ARTICLE

THE CULTURE OF SCIENCE AND THE REGULATION AND LITIGATION OF BIODEFENSE RESEARCH

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1.0 INTRODUCTION

The headlines of the local newspaper in a West Texas city of about 200,000 population read "Professor Admits to Lie About Plague" followed by the statement that "the world renowned researcher who turned an international spotlight on Lubbock with claims of missing samples of plague admitted Wednesday to federal authorities that he lied about what happened to the bacterial agent, court records show."[1]

The impact of this news on January 13, 2003 was nationwide. Within hours of the report of the stolen or missing plague to the FBI, the President of the United States was briefed about the possible biocrime. On the financial front, cattle and pork futures plummeted. The futures reached a "limit down" status, meaning that the exchange halted trading for the day because the market had reached its limit established for a decrease in value for one day. For one month's contracts, the drop resulted in a loss of $1,049 per steer for April 2003 contracts.[2] Although plague does not affect cattle or

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1. Kerry Drennan, *Professor Admits to Lie About Plague*, THE LUBBOCK AVALANCHE-J. (Texas), Jan. 17, 2003, at A1.

2. All cattle contracts were down, but April, June, and October contracts were down the limit allowed, which represented the cattle most ready for market, on Wednesday, January 15, 2003. In a telephone interview in March 2003 with analyst Dave Weaber of Cattlefacts in Denver, CO, Weaber said that the fed cattle futures continued to decline, but June contracts had recovered half of what was lost and October had recovered one-third of what was lost the day of the announcement. He thought that the announcement of the missing plague could account for some, but not all, of the decline in the markets on that day.

pork, the perception of how it would affect the cattle market in the Panhandle of Texas was clearly important in the financial market. The impact was felt locally, too. Local residents telephoned the FBI and the local Department of Public Health with concerns about their safety. Hours after the announcement, the FBI announced that the plague had been located, and the fear subsided. After almost two years, Dr. Thomas Butler, the plague scientist, had lost his license to practice medicine and was checking into a federal prison in Ft. Worth, Texas for a two-year term.

Biodefense researchers were saddened and angered to see a colleague in handcuffs as he was taken into custody by the FBI—the result of almost a decade of growing legislative reactions to the threat to public health and national security, further fueled by the reality of the anthrax attacks of 2001. Another scientist, Professor John Rosenberger of the University of Pittsburg, who otherwise had stellar and honorific careers in scientific research, retired as part of a plea bargain in a criminal case against him for violating the select agent regulations. Institutions of worldwide repute for excellence in leadership in scientific research in dangerous pathogens—Texas A&M University and USAMRIID, the U.S. Army's biodefense research institution—have been fined and/or suspended from all research in these very areas. Scientists have been under scrutiny and investigated to the extent that their careers have been negatively impacted. The highest profile of these was Steven Hatfill who ultimately settled with the federal government for around $5 million for being named a "person of interest" and pursued relentlessly, disrupting his academic appointments and career.

The mere suggestion of a biodefense laboratory has driven communities to form organizations to protest their location, and litigation through environmental statutes has been utilized in their effort. One non-profit organization, The Sunshine Group, was formed with an objective of investigating the "proliferation" of biodefense laboratories in the United States as a result of the increased capacity building for research following the anthrax attacks of 2001.

After the five-year mark for implementation of the select agent regulations in 2008, a legislative review of the program resulted in proposed legislation. The objective was a complete review of the entire design of the program, although consideration of the legislation was interrupted by the presidential election in fall 2008. Some questions asked were: Is this a regulatory regime that can ensure the safety of the public and the security of our homeland and nation? Do we have any other regulatory choices?

Prior to 1996, the biodefense research community had scientific ethics as their guiding principle to limit research plans that went beyond those boundaries. Indeed, the first generation of regulation of biodefense research was directed not toward the scientist and the biological agents in the laboratory, but toward the interstate shipment of the biological agents with which they worked. The Public Health Security and Bioterrorism Response and

Preparedness Act of 2002, as well as the USA PATRIOT Act of 2001, created a second generation of regulations for the purpose of increasing national and homeland security in an academic environment and expanded the criminal provisions of the Bioterrorism Act, closing the gap between the intentional act of bioterrorism and the violation of standards, now also potentially criminal. In an effort to gain control of this scientific research complex engaged in research with potential biological weapons, Congress responded with new controls. Building upon an existing regulatory regime of transportation of select agents, a new generation of regulations was promulgated by the CDC from this legislation which added possession, storage, and use of select agents. The culture of the research scientist and the implementation of these regulatory mechanisms have led to a clash of interests—those of research for humankind and those of national security. Can these two interests co-exist? Which interest should yield to the other, and to what degree, in an optimal, balanced regulatory system?

This article examines the historical development of the select agent rules, the civil and criminal aspects of these rules, and how they have impacted the biodefense research community, including those members who have been found in violation of these rules. This examination of the development of the select agent rules captures some of the contrasting interests between the culture of science and the culture of law. This study can provide insight into the processes that drive science, which can be useful to lawmakers and regulators and to those in the legal academy in the interdisciplinary area of law and science. The development of environmental law and regulation through the 1970s and 1980s provides a model for examining the new regime of regulation of biodefense research through the select agent rules. Finally, this article considers whether the normative regulatory processes effectively achieve the legislative goals of national and homeland security in the area of life sciences biodefense research.

2.0 The Development of the Regulatory Framework of Select Agents

The regulatory framework that requires the regulation of biological agents which may be potential bioweapons began with a need to regulate the transportation of biologics and pathogens.[3] Since 9/11 and the anthrax attacks of the fall of 2001, that regulatory framework was used to build a new generation of regulations. These regulations have been shaped as a result of incidents involving biological agents, moving Congress to act to address the threat.

The first domestic law to address bioterrorism, the Biological Weapons Anti-Terrorism Act, was passed in 1989. This law made it a crime to

3. 42 C.F.R. § 73.12–13 (2005), *reprinted in* 49 U.S.C. § 5105 (2005).

intend to use biological agents as a biological weapon.[4] The law was passed in part as an international obligation under the Biological Weapons Treaty of 1972. However, the United States had already experienced its first modern biological attack in 1984, when a cult in Oregon poisoned salad bars in the community with *salmonella* bacteria in an attempt to influence the outcome of an election. This Biological Weapons Act required a criminal standard of "intent to use" any of a list of biologicals as weapons. Congress took care in the construction of the statute to make criminal only those who possessed biological agents "for other than peaceful purposes." This placed no limits on researchers who used these agents for typical research, and indeed, it was Congress's intent to avoid obstructing scientists in their work.

In 1995 and 1996, Larry Wayne Harris obtained plague bacteria from the American Type Culture Collection using letterhead from a laboratory. This incident moved Congress to pass the Antiterrorism and Effective Death Penalty Act of 1996, which added that not only must the perpetrator have "intent to use [biological agents] as a weapon . . ." but also "attempts, threatens or conspires to do the same."[5] Larry Wayne Harris identified himself as a scientist[6] which contributed to the concern that prompted Congress to begin to regulate biological agents typically transferred by scientists in laboratories and academic institutions to other researchers, rather than merely making criminal the use or intent to use them as weapons.

The regulatory gap between possession of these agents and the attempt to use them as weapons began to close when Congress created the select agent regulatory framework.[7] The select agent framework "represents a legislative mandate to balance the regulatory oversight of agents and toxins that have the potential to pose a severe threat to public health and safety while maintaining availability of these agents and toxins for research and educational activities."[8] From 1996 until 2002, scientists could remain out of the reach of regulation of these agents unless they chose to ship them. Then, compliance with transportation labeling and notification requirements would be required. In the 1996 publication of the final rules, the CDC responded to concerns from scientists that mere possession would be governed by the regulations. They responded that "[t]his final rule and associated criminal penalties apply only to interstate and intrastate transfer

4. Biological Weapons Anti-Terrorism Act § 175, 18 U.S.C. § 175 (2006).

5. Antiterrorism and Effective Death Penalty Act of 1996, Pub. L. No. 104-132, § 511, 110 Stat. 1214, 1284 (1996) (codified as amended at 18 U.S.C. §175 (2002)).

6. The Associated Press, *Man Accused of Ordering Plague by Mail Found Guilty*, CHI. TRIB., Apr. 22, 1997. ("I am a scientist. I am absolutely of no harm to anyone.").

7. 42 C.F.R. § 73.12–13.

8. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg.13,294, 13,297 (Mar. 18, 2005) (to be codified at 42 C.F.R. pt. 73).

of these agents. Possession of these agents is outside the scope of this final rule . . . ."[9]

The anthrax attacks of 2001 following 9/11 prompted Congress to close the gap between possession and criminal intent to use or attempt to use a biological weapon. The USA PATRIOT Act criminalized the possession of an agent "of a type or in a quantity that, under the circumstances, is not reasonably justified . . . ."[10] The statute also added the expanded definition of weapon to include the development or possession of an agent "for other than peaceful purposes."[11]

The USA PATRIOT Act was effective immediately upon its passage on October 23, 2001, and the first person was charged under the new rules in November 2001. Tomas Foral, a graduate student at the University of Connecticut was charged with possessing an agent for no "reasonably justified" purpose. While a graduate student at the University of Connecticut, he was found in possession of anthrax from about October 27, 2001 until November 27, 2001. Foral was charged with "unlawfully retaining a portion of the anthrax that had been discovered in October, 2001 at a University of Connecticut research laboratory in Storrs. The charge [of] unlawfully possessing a biological agent carries a maximum term of incarceration of 10 years and a fine of as much as $250,000 . . . ."[12]

The second generation of the select agent rules was also set forth in the USA PATRIOT Act. The new regulations required informational disclosures, security background checks, security plans for laboratories, and registration of facilities and personnel where select agents were housed. This second generation was an interim final rule in December 2002, and became effective February 7, 2003.[13] These rules effectively changed the culture of biodefense research from one of fetterless freedom in the laboratory to one of controlled security and accountability to a regulatory authority.

2.1 Mere Possession and Criminal Intent

In 1996, scientists feared that mere possession would make them criminals, and indeed, Congress sought to limit the rules so as not to impede legitimate research of scientists. The CDC assured scientists that

> [t]his final rule and associated criminal penalties apply only to interstate and intrastate transfer of these agents. Possession of these agents is outside the scope of this final rule; however, [an] individual in possession of a 'biological agent or toxin . . . for use

9. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. 55,190, 55,194 (Oct. 24, 1996) (to be codified at 42 C.F.R. pt. 72).

10. 18 U.S.C. § 175 (2002).

11. *Id.*

12. Press Release, U.S. Dep't of Justice, (Nov. 19, 2002), *available at* http://roundtable.healthsafe.uab.edu/pdfs/doj_pr_11_19_02.pdf.

13. 42 C.F.R. § 73.6, 73.7, 73.10, 73.11, 73.12 (2008).

> as a weapon' as defined in Title 18 of the U.S. Code, may be subject to separate criminal penalties (18 U.S.C. 175 et seq.).[14]

The gap between the regulation for movement of select agents and the intent to use them as weapons left many activities unregulated, ranging from the work of a clandestine scientist to the legitimate work of the government scientist.

In 1996, scientists were concerned about the inadvertent or unintentional mistake that could make criminals of scientists. In particular, the question was raised to make the required mental state required for the crime very clear. The criminal state of mind required to be convicted under the rules governing select agents, the CDC explained, was found in two criminal statutes:

> Title 18, United States Code, Section 1001 applies to false statements made to the Federal Government in connection with the rule. Such false statements may be made in connection with a facility's application to become a registered entity, completion of CDC Form EA-101 for transfers of select agents, and in other circumstances. To constitute a criminal violation, Section 1001 requires that the false statement be made "knowingly and willfully." Other violations of the rule are covered under Title 42, United States Code, Section 271. This violation is classified as a misdemeanor and requires a "knowing" mental state by the defendant. Thus, both of these criminal statutes subject offenders to punishment for knowing conduct.[15]

Among the first to be charged under the criminal provisions of the new post-9/11 regulation, 42 C.F.R. § 73, was Associate Professor Steven Kurtz of the University of Buffalo. In 2004, Professor Kurtz was arrested for possession of bacteria in his home. Professor Robert Ferrell, Department of Human Genetics at the University of Pittsburg had supplied the bacteria to Professor Kurtz, an artist who depicts biotechnologies in art forms. Kurtz had asked Professor Ferrell for biological materials, and Ferrell ordered *serratia marcescens* and other innocuous bacteria.[16] However, since the bacteria was not a select agent, it did not fall within the scope of the select agent regulation. Despite this discovery, the U.S. Attorney's Office continued to investigate the case against both Ferrell and Kurtz.

In another case, Professor John K. Rosenberger of the University of Delaware, an expert in avian influenza, was charged with smuggling an avian flu virus into Maine and then to a laboratory in Delaware in 1998. Rosenberger pleaded guilty in September 2004 to violation of the select agent rules. Although Rosenberger is recognized as an international author-

14. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. at 55,194.

15. *Id.*

16. *Serratia marcescens*, a usually harmless bacteria, has a bright red color.

ity on avian influenza virus, a felony conviction would permanently bar him from ever working with any select agent again.

The select agent rules and the bioweapons criminal statute have effectively closed the gap between the criminal and the mere possession of select agents and potentially subject biodefense researchers to one or both of these statutes, as illustrated in the preceding examples.

In addition to the select agent rules, the transportation of select agents continues to be an important part of tracking biological agents. The transportation requirements criminalize the failure to complete shipping papers, the failure to mark shipments, and the failure to affix a Class 6.2 shipping label indicating a biohazard. Imports are controlled by U.S. Customs and exports must be permitted by the Department of Commerce.

It was the exportation of the plague bacteria which carried the longest prison sentence for Professor Thomas Butler of Texas Tech University. The unauthorized export of any commercially controlled item is criminal. One of the disturbing parts of the case was that Dr. Butler had carried the plague onto a commercial airline on which he was a passenger, in what was commonly referred to as the "VIP" (vial-in-pocket) technique. There was no conviction for carrying plague in this manner, because there is no civil or criminal penalty for this action under 42 C.F.R. § 72 since it was not put into interstate shipment. Although 42 C.F.R. § 73 was in a notice and comment period before becoming a final rule, the VIP issue was never addressed, and it remains an unclear violation of the interstate shipment regulations under another title. If the CDC wishes to proscribe this behavior, it should do so in an express rule which does not leave the regulated community unsure about its prohibition.

The prohibition against certain types of experiments is another section of the select agent program which attempts to limit the types of experiments that might be done on biological agents which would make them more useful as weapons.

3.0 The Normative Regulatory Approach

The normative approach to regulation begins with the triggering evaluation of the need for a regulation, where "[i]t is essential to ascertain that there is a legitimate market failure before determining that a regulation is warranted."[17] Second, a cost-benefit analysis should be done; third, the policy choices should be cost-effective; and fourth, there should be balancing of the benefits and costs of policies.[18] However, the efforts to protect the public health and safety from biological agents are not driven by market

17. W. Kip Viscusi, Fatal Tradeoffs: Public and Private Responsibilities for Risk 249 (1992).

18. *Id.* at 249–51.

failures but by social values, where "[t]he ultimate object of social regulation policies is to influence health, safety, and environmental outcomes."[19]

The normative approach to regulation and the economic theory of regulation may explain the 1996 initial regulations after the arrest of Larry Wayne Harris, which focused on the regulation of the transportation of biological agents. Certainly, it was within the scope of the Commerce Clause to regulate articles of commerce moving in interstate commerce. It internalized previously externalized costs of risk to the public in the transportation of select agents. However, the anthrax attacks in fall 2001 changed what had been considered a negligibly low probability event to one with a real probability and high consequences. The increase in the perception of the risk triggered the need to create the new regulatory scheme. The economic theory of regulation would continue to drive the interest in research, but the government became an important participant in the market by regulating itself in national laboratories, as well as the academic and private sector.

Social regulation might seek to internalize previously externalized costs. For example, environmental regulation of hazardous waste applies a "polluter pays" principle, where the costs of disposal are paid by the generator rather than literally sending it down the river to devalue real property values and the health of the downstream human inhabitants and environment.

Normative approaches also seek to maximize existing models by adapting them to new regulatory subjects. The second generation of select agent rules was triggered by the post 9/11 experience of the anthrax attacks in fall 2001. Within the legislative mandate in the 2002 legislation, the CDC considered other models of regulation with similar objectives of public health and safety. The models considered were the Nuclear Regulatory Commission (NRC) licensing model for regulating the use of radioactive materials; the National Committee for Clinical Laboratory Standardization (NCCLS) certification program for hospitals; Institutional Biosafety Committees as utilized with the application of the NIH Recombinant DNA Guidelines; the U.S. Department of Agriculture's Animal Plant and Health Inspection Service (USDA/APHIS) program to regulate the import and transfer of restricted animal pathogens; the American Association for Accreditation of Laboratory Animal Care (AAALAC) Program; and the CDC program to permit the import of etiological agents.[20]

The regulatory approach of the federal government in carrying out the legislative mandate to protect public health and safety from bioterrorism or "biocarelessness" is one of oversight, targeting listed biological agents, facilities where they are located, and persons who have access. The target,

19. *Id.* at 285.

20. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg.13,294, 13,294 (Mar. 18, 2005) (to be codified at 42 C.F.R. pt. 73).

biological agents, has some similarities to the effort to regulate hazardous waste—namely, its quantity is unpredictable and requires self-reporting by the generator. However, unlike hazardous waste, biological agents can be multiplied by simply growing more of them, and they are stored in petri dishes, slants, and test tubes, rather than fifty-five-gallon drums, making detection a major distinction.

The economic theory of regulation stated by Judge Richard Posner holds that "legislation is a good demanded and supplied . . . so that legislative protection flows to those groups that derive the greatest value from it, regardless of overall social welfare . . . ."[21] That is, legislative action works like economics, driven by costs and benefits. This explains the regulatory scheme for hazardous waste, where the regulated community in hazardous waste is the industrial generator in the private sector. While the regulatory scheme for hazardous waste may be considered to be part of the costs of doing business, from an economics perspective, the regulatory scheme for biological agents does not generate income to justify the increased costs of "doing business" which is caused by this regulation. However, increases in funding for biodefense research provide the economic incentive to continue to participate in the regulatory scheme, by both the individual researcher and the researcher's institution.

The regulation also fails to internalize previously externalized costs, like the Superfund legislation which forces the private chemical company to pay for waste treatment rather than externalizing costs through property devaluation and health effects on people and animals. There are no demonstrable external costs from select agents in a laboratory that have been remedied by requiring internalized recordkeeping of quantities of them.

This incentive to continue and increase biodefense research has been widely disclaimed in the popular science journals and media, citing instead that the increased regulatory burden and security measures will cause biodefense researchers to abandon this research. To the contrary, the CDC has concluded in their cost/benefit analysis that there has been no loss of biodefense research, and, if there had been, it would be highly speculative to attempt to quantify it. In March 2005, in publishing the final rule for 42 C.F.R. § 73, the CDC had this comment:

> We agree that the RIA [risk impact assessment] has not attempted to quantify the value of lost research and other indirect institutional effects [of the new select agent rules]. . . . First, based on our experience with the pre-notification and registration process, we believe there will be few instances where universities abandon lines of research in response to the rule. Out of the 200 or so entities that transferred or destroyed their select agents rather than registering under the rule, we believe that the majority did so for

21. Richard A. Posner, *Economics, Politics, and the Reading of Statutes and the Constitution*, 49 U. CHI. L. REV. 263, 265 (1982).

> reasons that do not threaten future research, as suggested by the following three typical examples: (1) Researchers who already have completed efforts under past research grants; (2) universities that continue their select agent research but at fewer locations within the university system; and (3) hospitals that had used select agents for purposes other than research (e.g., quality assurance testing) but which can readily substitute other agents. Second, even if an institution did discontinue its research, we expect that this research would not be "lost." Instead, other universities likely would pick up these research lines, particularly research efforts funded through grants. Therefore, any research effects are likely to be small including, in particular, any shift of knowledge on select agents to outside of the U.S. Third, to the extent that any net reduction in research or other negative institutional effects were to occur, quantification of these effects would be highly speculative.[22]

So, it would seem the economic theory of regulation is consistent with the select agent rules which target the researcher and the researcher's institution.

The CDC's cost/benefit analysis of the regulation considered the costs by first identifying the regulated community in the regulation: facilities and persons with access. It estimated that not more than 817 institutions and facilities are expected to register, and from 2,400 to 10,000 persons with access are expected to be subject to the regulations.[23] The CDC considered that most of the entities seeking registration would already be "for the most part in compliance with these regulations." It attributes 60 percent of the cost to be for "limiting access to select agents and work areas; developing and implementing a security plan; developing and implementing a safety plan; and obtaining risk assessments for existing staff." The benefits are the safety and prevention of financial loss from chaos caused from a release of a select agent or toxin into the environment, whether accidental or intentional.[24]

The regulatory approach sought by the CDC was a focus on the agents themselves for protecting public health, and, interestingly, not the laboratory or the institution, which arguably is a more predictable regulatory tar-

22. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,294, 13,313–14.

23. Possession, Use, and Transfer of Select Agents and Toxins, 67 Fed. Reg. 76,886, 76,894–95 (Dec. 13, 2002) (to be codified at 42 C.F.R. pt. 73). This regulation applies predominantly to academic institutions and biomedical centers; commercial manufacturing facilities (the pharmaceutical industry); federal, state, and local laboratories, including clinical and diagnostic laboratories; and research facilities. Eight hundred seventeen facilities are expected to register and an additional 350 entities are believed to be exempt. The range of numbers of people who have access to select agents and toxins is from three (in small commercial or state facilities) to over 100 in large academic institutions.

24. *Id.* at 76,895–96.

get than select agents which rely solely on self-reporting of their existence and their quantities in order to be regulated. The CDC explained that they considered the Nuclear Regulatory Commission's program to regulate radioactive material as the target, but radioactive material is not self-replicating like biological material.

4.0 A Regulatory Process

4.1 Constitutional Basis for Federal Regulation

The Antiterrorism and Effective Death Penalty Act of 1996 authorizes the Secretary of Health and Human Services (HHS) to regulate the transfer of certain agents harmful to humans. The CDC is the agency within HHS responsible for promulgating this regulation. This rule is designed to ensure that select agents are not shipped to parties who are not equipped to handle them appropriately or who otherwise lack proper authorization for their requests, and to implement a system whereby scientists in research institutions may continue transferring and receiving these agents without undue burdens. Respondents include facilities such as those operated by government agencies, universities, research institutions, and commercial entities.[25] The USA PATRIOT Act broadened the bioterrorism crime. The Public Health and Bioterrorism Preparedness Act of 2002 created the second generation of select agent rules.[26]

4.2 Choosing a Regulatory Target—What is Being Regulated?

Select agents also include its elements of pathogenicity. The regulated select agents, as described in the comments with the final rule, also include

> genetic elements from a select agent, that contain a nucleic acid sequence(s) which, if inserted into an appropriate host system, are reasonably believed capable of producing disease or toxicosis. Genetic elements from a select agent that contains a nucleic acid sequence(s) which, if inserted into an appropriate host system, do not cause disease or toxicosis are not subject to the final rule.[27]
>
> "*Select agent*" is defined as "a microorganism (virus, bacterium, fungus, rickettsia) or toxin listed in Appendix A of this part. The term also includes: (1) Genetically modified microorganisms or genetic elements from organisms on Appendix A of this part, shown to produce or encode for a factor associated with a disease, and (2) Genetically modified microorganisms or genetic elements

25. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. 55,190, 55,196 (Oct. 24, 1996) (to be codified at 42 C.F.R. pt. 72).

26. 42 C.F.R. § 73 (2005).

27. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. at 55,195.

> that contain nucleic acid sequences coding for any of the toxins on Appendix A of this part, or their toxic subunits.[28]
>
> A select agent is selected for the list considering these four criteria:
>
> (1) The effect on human health of exposure to the agent or toxin; (2) the degree of contagiousness of the agent or toxin and the methods by which the agent or toxin is transferred to humans; (3) the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent any illness resulting from infection by the agent or toxin; and (4) any other criteria, including the needs of children and other vulnerable populations, that the Secretary considers appropriate.[29]

4.3 Genetic elements, Recombinant Nucleic Acids and Recombinant Organisms

The interim final rule also regulated genetic elements, recombinant nuclei acids and recombinant organisms as select agents and toxins, where:

> (1) Select agent viral nucleic acids (synthetic or naturally derived, contiguous or fragmented, in host chromosomes or in expression vectors) that can encode infectious and/or replication competent forms of any of the select agent viruses.
> (2) Nucleic acids (synthetic or naturally derived) that encode for the functional form(s) of any of the toxins listed in paragraph (d) of this section if the nucleic acids:
> (i) Are in a vector or host chromosome;
> (ii) Can be expressed *in vivo* or *in vitro*; or
> (iii) Are in a vector or recombinant host genome and can be expressed *in vivo* or *in vitro.*
> (3) Viruses, bacteria, fungi, and toxins listed in paragraphs (a) through (d) of this section that have been genetically modified.[30]

Even this description is inadequate to address the rapidly changing science with synthetic genomics and nanotechnologies which involve multidisciplinary laboratories, some of which are primarily engineering or physics laboratories and would not be subject to these regulations in some cases.

28. *Id.* at 55,199.

29. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. 13,294, 13,296 (Mar. 18, 2005) (to be codified at 42 C.F.R. pt 73) ("The Secretary directed the CDC to convene an inter-agency working group to determine which biological agents and toxins required regulation based on the criteria noted above. In June 2002, the CDC convened an interagency working group to review the current list of select agents and toxins and develop recommendations for a select agent list.").

30. *Id.* at 13,298.

4.4 The Exemptions

4.4.1 The Attenuated Strain Exemption

Attenuated strains may be exempted from regulation.[31] This permits the opportunity for the select agent to be shipped, possessed, or utilized in a laboratory and escape regulation. Attenuated strains are further required to not be "a threat to public health" in order to qualify for this exemption. This might presumably exclude any form of smallpox, although it is not specifically excluded. This further qualification requires a risk assessment in order to determine whether the attenuated strain is not a threat to public health, but the regulations do not specify how this determination is made. Although this is intended to be helpful to clinical diagnostic laboratories, it provides a regulatory gap for misuse of these materials.

4.4.2 Prion Agents

The CDC decided to exclude prion agents from regulation, notwithstanding the comments that these prions could impact the success of public health programs. Creutzfeldt-Jacob Disease and Kuru were two prions that were identified as possible select agents, but the agency declined to include them on the list[32]—notwithstanding the fact that Richard Preston, in his novel, *The Cobra Event,* featured the Creutzfeldt-Jacob Disease as a component of an engineered bioweapon that was said to have inspired President Clinton to begin the new department, DTRA, in the Department of Commerce to fund countermeasures to bioterrorism and other forms of terrorism.[33]

31. *Id.* ("The Act sets the criteria for excluding attenuated strains, *i.e.,* they may be excluded if they do not pose a severe threat to public health and safety, (42 U.S.C. 262a(a)).").

32. *Id.* at 13,296 ("One commenter asserted that the Creutzfeldt-Jacob Disease and Kuru agents should be added to the list of HHS select agents and toxins. The commenter noted that the 'Arguments for omission include the difficulty of obtaining these agents, the extreme difficulty of replicating them, low infectivity by the oral route, and the absence of person-to-person infectivity.' The commenter then argued that they should be included based on the conclusions 'that a single real or claimed incident of contaminating a childhood vaccine with a prion would cause indescribable anguish' and that 'The difficulty of confirming or refuting a claim that prions had been added to a vaccine would cripple most legitimate public health programs and result in epidemics of preventable diseases.' The commenter concluded by stating that 'In my judgment, the remote but extreme risk fully justifies the cost of including prions that are infectious to humans.' We made no changes based on this comment. Based upon the criteria that the HHS Secretary must consider, it was the consensus of the Secretary's Select Agent and Toxin Working Group that Creutzfeldt-Jacob Disease (CJD) and Kuru agents should not be added to the list because the degree of contagiousness of prions are too low to pose a significant mass casualty threat. While they are infectious under some circumstances, such as cannibalism in New Guinea causing Kuru or Creutzfeldt-Jacob Disease by the consumption of infected bovine central nervous system tissue, there is no evidence of contact or aerosol transmission of prions from one human to another.").

33. Judith Miller & William J. Broad, *Exercise Finds U.S. Unable to Handle Germ War Threat*, N.Y. TIMES, Apr. 26, 1998, § 1, at 1.

Exempting prions is not qualified by the risk to public health, and therefore creates another gap in regulation, including the laboratory security requirements of 42 C.F.R. § 73.

4.5 The Exceptions

4.5.1 The Clinical Specimen Exception

The largest gap in the select agent rules is the clinical specimen exception, which permits clinicians to transport any specimens from patients without falling within the scope of the select agent rules. A clinician who takes fluid from a bubo of a bubonic plague victim knows almost certainly that the specimen contains plague, but because it is not analyzed as such, it is still a clinical specimen under the regulation. Knowing this, one commenter to the regulations in 42 C.F.R. § 72 "wanted to know if tissue samples that only contain small amounts of the agent or that may only be suspected of containing a pathogen would be covered by the final rule."[34] The CDC responded by focusing on the suspected material, but added again the exception language: "All materials that are known or reasonably suspected of containing a select agent, including tissue samples, unless exempted as a human or veterinary clinical specimen, are subject to this regulation."[35] This signaled an implicit agreement by the agency that such a broad exemption should exist for a specimen even though it might be suspected of containing a select agent, presumptively to avoid the burden to clinicians who are treating patients and may or may not be involved in research.

4.5.2 Laboratory Exception

A second exemption for facilities exists for CLIA laboratories which are certified to diagnose diseases and may possess select agents as a reference sample for verification of their test.[36] However, one of the most significant accidents since the promulgation of these new regulations was the CLIA laboratory receipt of a mistaken shipment of a non-virulent strain of influenza for use as a diagnostic. The CLIA laboratories were the recipients of a virulent flu strain (virulent by mistake) which was sent throughout the United States as a reference sample to confirm the existence of flu. These laboratories were exempt from the security requirements of regulated labo-

34. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. 55,190, 55,191 (Oct. 24, 1996) (to be codified at 42 C.F.R. pt. 72).

35. *Id.*

36. *Id.* at 55,196 ("(2) Exemption of CLIA certified laboratories: Clinical laboratories certified under the Clinical Laboratory Improvement Amendments of 1988, (42 U.S.C. 263a) (CLIA), that utilize these select agents for diagnostic, reference, verification, or proficiency testing purposes are exempt from the provisions of § 72.6.").

ratories, and all quality control measures were outside the scope of the regulation.

4.5.3 Natural Environment Exception

The third exception provides a gap in the select agent rules which would allow the would-be terrorist to remain undetected among a menagerie of animals which might provide a living laboratory for the terrorist. The final rule states that a select agent or toxin under these rules does not include any select agent or toxin that is "in its naturally occurring environment provided it has not been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source."[37] The CDC provides some examples of this natural infection: "Select agents in their naturally occurring environment could include animals that are naturally infected with a select agent or toxin (e.g., macaques that are naturally infected with *Cercopithecine herpesvirus 1* or milk samples that contain *Coxiella burnetii*."[38] If the animal is intentionally collected, then the would-be terrorist could not legally house these animals because of presence of the disease—for example, a prairie dog carrier of bubonic plague or tularemia. An antibiotic resistant plague could be created among the animals without ever extracting the plague bacteria and the prairie dogs could be sold as pets, launching an outbreak of tularemia and plague.[39] However, if it is the intentional collection of the select agent or toxin that the rule precludes, then keeping the animals poses no violation.

The CDC explains the rule that it is the extraction of the select agent or toxin by taking tissue from the animal rather than the collection of the animal that is the violation:

> However, a select agent or toxin that has been intentionally introduced, cultivated, collected, or otherwise extracted from its natural source, including tissues from animals or agents or toxins obtained from milk samples that have been naturally infected with a select agent or toxin, is subject to this part . . . .[40]

But discovery of the presence of a select agent or toxin in the animals is not required by the CDC unless the discovery was made due to the intentional acts described above.

Any individual or entity that intentionally extracts and discovers that a select agent exists is then required to report it to the CDC: "[I]n such a case

37. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg.13,294, 13,298–99 (Mar. 18, 2005) (to be codified at 42 C.F.R. pt. 73).

38. *Id.* at 13,299.

39. There was an outbreak of tularemia from pet prairie dogs reported to the CDC which required treatment of all those exposed and the destruction of potentially infected animals over several states. This could have been similar to a would-be terrorist attack, and might have been suspected as one, if the prairie dogs had been randomly placed in several states, for example.

40. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,299.

the entity is required to report the select agent or toxin upon identification."[41] This explanation fails to describe how that reporting entity would avoid prosecution under other parts of the rule which require registration of the facility and safety plans, as well as security risk assessments of all those who have contact with the select agents. The possibility of such an entity making such a report is practically nonexistent without further explanation by the CDC that there would be no penalty for doing so.

4.6 Failure to Exempt the Disclosures from FOIA

4.6.1 Information for the Public

The collection of information by the federal government inevitably leads to the question of its accessibility by the public through the Freedom of Information Act (FOIA). During the comment period for the 1996 regulations which established a list of registered facilities, concerns were raised about the availability of a list of institutions housing select agents. The concern was that such "a publicly available list of registered facilities would serve as a 'roadmap' to would-be terrorists of facilities possessing these dangerous agents."[42] Another concern was that the database and transfer forms may contain proprietary information.[43] This information was not exempted from FOIA. Instead the burden was on the submitter to pursue legal action to prevent the release of the information upon notification to the submitter that the information had been requested.[44]

Further, the FOIA exception did not protect information that might be a threat to the security of the laboratory where select agents are stored in the case where public institutions are regulated by state open records statutes, and although the information at federal agencies may be protected, the state institution itself may be required to disclose almost limitless records on the storage, location, and amounts of select agents that may be in a state institution. For example, the University of Texas was sued by the Texas Attorney General for failing to disclose information about its select agent program pursuant to a state open records request by the non-profit organization, The Sunshine Group. The Texas legislature has introduced legislation to provide for an exception to the open records act in order to protect information that might be a threat to laboratory security.

It is clear from published statements from the CDC that it considers the identification of location to be a possible threat to security. For example, it has given facilities the option of posting a sign on the door of the

41. *Id.*

42. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. 55,190, 55,194 (Oct. 24, 1996) (to be codified at 42 C.F.R. pt. 72).

43. *Id.*

44. *Id.* at 55,195.

laboratory describing what select agent is stored inside, if the entity believes it may be a threat to security.[45]

5.0 The Laboratory as the Regulatory Target

The National Committee for Clinical Laboratory Standardization (NCCLS) model for certifying hospitals, or the American Association for Accreditation of Laboratory Animal Care (AAALAC) Program model would have targeted the facility and made institutions rather than researchers and select agents the target.

Although the CDC considered the Institutional Biosafety Committees (IBCs) as utilized with the application of the NIH Recombinant DNA Guidelines, violation of these guidelines results in loss of federal funding rather than criminal sanctions like the select agents rules. Should the IBCs, whose members are employed by the institution, be utilized where conflict would exist where facilities and institutions are to be accountable and potentially civilly liable under the select agent rules? The very problem of self-reporting by the researcher would leave IBCs and their institutions without knowledge of the existence of select agents, should the researcher decide not to report. In fact, Thomas Butler in *United States v. Butler*, had failed to disclose his possession of plague bacteria to university officials, and it was not until he reported it as "stolen" that the institution became aware of his activities which included possession of the bacteria in his laboratory.[46] His activities were presumably secret because of the financial arrangements with pharmaceutical companies which were not disclosed to the university, resulting in diversion of funds from the institution and, ultimately, criminal penalties for Butler.

5.1 The Biological Safety Laboratory BSL Vagueness:

> Incorporation of the BMBL. Some commenters questioned incorporating the BMBL into the regulation because, in their view, the BMBL provides "guidelines" that are vague, and lack specificity and sufficient detail. One commenter recommended that the BMBL be augmented or updated to provide a clear objective standard. Because the BMBL serves as the only nationally and internationally recognized source for biosafety requirements for laboratories, the final rule retains the incorporation of the BMBL. The BMBL provides the minimum requirements for BL-2, 3, and

45. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,306 ("In this final rule, 42 C.F.R. 73.12 (Biosafety) provides that an individual or entity should consider the BMBL and NIH Guidelines when developing a biosafety plan. However, it is the entity's responsibility to determine if posting biohazardous signs on access doors would compromise laboratory security.").

46. United States v. Butler, 429 F.3d 140 (5th Cir. 2005).

> 4 laboratories and animal facilities and is readily applicable to a facility registration and inspection process.[47]

In a survey conducted in 2008 among biodefense researchers in the U.S., almost half of the respondents would prefer clear guidance to the vagueness of the BMBL, which is used as an enforcement tool rather than as guidance. The other half wanted to leave the BMBL as it is currently used. This suggests that, after five years of use, what might typically be more acceptable as the status quo is questioned as unclear after more than five years of implementation of this regulatory aspect of the rule.

A safety plan is also required by 42 C.F.R. § 73.12, which vaguely refers to considering the incorporation of the BSL requirements.[48] This cannot be used as an enforcement tool without being subjected to the notice and comment process of rulemaking under the Administrative Procedure Act, which subjects the regulated community to enforcement without constitutional requirement of due process.

6.0 What is the Objective of the Regulation?

6.1 Public Health and National Security

Biosafety is a regulatory objective which attempts to regulate safe handling and storage of the select agents. On the other hand, biosecurity is a regulatory objective which attempts to safeguard the storage of select agents from intentional or accidental access to unregistered individuals.

"National Security" as a goal of the statute is largely derived from the description of the objectives of biosecurity, but it is explicitly mentioned in the section of the rule requiring security risk assessments (SRAs), indicating that the purpose of the select agent rules includes a national security goal. In comments to the regulation, former CIA Director Bobby Inman wrote that "Science and national security have a symbiotic relationship . . . . In the long history of that relationship, the suggestion is hollow that science

47. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. at 55,191.

48. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,308 ("The amended interim final rule provided that an entity subject to the part 73 regulations must develop and implement a safety plan and in developing a safety plan, an entity should consider: '(1) The biosafety standards and requirements for BSL 2, 3, or 4 operations, as they pertain to the respective select agents, that are contained in the CDC/NIH publication, "Biosafety in Microbiological and Biomedical Laboratories" including all appendices except Appendix F. (2) The specific requirements for handling toxins found in 29 CFR part 1910.1450, "Occupational Exposure to Hazardous Chemicals in Laboratories" and/or 29 CFR part 1910.1200, "Hazard Communication," whichever applies and specific requirements for handling toxins found in Appendix I in the CDC/NIH publication, "Biosafety in Microbiological and Biomedical Laboratories." (3) For provisions of the safety plan relating to genetic elements, recombinant nucleic acids and recombinant organisms, the "NIH Guidelines for Research Involving Recombinant DNA Molecules," (NIH Guidelines). This includes, among other things, provisions regarding risk assessment, physical containment, biological containment, and local review and applies to all recombinant DNA research, regardless of funding.' ").

might (or should somehow) be kept apart from national security concerns, or that national security concerns should not have an impact on 'scientific freedom.' "[49]

One of the more controversial areas of the regulation has been the "access" definition, a feature of meeting the biosecurity goal of the statute.

6.2 Who Has Access?

During the rulemaking process, comments about the meaning of "access" in 42 C.F.R. § 73.10 that were received before the final rule was published on March 18, 2005, indicated that "the use of the terms 'area' and 'access' were confusing. Thus the term 'area' was eliminated unless it is in clear context."[50] The rule was evidently still vague because the agency added an explanation that "[a]n individual will be deemed to have access at any point in time if the individual has possession of a select agent or toxin (e.g. ability to carry, use, or manipulate) or the ability to gain possession of a select agent or toxin."[51]

In response to comments, the agency described who was an unauthorized person who could not have access and explained that "unauthorized persons are those unescorted individuals who do not have access approval from the HHS Secretary or Administrator and who are in areas where they could gain access to select agents or toxins."[52] This gave some guidance in that every individual would require an escort, but was problematic for cleaning personnel or maintenance personnel and raised a question as to what extent they required escorts. To address this regulation, many cleaning companies became specialized and obtained clearances for cleaning personnel who then became authorized to have access to select agents for security purposes; from a practical perspective, though, they had no training for biosafety aspects of having access to select agents.

6.3 Security Risk Assessments for Those Who Have Access

Security risk assessments (SRAs) are required for individuals who are authorized and have access to select agents. The CDC refused to make changes based on the commenters' assertions during the comment phase of the regulatory process, which asked for the portability of registrations so that scientists could conduct research at multiple institutions, part of the culture and practice of biological research.[53] Sometime after the final publi-

49. Admiral Bobby Ray Inman, *Federal Restraints on Research*, IEEE SPECTRUM, May 1982, at 60.

50. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,295.

51. 42 C.F.R. § 73.10 (2005).

52. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,307.

53. *Id.* at 13,304 ("Commenters asserted that the regulations should allow security risk assessment approvals for individuals to be portable from entity to entity, from location to location, and from project to project. One commenter recommended that an individual's clearance remain

cation, the CDC agreed to this change, but only after rejecting the comments initially and then acquiescing after publication.

However, the CDC, APHIS, and the U.S. Attorney General agreed that an additional SRA was not needed where an individual was visiting another facility to work with select agents. However, the "Responsible Official "of the destination facility was required to write a letter to clarify this approval and to note that the individual has a current SRA. The host institution was then required to amend their registration accordingly.

However, the CDC, APHIS, and the Attorney General have agreed to, and have already implemented, a policy where an additional security risk assessment is not needed in cases where an individual has a current security risk assessment and will be merely visiting another entity.[54] This excessively burdensome requirement ensured that the time to acquire such an approval was often long after the need for the individual to visit had passed, making this largely an unworkable policy.

6.4 Who Cannot Have Access:

The biosecurity aspect of the regulations regarding access derives its authority from the bioterrorism criminal statute prohibiting possession or use of biological weapons. This rule also defines who should be "restricted persons" that are denied access to select agents.[55] These criteria are substantively the same as for those required to have a permit to buy a firearm, suggesting again that the normative approach to regulation was taken by regulators, i.e., to utilize an existing model of regulation which sought to protect public safety. However, the regulation, as is the case with handgun control, may not meet the goals and objectives of the legislation.[56]

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valid if the scientist moves to another institution as long as the scientist's new employer amends its registration document promptly to include the individual. The commenter also recommended 'that the Department clarify that an individual's clearance will continue to be valid if his or her laboratory is relocated among any of the facilities under the oversight of the entity's Responsible Official" and added that 'The change in location should, of course, be reflected in a timely amendment of the entity's registration.' We made no changes based on these comments.").

54. *Id.* ("If a registered entity wants a visiting individual to have access to select agents or toxins, the RO of home entity will have to send to the RO of host entity a letter stating that the individual is currently identified on the home entity's Select Agent registration and that the individual has a current SRA approval. The host entity RO can then submit this letter and an amendment to their registration. Once the visit is complete, the host entity would then amend their registration to remove the visiting individual's name. In some circumstances the host entity may decide to leave the individual on the registration, if the same individual will be visiting the entity again. Specific guidance on the process has been made available to the public on the Select Agent Program web site. In addition, in this final rule, we have added the requirement that an individual with access to select agents or toxins must have the appropriate education, training, and/or experience to handle or use such agents or toxins. We believe this requirement is necessary to ensure that the individual has the appropriate education, training, and/or experience to handle such agents or toxins.").

55. 18 U.S.C. § 175b (2005).

56. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,305 ("[The commenters] argued that the term 'restricted person' would cover an individual who re-

7.0 Prohibitions on Certain Types of Research

The dual-use dilemma, which refers to biological research which can be used for both benevolent as well as malevolent purposes, and bioethics underlie the objectives of the prohibition on certain types of research in addition to the goals of biosafety and biosecurity. Targeted in 42 C.F.R. § 73 is the prohibition of certain types of research with select agents. In 1996, the CDC explained that

> [t]he deliberate transfer of a drug resistance trait to microorganisms listed in this Appendix that are not known to acquire the trait naturally is prohibited by NIH 'Guidelines for Research Involving Recombinant DNA Molecules,' if such acquisition could compromise the use of the drug to control these disease agents in humans or veterinary medicine.[57]

The amended interim final rule for 42 C.F.R. § 73 in 2003 stated that "an entity may not conduct certain experiments unless approved by the HHS Secretary after consultation with experts." No specific body of experts was identified, and the agency left open the flexibility to consult any expert "as needed for decision making" and that they would "consult with subject matter experts as necessary."[58]

The normative approach is simply utilizing existing models for regulating select agent use. The CDC used the IRB model of reviewing DNA experimentation to apply to experiments in biodefense, and indeed, from the CDC explanation, it is clear that they consider this to be nothing more than an extension of the scope of experimentation monitoring of recombinant DNA research. The regulatory goal of the DNA monitoring model is to protect public safety and prevent unethical and unscientific research from being funded or supported by the institution. The goal of the select agent experimentation is also to protect public health and safety; but in contrast to the DNA experimentation concerns, the biodefense research is also intended to prevent the creation of dangerous knowledge which could be acquired by bioterrorists in their efforts to develop weapons with regard to not only a public health risk, but a national security risk. Is the IRB model appropriate for the protection of national security interests as well as public health interests?

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ceived a dishonorable discharge from the U.S. military for homosexuality and could not understand how precluding such individual from ever working on select agents would protect the security of the United States. Commenters also argued that 'it is predictable that some individuals who are currently productive, respected members of the scientific community and who have performed work with select agents or toxins meet one or more of the definitions of a 'restricted person.' We made no changes based on these comments.").

57. Additional Requirements for Facilities Transferring or Receiving Select Agents, 61 Fed. Reg. 55,190, 55,200 (Oct. 24, 1996) (to be codified at 42 C.F.R. pt. 72).

58. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. at 13,308–09.

One of the inherent problems with biodefense research is the need to build organisms on which to experiment to determine the efficacy of antibiotics. This would necessitate the building of organisms with potentially antibiotic resistant characteristics, and is a typical approach to determining efficacy at the earliest stage of countermeasures research. Potentially, this would be prohibited under this regulation and would require an extensive review process. Comments made during the comment phase indicated that this was a problem, but the CDC again refused to make any changes to the rule.[59]

The normative approach utilizing existing models used the IRB model of reviewing DNA experimentation to apply to experiments in biodefense. The regulatory goal of the DNA monitoring model is to protect public safety and prevent unethical and unscientific research from being funded or supported by the institution. The goal of the select agent experimentation is also to protect public health and safety, but in contrast to the DNA experimentation concerns, the goal of the effort is to place "stringent scrutiny" on these areas of research. The "stringent scrutiny" explained by the agency is to provide for the future experimentation that they may not have contemplated. Commenters also suggested additional kinds of research that should be restricted, but the agency declined to add these experiments.[60]

Although the CDC indicated that they would propose new rules for additional experiments in 2005, as of this date no proposal has been made for consideration of additional kinds of prohibited experiments. The explanation was simply that they would continue to "study" these kinds of experiments and what "should be added to § 73.13. Experiments will be proposed for addition to the listing of restricted experiments as warranted, through the publication of a proposed amendment for public comment."[61]

One commenter questioned whether the HHS secretary could limit or proscribe research: The CDC responded:

59. *Id.* at 13,309 ("The commenter asserted that if strictly imposed, the restricted experiment provisions would limit this standard research practice and provided an example concerning antibiotic resistance application. The commenter stated 'Transposon insertion libraries are common experimental creations used to generate gene knockouts and study the effect on expression and phenotype' and 'this often results in an array of genomes containing antibiotic resistance markers used for selection and screening.' The commenter then argued that 'The method is common enough not to need approval from a cabinet level position and too burdensome if approval is needed for each of several thousand insertional mutants that would be created for a single genome.' We made no changes based on this comment.").

60. *Id.* ("One commenter argued that the following experiments should be added to the reserved paragraph based on the conclusion that they warrant such stringent scrutiny (i.e., should be allowed only if approved by the HHS Secretary after consultation with experts): (1) Experiments involving construction of vaccine-resistant select agents or toxins. (2) Experiments involving increasing the environmental stability of select agents or toxins. (3) Experiments involving powder or aerosol production of select agents or toxins (other than preparation of lyophilized reference specimen <10 mg). (4) Experiments involving powder or aerosol dispersal of select agents or toxins.").

61. *Id.*

> We believe we have such authority. In this regard, the Act at 42 U.S.C. 262a(c) states that the "Secretary shall by regulation provide for the establishment and enforcement of standards and procedures governing possession and use of listed agents and toxins . . . in order to protect public health and safety.[62]

8.0 What Will the Third Generation of Select Agent Regulation Look Like?

An effort will be made to fill the existing gaps. Although the coverage of the regulation extends to both the private sector and the public sector, there is no regulation of laboratories that supply the biological agents in the first place. The first order of business should be to target the source of the biological agents. For example, when a suspect is being investigated who has possession of a biological agent, the first priority is to find the source or supplier which is often one of the supply laboratories like American Type Culture Collection. Three of the four incidents with biological agents described in this article show that the biological agents were obtained from somewhere other than the suspect's own laboratories: Larry Wayne Harris, Prof. Robert Ferrell, and Prof. John K. Rosenberger. Two of these three received the biological agents from a supply laboratory—American Type Culture Collection.

There are an estimated 453 laboratories in the world in 67 countries which supply biological agents. Not only will they ship ordinary biological supplies, but eighteen of these laboratories will ship, for example, bubonic plague samples. Keeping these channels open for academic research is vital to the worldwide research community. The United States controls the importation of select agents through 42 C.F.R. § 73.16(iii), while U.S. Customs has regulatory authority over importation permits. The inability to control the supply laboratories outside of the United States ensures a steady supply for any purchaser.

The CDC registration process as a condition of receiving U.S. funding for international laboratories is a foray into the international arena. The next step might be to partner with the World Health Organization (WHO), which has developed laboratory biosecurity guidelines, to create a laboratory registration process which would be a prerequisite for U.S. funding.

9.0 Analysis of Regulations

The select agent rules are enforcement-intensive and therefore resource-intensive. This administratively burdensome design does not make this model useful to less wealthy countries seeking appropriate biosafety and biosecurity regulatory models. The benefit of predictability and notice about how one is being regulated is also a weakness of this regulatory

62. *Id.*

model. The problems of modeling an inventory program of biological, self-replicating organisms after a radiological inventory program are self-evident. Many of the enforcement examples have been related to this inventory issue, making the regulatory system at risk of outweighing the benefit of its burden. The most important information from the inventory rule is simply the type of organism that is being inventoried and not the quantity, which is largely irrelevant. This descriptive information, not quantitative information, dictates the laboratory security level through the BMBL guidance and the risk assessments of the individuals with access. In a national survey of biodefense researchers in 2008, the researchers were given several choices concerning the usefulness of the select agent inventory rule, and almost one-quarter of the respondents thought that the regulation was not useful.[63]

The limiting of experiments is also vaguely unhelpful to national security. However, the fact that they are managed by the IBC makes this a reasonable regulation with local accountability—both the individual and the institution are responsible for experiments conducted. However, there are no civil or criminal penalties for violating the experiments rule (only withholding of funding).

The institution as a target through the requirement for a security plan and compliance with the BMBL guidance proves to be the most important measure to protect public health and national security, yet the BMBL guidance is incorporated only by reference to be "considered" by the entity or individual in their security plans.[64]

10.0 Conclusion

Because compliance with the BMBL laboratory safety standards is sufficient to gain NIH funding in other countries, the CDC must conclude that this standard sufficiently protects public health and national security. If it is sufficient for the safety of these laboratories, why is disclosure of select agents and their ever-changing inventories required to make laboratories safe, merely because they are located in the United States? Withholding funding is a sanction which can be administered by NIH, and the one which drives international laboratories to comply with the CDC's requirements. Yet, the CDC has chosen not to require compliance with select agent rules, but only with BMBL standards.

The BMBL Guidance, based on specific proscriptive requirements, is incorporated by reference to the regulation of select agents, but the violation of these requirements carries no penalties. The only penalty is loss of federal funding, which leaves the private laboratory (which receives no

63. National Biodefense Research Survey, presentation, American Society of Microbiology, February 2009, Baltimore, MD.

64. Possession, Use, and Transfer of Select Agents and Toxins, 70 Fed. Reg. 13,294, 13,306 (Mar. 18, 2005) (to be codified at 42 C.F.R. pt. 73).

CDC funding) with no economic incentive to comply with the proscriptive requirements of the guidance. Future regulations will ultimately consider incorporating the safety standards into the regulations, because it is the environment in which the biological agents are stored which directly relates to the safety of the public.

Third, the clinical specimen exception has been a glaring hole in the otherwise seamless domestic regulatory scheme. The clinical specimen, often more likely than not to contain a select agent, requires no advance notice of transportation, registration of the person with access or registration of the facility, or transportation permits or import or export permissions. Clearly, the withdrawal of fluids from buboes of a bubonic plague patient, before confirmation, has such a high likelihood of being positive that applying this sweeping clinical specimen exception simply invites unregulated shipment of dangerous pathogens. This sweeping exception of clinical laboratories is an example of the rule of "agency capture," where the regulated community "captures" the agency and the agency begins to meet the demands of the regulated community in order to avoid unwanted political pressure.

Fourth, the exemption of select agents in the natural environment would allow the fringe operator to maintain a living laboratory without falling into the scope of either the select agent rules or the crime of bioterrorism. The technology to obtain anthrax or other select agents from the natural environment leaves this wide gap in the control of select agents.

Fifth, restricted experiments are already controlled by scientific ethics which, if violated, may result in suspension of grant funding. The restricted experiments rule adds little to the existing regime. The notion of academic freedom does not imply that there can be no constraints on activities, but these activities must conform to a standard of professional methods and conduct within the discipline of the research which may include a code of ethics and restrictions on behavior.

11.0 RECOMMENDATIONS

The normative approach—identifying the target of regulation as "select agents" and developing a performance-based or standards-based regulation to control them, first in transportation, then within the laboratory—relies too much on the normative as a measure of success rather than on true workability in the regulated community. When the gaps in the regulation are examined, the dual goals of public health and safety and national security should be the focus rather than the ease of enforcement for the regulators. One of the goals thwarted by this regulatory regime is the need for scientists to collaborate freely with colleagues nationally and internationally to achieve the objectives of biodefense countermeasures.

Registering scientists to also allow portability of their registration was a long-sought goal, which was eventually amended by the CDC. This was a positive response to feedback from the regulated community, and allowed any registered scientist to possess any of the select agents that may be on a list as an appendix to their registration. However, the enforcement objective of controlling select agents cannot be achieved by a system which cannot account for the replication of biological organisms, which will ultimately prove administratively infeasible and counterproductive to biodefense goals.

Laboratory safety with specific BMBL guidelines should be extended internationally contingent on funding to organizations that collaborate with U.S. scientists.

The attached chart describes factors in several cases involving select agents that are regulated by the select agent regulations. The commentary suggests that even fully implementing the select agent regulations would not have prevented any of these incidents. Given these weaknesses in the regulation, the target of the regulation should be reconsidered. Rather than making the select agent the target of the regulation, the commentary suggests that a more effective target might be the facilities and the individuals working with the select agents. More focus on specific regulations and certification of facilities without the vagueness of the guidance used as an enforcement tool would address the biosafety problem inherent in the design of the regulations. The focus on better security risk assessments (SRAs) of individuals who are then left to their own professional standards in working and storing select agents within the framework of the facilities certification is also suggested as a better target for the regulation and more likely to achieve the goals of biosecurity and biosafety.

Year of incident	1984	1995	2001	2001	2003	2004	2004
Responsible party	Rashmeeshee, Oregon cult community	Larry Wayne Harris	Allegedly, Bruce Ivins	Foral, graduate student	Butler, professor, MD, Infectious diseases	Ferrell, professor, human genetics scientist Kurtz, professor, art	Rosenberger, professor, specialist in avian viruses
Type of target	Salmonella	Plague	Anthrax	Anthrax	Plague	Serratia marcensens	Univ of Delaware
Select agent inventory—would inventory have helped?	No	No	No	Yes	No	No	No
institution	State licensed CLIA lab		USAMRIID	Univ of Connecticut	Texas Tech University	Univ of Pittsburg Univ of Buffalo	Univ of Delaware
Security plan of the Laboratory and "access"	Taken from their own controlled laboratory	Taken through mail and to home and car	Purportedly developed in the laboratory and taken out to mail	Stayed within the laboratory	Collected clinical samples in Tanzania, but transported in and out of the United States and across state lines	Through mail and between professors from ATCC to the laboratory of Ferrell to the art studio of Kurtz	From domestic birds in the Soviet Union, Hand-carried to the U.S. and from Univ of Delaware to Maine vaccination production facility
Individual SRA Would SRA have alerted authorities?	Yes, Association with radical group	Yes, Association with radical group	Ivins had passed the required background check, required only once	No, No known association that has been made public	No, Long history of distinguished research in plague	No, Ferrell (who obtained the agent) Long history of distinguished research in human genetics Yes, Kurtz, activist against biotechnology	No, Long history of distinguished research in avian flu viruses.
Other possible regulatory approaches			More frequent psychological checks				
select agent source	Their own licensed lab	ATCC	?	Old samples within the same laboratory	Samples from infected patients	Ordered from ATCC?	Smuggled into the United States from Russia