Dual Use Research of Concern: Balancing the Risks and Rewards of Current and Future Life Sciences Research

by

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ABSTRACT

In 2011, two studies funded by the National Institutes of Health (NIH) which demonstrated the transmissibility of H5N1 (avian influenza) to mammals caused an uproar in the scientific community. Researchers engineered H5N1 viruses to make them transmissible by respiratory droplets between ferrets, an animal commonly used to model human influenza infection. These studies provided critical information to scientists and public health officials by demonstrating that H5N1 viruses can be mutated to enable them to spread among certain mammals perhaps even among humans. The generation of these strains raised safety and security concerns centered on whether the strains could be released accidentally or used for malevolent purposes that could threaten public health or national security. These experiments triggered a global discussion for five months regarding the benefits and risks of funding, conducting research, and publishing these types of studies. As a result, the influenza community initiated a voluntary moratorium for 60 days that actually lasted over a year while the U.S. National Science Advisory Board for Biosecurity (NSABB) restricted publication of the results.

As a direct outcome of the H5N1 experiments, the Dual Use Research of Concern Policy was released in March 2012 in an attempt to oversee this type of research. The dual use policy is not intended to restrict science but to support public health and national security. However, if the only country moving forward with a dual use policy is the U.S., then it will inhibit research while other countries make cutting edge discoveries in life sciences. The policy demonstrates the need for achieving consistency within the life science field of research throughout the globe. Fostering transparency at an institution leading up to the publication of research results will protect public health and the institution.
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CHAPTER I
INTRODUCTION

The National Institutes of Health (NIH) and other national and international agencies support the publication of federally funded, fundamental research. Fundamental research is defined as basic and applied research in the areas of science and engineering where the resulting information is intended to be published and shared broadly within the scientific community with no governmental restrictions ("Deemed exports and," n.d.). The technology used during the research is publicly available and may even be a part of the published information ("Deemed exports and," n.d.).

Unfettered distribution of these data drives innovation and job creation while advancing technology and science. However, in a limited number of cases, the methods and data collected may pose a security threat which requires the federal government to re-classify or even prohibit publication of this fundamental research (Gottron & Shea, 2012).

In late 2011, two federally funded research groups headed by Ron Fouchier (Erasmus Medical Centre, Rotterdam, Netherlands) and Yoshihiro Kawaoka (University of Tokyo, Japan, and University of Wisconsin-Madison, United States) submitted manuscripts detailing methods for increasing human-to-human transmissibility of H5N1 avian influenza virus (bird flu). Both groups had genetically modified the highly pathogenic avian influenza H5N1 virus through reassortment with the H1N1 (swine) influenza virus, directed mutation and passage experiments. The resulting viral mutants could be transmitted via aerosol among ferrets, a model for influenza transmission in human beings ("Avian influenza and," 2012). The submission of these two manuscripts to the scientific journals Nature and Science caused uproar in the scientific
community and led to an unprecedented recommendation from the U.S. National Science Advisory Board for Biosecurity (NSABB) for the publication of the research be put on hold.

In the U.S., NSABB requested that the methods used to enable transmission of the H5N1 virus from mammal to mammal and the results of the experiment be redacted before the articles were released to the public. The NSABB feared that the exact details of the scientific methods used and the mutations involved could pose a significant biosafety risk. In the Netherlands, the paper by Fouchier was delayed from being released by the Dutch government which believed that the work may have violated export control rules, related to dual use and government regulated technology (Enserink, 2012). The NSABB also recommended a 60 day moratorium on all similar research while the risks were assessed. Leading influenza scientists around the world agreed to the moratorium. The World Health Organization (WHO) did not agree with NSABB’s recommendation of redacting information in the articles before publication. They felt that widely sharing the results of the papers would provide significant public health and scientific value (Cohen, 2012); however, the WHO did agree to the moratorium until the risks could be further evaluated (Cohen & Enserink, 2012).

*Science* and *Nature* both agreed to the NSABB recommendation to redact the information, with the understanding that the information would be made available to researchers and organizations with a legitimate reason for access including governments of countries with endemic H5N1, influenza research institutions around the world, and pharmaceutical companies. The research groups agreed to these conditions, although many of them along with others in the broader scientific community viewed the proposal as censorship ("Avian influenza and," 2012). The WHO did not support making the information available to certain groups citing that it would
be too difficult and time consuming to come up with a mechanism of distribution and to determine who would be able to receive the data (Cohen, 2012).

The recommendation to postpone publication and to redact details of the methods used to mutate the virus to enable aerosol transmission in mammals sparked fierce debate among the scientific community, government agencies, non-governmental organizations, and biosafety specialists who all presented valid data to support the benefits and risks of such research ("Avian influenza and," 2012). In the process of weighing the potential risks and benefits of these papers, it became clear that, when possible, to assess research with DURC potential before the initiation of the project and before the results are submitted for publication (Fauci & Collins, 2012).

The H5N1 dilemma highlighted a challenge for the scientific community and regulatory agencies at the intersection of two important concepts: scientific discovery and social responsibility. Scientists must look at their research from two different points of view: adherence to accepted standards of scientific practice in both conducting and reporting research and the social consequences of applying research findings. It raises two important questions:

1. How much of a researcher’s methods must be accessible in order to assess the integrity of the findings?
2. What is the scientist’s social responsibility when the research has dual use applications? (Frankel, 2012).

The intervention of national and international government parties into the publication process brought to the surface the old but recurring question: what is the role of government in regulating science, and what is the relationship between science and society? In the past science was left to the scientists. Now scientists are subject to stakeholders who see scientific results as part of a larger goal whether it be profit, funding, patients seeking a cure, politicians seeking
votes, or the global community seeking assurance that the science is safe. As a result, many biosafety, scientific, and government groups are demanding accountability from the scientific community. Determining the level of regulation that meets the needs of the majority of stakeholders is a balancing act that will require ongoing and improved negotiation moving forward (Frankel, 2012).

It has been a challenge for national and international governments to respond to the H5N1 influenza controversy as they try to balance increasing public pressure for greater government oversight of scientific research with the need to support researchers in preparing for another pandemic. The U.S. Policy for Oversight of Life Sciences Dual Use Research of Concern was published in March 2012 in an attempt to regulate publication of life sciences research. It was designed to establish regular reviews of U.S. government funded research involving 15 high consequence pathogens deemed Dual Use Research of Concern (DURC). These same agents are regulated by the Centers for Disease Control and Prevention (CDC) select agent program. These 15 pathogens were selected because they have the potential to be deliberately misused, causing mass fatalities or destructive effects to the economy, vital infrastructure or public confidence ("United States government," 2012). This is a significant change for U.S. based researchers in dual use life science research because in the past it has always been up to the research community to decide what, how, and when research would be published (Frankel, 2012).

Governments in other countries have taken notice of the U.S. policy on DURC and are taking another look at their own programs. If changes are made in how life science research results are published, the U.S. and other countries will need to agree on a core set of principles to safely regulate the publication of research while promoting discovery and innovation. A level of regulation will have to be determined that takes into account all stakeholders (Frankel, 2012).
The debate about the publication of scientific research with potential security implications cuts across multiple policy issues including supporting federal research, maintaining homeland security, and sustaining research information. The controversy surrounding the decision to partially publish these experiments demonstrates flaws in existing mechanisms to identify and balance the potential public health benefits and security trade-offs (Gottron & Shea, 2012).

Policymakers and stakeholders face difficult decisions when trying to balance the potential benefits of this research against potential harm such as an accidental release or bioterrorism. Public health experts agree that an influenza pandemic in the future is inevitable (Petsko, 2005). Most experts also agree that such research may increase the risk that an influenza outbreak could occur through accidental or deliberate release of a modified virus (Frankel, 2012). The outbreak of smallpox from a research lab in Birmingham England in 1978 supports this rationale ("Smallpox global alert," 2012).

This paper will discuss the future of life sciences research as the science community and government move forward and make decisions about regulating DURC and at what level the research should be regulated. This paper will add to the body of knowledge regarding the risks and rewards of regulating cutting edge research as it relates to public health. It will also discuss how over-regulation of scientific research can serve as deterrent to researchers performing key studies that have great benefit to public health and welfare.
CHAPTER II
BACKGROUND/LITERATURE REVIEW

Definitions

Life Science Research

Life science refers to the study of living organisms including, microbes, and human beings, animals, fungi, and plants ("Committee on Research," 2004). It includes the fields of biology, aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, synthetic biology, environmental science, public health, modeling, engineering of living systems, and many other types of scientific study. The phrase “life sciences” is meant to encompass the diverse approaches for understanding life at the levels of ecosystems, organisms, organs, tissues, cells, and molecules ("Committee on Research ," 2004).

Research in life sciences in the last century has provided advances in agriculture and industrial development while transforming the practice of medicine. In the field of biopharmaceutical products, major breakthroughs have been made including human recombinant insulin for the treatment of diabetes, a vaccine against hepatitis B, and medicines for cancer therapy, arthritis, multiple sclerosis, and cystic fibrosis (“Committee on Research ,” 2004).

Better understanding of the principles of genetics, biochemistry, the structure of DNA, and the discovery of gene-splicing technology have greatly advanced biological or life sciences. The discovery of genetic engineering was a major accomplishment for the scientific community. Genetic engineering allows for the modification and transfer of genetic material from one organism to another including from one species to another. These scientific advances are directly related to the sharing of knowledge among scientists and people and ideas moving freely
between universities, government agencies, and private industry. Large numbers of foreign nationals including graduate and post-doctoral students have greatly contributed to biological science discoveries (“Committee on Research” 2004). The same technology that has enabled so many advances in medicine and pharmacy also pose a potential threat to society because it can be used to create biological weapons. Biotechnology presents a “dual use” dilemma in which the same discoveries can be used to either help people or misused for bioterrorism purposes (“Committee on Research,” 2004).

**Dual Use**

In the language of the Department of Commerce (DOC) or International Traffic and Arms (ITAR) regulations, dual use refers to technology intended for civil end use while also having a military application. Technology encompasses more than just a product, it also includes how to produce and use the product (“Committee on Research,” 2004). In the life sciences field, the definition of dual use is “biological research with a legitimate scientific goal that could be misused by rogue states, terrorist organizations, or individuals to pose a biological threat to public health or national security” (Fauci & Collins, 2012).

Life sciences research is important for improving public health, agriculture, and the environment, while strengthening national security and the economy. However, the same research intended to improve health, welfare, and safety, can also provide information or technologies that could be used in a malicious manner. For example, information from *Yersinia pestis* (plague) vaccine research can be misapplied to create an antibiotic resistant pathogen to be used as a biological weapon. This threatens the health and safety of humans, animals, plants, and the environment. Research providing new technologies or information with the potential for both
beneficial and disadvantageous applications is called "dual use research" (“NSABB frequently asked”).

**Dual Use Research of Concern**

Dual use potential is found in the majority of life sciences research. There is, however, a smaller subset of life science research with a higher potential for providing knowledge, technology or end products that can be used to threaten public health or national security. There are 15 organisms in this subset including the seven experiments of concern that fall into the category of "dual use research of concern" or DURC (“NSABB frequently asked”).

**Seven Experiments of Dual Use Research of Concern**

The NSABB has identified seven types of research that may fall under the category of dual use research of concern. These research projects warrant close attention to the dual use nature of the experiment by the researcher when being designed, conducted, and published (Unites States government,” 2012). These include research that might:

1. Enhance the harmful consequences of the agent/toxin; Example - experiments designed to make seasonal flu as virulent as the pandemic 1918 influenza virus.

2. Disrupt immunity to or the effectiveness of an immunization against the agent/toxin without clinical or agricultural justification; Example - inserting an immunosuppressive cytokine into a viral genome to make the immune response less effective.

3. Confer to the agent/toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent/toxin or facilitates their ability to evade detection methodologies; Example – altering the sensitivity of the bacterium *Yersinia pestis* (plague) to doxycycline, the antibiotic used to treat plague infections.
4. Increase the stability, transmissibility, or the ability to disseminate the agent or toxin;
   Example – genetically modifying a pathogenic thermophilic bacterial strain to grow at ambient temperatures.

5. Alter the host range or tropism of the agent/toxin. Example - altering a mosquito-transmitted virus so that it is transmissible to a new species of mosquito

6. Enhance the susceptibility of a host population to the agent/toxin; Example - modification of a pathogen to allow it to evade a crucial host immune response.


**History of Biological Warfare**

**14th to 18th Century**

Thousands of microorganisms are potentially pathogenic; however, very few have been developed to be disseminated as biological weapons (“Committee on Research,” 2004). While recent events have led most Americans to believe that biological and chemical warfare is a recent development, in fact biological warfare has been around since the 14th century. Early on people recognized the potential impact of infectious diseases on armies. Since ancient times, cadavers, animal carcasses, and pathogens have been used as weapons to contaminate water sources including the wells and reservoirs of armies and civilian populations under attack.

One of the earliest records of biological warfare was the use of fomites in the 14th century (Christopher, Cieslak, Paviln, & Eitzen, 1997). Fomites are inanimate objects such as clothing and bedding capable of carrying infectious microorganisms that can be transmitted from one person to another (“Merriam Webster,” 2013).
During the 14th century siege of Kaffa, the attacking Tartar army contracted bubonic plague. In an attempt to weaken the Kaffa forces, the Tartars catapulted the cadavers that died of plague into the city to start an epidemic. An outbreak occurred soon after resulting in the Tatars defeating Kaffa (Christopher et al., 1997).

Smallpox was used as a biological weapon against Native Americans during the French and Indian War in the 18th century. The British forces in North America deliberately used smallpox to reduce the number of Native Americans that were “hostile to the British”. An outbreak at the British headquarters in Fort Pitt resulted in the opportunity for the British to use fomites in the form of blankets from hospitals to be given to the Native Americans. This modern day adaptation of the Trojan horse was followed by an epidemic of smallpox in the Native American community (Christopher et al., 1997).

19th Century Advances

In the 1800’s Augustinian monk Gregor Mendel discovered the concept of dominant and recessive genes using his cultivation of 29,000 plants that he grew in his experimental garden at the monastery. Mendel noticed that the plant’s traits did not blend together when cross-pollinated. He recognized that traits remained intact through generations carried by what he called “factors” which was later called genes. He was considered the “Father of Genetics” (O’Carroll, 2011).

In 1884, Robert Koch and Friedrich Loeffler developed Koch's postulates which were published in 1890. These postulates defined four criteria that established a causal relationship between a pathogen and the outbreak of a disease. Koch applied the postulates to establish the pathogenic origin of anthrax and tuberculosis and since then many other disease-causing organisms have been linked to illness using the criteria. Koch’s postulates along with the
development of modern microbiology in the 19th century provided the capability to isolate and culture pathogens (Racaniello, 2010).

19th to 20th Century

Over the past 100 years pathogens have been chosen and modified to be used as strategic and tactical weapons. Studies show that Germany had an established biological warfare program during World War I that involved covert operations with neutral trading partners of the Allies to infect livestock and contaminate animal feed to be exported to Allied troops (Christopher et al., 1997). Every major nation involved in World War II including the United States, Germany, Japan, Canada, France, and the former Soviet Union had a biological weapons program in place. During the Sino-Japanese War of 1937 Japan used Yersinia pestis (plague) to attack 11 different cities. It was reported that conservatively 700 Chinese died from the plague (“Committee on Research,” 2004). During World War II, Japan had a secret biological warfare program in a remote part of Japan where they perfected the culturing and dissemination of organisms. After the war much of the information from this lab ended up in Fort Detrick in Frederick, Maryland. It is still held in the National Archives in the U.S. (“Committee on Research,” 2004).

The U.S. also had a strong biological warfare program with its origins in World War II. The program began in 1942 and was housed at Fort Detrick in Maryland. The researchers at Detrick concentrated their work on the pathogens anthrax and botulism. The biological warfare work was carried out in four U.S. facilities from 1942 until 1969 when the U.S. decided to renounce its biological weapons program.

The largest biological weapons compound was established in the former Soviet Union. They had two programs in place for many years. One of which was a military controlled group begun in the 1920’s and the other a top secret program that was managed by civilians from 1972
until 1992 – long after the U.S. stopped its biological weapons’ program. The Soviet program was the most sophisticated biological weapons program in the world. In early 1990 there were approximately 60,000 people working in research, development and production. They stockpiled hundreds of tons of anthrax spores and tons of other pathogens that included the plague and smallpox (“Committee on Research,” 2004).

2001 to Present

2001 Anthrax Attacks. September 11th, 2001 will always be remembered as one of the worst days in American history. That morning the World Trade Center collapsed killing approximately 3,000 people while at the Pentagon in Washington D.C. 200 lives were lost. That same day an airliner went down in a field in Pennsylvania targeted for Washington, D.C. These three events shaped the thoughts and attitudes of a new generation about travel, personal safety, and the threat of terrorism.

Unbeknownst to anyone, seven days after the attacks of 9/11 another terrorist attack was underway. On September 18th, 2001, six anthrax filled letters were mailed via the U.S. Post Office causing hysteria and fear throughout the nation (Day, 2003). On September 27, 2001, a photo editor in the office of the tabloid newspaper The Sun became sick with a flu-like illness in Boca Raton, FL. On October 2nd he was admitted to the hospital where he died on October 5th of inhalation anthrax. Cases of cutaneous anthrax were reported among workers at the National Broadcasting Company, American Broadcasting Company, and Columbia Broadcasting Company and at Post Offices in New York City, N.Y. During this same time, more incidents of cutaneous and inhalation cases were reported from workers at a post office in Trenton, N.J. (Higgins et al., 2003).
On October 12th, 2001 the Federal Bureau of Investigation (FBI) announced that a letter contaminated with anthrax had been processed in a postal distribution facility in Hamilton, N.J. They knew that at least 4 contaminated letters had been processed at this facility exposing approximately 1100 workers. Two cases of inhalation anthrax and three cases of cutaneous anthrax were confirmed with another case of cutaneous anthrax suspected. By the third week in October, 70% of the residents in New Jersey were worried that they or someone in their family had been exposed to anthrax. Government agencies including the CDC, USDA, and the NJ Department of Health were overwhelmed with calls related to bioterrorism (Chess & Clarke 2007).

**2005 Paper: Dual Use of Concern and Reconstructed 1918 Influenza Virus.** In 1918 as World War I was drawing to a close, an influenza pandemic that began the year before was raging uncontrolled throughout the globe. The 1918 virus had tremendous morbidity and mortality, infecting approximately 500 million people worldwide and killing at least 50 million people, roughly 3% percent of the world’s population (Fauci & Collins 2012) (Figure 1). In 2005, two teams of researchers including the CDC and other scientists pieced together the genetic elements of the 1918 virus, reconstructing the deadly pathogen that caused the “Spanish Influenza” pandemic. To obtain the virus samples, researchers traveled to Alaska where most of the villagers had died 80+ years ago after the flu reached their village. The researchers obtained permission to collect lung samples from an Inuit woman who had died of Spanish flu in 1918 and whose body remained preserved after being buried in the frozen tundra (Figure 2).

The researchers’ goal was to study the extraordinary virulence of the virus. The researchers defended their work saying that the live virus provided information that could be used to counter future outbreaks of a similar pathogenic flu strain. They also felt that it would aid
FIGURE 2.1

HISTORIAL PHOTO OF THE 1918 SPANISH INFLUENZA WARD AT CAMP FUNSTON, KANSAS, SHOWING THE MANY PATIENTS ILL WITH THE FLU

A ward at Camp Funston, Kansas showing the many ill patients who caught the 1918 Spanish influenza. Photograph by an unknown U.S. Army photographer. (Camp Funston, 1918)

Permission: Public domain (before 1923) & U.S. Government
Photo credit/Source: U.S. Army via Wikimedia Commons
FIGURE 2.2
THE 1918 SPANISH FLU IN LABRADOR

Hebron, Labrador, ca. 1900 The Spanish influenza appeared at the Inuit village of Hebron in October 1918 after a supply ship arrived there from St. John’s with an infected crewmember on board. By 19 November, 86 of Hebron’s 100 residents had died from the influenza. A further 74 people died in surrounding communities, cutting the area’s population to 70 from 220. ("Hebron, labrador, ca. 1900," 1918)

Photo Credit/Source: Newfoundland and Labrador Heritage
Permission: Public domain (before 1923)
used to counter future outbreaks of a similar pathogenic flu strain. They also felt that it would aid in vaccine development efforts in order to protect the public against future pandemics. However, many worried that the research could be misused for malevolent purposes (Dual Use, 2012). The appalling statistics from the pandemic help explain the controversy caused by the virus reconstruction and publication of the results in *Science* magazine in 2005 (Dual Use, 2012).

The research team’s findings indicate that the 1918 virus was an avian strain that naturally mutated to become able to infect humans. This was an interesting finding because the strain of H5N1 influenza virus that is currently circulating is also an avian strain. To reconstruct the strain the researchers used reverse genetics. They took gene sequences of the RNA and inserted it into bacteria and then introduced these genes into cell culture to form the virus. In October 2005, the reconstructed 1918 influenza was declared a Select Agent and is strictly regulated in the lab and treated as a potential bioweapon by the CDC. It is also considered a dual use agent by the NIH, CDC, and NSABB (“1918 killer flu,” 2005).

The research on the 1918 influenza virus demonstrates the dilemma that can arise with conducting and the publication of dual use research. Many are worried the virus that killed 1 in 40 people 87 years ago will pose a threat to public health if it were accidently released from a lab or ended up in the hands of a bioterrorist organization (“1918 killer flu,” 2005).

**Publication of Controversial Research**

Since the 1990’s the debate about the possible control or censorship of dual-use research in life science research has mounted. The timeline for concern began with the terrorist attacks on September 11th, 2001 and the anthrax letters in the U.S. mail the following week. These events were followed by the 2001 report in the *Journal of Virology* about researchers that re-engineered a mousepox virus to sterilize the mouse population that unexpectedly produced a much more
virulent virus. In *Science* magazine in 2002, researchers reported that they had reconstructed the poliovirus from chemically synthesized oligonucleotides that were linked together and then transfected into cells. That same year in *Proceedings from the National Academy of Sciences*, researchers reported that their work on the immune response to a virulence gene from vaccinia (the vaccine strain for smallpox), included information on how to increase viral virulence. All of these experiments raised fears about their potential for bioterrorism (Dual Use, 2012).

The publication of the H5N1 papers in 2012 brought the dual use debate to the forefront. The discussion centered around several questions: Should the publication of research that could be used for malevolent purposes be restricted? If the research is restricted to what extent should it be restricted? How and who will restrict the publication? No consensus has been reached on these questions but the publishing of the H5N1 papers forced governments, funding agencies, scientists, and scientific journals to confront this issue after many years of controversial experiments being published in the public domain.
CHAPTER III

DUAL USE RESEARCH/DUAL USE RESEARCH OF CONCERN

History

The terrorist attacks of September 11, 2001 coupled with the subsequent anthrax attacks highlighted the dilemma that information gained from life sciences research can also be used for nefarious purposes that can threaten national security and public health. There has been increased demand for more oversight of life science research that may be subverted for malevolent purposes and the need for new biosecurity measures to minimize the risk posed by such research (NSABB, 2007).

Stricter regulation of dual use biological research began in earnest in 2003 when the U.S. National Academies recommended that the government and research community work together to identify research of concern as well as design and implement a system to evaluate such research before it was published (Malakoff, 2012). Mitigating the threat of dual use research has been the content of two National Academies reports and international forums including the InterAcademy Panel and the Biological Weapons and Toxins Convention (BWTC) (Wolinetz 2012.) In response to these groups, the U.S. Government in 2004 established the National Science Advisory Board for Biosecurity (NSABB) to provide advice, guidance, and leadership regarding the oversight of dual use life sciences research.

Regulatory Agencies and Oversight

The regulatory structure for life sciences research has evolved over the last five decades. Responsibility for regulation in the U.S. in the fields of biotechnology research in life sciences falls under the jurisdiction of several federal agencies: National Science Advisory Board for
Biosecurity (NSABB), National Research Council (NRC), National Institutes of Health (NIH), Food and Drug Administration (FDA), Environmental Protection Agency (EPA), Human Health Services, U.S. Department of Agriculture (USDA), and Department of Justice (DOJ) (“Committee on Research,” 2004).

**National Science Advisory Board for Biosecurity (NSABB)**

The NSABB is an oversight committee tasked with proposing a framework for the identification, review, conduct, and communication of life sciences research with dual use potential. Their role is to consider both the protection of national security and progressing life science research; however, it is not NSABB’s role to restrict science. The group strongly promotes the free and open exchange of information in the life sciences area. They believe the way to address dual use concerns are to raise awareness of the issues while strengthening the scientific culture within the research community by increasing understanding and responsibility. The NSABB believes in instituting new oversight measures in order to minimize the risk of misuse of research information. It also recommends strategies and develops tools to help researchers communicate results of research with dual use concerns (NSABB, 2007).

**National Research Council (NRC)**

The National Research Council (NRC) takes the role of improving government decision making and public policy. Their goal is to increase public understanding while educating and disseminating information in the fields of science, engineering, technology, and health. The council publishes independent expert reports in order to drive the U.S. policy process. Their objective is to improve people’s lives around the world. This group published the book, *Biotechnology Research - An Age of Terrorism in 2004*, the first report that dealt specifically with national security and the life sciences. In biosafety circles, this book is referred to as the

National Institutes of Health, Food and Drug Administration, and Environmental Protection Agency

The NIH is a regulatory body that sets standards and procedures for the research it funds for recombinant DNA. Recombinant DNA is research with DNA sequences that result from the use of laboratory methods (molecular cloning) to bring together genetic material from multiple sources, creating sequences that would not otherwise be found naturally in biological organisms.

Research involving human gene therapy falls under a special category under the NIH guidelines and the FDA. Both groups are required to review the research protocols before the initiation of the research. If recombinant material is going to be released to the environment for crop improvement or other environmental applications the Environment Protection Agency (EPA) is required to be involved (“NIH Guidelines,” 2011).

Human Health Services (HHS), U.S. Department of Agriculture (USDA), Department of Justice (DOJ) – Oversight of the Select Agent Program

Select agents and toxins are biological agents and toxins that have been determined to have the potential to pose a severe threat to public health and safety, to animal or plant health, or to animal or plant products. To advance scientific knowledge about biological agents and toxins while increasing knowledge about biological countermeasures, academic, commercial, and government institutions have been authorized by the U.S. government to carry out research with these agents (Besser, 2007).

Select agent oversight is a shared federal responsibility between Human Health Services (HHS), the U.S. Department of Agriculture (USDA), and the Department of Justice (DOJ).
Congress authorizes HHS to regulate the possession, use, and transfer of biological agents and toxins (select agents) that could pose a severe threat to public health and safety. The Secretary of HHS assigned this authority to the CDC. Congress gave the USDA the authority to regulate select agents that pose a severe threat to animal and plant health and/or animal and plant products. The DOJ is responsible for conducting background checks, called Security Risk Assessments (SRA), of individuals that have access to laboratories where select agent work is being conducted. The regulation of the possession, use, and transfer of select agents by the HHS, USDA, and DOJ strengthens the U. S. bioterrorism prevention strategy (Besser, 2007).

Legislation and Regulation

**Antiterrorism and Effective Death Penalty Act of 1996**

No program for oversight of select agents existed in the U.S. before 1996. Congress passed the Antiterrorism and Effective Death Penalty Act in 1996 following an incident where a person without a research need ordered plague strains from a supplier of biological agents. After the arrest, government officials realized they had no legal right to charge the individual with a crime other than mail fraud (“Backgrounder the select,” 2002).

The Act of 1996 authorized the Secretary of HHS to regulate the transfer of select agents harmful to humans. The HHS requested that CDC develop regulations that would manage select agents to protect the public without hindering scientific research. As a result of the Act, the CDC was designated the agency within HHS responsible for enforcing this regulation (“Backgrounder the select,” 2002). The regulations that went into effect on April 1997 (42 CFR 72.6), issued by the Secretary of HHS, established a list of biological select agents that have the potential to pose a severe threat to public health and safety.
United States PATRIOT Act

In 2001, Congress strengthened the select agent program by passing the Uniting and Strengthening America by Providing Appropriate Tools Required to Intercept and Obstruct Terrorism Act of 2001 (USA PATRIOT Act). This expanded the regulations by restricting the shipping, possession, and receipt of select agents. The USA Patriot Act establishes requirements for the appropriate use of select biological agents. It also identifies those persons who should be restricted from working with select agents, and imposes criminal and civil penalties for the inappropriate use of select agents ("Backgrounder the select," 2002).

Public Health Security and Bioterrorism Preparedness and Response Act of 2002

In 2002, Congress passed another act called the Public Health Security and Bioterrorism Preparedness and Response Act which significantly strengthened oversight of select agents. This act strengthened the regulatory authorities of HHS under the Antiterrorism and Effective Death Penalty Act of 1996 and granted similar regulatory authority to USDA for select agents that present a significant threat to animal or plant health, and/or animal or plant products. It also required coordination and agreement between HHS and USDA on program activities such as the development of regulations, reporting forms, and approval of changes to regulated laboratories’ registrations and the inspection process for select agents regulated by both agencies ("Backgrounder the select," 2002).

Over the years, the Bioterrorism Act has been augmented through a series of additional regulations. The HHS published an interim final rule—the “Possession, Use, and Transfer of Select Agents and Toxins” Interim Final Rule (42 CFR 73, 9 CFR 121, and 7 CFR 331) (effective on February 7, 2003)—which implemented the relevant provisions of the Bioterrorism Act. A later Final Rule became effective on April 18, 2005. On October 20, 2005, HHS
established an Interim Final Rule adding reconstructed replication competent forms of the 1918 pandemic influenza virus containing any portion of the coding regions of all eight gene segments to the HHS select agent list. These regulations are referred to as the “select agent regulations.” The regulations were recently updated and implemented on October 5, 2012 (“National select agent,” 2005).

**U.S. Policy for Oversight of Life Sciences Dual Use Research of Concern 2012**

Although numerous situations and governmental responses highlighted the issue of biosecurity relating to dual-use research of concern, NSABB recommended that manipulations of the H5N1 virus which had increased its transmissibility not be published. This action set off a bioethical debate over balancing global security, public health and the integrity of science.

In an attempt to draw the boundaries between science and society, the U.S. Government published in March 2012, the *U.S. Policy for Oversight of Life Sciences Dual Use Research of Concern*. This policy was designed “to establish regular review of United States Government funded or conducted research with certain high consequence pathogens and toxins for its potential dual use research of concern” (DURC) (“United States government,” 2012, p. 1). The policy identified 15 high risk pathogens and toxins and required funding agencies to identify all federally funded research involving these agents within 60 days. Within 90 days the agencies were required to report all instances of research involving the 15 agents that could be considered dual use. Furthermore, the funding agency, institution, and lead scientists of studies found to have dual use risks were charged with creating risk mitigation plans. This could include modification of methodology, moving research to more secure labs, and alteration of how the research is communicated to the public and scientific community (“United States government,” 2012).
Previously, research done at the NIH and the CDC was reviewed for possible dual use. The new policy would apply this same standard to all research carried out with NIH or CDC funding. These reviews are to be performed for all current studies as well as future studies. It also appears this will affect research funded by other government agencies such as the USDA and the DOD.

Under Purpose and Principle of the Dual Use Research of Concern policy, it states:

The United States Government will facilitate the sharing of the results and products of life sciences research conducted or funded by United States Government agencies, and honor United States Government obligations within relevant international frameworks and agreements, while taking into account United States’ national security interests.

(“United State government,” 2012, p. 1)

It also states:

In executing this Policy, the United States Government will abide by and enforce all relevant Presidential Directives and Executive Orders, all applicable laws and regulations, and support the implementation of legally binding treaties, commitments, and United Nations Security Council resolutions prohibiting the development and use of biological agents as weapons. (“United States government,” 2012, p. 1)

At a glance, this is good news for science because the current U.S. policy for sharing of the results and products of research related to national security is governed by a Presidential National Security Decision Directive issued in 1985 stating that fundamental research will remain unrestricted. However, as the policy is read further, the boundaries become less clear. The federal government according to the policy has the responsibility to consider “risk mitigation measures” including “determining the venue and mode of communication”
content, timing and the extent of distribution of the information) to communicate the research responsibly” (“United States government,” 2012 p. 3). If the measures are not adequate the government has the authority to “classify the research” (“United States government,” 2012 p. 3) or “not provide or terminate research funding” (“United States government,” 2012 p. 4). The potential that a project could be undertaken only to find at a later date that the research is classified at a level which restricts publication or terminates funding is not an atmosphere conducive to good science. These broad restrictions will discourage researchers from going into this field of work (Frankel, 2012).

This new policy changes the established approach of the research community deciding on what, how and when research is published. It regulates researchers within the U.S. but what will it mean for international research? The policy applies to U.S. scientists in collaborations with non-U.S. scientists making research a little more difficult for both sides due to the cloudy issue of oversight. The policy may also put the U.S. at a disadvantage for competing in cutting edge research. The policy does state the need to pursue “engagement with our international partners” (“United States government,” 2012 p. 1) but provides no details or how this will be accomplished. As demonstrated in the case of Ron Fouchier in the Netherlands, publication was held up because his country required an export license to release the technology used to make the mutations in the H5N1 influenza virus. They determined the research was “applied” rather than “basic” thus putting more restrictions on the research. If this becomes the norm in other countries it will considerably slow down research collaborations. Governments will need to start reconciling policy difference where policies currently exist. Governments including agencies like the WHO need to agree on a core set of principles that reflect global consensus on fostering international cooperation. They will have to work together on policies including those dealing
with the dissemination of dual use research to diminish the potential for misuse by bioterrorists (Frankel, 2012).
CHAPTER IV

IMPLICATIONS OF FEDERAL DUAL USE POLICY ON LIFE SCIENCES RESEARCH

The recent review of the H5N1 avian influenza papers by the NSABB demonstrates the challenge of making decisions about mitigating the risks of DURC while at the same time implementing a workable system that encourages collaboration across the worldwide research community. The discussion on whether or not to publish the papers lasted almost five months including an international summit of influenza experts and other researchers which failed to reach consensus in its final decision to recommend publication. This review process dealt with only two publications on two similar projects making the burden of review and risk mitigation applied to a broader body of research almost incomprehensible.

Questions have been raised since the H5N1 debate and the publication of the DURC policy.

- Who at the federal level will be responsible for conducting a review to identify all current or proposed research for DURC potential?
- What expertise is needed to conduct the review?
- While a timeline for reporting findings to the U.S. Government has been established, what is the timeline for reporting to the researcher and institution so they can move forward and develop a risk mitigation plan?
- How does the timing of the DURC review fit into all the other regulatory reviews and funding deadlines?
It is obvious there will need to be open communication lines and processes put into place or research will come to a halt.

How will disagreements over the risk mitigation plan or the identification of a research project as DURC be handled? The H5N1 case demonstrates the difficulty of obtaining consensus among experts. Determining what is an acceptable and unacceptable risk is very subjective and is based on background, experience, and education, which can hold up the process. The policy does not mention an appeals process for the researcher or provide contact names of research agencies.

The elements of the risk mitigation plan are not well defined, simply stating that there will be an ongoing review at the institutional level. It provides no guidance as to who at the institution should be given the task of ongoing reviews. Will this task be given to the Institutional Biosafety Committee (IBC) that currently reviews recombinant DNA on campuses nationwide? If so, what additional resources will be available to support these new responsibilities? To whom will the IBC report their findings? Will the IBC develop a reporting relationship with the NSABB as they currently do with the NIH for recombinant DNA research? Will a local DURC policy with guidelines be published to aid institutions in implementing this policy?

Research universities are under increasing federal compliance demands. Discouraging researchers or institutions from federally funded research with select agents or delaying research with additional layers of review can only hurt national security and public health outcomes. This was never the intent or purpose of the DURC policy (Wolinetz, 2012).

What dual-use life sciences research will look like in the U.S. and how and when it will be disseminated is open for discussion with the need for a more defined oversight plan. The DURC policy in its current form has not enhanced nor restricted responsible science but rather
provided an opportunity for discussion as we communicate with other nations to resolve this very complex issue (Frankel, 2012).
CHAPTER V
CONCLUSIONS & RECOMMENDATIONS

Conclusions

It is important to note that the dual use policy does not fully address dual use in life science research. The DURC policy is limited to experiments involving the 15 of the 80 agents already regulated by the select agent program. This raises the question as to whether the DURC is a redundant federal policy. Select agents are already strictly regulated by the CDC requiring background checks on all staff allowed entry into a lab. It also requires the facility to be licensed to work with the agents. To make the select agent program stronger from an internal threat, the regulations were recently changed to include a personal reliability program including criminal background checks.

It is interesting that many case studies of DURC that have been documented by NSABB as evidence for the need for more oversight would not be covered by this policy. For example, the de novo synthesis of polio virus and the Australian mousepox experiment would not have been regulated by this policy. The majority of biological scientists are surprisingly unaware of dual use research and the role of the NSABB.

It is also thought-provoking that the NSABB webpage describes experiments that are considered dual use while the agent used in the experiment is not listed in the DURC policy. An example from the webpage is listed below.

Ann, a post-doctoral fellow, is working with Peter, a senior researcher, on a study of antimicrobial resistance in gram-positive pathogenic bacteria. Ann is studying recently isolated strains of *Streptococcus pneumoniae* that have developed antibiotic resistance
and cause significantly increased pneumonia morbidity and mortality. She has identified a gene that she believes is responsible for the resistance, one that encodes part of a membrane-bound pump that removes materials from bacterial cells. With that gene, she has created a variant with increased capacity and heightened resistance. (“Dual Use Research,” 2012, p. 42)

Although this research has public health benefits, it could also be used for malevolent purposes.

After reading the DURC policy, it is clear that the policy limits the scope of listed agents to prevent over identification of legitimate research that does not pose much of a risk to limit the associated burden of review that would be required for institutions. However, the redundancy with the select agent program and its clear failure to capture experiments that are commonly agreed to be DURC raises the question if it addresses the DURC issue in life science research at all.

The recent review and re-review of the H5N1 avian influenza publications by the NSABB demonstrates the difficulty in making decisions about how to mitigate the risks of DURC even as it supports the need for a workable system to address the real risks associated with some biological research. The decision making process for the H5N1 experiments took five months and an international summit of experts to come to a conclusion. It asks the question: is the DURC policy feasible or is it going to hinder research results? If other countries don’t put the same type research review system in place, then they may move ahead in the research arena.

The delicate balance of regulating public safety and continued support of scientific research will rely heavily on consistency between U.S. and foreign policies regarding DURC. Without international cross-talk and uniformity, it is conceivable that DURC policies will serve to drive U.S. researchers to conduct research outside of the U.S. and to handicap researchers who
continue to work within the U.S. The outcome of either of these scenarios is that the important work being done by U.S. scientists to prevent disease and design better vaccines and therapeutics for some of the most nefarious pathogens will be minimized.

Ongoing research in countries such as the Soviet Union makes one wonder what happened to the tons of anthrax spores and plague that were manufactured for years in their bioweapons program. If world oversight of DURC is not established, what research results will be published from these countries that manufactured many of the 15 agents on the DURC list? While there is much controversy and many unanswered questions about the federal dual use policy, institutions will be required to move forward at a local level to implement a dual use policy for their institution and research community.

**Recommendations**

The U.S. Government Policy for Institutional Oversight of Life Science Dual Use Research of Concern was officially proposed for local oversight on February 21, 2013. This first stage of implementation will require the development of a formal local policy and process in compliance with the new regulation, occurring at a local IBC level. The formal local policy and process will establish a program for education, training, review, and decision-making involving a Dual Use Research Review Committee (DURRC) and related institutional input.

To implement dual use at a local level, the second stage must involve education and training programs for all persons involved in scientific research and scientific policy within an institution. Mandatory training should begin with the IBC and move outward into the research community to include research faculty, staff, and students. The Biological Safety Officer should lead the effort on implementing the training and enforcing compliance. Regulations change periodically, so the training must be reviewed and updated at least annually or when changes
occur, and researchers must be required to be current in their training. If a select agent were involved in the research, the NSABB should be consulted for advice before moving forward with the research.

The NSABB stated:

Researchers are the most critical element in the oversight of dual use life sciences research. They know the work best and are in the best position to anticipate the types of knowledge, products, or technologies that might be generated, the potential for misuse, and the degree of immediacy of that threat (“NSABB,” 2007 p. 18).

As a result, institutions need to establish processes to allow researchers to evaluate and monitor their research programs for DURC. The guidelines and review processes at an institutional level should be designed with input from research personnel with the IBC taking the lead. These guidelines should be designed to encourage collaborations and not restrict the publication of results.

To minimize research delays, as part of submitting a grant, researchers should be required to screen their proposed research using a set of questions that will identify potential issues related to DURC. The eight questions below should apply to research grants. Does the proposed research:

1. Enhance the harmful consequences of a biological agent or toxin?
2. Disrupt immunity or effectiveness of an immunization without clinical and/or agricultural justification?
3. Confer to a biological agent or toxin resistance to clinically and/or agriculturally useful prophylactic or therapeutic interventions against agent or toxin?
4. Facilitate their ability to evade detection methodologies?
5. Increase the stability, transmissibility, or the ability to disseminate a biological agent or toxin?

6. Alter the host range or tropism of a biological agent or toxin?

7. Enhance the susceptibility of a host population?

8. Generate a novel pathogenic agent or toxin, or reconstitute an eradicated or extinct biological agent?

Providing the tools upfront that researchers need to evaluate research is a big step towards finding a balance between the research and regulations. For instance, a mitigation plan template should be developed at each institution which will aid researchers in complying with regulations once dual use research has been identified. The research should be reviewed by the IBC to determine if it is dual use in nature. If a mitigation plan needs to be implemented, the IBC must approve the plan before research begins. Aiding researchers up-front will protect the institution while not making them feel over-regulated and overburdened in continuing their work.

Transparency in research projects builds trust in the non-scientific community. Many scientists already feel over regulated by funding agencies and other state and local regulations. If the researchers’ work is classified as dual use by the IBC, the researchers will be burdened with extra layers of regulation including developing a mitigation plan. Under the stress of this additional burden, researchers may believe that the institution is thwarting their research and may inhibit them from being transparent. It is crucial that the IBC receive endorsement from institution leaders so that the burden of enforcement does not lie solely on the IBC. Researchers must realize that the IBC is protecting their research because non-compliance with the new policy may endanger federal funding for researchers as well as the entire institution.
The intent of dual use research oversight is not to hinder research but to foster a responsible, safe, and open research environment. It is researchers’ responsibility to inform the scientific community, public, and policy makers of the potential dangers of their work while helping the same groups realize the risks and lost opportunities associated with restricting the flow of scientific information.

The role of the IBC in this process is to facilitate communication with the federal government while simplifying the process for the researchers. The communication of the IBC with the researchers and the federal government will aid in transparency of research results that will benefit the institution. It will take everyone’s cooperation to implement this new policy and to streamline the process so it does not inhibit research at the laboratory level.
REFERENCES


Section I: Purpose and Principles
1) The purpose of this Policy is to establish regular review of United States Government funded or conducted research with certain high-consequence pathogens and toxins for its potential to be dual use research of concern (DURC) in order to: (a) mitigate risks where appropriate; and (b) collect information needed to inform the development of an updated policy, as needed, for the oversight of DURC. The fundamental aim of this oversight is to preserve the benefits of life sciences research while minimizing the risk of misuse of the knowledge, information, products, or technologies provided by such research.

2) This Policy complements existing United States Government regulations and policies governing the possession and handling of pathogens and toxins. Currently, the Select Agent Regulations ensure appropriate oversight of biosafety and biosecurity of the possession and handling of pathogens and toxins that have the potential to pose a severe threat to human, animal, or plant health, or to animal and plant products. In addition, recommendations from Federal advisory bodies such as the National Science Advisory Board for Biosecurity (NSABB) have helped inform United States Government policies for identifying and managing DURC. This Policy will be updated, as needed, following domestic dialogue, engagement with our international partners, and input from interested communities including scientists, national security officials, and global health specialists.

3) The following principles guide implementation of this Policy:
   a) Life sciences research is essential to the scientific advances that underpin improvements in the health and safety of the public, agricultural crops and other plants, animals, the environment, materiel, and national security. Despite its value and benefits, some research may provide knowledge, information, products, or technologies that could be misused for harmful purposes.

   b) Accordingly, some degree of Federal and institutional oversight of DURC is critical to reducing the risks to public health and safety, agricultural crops and other plants, animals, the environment, materiel, and national security.

   c) Measures that mitigate the risks of DURC should be applied, where appropriate, in a manner that minimizes, to the extent possible, adverse impact on legitimate research, is commensurate with the risk, includes flexible approaches that leverage existing processes, and endeavors to preserve and foster the benefits of research.

   d) The United States Government will facilitate the sharing of the results and products of life sciences research conducted or funded by United States Government agencies, and honor United States Government obligations within relevant international frameworks and agreements, while taking into account United States’ national security interests.

   e) In executing this Policy, the United States Government will abide by and enforce all relevant Presidential Directives and Executive Orders, all applicable laws and regulations, and support the
implementation of legally binding treaties, commitments, and United Nations Security Council resolutions prohibiting the development and use of biological agents as weapons.

**Section II: Definitions**

1) For the purpose of this Policy, DURC is life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.

2) “Life sciences” pertains to living organisms (e.g., microbes, human beings, animals, and plants) and their products, including all disciplines and methodologies of biology such as aerobiology, agricultural science, plant science, animal science, bioinformatics, genomics, proteomics, synthetic biology, environmental science, public health, modeling, engineering of living systems, and all applications of the biological sciences. The term is meant to encompass the diverse approaches for understanding life at the level of ecosystems, organisms, organs, tissues, cells, and molecules.

3) Extramural research is that which is funded by a department or agency under a grant, contract, cooperative agreement, or other agreement and not conducted directly by the department or agency.

4) Intramural research is that which is directly conducted by a department or agency.

**Section III: Scope**

Under this Policy, review will focus on research that involves one or more of the agents or toxins listed in Section (III.1) below, which pose the greatest risk of deliberate misuse with most significant potential for mass casualties or devastating effects to the economy, critical infrastructure, or public confidence, and produces, aims to produce, or is reasonably anticipated to produce one or more of the effects listed in Section (III.2) below:

1) Agents and toxins2:
   a) Avian influenza virus (highly pathogenic)
   b) *Bacillus anthracis*
   c) Botulinum neurotoxin
   d) *Burkholderia mallei*
   e) *Burkholderia pseudomallei*
   f) Ebola virus
   g) Foot-and-mouth disease virus
   h) *Francisella tularensis*
   i) Marburg virus
   j) Reconstructed 1918 Influenza virus
   k) Rinderpest virus
   l) Toxin-producing strains of *Clostridium botulinum*
   m) Variola major virus
   n) Variola minor virus
   o) *Yersinia pestis*

2) Categories of experiments:
   a) Enhances the harmful consequences of the agent or toxin;
b) Disrupts immunity or the effectiveness of an immunization against the agent or toxin without clinical or agricultural justification;

c) Confers to the agent or toxin resistance to clinically or agriculturally useful prophylactic or therapeutic interventions against that agent or toxin or facilitates their ability to evade detection methodologies;

d) Increases the stability, transmissibility, or the ability to disseminate the agent or toxin;

e) Alters the host range or tropism of the agent or toxin;

f) Enhances the susceptibility of a host population to the agent or toxin; or

g) Generates or reconstitutes an eradicated or extinct agent or toxin listed in Section (III.1) above

Section IV: Department and Agency Responsibilities

1) Federal departments and agencies that conduct or fund life sciences research should implement the following actions:

a) Conduct a review to identify all current or proposed, unclassified intramural or extramural, life sciences research projects that fall within the scope of Section III. This review will include, at a minimum, initial proposals and any progress reports.

b) Determine which, if any, of the projects identified in Section (IV.1.a) meet the definition of DURC in Section (II.1) of this document.

c) Assess the risks and benefits of such projects, including how research methodologies may generate risks and/or whether open access to the knowledge, information, products, or technologies generates risk.

d) Based on the risk assessment, in collaboration with the institution or researcher, develop a risk mitigation plan to apply any necessary and appropriate risk mitigation measures.

In addition:

i) For DURC that is proposed and not yet funded, departments and agencies will assess whether to incorporate risk mitigation measures in the grant, contract, or agreement.

ii) For currently funded DURC, funding departments and agencies will consider modifying the grant, contract, or agreement to incorporate risk mitigation measures. If such modifications are not possible or desirable, departments and agencies will seek voluntary implementation of mitigation measures by the institution.

e) A risk mitigation plan may include, but not be limited to, the following risk mitigation measures:

i) Modifying the design or conduct of the research.

ii) Applying specific or enhanced biosecurity or biosafety measures.

iii) Evaluating existing evidence of medical countermeasures (MCM) efficacy, or conducting experiments to determine MCM efficacy against agents or toxins resulting from DURC, and where effective MCM exist, including that information in publications.

iv) Referring the institution to available DURC educational tools such as:

http://oba.od.nih.gov/biosecurity/biosecurity.html

v) Regularly reviewing, at the institutional level, emerging research findings for additional DURC.

vi) Requesting that institutions notify funding departments or agencies if additional DURC is identified, and propose modifications to the risk mitigation plan, as needed.

vii) Determining the venue and mode of communication (addressing content, timing, and possibly the extent of distribution of the information) to communicate the research responsibly.

viii) Reviewing annual progress reports from Principal Investigators to determine if DURC results have been generated, and if so, flagging them for institutional attention and applying potential mitigation measures as described above, as necessary.

ix) If the risks posed by the research cannot be adequately mitigated with the measures above, Federal departments and agencies will determine whether it is appropriate to:

(a) Request voluntary redaction of the research publications or communications 3;
(b) Classify the research:
(i) In accordance with National Security Decision Directive/NSDD-189, departments and agencies will make classification determinations within
(ii) Departments and agencies may consider whether to refer classified research to another department or agency for funding.
(c) Not provide or terminate research funding.

2. Federal departments and agencies are requested to report the following to the Assistant to the President for Homeland Security and Counterterrorism: a) Within 60 days of issuance of this Policy, the following results of the review conducted in response to Section (IV.1.a): i) Aggregate number of current and proposed unclassified, intramural, and extramural research projects identified that include work with one or more of the agents and toxins in Section (III.1).
   ii) Aggregate number of current and proposed unclassified, intramural, and extramural research projects that include work with one or more of the agents and toxins in Section (III.1) and produces, aims to produce, or are reasonably anticipated to produce one or more of the effects listed in Section (III.2).

b) Within 90 days of issuance of this Policy, the following results of the review conducted in response to Sections (IV.1. b. c. and d): i) Number of unclassified current and proposed DURC projects.4
   ii) Number of current projects identified as DURC through initial proposals versus progress reports. 5
   iii) Summary of risks, mitigation measures already in place that address those risks, any additional mitigation measures that have been proposed or implemented, and number of projects to which each mitigation measure would be applied.

3) Following completion of the reporting requirements in Section (IV.2), Federal departments and agencies are requested to submit periodic reports on items in Section (IV.2.a. and b) biannually.
4) Federal departments and agencies should implement Section IV in accordance with their relevant and applicable authorities, regulations, and statutes.
5) For additional guidance on how to conduct the risk assessment identified in Section (IV. 1.c), departments and agencies may refer to the “Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information,” which identifies useful assessment tools and is available at: http://oba.od.nih.gov/biosecurity/biosecurity_documents.html.

Section V: Consultation
As necessary and appropriate, the United States Government will continue to consult with the NSABB (in compliance with provisions of the Federal Advisory Committee Act) or convene the Countering Biological Threats Interagency Policy Committee for guidance on matters relating to the review and conduct of DURC and the mitigation of DURC risks. (“United States government, 2012”)