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For the Hearing "Germs, Viruses, and Secrets: The Silent Proliferation of Bio-Laboratories in the United States"

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Thank you for inviting the Center for Arms Control and Non-Proliferation to discuss issues related to the recent and rapid expansion of high containment laboratory research and research capacity in the United States. Since 1980, the Center has been working to protect the American people from the threat of nuclear, chemical and biological weapons. Here I discuss some of the public health and national security risks associated with the expansion of bioweapons-related research and development, and I propose some steps our nation can take to help mitigate these risks.

Over the last six years, the Federal government has dramatically increased US research and development activity and infrastructure focused on biological weapons agents. This continuing expansion promises new capabilities for detecting and responding to potential bioweapons attacks and natural infectious disease outbreaks. It also creates increasing risks to laboratory personnel, public health and national security. In order to reduce these risks, we need

- Strong and effective biosafety and biosecurity practices and oversight mechanisms
- Transparency to guarantee public accountability, and
- Rigorous and transparent interagency needs assessment and strategic planning to match research and infrastructure capacity with national needs.

Our current biosafety and biosecurity system is plagued by significant and systemic weaknesses, inadequate oversight and transparency, and a lack of rigorous interagency needs assessment and strategic planning. Unless corrective action is taken, the risks to our nation and its people from accidental or deliberate disease outbreaks arising from our own activities and institutions will continue to rise. The US biosafety and biosecurity system needs to be made more coherent, more comprehensive, more effective, and more transparent:

- Congress should mandate, and DHHS and USDA should develop, biosafety and biosecurity training standards and minimum core competencies for work with high-risk biological agents, including a plan for meeting national training needs
- Congress should mandate, and DHHS and USDA should develop, operate and maintain a universally mandatory and transparent Biosafety/Biosecurity Incident Reporting System
- Congress should mandate, and DHHS and USDA should develop, establish and maintain a national licensing system and registry for all BSL-3 and BSL-4 facilities in the United States, including an integrated and effective auditing process
- Congress should mandate institutional compliance with the performance-based guidelines contained in *Biosafety in Microbiological and Biomedical Laboratories* and the NIH Guidelines
- Congress should mandate independent Institutional Biosafety Committee (IBC) review of all research projects involving bioweapons agents and other high-risk pathogens and activities, not just those involving certain categories of rDNA research
- Congress should make all three of the above requirements legally binding for all institutions – government, academic and private – not just those receiving funds from NIH, including all institutions which conduct classified research activities, so as to help ensure universal application of and compliance with these requirements
- DHHS and USDA should define and fund the development of the training and infrastructure needed to implement such IBC review
- Congress should consider consolidating all CDC and NIH OBA responsibilities and authorities relevant to implementing, monitoring and enforcing the above requirements into a single office located within the Office of the Secretary DHHS, or in some other way improving the coherence of the US biosafety and biosecurity system
- Congress should require an annual report from DHHS and USDA detailing their efforts to implement and enforce all of the above requirements
- Congress should modify Section 351A(h) of Title III of the Public Health Service Act in order enhance accountability by more narrowly and accurately defining necessary and appropriate requirements for withholding information about activities involving potential bioweapons agents

- Congress should mandate that the Executive Branch work to promote the adoption of these strengthened biosafety and biosecurity requirements more broadly by other countries
- Congress should mandate comprehensive national needs and risk assessments for the continuing increases in the number of high containment research facilities and the number of institutions and individuals conducting bioweapons-related research

All too often in current debates, a wedge is placed between supporting important life sciences research on the one hand and preventing accidents and the malevolent use of the life sciences on the other. In fact, both are possible and necessary. Effective oversight and transparency of life sciences research activities contributes to enhancing public health and national security; it is the lack of adequate and appropriate oversight and transparency which adds to the risks we face today. Experience shows that stronger oversight of high-risk research and research facilities can be designed and implemented. (Davidson, et al, *Science*, 316, 1432-33, 2007; Lentzos, *Biosecurity and Bioterrorism*, 5: 55-61, 2007; Tucker, *Disarmament Diplomacy*, 84, Spring 2007). Regulations will need to be carefully designed to ensure that they reduce risk. They will also need to go beyond what is currently in place in the United States today.

Bioweapons-related research and development activities and capacity are increasing dramatically

For the last two years, the Center for Arms Control and Non-Proliferation has analyzed federal funding for bioweapons-related activities (see Appendix A for our analysis of the FY2008 budget). Our analysis shows that funding for bioweapons-related research and development has increased from approximately \$583 million in FY2001 to over \$3 billion in FY2007. For FY2008, the Bush Administration has requested over \$3.3 billion for such research and development. The increase has been particularly dramatic for civilian (i.e. non-DOD) research and development, which has gone from \$135 million in FY2001 to nearly \$2.4 billion proposed for FY2008. In sum, from FY2001 through FY2007, nearly \$17 billion in federal funds have been spent or appropriated for bioweapons-related research and development activities.

Of this \$17 billion, over \$1.7 billion has been appropriated for the construction of new high containment research facilities for bioweapons-related research. By high containment facilities I mean facilities that are designed for work with agents that may cause serious or potentially lethal disease through exposure to aerosols (called Biosafety Level 3 or BSL-3 facilities) and facilities that are designed for work with agents that pose a “high individual risk of life-threatening disease, which may be transmitted via the aerosol route and for which there is no available vaccine or therapy” (called Biosafety Level 4 or BSL-4 facilities).

Our preliminary analysis shows that, as a result of this funding, high containment research and development infrastructure is expanding rapidly along at least three dimensions:

- 1) **The absolute number of facilities.** Prior to 2002, there were three significant BSL-4 facilities in the United States. Today twelve are in operation, under construction, or in the planning stage. When completed, there will be in excess of 150,000 square feet of BSL-4 laboratory space (as much space as three football fields). The number of BSL-3 labs is also clearly growing, but ascertaining the amount of growth is difficult in the absence of accurate baseline information. There are at least 600 such facilities in the US.
- 2) **The average size of such facilities.** The average size of a new BSL-4 facility is three times that of those which existed previously. BSL-3 space is similarly growing. According to a June 2005 report, 66% of institutions responding to a survey on BSL-3 capabilities had <1000 square feet of BSL-3 space; in the ten new BSL-3 facilities for which such data is publicly available, average BSL-3 space is nearly 12,000 square feet.¹ (Constella Health Services, "Survey for Determining the Location, Capacity and Status of BSL-3 Laboratories," June 2, 2005). One very large and notable BSL-3 facility not included in the above calculation, a private facility identified as "BCF-01" in a January 2007 DHHS/DHS report to Congress on high containment facilities, recently expanded from 36,000 net square feet of BSL-3 space to 88,000 net square feet.
- 3) **The number and size of facilities capable of conducting aerosol exposure studies in mammals including non-human primates.** Specific data are not available, but the DHHS/DHS report indicates a substantial increase in both the number and size of such facilities. Such studies can raise particularly significant biosafety risks. Secrecy surrounding such facilities can cause significant international concern about the intent of their activities.

The current expansion in high containment infrastructure appears to have occurred in the absence of rigorous interagency needs assessment and risk-benefit analysis. For instance, the February 2002 NIAID Strategic Plan for Biodefense Research simply called for the establishment BSL-3 and BSL-4 capability at 6 – 12 regional Centers of Excellence for Bioterrorism and Emerging Infectious Disease research, but provided no explanation for how it arrived at that number. NIAID has exceeded these recommendations, funding the construction of 13 regional BSL-3 laboratories and 2 national BSL-3/BSL-4 laboratories, and building three additional intramural BSL-3/BSL-4 facilities.

Yet, in mid-2004, 8 months after announcing the awards for 11 of these facilities, NIAID officials acknowledged that they couldn't say for sure whether too much space, at least at BSL-3, had been planned because there was no accurate inventory of existing BSL-3 labs. A committee of federal

¹ Some of this increase may reflect design changes made to facilitate workflow in BSL-3 facilities, such as moving experiment set-up and other functions incidental to the experiment itself into the BSL-3 laboratory.

agencies was conducting a national needs assessment, and officials said that until it was completed about one year hence, they would not know “whether we need six times more, 12 times more, or 100 times more” space (The Scientist, May 24, 2004).

The needs assessment was probably that delivered by DHHS and DHS almost three years later, in January 2007 (“Report Regarding Biocontainment Facilities, A Report to Congress,” January 2007). It concludes that prior to the recent expansion of high-containment facilities, existing high-containment aerosol challenge and GLP capacity would likely have “limit[ed] progress in current development and acquisition programs.” However, the current expansion “should significantly increase model development and testing capacity.” The report does not assert that any further expansion is necessary at this time, implying that there will soon be adequate high containment capacity in the United States. No assessment was made regarding the distinct possibility that there might be an **overcapacity** of BSL-3 and BSL-4 facilities.

Nor does the report appear to consider the new facilities that have or are being built at the CDC, DHS, DOD and DOE. To be sure, some of these facilities are necessary. At the time of the anthrax attacks in 2001, the need for additional high level containment facilities to meet research needs for both biodefense and naturally occurring infectious diseases was clear. But in replacing these aging facilities, the Federal government is increasing its own BSL-3 and BSL-4 capacity 10-fold or more.

As already noted, no US government agency knows the identity and critical details about every BSL-3 and BSL-4 facility in the United States. A June 2005 report by NIAID stated that at least 277 facilities in 46 states had a total of 598 distinct “BSL-3 capable laboratories.” Of these, 7 had capabilities for non-human primate studies, 21 for aerobiology studies and 57 had FDA Good Laboratory Practices (GLP) capability (the extent to which these capabilities overlapped was not clear in the report). The January 2007 DHHS/DHS report found that 204 “entities” registered with the CDC Select Agent Program had a total of 633 distinct BSL-3 and BSL-4 “facilities.” Of these, 39 had the “capacity to conduct the animal studies necessary for medical countermeasure testing.” The number having capability for aerosol-challenge studies in animals including non-human primates, and the number that are GLP compliant, were not identified. The number having both capabilities was identified as being either three or six, depending on how one interprets the report. The report does not include any facilities not registered with the CDC Select Agent program, such as those whose work with biological agents (such as H5N1 highly pathogenic avian influenza virus) is covered only by USDA or facilities that conduct BSL-3 or BSL-4 level work only with non-select agents. (Bioweapons agents are not the only pathogens handled in high containment facilities. Some types of work with, for example, multi-drug resistant *Mycobacterium tuberculosis*, the SARS coronavirus, and certain influenza viruses are also conducted in BSL-3 or BSL-3+

facilities. While work on such agents is not the reason for the recent expansion of high containment facilities, considerations of biosafety do extend beyond bioweapons agents per se.)

Neither report identifies specific facilities or entities having BSL-3 and BSL-4 capabilities. Neither provides an indication that information such as the age and condition of the facilities and the identity of the agents studied in them was collected. Neither assesses the overall operational status of the existing facilities. The data collected for the NIAID report were presumably destroyed as planned 120 days after the report was issued. Thus, NIAID likely no longer has a record of which facilities have BSL-3 capabilities. The Sunshine Project currently maintains the most comprehensive, publicly available list of BSL-3 and BSL-4 laboratories in the United States.

The content, discrepancies and gaps in these two reports indicate that no US government agency maintains a comprehensive database of BSL-3 and BSL-4 laboratories in the United States. This problem is highlighted by the existence of a third report, from researchers at Los Alamos National Lab and elsewhere, that there were over 1400 BSL-3 facilities in the United States as of 2004 (Sassone, et al "Review and Assessment of New Biological Safety Level 3 (BSL-3) Facilities," 2004).

As far as can be determined, a thorough interagency needs assessment and risk-benefit analysis has still not been conducted. None of the above-mentioned reports assess the overall operational status of existing BSL-3 and BSL-4 laboratories, or the degree to which existing capacity is being utilized. The 2007 report comes closest, but focuses on the narrower question of GLP-compliant high-containment animal (including non-human primate) aerosol challenge capacity. The lack of a registry containing fundamental data on existing high containment facilities will continue to significantly impair planning.

The Committee may want to look into these issues further. The may also want to look into issues surrounding the siting of these laboratories, which have caused concerns in some local communities.

Research and development capacity is increasing in another extremely important way – the number of individuals who are working with bioweapons agents and other high-risk pathogens. The 15-fold increase in non-defense bioweapons-related research and development funding has generated a major increase in research and development activities, and in individuals having access to bioweapons agents. As of August 2007, over 14,400 individuals at 327 registered entities were approved by the CDC for access to one or more bioweapons agents (personal communication from Cassandra Willyard, Nature Medicine). Over 7200 individuals are approved to work with anthrax alone (Hartford Courant, Oct 8, 2006).

Finally, it is important to note that the recent expansion includes an increase in classified bioweapons-related research, and in activities that fall under the nebulous and ill-defined label of sensitive but

unclassified. In particular, the Department of Homeland Security is responsible for conducting threat assessment research. Such research involves the exploration of offensive aspects of biological weapons agents and delivery mechanisms for defensive purposes. Much of this research is clearly sensitive, and some of the results may need to be classified. The number of threat assessment projects currently underway is not publicly known, but will surely increase once DHS' National Biodefense Analysis and Countermeasures Center (NBACC) being built at Ft. Detrick, Maryland, is operational. The Defense Department also conducts a significant level of classified bioweapons-related research and development, and the Department of Health and Human Services has also been given original classification authority, although it has not yet utilized that authority extensively.

The expansion in bioweapons-related research and development funding and activities is not over. The current level of funding is supporting research and development activities that, for the most part, do not yet use the new high containment facilities being constructed. As these facilities come online, we can expect that bioweapons-related R&D funding and activities will increase still further. The number of researchers with access to bioweapons agents will probably continue to expand if all of our new high containment facilities are to be fully utilized. According to a USAMRIID official "[w]hen I look at the capacity for studies" being built in this US, the number of BSL-qualified researchers "has to be five-fold bigger than we [have] now." (The Scientist, May 24, 2004). At the time approximately 11,000 individuals were registered with the CDC (Baltimore Sun, June 27, 2004).

The expansion of high containment research and research facilities is generating increased risk to researchers, the public health, and national security.

The biosafety and biosecurity risks associated with the dramatic and ongoing expansion of high containment research and research facilities are both real and growing.

By "biosafety risks" I mean those risks related to the protection of laboratory personnel and the outside community and environment from the potential effects of unintentional exposure to or accidental release of hazardous pathogens and toxins. By "biosecurity risks," I meant the risks related to the protection of individuals, communities and nations from the potential consequences of the deliberate theft, diversion, or use of biological agents to cause harm. The report *Globalization, Biosecurity and the Future of the Life Sciences*, released early last year by the National Academies, warns that harm can arise from both the malevolent and the careless or negligent use of biotechnology and the life sciences. Biosafety and biosecurity are two parts of a whole, and the mechanisms and processes needed to mitigate biosafety and biosecurity risks are complementary and overlap significantly.

Concerns about biosafety are well-founded. The circumstances surrounding recent laboratory accidents, such as infections of laboratory workers with the causative agents for tularemia (at Boston University; Boston Globe, Jan 19, 2005), brucellosis and Q fever (both at Texas A&M; Dallas Morning-News, June 26, 2007), provide the most direct indication that not all existing high containment laboratories are being operated as safely as possible. Not only are accidents occurring, but there are widespread deficits in biosafety training of laboratory personnel and underreporting of biosafety incidents, both of which contribute to elevating biosafety risk. For instance, a 2006 report by the DHHS Inspector General revealed deficits in training at 3 of 15 universities inspected (Daniel Levinson, "Summary Report on Universities' Compliance," A-04-05-02006, June 6, 2006). CDC has typically recorded about 20 accident reports per year since 2004, but has received 32 reports since April 2007 (Science, Sept 28, 2007). Until recently, the University of Texas had reported only 3 of 15 reportable biosafety incidents since January 2000 to federal authorities (American-Statesman, Sept 9, 2007). UT Medical Branch in Galveston recorded 17 cases of "potential exposure" to infectious agents over the last five years, but reported only one (Dallas Morning News, July 4, 2007). And since 2002 there have been dozens of exposures to hazardous biological agents in Texas universities for which there is no reporting requirement (Dallas Morning News, July 27, 2006). It is doubtful that these problems are restricted to Texas alone. Finally, as discussed further below, there are significant and systemic problems with the Institutional Biosafety Committee system put in place to reduce biosafety risks.

Concerns about biosecurity risks associated with the current expansion are also well-founded. While the numerous biosecurity failures at Texas A&M stand out, they are not alone. The June 2006 report by the DHHS Inspector General found that fully 11 of the 15 institutions working with bioweapons agents had inadequate security controls and other weaknesses which "could have compromised the ability to safeguard select agents from accidental or intentional loss." This finding came after an earlier investigation of 11 universities found similar defects at each. The Inspector General has apparently levied fines ranging from \$12,000 to \$150,000 on 9 institutions **and** companies for biosecurity breaches (Science, Sept 28, 2007).

The occurrence of these biosafety and biosecurity incidents does not alone necessarily mean that the level of risk is increasing. But there are additional and very good reasons for believing that it is.

First, as more research is performed with dangerous pathogens by more people in more locations, there are more opportunities for biosafety or biosecurity breaches to occur. It is quite clear that in the absence of countervailing efforts to mitigate risk, the potential for a high-consequence accidental or deliberate release of a dangerous biological agent will increase at least linearly with the expansion in the number of high containment facilities, the amount of bioweapons-related and other high-risk research activities, and the number of individuals working with bioweapons agents and other particularly dangerous pathogens.

The increase in the number of people working with biological weapons agents is particularly worrisome from a biosecurity perspective. To make an effective biological weapon, i.e. one that is capable of killing not just a few, but large numbers of people, requires three essential ingredients – materials, equipment, and expertise. Contrary to what is commonly stated in the media and by some biodefense boosters, it is not so easy to create an effective biological weapon. It can't be done by one person with high school knowledge of biology working in a cave. Rather, the easiest way for a sub-state adversary such as Al Qaeda to acquire a bioweapons capability is for it to penetrate an existing research project that uses bioweapons agents, obtaining both agents and training. Nor should we ignore the possibility of a biologist becoming a terrorist. As Vice Admiral Robert Murrett, Director of the National Geospatial Intelligence Agency, recently noted, biological weapons are best tracked by monitoring scientists with the expertise to make them. According to Murrett, this is posing a major challenge for the intelligence community. (Intelligence official: Bioweapons scientists tough to track, Associated Press, Sept 26, 2007) It is worth asking how the large increase in the number of bioweapons scientists in the US is affecting the IC's ability to meet this challenge.

Second, the speed of the current expansion is probably further increasing the risk by stressing and possibly even overwhelming our current national capacity for rigorous biosafety and biosecurity training of the individuals working in the new high containment laboratories. The likely result will be a decrease in the average level of training and experience in working in these facilities. It is unclear whether the NIH or any other agency has begun to assess workforce training needs, or has begun to implement programs to meet those needs.

Third, the direction in which some pathogen research is expanding today increases the risk further yet, as researchers conduct experiments which are inherently more risky than those of the past. Researchers are sometimes now trying to enhance the virulence of pathogens to determine what makes them lethal. They are trying to enhance the transmissibility of pathogens to understand what makes them contagious and what makes them able to pass from one host species to another, such as from chickens to humans. For instance, researchers at the CDC and elsewhere are now conducting experiments with the H5N1 avian influenza virus to see if they can convert it to a form that is more easily transmitted from one person to another. While some of this research may bring benefits to health and society, it also clearly carries substantial safety risks.

Some of it also carries substantial security risks. Such research is very often inherently dual-use – the materials and knowledge derived from the research can be used for either harmful or peaceful purposes. The dual-use problem is a growing concern of those who think about preventing and responding to biological attacks. A good illustration of this issue is the recent successful recreation from scratch of the

1918 influenza virus, perhaps the single most deadly virus in human history. This virus was extinct until researchers from the CDC and other US institutions brought it back from the grave (Tumpey, et al, *Science* 310: 77-80, 2005). Not only have we now created a new and fearsome potential bioweapons agent, but by publishing the sequence of the viral genome we have provided much of the information needed for its recreation by others. Moreover, we have provided a plausible reason for them to do so: whether released deliberately or by accident, if the 1918 flu gains a foothold, it will know no borders. Everyone will be at risk. Yet not publishing such information once we've generated it might be a bigger problem, for it might suggest to some nations that we are withholding information critical to their own security and that of their citizens. It might leave the impression that we are actually up to no good.

Might we in fact be turning such work into the type of glamorous fetish and matter of institutional and national pride that could contribute to an unnecessary proliferation of high-risk research? For instance, should we be concerned when the scientific director of the facility in which the 1918 virus was recreated for a second time says "[w]e're very proud of this work ... it demonstrates our capabilities and that we're an important piece of the science machinery of the world." (Canadian Press, Jan 17, 2007). I do not mean to suggest that particularly risky activities such as these are common or widespread. They are not. But they are growing in frequency. These are difficult problems to solve, and they clearly indicate a need for strong and publicly accountable oversight of dual-use research.

Fourth, similar but possibly even more acute biosafety and biosecurity risks are associated with threat assessment research. Not only are we exploring offensive aspects of known bioweapons agents, we are also now exploring and possibly trying to create new biological threat agents. The rationale for these efforts is that we are engaged in a biological "arms race" between protective measures and potential malevolent applications of life sciences research and technology. While this "capabilities-based" approach to threat assessment is not without merit, it is also fraught with substantial danger. Where is the line between legal and illegal activities under the Biological Weapons Convention? How can we ensure that we aren't engaging in an arms race against ourselves, and that our attempts to keep up with the "threat curve" don't simply push that curve forward faster? Since other nations will recognize the unavoidably dual-use nature of our activities, will they misperceive our efforts as potentially offensive in nature, and respond by carrying out their own, similar activities? At the very least, by undertaking such research we will be providing a plausible justification for others to do the same. While some threat assessment research is important, there must be a rigorous process in place for ensuring that only those projects that are absolutely necessary are conducted, for mitigating risk, and for demonstrating that the work complies with our international obligations under the BWC. Strengthening oversight of this expanding and highly consequential area of dual-use research is essential.

All of these factors are increasing biosafety and biosecurity risks as our current expansion continues. None of them, nor even all combined, argue decisively against some expansion of high containment

bioweapons-oriented research and infrastructure. However, they do highlight the need for a fundamental re-examination of the extent of our expansion and, more generally, of our national strategy for confronting biological threats. And they make a compelling case for effective measures to mitigate the risks we are taking and the risks associated with the more general advancement of the life sciences.

Our biosafety and biosecurity system is not adequate to meet the increased risk

No activity involving a dangerous pathogen or toxin will ever be risk free. However, risk can be minimized through the combination of effective biosafety and biosecurity practices, management, oversight, enforcement, and accountability.

Unfortunately, the current US biosafety and biosecurity system has significant and systemic weaknesses. Despite the dramatic expansion in high containment research and research capacity, there has been no enhancement of biosafety oversight and regulation. Indeed, there are almost no legally binding biosafety rules or regulations, there is no comprehensive biosafety law, and there are no universally applicable biosafety guidelines. While there are biosecurity laws and regulations, there are significant gaps in those regulations, and there has been only partial and inadequate enhancement of biosecurity oversight and enforcement.

There are three distinct mechanisms in the United States that address biosafety and biosecurity: the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (NIH Guidelines), including the Institutional Biosafety Committee (IBC) system established by the Guidelines; the Select Agent Rules promulgated by APHIS and the CDC under the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, and several regulatory standards promulgated by the Occupational Safety and Health Administration (OSHA) (for a detailed review of each of these mechanisms, see Appendix B). Each has gaps and weaknesses.

The NIH Guidelines.

The NIH Guidelines, and the IBC system established by them, provide the only federally mechanism for increasing the likelihood that research projects adhere to biosafety guidelines. However, the Guidelines apply only to research projects involving recombinant DNA (rDNA). With two very narrow exceptions, there is no federal requirement for IBC or any other review of work involving bioweapons agents or other dangerous pathogens unless such work also involves recombinant DNA. Moreover, the Guidelines apply only to those institutions that receive NIH funding for rDNA research, and those institutions that receive funding from other federal agencies who have decided to adopt the Guidelines, such as the National Science Foundation. In addition, the Guidelines do not carry the weight of law. Instead, failure to comply with the Guidelines can result penalties up to and including the termination of NIH funding for research

involving rDNA at the institution. Finally, NIH does not effectively monitor or, when necessary, enforce compliance with the Guidelines.

In 1984, NIH and CDC developed the *Biosafety in Microbiology and Biomedical Laboratories* (the BMBL, now in its fifth edition) to provide guidance and advice to institutions and individuals on the safe handling and containment of infectious microorganisms and dangerous biological materials. Since that time, roughly two-thirds of the approximately 400 institutions with registered IBCs have chosen to assign their IBCs the additional responsibility of reviewing non-rDNA activities involving dangerous pathogens and other hazardous agents (Hackney, 2003). However, as noted by NIH Office of Biotechnology Activities (OBA), “this additional responsibility is assigned entirely at the discretion of the institution.”

Recent studies have revealed major weaknesses in the IBC system. For example, a 2003 survey of registered IBCs identified the following problems (Hackney, 2003):

- Limited resources – two-thirds of IBCs had less than one full-time equivalent staff member
- Lack of institutional involvement - nearly half were not required to make formal reports to their institution, suggesting that many institutions do not pay much attention to the effectiveness of their IBCs or their responsibilities under the Guidelines
- Lack of training - 80% of IBC members do not receive training, despite an NIH requirement that institutions are responsible for ensuring that they do
- Insufficient oversight of research – nearly 60% meet two times per year or less (one-third meet only “as needed”)
- Inadequate transparency and accountability - 50% do not make their minutes available to the public, in direct violation of the NIH Guidelines

A 2004 study by the non-governmental group known as the Sunshine Project found additional problems, including (Sunshine Project, “Mandate for Failure,” October 2004):

- Non-functional IBCs
- Blanket approvals for research, rather than specific project review
- Dramatic variation in the quality of IBC minutes, many of which did not offer “sufficient detail to serve as a record of major points of discussion and the committee’s rationale for particular decisions” as required by the Guidelines
- An apparently wide and uneven range of practices and procedures for IBC review of research from one institution to another
- Industry largely escapes from the IBC system altogether

The work of the Sunshine Project has revealed another significant weakness as well – ineffective monitoring, oversight and enforcement by NIH OBA, the office responsible for administering the NIH Guidelines. NIH OBA requires only that institutions file an annual report listing the members of their IBCs together with their biographies. As related in an April 2005 report in the Chronicle of Higher Education, NIH OBA “does not collect IBC minutes to confirm that they are reviewing research, and it does not require biosafety committees to certify that they are in compliance, as it does with institutional review boards.” (Institutional review boards are responsible for ensuring human subjects protection in research and are mandated by federal law.) In December 2004, NIH OBA announced that “[i]n the coming year, the NIH will be conducting site visits at selected institutions to obtain further information on IBC compliance with the *NIH Guidelines* and to educate institutions more directly about requirements that apply to the conduct of recombinant DNA research.” (Memo from Amy Patterson to All Institutions Receiving NIH Funding, Dec 6, 2004). The outcome of those visits remains unknown. As for enforcement, NIH OBA has no authority to conduct inspections and has rarely if ever exercised its fiduciary power to enforce the Guidelines in anything other than work involving human gene therapy.

The Select Agent Rule

The Select Agent Rule requires that institutions desiring to possess, use or transfer certain “select” biological agents or toxins (i.e. bioweapons agents) register with the Federal government, and that individuals wishing to have access to such agents or toxins undergo a background security check. They also provide the first universal and legally mandatory federal requirements for institutions to develop, implement and maintain biosafety, security, and incident response training and plans. Nonetheless, as with the NIH Guidelines, there are major weaknesses and gaps.

For example, the Rule applies only to the possession, use or transfer of select agents and toxins. It does not apply to any work with dangerous biological agents that aren’t so classified. Further, it does not set minimum standards for the content of the biosafety, security and incident response plans, nor does it require that entities submit their plans to the CDC for review at any time before or after they are certified, a gap that became apparent in the Texas A&M case. As with the case of IBCs, at some entities the plans may be quite good, while at others they may amount to little more than meaningless paperwork. Even more important than failing to ensure that this paperwork is in order, the Rule does not require that research projects involving potential bioweapons agents be subject to institutional review and oversight to ensure that they are being conducted safely and securely. Similarly, it does not require that biosafety level assignments for such work be determined by a risk assessment, or that institutions do anything more than “consider” the recommendations of the NIH Guidelines and the BMBL. Again, the incidents at Texas A&M have revealed some of the potential consequences of this gap that the CDC has known about, and ignored, for years. Yet further, in granting access approval for individuals, the CDC does not

require evidence that they are capable of safely and securely handling biological agents. Rather, the Rule requires that the entity's Responsible Official certify that the individuals are competent. This certification requirement is necessary, but is obviously not sufficient for guaranteeing that researchers have the skills they need. It is legitimate to question whether the Rule fulfills the statutory requirement that they ensure "proper training and appropriate skills to handle such agents and toxins." Finally, the Rule fails to define the meaning of "occupational exposure," thereby leaving uncertainty about the comprehensiveness and intent of the mandate to report such exposures. The consequences of this weakness are now widely apparent, as demonstrated by the accident reporting problems at Texas A&M and elsewhere.

Nonetheless, if effectively implemented, monitored and enforced, the Select Agent Rule could provide a reasonable foundation for beginning to strengthen some aspects of institutional biosafety and biosecurity. But it is not being effectively implemented, monitored and enforced by the CDC (this analysis does not consider USDA management of its Select Agent Program). This is apparent in the fact that in two successive reports the DHHS Inspector General has documented no significant improvement in institutional implementation of the Select Agent Rule. It is apparent in the fact that the CDC continues to learn about significant institutional compliance failures from others (a problem the CDC shares with NIH OBA when it comes to non-compliance with the NIH Guidelines). In the case of Texas A&M, either CDC's own inspections repeatedly failed to reveal significant institutional deficits, or the CDC failed to act effectively to correct those deficits. Quiet, informal and non-adversarial consultation with institutions to improve implementation of and compliance with the Select Agent Rule is absolutely essential, but it also must achieve demonstrable success. Can the CDC objectively demonstrate that there has been significant progress in institutional implementation and compliance?

The CDC refuses to make any of its inspection reports public, incorrectly citing a provision of the 2002 Bioterrorism Act as justification (see Appendix D). Thus, it is very hard to independently examine this question. More, very little is publicly known about how CDC conducts its inspections and interprets inspection results, about the competencies of the CDC inspection teams, or about what types of actions CDC takes in response to any weaknesses it finds. What are the standard operating procedures for CDC inspections? Do inspectors have a list of key indicators for determining if a deeper inspection is required? Such a list might both facilitate the inspection process and avoid needless alienation of those institutions that have a good record of compliance. Are more inspectors with better skill sets needed? Will the CDC now re-examine its inspection process? In short, does CDC know what it is doing?

Concerns about the CDC's regulatory abilities are not new. Chairman Stupak raised such concerns as far back as 1999 during a House Commerce Subcommittee hearing on the Threat of Bioterrorism in America. The need for better verification measures to monitor compliance was raised by Senator Feinstein during a Senate Judiciary Subcommittee hearing on Germs and Toxins as Domestic Terrorist Threats in 2001.

And a 2002 performance review of CDC's management of the Select Agent Program by GAO highlighted major deficits in CDC monitoring, inspections, databases and organizational structure (GAO-03-315, Nov 22, 2002). As this review was conducted before the new and significantly expanded Select Agent Rules went into effect, perhaps it is time for GAO to be asked to update its previous study of CDC's regulatory efforts in this critical area.

Finally, there are two significant gaps in the Select Agent Rules that remain completely unaddressed. First, registered institutions have no obligation to report occupational exposures or breaches of primary containment to State or local public health authorities. Second, the Rules, as interpreted by the CDC, provide almost no coverage for synthetic genomes. The recreation of the 1918 influenza virus shows how it has become possible to synthesize or clone DNA encoding the entire genome of a select agent virus and use this DNA to generate the virus essentially from scratch. Yet, the CDC interprets the Rules in such a way that the possession, use or transfer of such DNA is unregulated unless the DNA itself can be considered intrinsically infectious. Only a few of the viruses of bioweapons concern, such as Venezuelan Equine Encephalitis (VEE) and the tick-borne encephalitis viruses, fall into this category.

This means that it is currently entirely legal for an unregistered individual to possess, use or transfer nucleic acids comprising the entire genome, plus all the materials needed to generate infectious virus from these nucleic acids, for select agent viruses such as including the 1918 influenza virus, ebolavirus and perhaps in the not too distant future, smallpox (Mark Hemphill (CDC), presentation to "Synthetic Genomics Workshop 3," May 31-June 1, 2006, CSIS, Washington DC.). Only when that individual actually makes the virus itself will he or she be in violation of the law.

I do not say this to raise unnecessary alarm. To be sure, generating a virus in this way is far from trivial. The knowledge of how to do so exists for only a few viruses of major bioweapons concern today, and even in those cases it could easily take a skilled postdoc substantial time to achieve success. But for the 1918 influenza virus and ebolavirus, it has already been done. It is not hard to imagine that a skilled terrorist or rogue scientist could work in a government, university or corporate lab, perhaps under cover of a different project, to assemble one of these viruses. No one would be the wiser and, if by chance the individual was discovered, s/he could not be prosecuted unless s/he actually possessed the virus itself. Clearly a careful reconsideration of the Select Agent Rule, or at least of its interpretation by the CDC, is in order.

The OSHA Standards

The third mechanism, addressing biosafety only, is embodied in several OSHA regulations. These are described in more detail in Appendix B. The important point for this discussion is that they are limited to

regulating work with certain toxins and work with human blood and other potentially infectious human bodily fluids. Moreover, reporting requirements under these standards apply only when there is a work-related fatality or hospitalization of three or more individuals.

This analysis of the existing US biosafety and biosecurity system shows that it has significant and systemic weaknesses. The system lacks coherence, with multiple different reporting requirements, reporting standards, and agencies to report sometimes similar information to. It lacks clarity about certain critical institutional responsibilities. It lacks transparency and accountability at all levels - reasonable and salient information about the management, operation and oversight of high containment facilities and the US biosafety and biosecurity system that should be public is not public. It lacks universal applicability, leaving gaps in our biosafety and biosecurity web of prevention. The expansion of high containment research and development facilities and dual-use research activities is now stretching that web, rending those gaps ever wider. The time to fix the US biosafety and biosecurity system is now, BEFORE we face any serious consequences of our inaction.

Recommendations

Emerging new risks necessitate corresponding changes in risk mitigation efforts if risk is to be maintained at a steady low level. The United States can rightly be proud that we have often been a world leader in biosafety and biosecurity. From its beginnings in the 1960s to the publication of the NIH Guidelines in 1976, the first edition of the BMBL in 1984, and the first laws governing the handling of bioweapons agents in 1996, the US biosafety and biosecurity system has seen continual improvements in response to demonstrated gaps and emerging risks. It has provided a model for emulation around the world.

We should be continuing this proud tradition. In some ways we are. For instance, the State Department's still expanding Biosecurity Engagement Program (<http://www.bepstate.net/>) and Sandia National Lab's International Biological Threat Reduction Program (<http://www.biosecurity.sandia.gov/>) are working closely with other nations to develop systems, practices and "cooperative international programs that promote the safe, secure and responsible use of biological materials that are at risk of accidental release or intentional misuse." (<http://www.bepstate.net/>)

Yet, how are these efforts made easier by the problems in our own biosafety and biosecurity system? Can we say that we are truly a leader when it comes to complying with our obligations to under the Biological Weapons Convention and UN Security Council Resolution 1540?

Biological Weapons Convention, Article IV:

Each State Party to this Convention shall ... take any necessary measures to prohibit and prevent the development, production, stockpiling, acquisition, or retention of the agents, toxins, weapons, equipment and means of delivery specified in article I of the Convention, within the territory of such State, under its jurisdiction or under its control anywhere.

UN Security Council Resolution 1540:

[A]ll States ... shall adopt and enforce appropriate effective laws which prohibit any non-State actor to manufacture, acquire, possess, develop, transport, transfer or use nuclear, chemical or biological weapons and their means of delivery, in particular for terrorist purposes

[A]ll States shall take and enforce effective measures to establish domestic controls to prevent the proliferation of nuclear, chemical, or biological weapons and their means of delivery, including by establishing appropriate controls over related materials and to this end shall:

- (a) Develop and maintain appropriate effective measures to account for and secure such items in production, use, storage or transport;
- (b) Develop and maintain appropriate effective physical protection measures;

The United States should be a strong and consistent world leader in biosafety and biosecurity, and we should take every reasonable step to ensure the safety and security of our people. Today, the US biosafety and biosecurity system must be made more coherent, more comprehensive, more effective, and more transparent if laboratory workers and the public health are to be adequately safeguarded. Congress and the Federal government can and should take the following actions to help achieve this goal:

Training

Training standards and core competencies. Congress should mandate, and DHHS and USDA should develop, biosafety and biosecurity training standards and minimum core competencies for work with high-risk biological agents, including a plan for meeting national training needs. Agent-specific, BSL-specific and facility-specific (mentored) training should all be required, as should regular refresher training to maintain competence as biosafety and biosecurity needs, practices and facilities evolve. Institutions should be required to keep a detailed record describing the training received by each individual and evidence of competency relevant to the work to be performed. Individual competency should be demonstrated by practical, and not only written, examination prior to being permitted to carry out independent research activities.

Reporting

National Biosafety/Biosecurity Incident Reporting System. Congress should mandate, and DHHS and USDA should develop, operate and maintain a **universally mandatory and transparent** Biosafety/Biosecurity Incident Reporting System (NBIRS). All biosafety and biosecurity incidents (both accidents and near-misses) involving risk group 3 and risk group 4 biological agents, and risk group 2 select agents, would be reportable (See Appendix E for an explanation of risk groups). DHHS and USDA should establish clear reporting criteria and requirements, such as, for example, a requirement that any incident resulting in an occupational exposure as defined by 29 CFR 1910.1030 (See Appendix B) be reported. Other requirements would be to provide specific information on the identify of the agent(s) involved in the incident and an analysis of the cause, effect, and responses taken, in order to enable community-wide learning and safety/security enhancement.

Incident reporting under the NBIRS would be mandatory for all public and private institutions, regardless of whether the conduct classified research. A provision for the withholding of personal, but not of institutional, information could be included for the purpose of guaranteeing individual personal privacy. Similarly, a provision for withholding information while law enforcement authorities are involved in responding to an incident should be included. DHHS and USDA should conduct ongoing monitoring and analysis of the information received, and issue community-wide recommendations for biosafety and biosecurity enhancement as needed. They should issue an annual public report listing the number and categories of incidents by institution and biological agent, and any corrective actions taken. This level of transparency is important for ensuring public accountability and strengthening biosafety and biosecurity practices. It will also provide international reassurance about our bioweapons-related activities.

Finally, institutions should take steps to instill a culture of responsibility, not a culture shame and embarrassment, among researchers. Researchers should know that their responsible behavior will be rewarded, not punished.

State and local notification. Congress should mandate notification of state and local public health and emergency response authorities by the Secretary DHHS or USDA within 12 hours of any accidental or deliberate breach of containment (theft, loss or release, including potential exposure of one or more laboratory personnel, of a biological agent) involving a select agent or a risk group 3 or 4 agent.

Monitoring, oversight and enforcement

Facility licensing and registration. Congress should mandate, and DHHS and USDA should develop, establish and maintain a national licensing system and registry for all BSL-3 and BSL-4 facilities in the

United States, including an integrated and effective auditing process. Criteria and minimum licensing requirements for different general categories of facilities (animal vs. human pathogens, BSL-3 vs. BSL-3Ag vs. BSL-4, etc) should be developed to facilitate the licensing process. Given the wide variations that exist among facilities built at different times for different purposes, a formal public process should be established for issuing any necessary variances. The registry should include information needed for a national inventory of high containment capabilities in the United States in order to facilitate national needs assessments. Information of this type is already collected from institutions applying for registration under the Select Agent Rule, providing a useful model for broader applicability. An integrated and effective auditing process, including a clear and relevant list of key indicators for identifying biosafety and biosecurity deficiencies should be developed. Licensed facilities should be audited regularly (on an annual to triennial basis) to ensure that the minimum required standards for their license category. Evidence of possession of a license should be required with all relevant applications for federal funding.

A national list of all licensed facilities, including a description of their activities, should be publicly available. Any information collected as part of the licensing and registration process which reveals the precise location of select agents, and personal identifying information about individuals who handle them, should remain out of the public eye. General information about which institutions work with which select agents does not pose a significant security risk and should be public. Facilities which conduct classified research should be included on this public national list, but may be allowed to provide more general descriptions of their activities. Current Federal law prohibiting US government agencies from releasing the types of information that would be included in this list should be amended. This level of transparency is important for ensuring public accountability and strengthening biosafety and biosecurity practices. It will also provide international reassurance about our bioweapons-related activities.

The BMBL and NIH Guidelines. Congress should mandate institutional compliance with the BMBL and the NIH Guidelines. Arguments are sometimes made that mandating compliance with the BMBL and the NIH Guidelines would interfere with the individual and institutional flexibility needed to conduct research safely, and that incorporating them into the rulemaking process would make it more difficult to update and revise the recommendations as needed. In recognizing the importance of flexibility and currency for effective biosafety practices, these arguments make an important point. However, they do not consider that the BMBL and the NIH Guidelines contain mainly performance-based recommendations, not hard and fast rules. Mandating compliance with these recommendations and guidelines would simply establish them as performance-based requirements. The OSHA regulation on blood borne pathogens (29 CFR 1910.1030) establishes similar performance-based requirements. It does not impede the adoption of up to date best practices.

Scientists support mandating compliance with the BMBL and the NIH Guidelines. In comments on the Interim Final Select Agent Rule submitted to CDC on February 6, 2003, the American Society for Microbiology advocated that the Rule mandate compliance with the most recent versions of the BMBL and the NIH Guidelines. The ASM is the largest single life science society in the world, with over 43,000 members from a wide range of disciplines. The ASM noted that this “could mandate the state of the art approaches for safety and security.” Further, ASM explained that “the CDC will have to update the regulations through rulemaking ... to ensure that when these documents are updated and revised the most current version is incorporated by reference in the regulation.” In other words, mandating compliance with these documents would not impede their regular updating and revision. In fact, the ASM noted that mandating compliance with these guidelines would allow “for appropriate updating as the guidelines evolve as the result of research progress.” Mandating compliance with the BMBL and the NIH Guidelines is long overdue.

Institutional Biosafety Committee Review. Voluntary compliance with biosafety and biosecurity guidelines is not working. This much is obvious from the discussion in the section above. Congress should mandate Institutional Biosafety Committee (IBC) review of all research projects involving risk group 3 and 4 biological agents, risk group 2 select agents, and other high-risk activities, not just those involving certain categories of rDNA research. This review should consider biosafety, biosecurity, and dual-use issues. DHHS and USDA should develop a standard, performance-based process for such IBC review, and should establish a set of mandatory requirements (training and expertise) for IBC members. As well, they should develop a process for elevating particularly difficult issues, and certain narrowly-defined types of particularly dangerous research, for higher level review. The minutes of IBC meetings should include a work summary and offer sufficient detail to serve as a record of major points of discussion and the committee’s rationale for particular decisions.

Responsibility for compliance should be placed at the institutional, not the individual, level. Individual researchers must play a critical role in any review, but the review process should be carried out by an independent body capable of bringing in a wide range of relevant expertise. To ensure universal application of and compliance with these requirements, this mandate should be legally binding on all institutions – government, academic, and private – not just those receiving funds from NIH. This should include all institutions which conduct classified research activities. IBC minutes should be provided to the office described below as evidence that the IBC is complying with these requirements. Public membership on the IBC should continue to be required, as should public access to IBC minutes. Consideration will need to be given as to whether, when and how certain research information, proprietary business information, or national security information should be reasonably protected. Different approaches will likely be required for these different classes of information.

DHHS and USDA should define and fund the development of the training and infrastructure needed to implement such IBC review. The IBC system is in a state of disrepair. In order to effectively meet the requirements for IBC review outlined above, the system will either have to be fixed, or replaced. As there is no other system in place which could act as a replacement, and as some institutions appear to have strong and effective IBCs, repairing the IBC system is the preferred option. Funding for this purpose should be provided out of current U.S. biodefense research and development budgets (2% of proposed DHHS and USDA biodefense R&D funding for FY2008 would total \$35 million).

[The NIH Guidelines] have given colleges too much “poetic license.” [R]eplacing them with a law would “remove the inconsistencies.” ... “People who like to flout guidelines can’t flout rules.”

Philip Chandler, Chairman, Medical College of Georgia IBC (Chronicle of Higher Education, April 29, 2005)

Consolidation of monitoring and enforcement. Compliance will be enhanced if regulations are clear, coherent, and integrated. Compliance requires effective monitoring and enforcement – a law not monitored and enforced may be little better than a voluntary guideline. The lack of coherence and integration in the biosafety and biosecurity system, and the administrative, management and likely capacity and capability deficits at in the CDC Select Agent Program and NIH OBA call out for attention. Congress should consider consolidating all CDC and NIH OBA responsibilities and authorities relevant to implementing, monitoring and enforcing the above requirements into a single office located within the Office of the Secretary DHHS. This would help improve coherence in the biosafety and biosecurity system and make it easier for Congress to guide the process of improving monitoring and enforcement of existing and new rules and regulations. At the Secretarial level, DHHS likely has enough distance from the research process that the problems caused by the potentially conflicting objectives of regulation and promotion may be less intense than they are at CDC and NIH. At the same time, DHHS likely possesses and will be able to call on the scientific and institutional knowledge and expertise needed to effectively monitor and enforce biosafety and biosecurity regulations. Absent the consolidation recommended here, Congress will need to find another way to improve coherence, monitoring and enforcement.

Annual report. In order to further strengthen DHHS and USDA implementation, monitoring and enforcement of all of the above requirements, Congress should require that these agencies submit an annual report detailing their efforts in this regard.

Transparency

Amend Section 351A(h). Section 351A(h) of Title III of the Public Health Service Act provides an overly broad exemption for disclosure of certain information pertaining to entities registered under the Select Agent Rules (Appendix C). Moreover, the CDC is interpreting this exemption even more broadly than provided for in the Act (Appendix D). Section 351A(h) is making it easier for institutions and Federal agencies to cover up their mistakes. Meant to strengthen US national security, this Section as currently conceived instead weakens biosafety and biosecurity, and thus national security. It does so by impeding public accountability of institutions and Federal agencies, and by reducing our ability to reassure others that our bioweapons-related research and development activities comply with our obligations under international law. The Section should be amended to more narrowly and accurately define necessary and appropriate requirements for withholding information about activities involving potential bioweapons agents.

Promotion

International promotion. Biosafety, biosecurity and dual-use research are issues of international concern. Congress should mandate that the Executive Branch work to promote the adoption of these strengthened biosafety and biosecurity requirements more broadly by other countries.

Needs and Risk Assessments

Needs assessment for high containment labs. As discussed earlier, no comprehensive interagency needs assessment for determining our high containment laboratory requirements has been performed. Congress should mandate that DHHS, DHS, DOD and USDA conduct a comprehensive interagency assessment to determine current and anticipated US needs for BSL3 and BSL4 facilities. The needs assessment should include, but not be limited to, all information gathered as part of the BSL-3/BSL-4 facility licensing and registration process described above. Congress should further mandate that GAO assess and report on the quality of the interagency needs assessment, including the processes and data used.

Risk Assessments. Congress should mandate, and the GAO should conduct, independent evaluations of safety risks and security risks associated with the recent and continuing increases in the number of institutions and individuals performing bioweapons-related and other high-risk research. Given the widespread concerns that exist in some communities, the assessments should include consideration of siting issues.

Funding moratorium. Congress should impose a moratorium on all future funding for the construction or expansion of BSL-3 and BSL-4 facilities pending completion and review of the above assessments.

Appendix A - Federal Funding for Biological Weapons Prevention and Defense, Fiscal Years 2001 to 2008

Introduction

Since the 2001 terrorist attacks on the United States, the U.S. government has spent or allocated over \$40 billion among 11 federal departments and agencies to address the threat of biological weapons. For Fiscal Year 2008 (FY2008), the Bush Administration is proposing an additional \$6.77 billion in bioweapons-related spending, approximately \$550 million (9%) more than the amount that Congress appropriated for FY2007.² U.S. funding for bioweapons-related activities focuses primarily on research, development, and acquisition of medical countermeasures and protective equipment, enhancing medical surveillance and environmental detection of biological weapons agents, and improving state, local, and hospital preparedness. The Department of Defense proposes to double the amount of money that it spends on efforts to prevent the development, acquisition and use of biological weapons by states and terrorists and other non-state actors in FY2008. However, activities aimed at prevention still account for less than 2% of all federal bioweapons-related funding since FY2001. Further strengthening of prevention efforts, including a commitment to broad cooperative international action, are essential for improving our nation's security.

Annual bioweapons-related programs and funding for the following departments and agencies from FY2001 to FY2008 are summarized in Table 1: the Department of Agriculture (USDA), the Department of Commerce, the Department of Defense (DOD), the Department of Energy (DOE), the Department of Health and Human Services (DHHS), the Department of Homeland Security (DHS), the Department of State, the Department of Veterans Affairs (VA), the Environmental Protection Agency (EPA), the National Science Foundation (NSF), and the United States Postal Service (USPS). Table 1 also includes funding for Project BioShield, a ten-year program to acquire medical countermeasures to biological, chemical, radiological and nuclear agents for civilian use. As illustrated in Figure 1, annual bioweapons-related spending grew rapidly from FY2001 to FY2004. Excluding Project BioShield and one-time funding for the US Postal Service in FY2005, federal bioweapons-related funding has remained roughly steady at approximately \$6.5 billion/year since FY2004.

Cumulative total funding by agency for the entire FY2001 to FY2008 period (\$48.33 billion if the FY2008 request is funded in full) is illustrated in Figure 2, with DHHS funding broken down into its constituent agencies and offices (Food and Drug Administration (FDA), Health Resources and Services Administration (HRSA), the Centers for Disease Control (CDC), National Institutes of Health (NIH), and the Office of the Secretary (OS) plus the Agency for Healthcare Research and Quality (AHRQ)). Over 90% of all bioweapons-related funding goes to three lead departments: Health and Human Services, Defense, and Homeland Security (through which Project BioShield is funded).

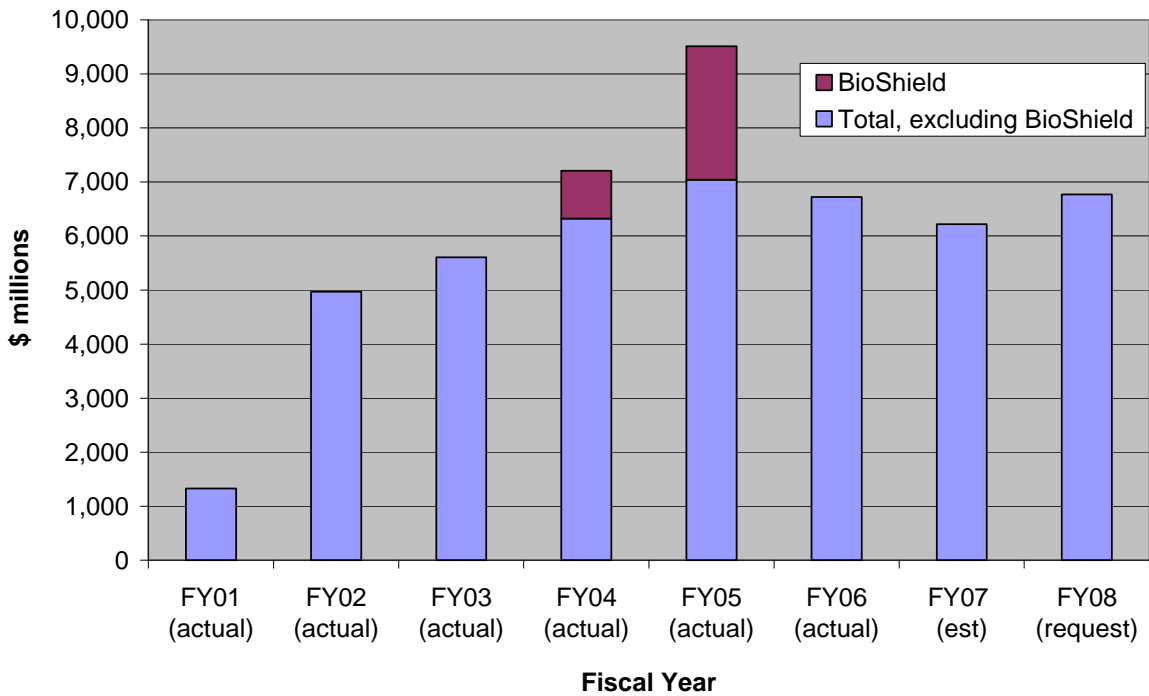
In contrast to other preparedness efforts, biodefense research, development, testing, and evaluation (RDT&E) can be dual-use in nature: scientific knowledge, methods, and materials that can be used to protect against biological weapons can often also be used to develop biological weapons. The dual-use problem has become a significant national and international policy concern. In the United States, the National Science Advisory Board for Biosecurity (NSABB) has been established under the auspices of

² The estimates presented here differ from those in our FY2007 budget analysis. More refined analysis of Defense Department funding resulted in a reduction of \$250 - \$300 million annually, due to allocations within the Chemical and Biological Defense Program for chemical and radiological countermeasures. Project BioShield funding was previously reported as annual obligations listed in federal government budget documents. These data are no longer valid given the cancellation of a major BioShield contract, (discussed in Homeland Security analysis section). All Project BioShield funding is now reported in the year that it was appropriated.

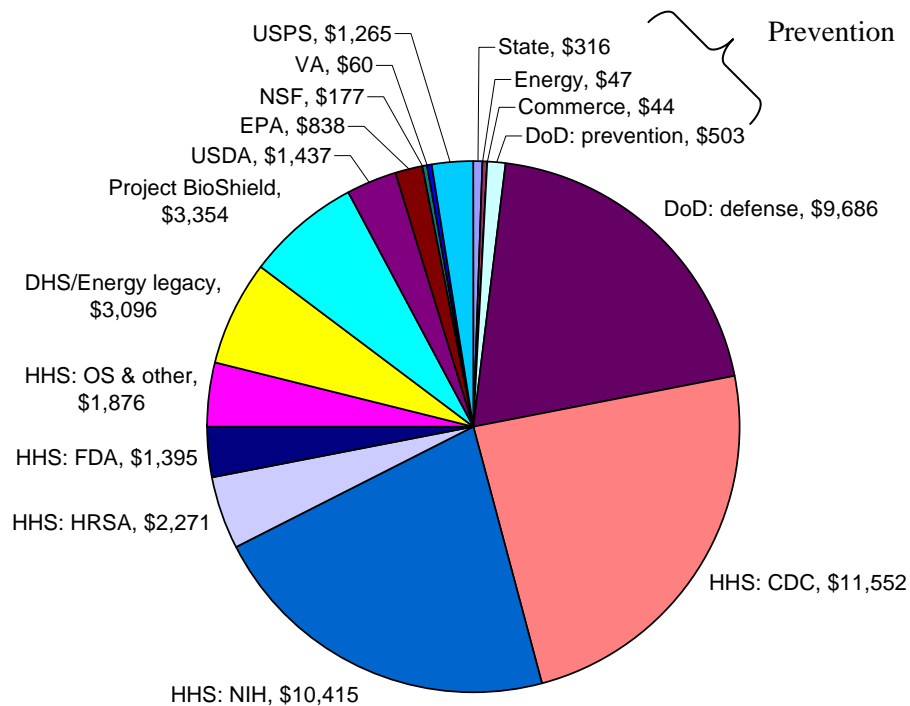
Table 1. Federal Funding for Bioweapons Prevention and Defense, by Agency, FY2001 – FY2008 (in \$ millions)

Department/Agency	FY01 (actual)	FY02 (actual)	FY03 (actual)	FY04 (actual)	FY05 (actual)	FY06 (actual)	FY07 (estimate)	FY08 (request)	FY01-FY08
Agriculture	7	42	204	111	298	247	187	341	1,437
Commerce	3	4	5	7	6	5	7	7	44
Defense	734	1,046	1,053	1,246	1,335	1,679	1,406	1,690	10,189
Energy	4	5	5	5	5	11	7	5	47
Health and Human Services	324	2,980	4,035	3,704	4,148	4,090	4,044	4,182	27,507
Homeland Security/ Energy legacy	40	85	119	1,038	554	523	397	340	3,096
Project BioShield				885	2469				3,354
State	20	49	35	46	44	37	42	43	316
Veterans Affairs			27	23	9	0	1	0	60
Environmental Protection Agency	20	155	95	114	111	103	103	137	838
National Science Foundation		17	26	27	27	27	28	25	177
US Postal Service	175	587	0	0	503	0	0	0	1,265
Total	1,327	4,970	5,604	7,206	9,509	6,722	6,222	6,770	48,330
Total, excl. BioShield	1,327	4,970	5,604	6,321	7,040	6,722	6,222	6,770	44,976

**Figure 1. Total Federal Funding for Bioweapons Prevention and Defense
FY2001 - FY2008**



**Figure 2. Total Federal Funding for Bioweapons Prevention and Defense by Agency
FY2001 – FY2008 (\$ millions)**



theNIH, with *ex officio* representation from 18 Federal departments, agencies, and offices, in order to “provide advice, guidance, and leadership regarding biosecurity oversight of dual use research” to the Secretary of DHHS, the Director of the NIH, and the “heads of all federal departments and agencies that conduct or support life science research.”³

Cumulative funding for biodefense RDT&E from FY2001 through FY2008 will reach \$20 billion, over 40% of all bioweapons-related funding since FY2001 (Table 2). Of this, approximately \$1.9 billion has thus far been spent, allocated, or requested for improving existing or building at least 20 new high containment research facilities around the country, including 7 new biosafety level 4 (BSL-4) facilities for conducting work on dangerous pathogens such as the ebola viruses and other hemorrhagic fever viruses. The Departments of Defense and Homeland Security are expected to request up to another \$1.25 billion over the next five years for two of these BSL-4 facilities.

In contrast, cumulative funding for efforts to prevent the development, acquisition, and use of biological weapons is expected to reach approximately \$874 million in FY2008 (Table 3). This is less than 2% of the total funding for biodefense RDT&E during the same time period. FY2008 sees the first substantive increase in funding for prevention efforts since FY2004. If approved by Congress, funding for prevention activities as a percentage of total bioweapons-related funding will increase to 3%, returning it to pre-2001 levels. Approximately 90% of prevention funding goes to the Departments of Defense, Energy and State for Cooperative Threat Reduction efforts, primarily in states of the former Soviet Union. Other prevention-related funding is provided to the Department of Commerce for Export Controls on materials and equipment that could be used to develop biological weapons, and to the Select Agents programs at the

³ biosecurityboard.gov

CDC and USDA which regulate the possession, use, and transfer of potential biological weapons pathogens and toxins. The NSABB also receives roughly \$1 million per year for its activities.

Table 2. Funding for Biodefense Research, FY2001 – FY2008 (in \$ millions)

Department/Agency	FY01 (actual)	FY02 (actual)	FY03 (actual)	FY04 (actual)	FY05 (actual)	FY06 (actual)	FY07 (estimate)	FY08 (request)	FY01-FY08
Facilities									
USDA	7	30	143	0	121	58	0	16	375
DOD						21	29	150	200
DHHS		92	743	0	149	30	25	0	1039
DHS			30	108	68	36	23	n/a ^a	265
<i>Facilities, Subtotal</i>	<i>7</i>	<i>122</i>	<i>916</i>	<i>108</i>	<i>338</i>	<i>145</i>	<i>77</i>	<i>166</i>	<i>1879</i>
Programs									
USDA		9	12	20	29	34	32	81	217
DOD: Army		17	19	22	19	16	25	16	134
DOD: DARPA	146	172	158	142	155	133	113	99	1118
DOD: CDBP	302	488	505	578	565	844	773	827	4882
<i>DOD, Subtotal</i>	<i>448</i>	<i>677</i>	<i>682</i>	<i>742</i>	<i>739</i>	<i>993</i>	<i>911</i>	<i>942</i>	<i>6134</i>
DHHS: FDA	6	46	53	53	57	57	55	57	384
DHHS: CDC	29	20	20	18	17	14	14	0	132
DHHS: NIH	53	198	810	1821	1593	1604	1610	1628	9317
DHHS: OS/BARDA							54	189	243
<i>DHHS, Subtotal</i>	<i>88</i>	<i>264</i>	<i>883</i>	<i>1892</i>	<i>1667</i>	<i>1675</i>	<i>1733</i>	<i>1874</i>	<i>10076</i>
DHS: S&T ^b			53	218	247	244	196	183	1141
DOE	40	85							
VA	n/a	n/a	27	23	9	0	1	0	60
EPA: S&T	0	5	17	33	51	46	46	67	265
NSF	0	17	26	27	27	27	28	25	177
<i>Programs, Subtotal</i>	<i>576</i>	<i>1057</i>	<i>1700</i>	<i>2955</i>	<i>2769</i>	<i>3025</i>	<i>2947</i>	<i>3172</i>	<i>18201</i>
Research, Total	583	1179	2616	3063	3107	3170	3024	3338	20080

^a n/a: no information available.

^b Based on estimate that 60% of non-facility Biological and Chemical Division funding from FY2003 - FY2007, and 80% in FY2008, is devoted to biodefense RDT&E.

Table 3. Funding for Bioweapons Prevention Activities, FY2001 – FY2008 (in \$ millions)

Department/Agency	FY01 (actual)	FY02 (actual)	FY03 (actual)	FY04 (actual)	FY05 (actual)	FY06 (actual)	FY07 (estimate)	FY08 (request)	FY01-FY08
USDA:APHIS:					3	3	3	7	16
Select Agents									
DOD: CTR	12	17	55	68	69	70	68	144	503
DHHS: CDC:	5	5	5	5	5	5	5	5	40
Select Agents ^a									
State: Nonproliferation Programs	16	45	20	29	27	25	31	32	225
Commerce: Export Controls	3	4	5	7	6	5	7	7	44
DOE: NIS Programs	4	5	5	5	5	5	7	5	41
Prevention, Total	40	76	90	115	116	114	122	201	874

^a HHS and CDC do not provide data on funding for the Select Agent Program. This is an estimate based on USDA data and CDC data from FY2002 (from GAO-03-315R "CDC Select Agent Program," 11/22/02).

Appendix B – Biosafety and Biosecurity Rules and Guidelines

The NIH Guidelines

The first mechanism, which addresses biosafety only, is the system established by the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (NIH Guidelines). The NIH Guidelines apply to all institutions that receive funding from NIH and conduct research involving recombinant DNA (rDNA). Such institutions are responsible for ensuring that all research covered by the Guidelines is conducted in accordance with the provisions of the Guidelines (Section IV-B-1). Among their responsibilities, they must establish an Institutional Biosafety Committee (IBC) and file an annual report listing the names and biographies of all IBC members with the NIH Office of Biotechnology Activities (OBA) (at present, approximately 400 IBCs are so registered with OBA). Institutions must also appoint a Biological Safety Officer (BSO) if they conduct rDNA research at BSL-3 or BSL-4. They must “ensure appropriate training” for the IBC Chair, the BSO, and all relevant personnel regarding biosafety and implementation of the Guidelines, and they must establish a health surveillance program if they conduct rDNA research at BSL-3 or higher. Investigators must subject all research involving rDNA to a risk assessment in order to determine the appropriate containment level for their work (Section II-A). The Guidelines provide recommendations to facilitate this process, including the categorization of biological agents into one of four “risk groups.” (Section II and Appendix B). The IBC must provide independent prior review and approval for certain rDNA research (defined in Sections III-A to III-D). To enhance transparency and public accountability, institutions are required to provide public access to IBC meeting minutes, which “should offer sufficient detail to serve as a record of major points of discussion and the committee’s rationale for particular decision.” (Section IV-B-2). Finally, institutions or their IBCs must report any “significant problems [or] violations” of the NIH Guidelines, and any “significant research related accidents or illnesses” involving rDNA, to OBA within 30 days (Section IV). Spills or accidents that result in “overt” exposure at BSL-2, or “overt or potential exposure” at BSL-3 and BSL-4 must be reported immediately (Appendix G). Failure of an institution to comply with the Guidelines can result penalties up to and including the termination of NIH funding of research involving rDNA at the institution (Section I-D).

There are a few absolute prescriptions in the NIH Guidelines. For instance, any experiments involving the introduction of rDNA into Risk Group 4 agents must be conducted at BSL-4. Experiments in which DNA from such agents is transferred into other microorganisms may be performed at BSL-2, but only after it has been demonstrated that “only a totally and irreversibly defective fraction of the agent’s genome is present in a given recombinant.” In the absence of such a demonstration, the work must be performed at BSL-4. Finally, containment conditions for all experiments involving the transfer of DNA from the smallpox virus into other microorganisms must be determined by OBA following a case-by-case review (Section III-D). In addition, two specific types of research require approval by the NIH Recombinant DNA Advisory Committee (RAC) and/or the NIH or another federal agency with jurisdiction for review and approval (Sections I-A, III-A, III-B). These are any experiments involving the cloning of genes coding for toxin molecules having a median lethal dose of less than 100 nanograms per kilogram body weight, and any experiments involving the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally “if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture.” (There are also requirements for review and approval of human gene therapy experiments, but these are not discussed further here). Experiments involving the cloning of less potent toxin genes must be registered with OBA prior to their initiation (Appendix F).

The Select Agent Rules

The second mechanism, addressing both biosafety and biosecurity, is provided by the Select Agent Rules promulgated by APHIS and the CDC under the Public Health Security and

Bioterrorism Preparedness and Response Act of 2002. This discussion is based on the Rule promulgated by CDC (at 42 CFR 73). The Select Agent Rules define a list of “select” biological agents, toxins and genetic materials that “have the potential to pose a severe threat to public health and safety, to animal health, or to animal products” and provide for the registration and oversight by the federal government of all entities in the United States who possess, use or transfer such agents, with certain exemptions. The possession, use or transfer of a select agent without a certificate of registration is illegal under federal law. As outlined in Section 73.7, to obtain a certificate of registration an entity must designate a Responsible Official (RO), and both the entity and RO must undergo a security risk assessment by the Justice Department. Certificates of registration are valid only for specific physical locations, specific select agents or toxins, and specific activities. Registered entities may not provide an individual with access to a select agent or toxin unless the individual receives access approval from the federal government following a security risk assessment.

The Rules specify that a registered entity must maintain a complete inventory of all select agents and toxins, including their names, characteristics, storage locations, dates accessed, and uses (42 CFR 73.17). The entity must adhere to specific security requirements “or implement measures to achieve an equivalent or greater level of security,” and must develop and implement a written security plan which includes certain specified types of information and is “sufficient to safeguard the select agent or toxin against unauthorized access, theft, loss or release.” (42 CFR 73.11). The entity must also develop and implement a written biosafety plan that is “commensurate with the risk of the agent or toxin, given its intended use.” The plan “must contain sufficient information and documentation to describe the biosafety and containment procedures,” which “must be sufficient to contain the select agent or toxin.” In developing the plan, the entity “should consider” the BMBL, the NIH Guidelines, and the OSHA regulations at 29 CFR 1910.1200 and 1910.1450 (see more below)(42 CFR 73.12). The entity must also develop and implement a written incident response plan which fully describes the response procedures in case of theft, loss or release of a select agent or toxin and contains certain basic emergency response information (42 CFR 73.14). Each of these plans must be reviewed, evaluated and revised as necessary on an annual basis.

Each individual with access to select agents and toxins “must have the appropriate education, training, and/or experience to handle or use such agents or toxins.” (42 CFR 73.10(c)). The registered entity must “provide information and training on biosafety and security to each individual with access approval ... before he/she has such access,” and must also provide information and training on biosafety and security to each individual not approved for access before he/she works in or visits areas where select agents or toxins are handled or stored. The training “must address the particular needs of the individual, the work they will do, and the risks posed by the select agents or toxins,” and refresher training must be provided annually. A record of such training, including the date of the training, a description of the training, and the means used to verify that the individual understood the training, must be maintained. (42 CFR 73.15).

The entity must obtain prior federal approval before conducting any experiment with a select agent or toxin that involves the deliberate formation of rDNA containing genes for toxins having a median lethal dose of less than 100 nanograms per kilogram body weight, or the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally “if such acquisition could compromise the use of the drug to control disease agents in humans, veterinary medicine, or agriculture.” (42 CFR 73.13)

The entity must immediately notify the CDC and other appropriate Federal, State or local authorities upon discovery of the theft or loss of a select agent or toxin. It must immediately notify the CDC upon discovery of a “release of an agent or toxin causing occupational exposure or the release of a select agent or toxin outside the primary barriers of the biocontainment area. In each case, written notice must also be filed within seven days. (42 CFR 73.19).

Finally, when applying for a certificate of registration, an entity must submit a CDC Form 1. The Form must include information on the biosafety level at which the specific registered activity will be conducted. The biosafety level “should” be determined by a biosafety risk assessment that “should” be based on the requirements at 29 CFR 1910.1450, the BMBL, and the NIH Guidelines. The RO must certify that the entity is capable of safely and securely handling the agents or toxins specified in the application, and that “information and training on safety and security for working with select agents and toxins” has been provided to each individual for whom access approval is requested. Certain other biosafety and security-related information must also be provided. The issuance of the certificate may be contingent upon inspection of the entity or the submission of additional information including a security plan, biosafety plan, incident response plan, or any other required documents (42 CFR 73.7(f)).

The third mechanism, addressing biosafety only, is embodied in several OSHA regulations. In 1992, OSHA established a legally binding standard for working with bloodborne pathogens (29 CFR 1910.1030). The standard requires the employers establish and regularly update and maintain a detailed written Exposure Control Plan designed to eliminate or minimize employee exposure to human blood or other human bodily fluids, tissues or organs that may contain infectious materials. It defines “occupational exposure” as “reasonably anticipated skin, eye, mucous membrane, or parenteral contact with blood or other potentially infectious materials that may result from the performance of an employee's duties.” The standard includes detailed requirements for engineering and work practice controls, personal protective equipment, waste management and disposal, employee training, and record-keeping. Similarly, OSHA has established a legally binding standard for work with hazardous chemicals, including certain toxins (29 CFR 1910.1450). Finally, OSHA requires that employers with 10 or more employees must record and report work-related fatalities and illnesses. Further, any fatality and any hospitalization of three or more individuals which occurs within 30 days of and is due to a work-related incident must be orally reported to OSHA within 8 hours (29 CFR 1904).

Appendix C - Section 351A(h) of the Public Health Service Act

As added by Title II of the Bioterrorism and Public Health Emergency Preparedness and Response Act of 2002

(h) Disclosure of Information.--

“(1) Nondisclosure of certain information.--No Federal agency specified in paragraph (2) shall disclose under section 552 of title 5, United States Code, any of the following:

“(A) Any registration or transfer documentation submitted under subsections (b) and (c) for the possession, use, or transfer of a listed agent or toxin; or information derived therefrom to the extent that it identifies the listed agent or toxin possessed, used, or by a specific registered person or discloses the identity or location of a specific registered person.

“(B) The national database developed pursuant to subsection (d), or any other compilation of the registration or transfer information submitted under subsections (b) and (c) to the extent that such compilation discloses site-specific registration or transfer information.

“(C) Any portion of a record that discloses the site-specific or transfer-specific safeguard and security measures used by a registered person to prevent unauthorized access to listed agents and toxins.

“(D) Any notification of a release of a listed agent or toxin submitted under subsections (b) and (c), or any notification of theft or loss submitted under such subsections.

“(E) Any portion of an evaluation or report of an inspection of a specific registered person conducted under subsection (f) that identifies the listed agent or toxin possessed by a specific registered person or that discloses the identity or location of a specific registered person if the agency determines that public disclosure of the information would endanger public health or safety.

“(2) Covered agencies.--For purposes of paragraph (1) only, the Federal agencies specified in this paragraph are the following:

“(A) The Department of Health and Human Services, the Department of Justice, the Department of Agriculture, and the Department of Transportation.

“(B) Any Federal agency to which information specified in paragraph (1) is transferred by any agency specified in subparagraph (A) of this paragraph.

“(C) Any Federal agency that is a registered person, or has a sub-agency component that is a registered person.

“(D) Any Federal agency that awards grants or enters into contracts or cooperative agreements involving listed agents and toxins to or with a registered person, and to which information specified in paragraph (1) is transferred by any such registered person.

“(3) Other exemptions.--This subsection may not be construed as altering the application of any exemptions to public disclosure under section 552 of title 5, United States Code, except as to subsection 552(b)(3) of such title, to any of the information specified in paragraph (1).

“(4) Rule of construction.--Except as specifically provided in paragraph (1), this subsection may not be construed as altering the authority of any Federal agency to withhold under section 552 of title 5, United States Code, or the obligation of any Federal agency to disclose under section 552 of title 5, United States Code, any information, including information relating to--

“(A) listed agents and toxins, or individuals seeking access to such agents and toxins;

“(B) registered persons, or persons seeking to register their possession, use, or transfer of such agents and toxins;

“(C) general safeguard and security policies and requirements under regulations under subsections (b) and (c); or

“(D) summary or statistical information concerning registrations, registrants, denials or revocations of registrations, listed agents and toxins, inspection evaluations and reports, or individuals seeking access to such agents and toxins.

“(5) Disclosures to congress; other disclosures.--This subsection may not be construed as providing any authority--

“(A) to withhold information from the Congress or any committee or subcommittee thereof; or

“(B) to withhold information from any person under any other Federal law or treaty.

Appendix E - Primer on Pathogen Risk Groups

The NIH Guidelines establish an agent risk group classification scheme that describes four general risk groups based on the infectivity and pathogenicity (ability to cause disease) of a biological agent, its virulence (severity of disease), the availability of preventive measures and effective treatments for the disease, and the route of transmission of the natural disease. The four groups address the risk to both the laboratory worker and the community. Risk groups correlate with but do not equate to biosafety levels (BSLs). A risk assessment is used to determine the appropriate BSL at which to conduct work with a pathogenic agent. The risk assessment is based on the risk group of the agent, its mode of transmission, procedural protocols, experience of staff, and other factors.

Risk Group 1

Agents that are not associated with disease in healthy adult humans.

Risk Group 2

Agents that are associated with human disease which is rarely serious and for which preventive or therapeutic interventions are *often* available. Examples: anthrax, salmonella, dengue, measles)

Risk Group 3

Agents that are associated with serious or lethal human disease for which preventive or therapeutic interventions *may be* available (high individual risk but low community risk). Examples: plague, tularemia, tuberculosis, hantaviruses, HIV

Risk Group 4

Agents that are likely to cause serious or lethal human disease for which preventive or therapeutic interventions are *not usually* available (high individual risk and high community risk). (High individual and community risk) Examples: ebola, Marburg,