuvants (vaccines)	1810 N Broadway Walnut Creek, CA 94596	UK
Escape Therapeutics	http://escapetherapeutics.com/	Private	Stem Cell Treatments	5941 Optical Court San Jose, CA 95138	UK
Eureka Genomics	https://www.eurekagenomics.com/ws/hom	Private	Screening	750 Alfred Nobel Drive, Suite 108 Hercules, CA 9	UK
Five Prime Therapeutics	http://www.fiveprime.com/	Public	Protein Therapy	Two Corporate Drive South San Francisco, CA 9	UK
Genomic Health	http://www.genomichealth.com/	Public	Genetic Testing	301 Penobscot Dr, Redwood City, CA 94063	UK
HTD Biosystems	http://www.htdcorp.com/index.html	Private	Contact clinical research	1061 Serpentine Lane, Suite E Pleasanton CA 9	UK
Hyperion	http://www.hyperiontx.com/	public	Drug Discovery	2000 Sierra Point Parkway, Suite 400 Brisbane,	UK
Igenica	http://www.igenica.com/	Private	Cancer Treatments	863 Mitten Road, Suite 102 Burlingame, CA 940	UK
Illumina	http://www.illumina.com/	Public	Gene sequencing	5200 Illumina Way San Diego, CA 92122 USA	UK
Impax Labs	http://www.impaxlabs.com/	Public	Drug Delivery	31047 Genstar Rd. Hayward, CA 94544	UK
Intarcia Therapeutics	http://www.intarcia.com/	Private	Drug Discovery	24650 Industrial Blvd, Hayward, CA 94545	UK

InteKrin	http://www.intekrin.com/index.html	Private	Drug Discovery	201 Redwood Shores Parkway, Suite 200 Redw	UK
Invitae	https://www.invitae.com/en/	Private	Genetic Testing	458 Brannan Street San Francisco, CA 94107	UK
Ipsen Biopharmaceuticals	http://www.ipsen.com/en/	public	Drug Discovery	2000 Sierra Point Pkwy, Brisbane, CA 94005	UK
Jennerex	http://www.jennerex.com/	Private	Cancer Treatments	450 Sansome Street, 16th Floor San Francisco,	UK
Juvaris	http://www.juvaris.com/	Private	Vaccines and Immunotherapay	Pleasanton, Ca 94566	UK
List Biological Laboratories	http://www.listlabs.com/contact.php	Private	Toxin Production	540 Division St, Campbell, CA 95008	UK
MacroGenics	http://www.macrogenics.com/index.html	Public	Cancer, Autoimmune Diseases and Infec	One Corporate Drive South San Francisco, CA 9	UK
MedImmune (AstraZeneca)	https://www.medimmune.com/about-medi	Public (ow	Infectious Disease Treatments	319 North Bernardo Avenue Mountain View, CA	UK
Medivation	http://www.medivation.com/	Public	Drug Discovery	525 Market Street, 36th Floor San Francisco, CA	UK
Mountain View Pharmaceutical	http://www.mvpharm.com/	Private	Drug Delivery	3475 Edison Way, Menlo Park, CA 94025	UK
MyoKardia	http://www.myokardia.com/	Private	Cardiovascualr Drugs	400 East Jamie Court, Suite 102South San Fran	UK
Neuraltus	http://www.neuraltus.com/	Private	ALS treatments	2479 E. Bayshore Road Suite 220 Palo Alto, CA	UK
Neurokos	http://www.neurokos.com/	Private	Neurology Treatment	2225 East Bayshore Road, Palo Alto, CA 94303	UK
Nexgenix	http://www.nexgenixpharm.com/overview_	Private	Drug Discovery	849 Mitten Road Burlingame CA	UK
Nizyme	http://www.nizyme.com/	Private	Drug Discovery	49 Amethyst Way, San Francisco, CA 94131	UK
Nora Therapeutics	http://www.noratherapeutics.com/	Private	Infertiliy Treatments	530 Lytton Avenue, 2nd floor Palo Alto, CA, 943(	UK
Oculus Innovative Sciences	http://oculusis.com/	Public	Drug Discovery and Treatments	1129 North McDowell Blvd. Petaluma, California	UK
Odyssey Thera	http://www.odysseythera.com/	Private	Drug Discovery	4550 Norris Canyon Road Suite 140 San Ramor	UK
Oxford BioTherapeutics	http://www.oxfordbiotherapeutics.com/	Private	Cancer Drugs	San Jose Biocenter, 5941 Optical Court, San Jos	UK
Oxigene	http://www.oxigene.com/	Public	Cancer Drugs	701 Gateway Blvd, Suite 210 South San Francis	UK
PCT Cell Therapy (Neostem)	http://pctcelltherapy.com/	Public (ow	Various Services	291 Bernardo Avenue Mountain View, CA 94043	UK
Personalis	http://www.personalis.com/	Private	Gene sequencing	1350 Willow Rd #202, Menlo Park, CA 94025	UK
Pharmacyclics	http://www.pharmacyclics.com/	Public	Drug Development	999 East Arques Avenue, Sunnyvale, California	UK
Portola Pharmaceuticals	http://www.portola.com/	Public	Drug Development	270 E. Grand Avenue South San Francisco, CA	UK
Principia Biopharma	http://www.principiabio.com/	Private	Cancer and Autoimmune drugs	400 East Jamie Court South San Francisco CA(	UK
Quanticel	http://www.quanticel.com/	Private	Cancer Treatments	1500 Owens Street, Suite 500 San Francisco, C	UK
Quark Pharmaceuticals	http://www.quarkpharma.com/	Private	Drug Discovery	6501 Dumbarton Circle. Fremont, CA 94555.	UK
Raptor Pharmaceuticals	http://www.raptorpharma.com/	Public	Drug Discovery	5 Hamilton Landing, Suite 160 Novato, CA 9494	UK
Redwood Bioscience	http://www.redwoodbioscience.com/#	Private	Antibody Developemnt	5703 Hollis St, Emeryville, CA 94608	UK
REG Life Sciences (Renewable	http://www.reglifesciences.com/	Public	biofuels	600 Gateway Blvd South San Francisco, CA 940	UK
Relypsa	http://www.relypsa.com/	Public	Drug Development	700 Saginaw Dr, Redwood City, CA 94063	UK
RenovoRx	http://www.renovorx.com/	Private	Drug Delivery	3114 David Avenue Palo Alto, CA 94303	UK
ResVerlogiX	http://www.resverlogix.com/	Public	Cardiovascualr Drugs	Suite 4010, 44 Montgomery StreetSan Francisco	UK
Revance Therapeutics	http://www.revance.com/	Public	Drug Delivery	7555 Gateway Blvd, Newark, CA 94560	BSL 2 and 3
Ruga	http://www.rugacorp.com/	Private	Cancer Drugs	550 Hamilton Avenue Suite 220 Palo Alto, CA 94	UK
SanBio	http://www.san-bio.com/	Private	Neuroglocial Treatments	231 S Whisman Rd, Mountain View, CA 94041	UK
Santen	http://www.santen.com/en/	Public	Broad Drug Discovery	2100 Powell Street, Suite 1600, Emeryville, Calif	UK
SMC Biotechnology	http://smcbio.com/	Private	Regenetic Medicine	SMC Biotechnology, Inc. 425 Broadway St. Red	UK
Somagenics	http://www.somagenics.com/	Private	RNAi	2161 Delaware Ave, Santa Cruz, CA 95060	UK
StemCells Inc	http://www.stemcellsinc.com/	Public	Stem Cells	7707 Gateway Blvd., Suite 140 Newark, CA 945(	UK
Sunesis Pharmaceuticals	http://www.sunesis.com/	Public	Cancer Drugs	395 Oyster Point Boulevard, Suite 400 South Sa	UK
Tacere Therapeutics (Benitec B	http://www.tacerebio.com/corporate.htm	Public (ow	DNA based Drugs	4900 Hopyard Rd, Suite 100 Pleasanton CA 945	UK
Telik	http://www.telik.com/	Public	Drug Development	2100 Geng Road, Suite 102, Palo Alto, CA 9430	UK
Threshold Pharmaceuticals	http://www.thresholdpharm.com/	Public	Cancer Treatments	170 Harbor Way, Suite 300 South San Francisco	UK
Titan Pharmaceuticals	http://www.titanpharm.com/	Public	Drug Delivery and Development	400 Oyster Point Blvd., Suite 505 South San Fra	UK
Tobira Therapeutics	http://www.tobiratherapeutics.com/discove	Private	HIV drugs	701 Gateway Blvd, Suite 200 South San Francis	UK
Tolerion	http://www.tolerioninc.com/	Private	Autoiimune Treatment	321 Dedalera Dr. Portola Valley, CA 94028	UK
Transcept Pharmaceuticals	http://www.transcept.com/	Public	Neurology Treatments	1003 W. Cutting Blvd Suite #110 Pt. Richmond, (	UK
Transgenomic	http://www.transgenomic.com/	Public	Sequencing	2032 Concourse Drive San Jose, CA 95131, US	UK
Trellis Bioscience	http://www.trellisbio.com/	Private	Antibody threapies	2 Corporate Dr, South San Francisco, CA 94080	UK
Trigemina	http://trigemina.com/	Private	Pain Therapy	809 Cuesta Drive # 109B Mountain View, CA 94(	UK

Ultragenyx	http://ir.ultragenyx.com/	Public	genetic Disease Treatmetns	60 Leveroni Ct, Novato, CA 94949	UK
Urigen Pharmaceuticals	http://www.urigen.com/	Public	Urology treatments	1700 N Broadway, Walnut Creek, CA 94596	UK
US World Meds	http://www.usworldmeds.com/company_o	Private	Drug Discovery	701 Gateway Boulevard Suite 250 South San Fr	UK
Vaxart	http://www.vaxart.com/	Private	Influenza Vaccines	385 Oyster Point Blvd #9a, South San Francisco	UK
Versartis	http://www.versartis.com/	Public	Endocrine treatments	4200 BOHANNON DRIVE SUITE 250 MENLO P	UK
VG Life Sciences	http://www.vglifesciences.com/contact/	Private	Broad Drug Discovery	121 Gray Ave. Ste 200 Santa Barbara, CA 9310	UK
VistaGen	http://www.vistagen.com/	Public	Stem Cell Treatments	343 Allerton Avenue South San Francisco, CA 9	UK
Vivus	http://www.vivus.com/home	Public	Drug Discovery	Mountain View, CA 94041 USA	UK
XDx	http://caredxinc.com/company	private	Diagnostics	3260 Bayshore Blvd, Brisbane, CA 9400	UK
Ascend Genomics	http://www.ascendgenomics.com/about/	Private	Genetic Cancer Testing	320 Hatch Drive Foster City, CA 94404	UK
Guardant Health	https://www.guardanthealth.com/	Private	Genetic Cancer Testing	2686 Middlefield Rd, Suite C,D,E Redwood City,	UK
Theranos, Inc.	http://www.theranos.com/	Private	Lab Testing	1601 S. California Avenue Palo Alto, CA 94304	UK
Singulex	http://www.singulex.com/	Private	Lab Testing	1701 Harbor Bay Parkway, Suite 200 Alameda, (	UK
Agilent Technologies Inc.	http://www.home.agilent.com/agilent/hom	Public	DNA therapeudics, diagnostics	395 Page Mill Road Palo Alto California 94303	UK
Life Technologies	http://www.appliedbiosystems.com/absite/	Private	Diagnostics	850 Lincoln Centre Drive Foster City California	UK
Celgene San Francisco	https://www.celgene.com/	Public	hematology, oncology, immunology	1500 Owens Street Suite 600 San Francisco Ca	BSL 2
Intexon	http://www.dna.com/	public	Synthetic Bio	201 Gateway Boulevard, 1st Floor South San Fr	UK
Roche Palo Alto		Public	Inflammatory Diseases, Virology	3431 Hillview Avenue Palo Alto California 9430	UK
Illumina Hayward	http://www.illumina.com/	Public	Sequencing	25861 Industrial Blvd. Hayward, CA 94545 USA	UK
Pfizer	http://www.pfizer.com/	Public	Research, borad drug discovery	230 East Grand Avenue South San Francisco C	UK

School	Facility Na	Research	Address	
Stanford University	Lorry Loke	Stem Cell Bio, Regenerative M	265 Campus Drive, 3rd Floor Stanford, CA 94305	BSL 2 facilities
Stanford University	Arastrader	cancer gene discovery, genomi	1050 Arastradero Rd Palo Alto, CA 94304	BSL 2 facilities
Stanford University	Beckman	genetic engineering, cell physic	279 Campus Drive West Stanford CA	BSL 2 facilities
Stanford University	Center for	molecular pharmacology, immu	269 Campus Dr, Palo Alto, CA 94304	BSL 2 facilities
Stanford University	Clark Cen	Bioengineering, Molecular Biol	318 Campus Drive West, Stanford, CA 94305	BSL 2 facilities
Stanford University	Sherman I	structural biology, biophysics, n	299 Campus Drive WestStanford, CA 94305	BSL 2 facilities
Stanford University	Stanford E	Blood Research and Cancer R	3373 Hillview Avenue. Stanford CA	BSL 2 facilities
Stanford University	Stanford C	Genomics, cancer genetics, se	855 S. California Avenue Palo Alto, CA 94304-1103	BSL 2 facilities
Stanford University	Stanford Medical Center		Stanford University Stanford, CA 9430	BSL 2 facilities
Stanford University	Lokey Che	Chemsitry and Biology	337 Campus Drive Stanford, CA 9430	BSL 2 facilities
Stanford University	Edwards Research Building		Stanford University Palo Alto, CA 94304	BSL 2 facilities
Stanford University	Stanford C	Cancer Research	875 Blake Wilbur Dr Clinic E Stanford, CA94305	BSL 2 facilities
Stanford University	Stanford C	Viral Research, Pathology rese	725 Welch Rd, Palo Alto, CA 94304	BSL 2 facilities
Stanford University	Cargnagie	Ecology, Plant Biology, Embryo	260 Panama Street, Stanford CA	BSL 2 facilities
Stanford University	Hopkins M	Marine Ecology, Biology and O	120 Ocean View Blvd., Pacific Grove, CA 93950,	BSL 2 facilities
Stanford University	Gilbert Biological Sciences Building		371 Serra Mall, Stanford, CA 94305	BSL 2 facilities
Stanford University	Herrin Biological Labs		385 Serra Mall, Stanford, CA, 94305	BSL 2 facilities
UC Berkley	QB3/Stanl	Biophysics	274 Stanley Hall Berkeley, CA 94720-3370	BSL 1,
UC Berkley	Etcheverry	Biomechanics, Mechanical Eng	6141 Etcheverry Hall University of California	BSL 1,
UC Berkley	Hearst Me	biomaterials	Hearst Memorial Mining Building Berkeley, CA 947	BSL 1 and 2
UC Berkley	Life Scien	Neurobiology, Immunology, Ge	University of California, Berkeley, CA 94720	BSL 1 and 2
UC Berkley	Li Ka Shin	Developmental Biology, Genetl	Li Ka Shing Center Berkeley, CA 94720-3220	BSL 1 and 2
UC Berkley	Barker Ha	Molecular & Cell Biology, Neur	Barker Hall University of California, Berkeley, Berke	\BSL 1 and 2
UC Berkley	Koshland	Molecular & Cell Biology, Plant	Koshland Hall Berkeley, CA 94720-3102	BSL 1 and 2
UC Berkley	Valley Life	otany, Biochemistry, Genetics,	Valley Life Sciences Bldg, University of California, I	BSL 1 and 2
UC Berkley	Lewis Hall	Biochemistry, Biophysics, Synt	Lewis Hall University of California, Berkeley, Berke	BSL 1 and 2
UC Berkley	Hildebran	Chemistry, QB3, Chemistry and	Hildebrand Hall University of California, Berkeley, I	BSL 1,2 and 3

UC Berkley	Wellman H	Environmental Science	Wellman Hall University of California, Berkeley, Be	BSL 1 and 2
UC Berkley	Latimer Ha	Chemistry, Biochemistry	Latimer Hall University of California, Berkeley, Berk	BSL 1 and 2
UCSF	AIDS Resi	Virology	50 Beale Street, Suite 1300 San Francisco CA 94105	
UCSF	Health Sci	Molecualr Biology, Immunology	513 Parnassus Avenue HSW-1601 San Francisco, CA 94143	
UCSF	Rock Hall	Molecualr Biology, Neuobiology	345 Rock Hall, UCSF Mission Bay Campus 1550 F	BSL 1 and 2
UCSF	Genentech	Biochemsitry, Biophysics, Immu	600 16th Street San Francisco, CA 94143-2140	BSL 2 and 3 (TB research being done)
UCSF	Byers Hall	Biochemsitry, Biophysics, Syste	1700 4th St. San Francisco CA 94158-2330	BSL 1 and 2
UCSF	QB3	Molecular Biology, nanotechnol	1700 4th Street, San Francisco, CA 94158	BSL 1 and 2
UCSF	Helen Dill	Cancer Biology, Molecular Biol	1450 3rd Street, San Francisco, CA 94158	BSL 1 and 2
UCSF	UC Hall	Pharmacology	533 Parnassus Ave ,San Francisco, California 941	BSL 1 and 2
UCSF	Med Scier	Pharmacology, Immunology	513 Parnassus Avenue HSW-1601 San Francisco,	BSL 1 and 2
UCSF	China Bas	Epidemiology, Biostastistics Ra	185 Berry Street W San Francisco CA 94143	BSL 1 and 2
UCSF	Sandler N	Neurobiology	675 Nelson Rising Lane, Suite 190 San Francisco,	BSL 1 and 2
UCSF	San Franc	pathology, neurology	1001 Potrero Ave San Francisco, CA 94110	BSL 1 and 2
UCSF	Blood Sys	Blood research, disease patho	270 Masonic Ave San Francisco CA 94118	BSL 1 and 2
UCSF	UCSF Mei	Pathology, Oncology, Rhuemat	505 Parnassus Ave., San Francisco, CA 94143	BSL 1 and 2
UCSF	UCSF Mei	Pathology, Oncology, Rhuemat	1600 Divisadero Street San Francisco, CA 94115	BSL 1 and 2
UCSF	San Francisco VA hopsital		4150 Clement Street San Francisco, CA 94121	BSL 1 and 2
UCSF	UCSF Mis	Oncology, Neurology	1855 Folsom Street, Room 226 San Francisco, CA	BSL 1 and 2
UCSF	UCSF Mei	Neurology, Endocrinology	400 Parnassus Ave, San Francisco, CA 94143	BSL 1 and 2
UCSF	Ray and D	Regenerative Medicine,Stem C	35 Medical Center Way San Francisco, CA 94143-	BSL 1 and 2
SFSU	Hensill Ha	Developmental Bio, Moelcular I	1600 Holloway Avenue . San Francisco . CA 94132	BSL 1 and 2
SFSU	Science B	Virology, Immunology, Clinical (	1600 Holloway Avenue . San Francisco . CA 94132	BSL 1/2 and building BSl 3
USF	Harney Sc	Biology, Biochemistry, Ecology,	2130 Fulton St. San Francisco, CA 94117-1080	
University of the Pacific	Biological	Stuctural Biology, Genetics, Imi	3301-3399 N Kensington Way, Stockton, CA 95204, USA	
University of the Pacific	Biology La	BioAcoustics, Developmental B	3601 Pacific Ave, Stockton, CA 95211	
University of the Pacific	Thomas J.	Pharmacology	3601 Pacific Avenue Stockton, CA 95211	
College of San Mateo	Science B	General Biology	700 West Hillsdale Boulevard, San Mateo, CA 94402	
Mills College	Moore Na	Biochemistry, Molecular Biolog	5000 MacArthur Blvd. Oakland, CA 94613	
Saint Mary's College of Californ	Sichel Hal	Microbiolgy, Molecular Biocolgy	1928 Saint Mary's Road, Moraga, CA 94575	
Saint Mary's College of Californ	Brousseau	Ecology, Microbiology, Immuno	1928 Saint Mary's Road, Moraga, CA 94575	
Touro University	College of	Microbiology, infectious disease	1310 Club Drive Vallejo, Ca 94592	BSL 1 and 2
Touro University	College of	Drug discover, Immunology, Ch	1310 Club Drive Vallejo, Ca 94592	BSL 1 and 2
Sonoma State University	Darwin Ha	Cell Biology, Ecology, Molecula	1801 East Cotati Ave Rohnert Park, CA 94928	
Public Institution Name		Research	Address	
Lawerence Livermore National	Lab Techniques (PCR, Diagnostics), Path		7000 East Avenue Livermore, CA 94550	BSL 1,2,3
Joint BioEnergy Institute	Biofuels, Bioenginnering, Synthetic Biolog		1 Cyclotron Rd Berkeley, CA 94720	BSL 1, 2
SF Department of Public Health:	HIV/AIDS	HIV/ AIDS, Virology, Epidemiol	25 Van Ness, Suite 500 San Francisco, CA 94102	BSL 2
San Francisco Department of P	Immunology, Epidemiology, Microbiology		101 Grove Street San Francisco, CA 94102	BSL 2
Santa Clara Public Health Dep	Immunology, Epidemiology, Microbiology		976 Lenzen Avenue San Jose, CA 95126	BSL 2
Alameda County Public Health	Immunology, Epidemiology, Microbiology		1000 Broadway, Suite 500, Oakland, CA 94607	BSL 2
Sonoma County Department of	Immunology, Epidemiology, Microbiology		3313 Chanate Road Santa Rosa, CA 95404	BSL 2
Solano County Public Health La	Immunology, Epidemiology, Microbiology		2201 Courage Drive, MS 9-200 Fairfield, CA 94533	BSL 2
County of San Mateo Health Se	Immunology, Epidemiology, Microbiology		225 W. 37th Avenue, Room No.113, San Mateo, C/	BSL 2
Lawrence Berkeley National La	micorbiology, synthetic biology, Bioenigne		1 Cyclotron Rd Berkeley, CA 94720	BSL 2