Trends in United States Biological Materials Oversight and Institutional Biosafety Committees

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Abstract: *Biological materials oversight in life sciences research in the United States is a challenging endeavor for institutions and the scientific, regulatory compliance, and federal communities. In order to assess biological materials oversight at Institutional Biosafety Committees (IBCs) registered with the United States National Institutes of Health, Office of Biotechnology Activities (NIH-OBA), a survey was sent to institutions obtained through a Freedom of Information Act request in early 2013. This research article will highlight the findings from the survey and literature review of current industry requirements, and highlight best practices and trends from survey data for trends in research administration.*

The goals of this research were to understand the scope of biological materials regulatory oversight in the United States, review results from a cross-sectional survey of Institutional Biosafety Committees conducted in 2013, and discuss trends for research administration compliance and best practices.

Keywords: *biosafety, research compliance, research administration, Institutional Biosafety Committee, biological safety, NIH Guidelines, recombinant DNA, synthetic DNA, biological materials, human gene transfer, gene therapy, animal research, life sciences research*

Introduction

Since 1975 when the Asilomar Conference convened over recombinant DNA technology and led to the creation of the National Institutes of Health (NIH) Guidelines for Research Involving Recombinant DNA Molecules (recently changed to Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules), advances in biotechnology and recombinant DNA (rDNA) have necessitated oversight and safety reviews of life sciences research with biological materials through Institutional Biosafety Committee (IBC) oversight in the United States (Berg, Baltimore et al. 1975, Jackson October 1972). Over time from the Guidelines initial implementation, it has become accepted by the scientific and biosafety communities that additional monitoring of non-rDNA biohazards by IBCs should occur (Talbot, King et al. 1981, Dutton and Hochheimer 1982, O'Reilly, Shipp et al. 2012).

In contrast to the detailed NIH requirements for oversight of federally funded research that involves human subjects, animals, and even recombinant DNA, no uniform standard exists for oversight over additional forms of biological materials used in research as there are for animals, radioactive materials, or human subjects. Since the current regulatory environment does not prescribe a one-size-fits-all solution for the regulation of all biohazards, each institution must craft its own mechanism knowing that there are layers of biohazard oversight beyond those prescribed in the regulatory environment (Harris, 2005). This flexibility presents institutions with a myriad of options and little guidance on how to oversee biohazards beyond those prescribed in the NIH Guidelines.

This research hypothesizes United States life sciences regulation for research involving biological materials fails to provide adequate biosafety and biosecurity oversight, and IBCs charged to oversee research with biological materials require additional regulatory guidance in order to protect people, product, and the environment. The expected outcomes will highlight regulatory limitations and statute gaps with biohazards in research, propose policy changes, and provide the regulated community current IBC practices and example methodologies for Institutional Biosafety Committees and institutions to adopt to enhance biosecurity and compliance with biological materials.

History of Recombinant DNA Technology and Oversight

Recombinant DNA (rDNA) technology is a relatively recent phenomenon. During a 1968 Senate Subcommittee hearing on a Joint Resolution to establish a new health science commission, Dr. Arthur Kornberg directed the subcommittee's attention toward the rapidly progressing field of molecular biology (Vettel, 1968). Dr. Kornberg noted important developments were near fruition and that the potential social impact of these advances could be far-reaching (Vettel, 2006). Dr. Kornberg was referring to discoveries which would provide the technical framework for the specialty commonly known as genetic engineering (Vettel, 1968). New techniques developing in this field would enable a researcher to recombine DNA, the hereditary material of the cell, in a very precise manner (Vettel, 1968). The rDNA introduced could provide a cell with the ability to manufacture products (for example, insulin) which were previously not part of the cell's make-up (Johnson, 2011).

In 1973, a group of scientists attended the Gordon Conference Session chaired by Drs. Maxine Singer and Dieter Sol to discuss the possibility of public health risks associated with genetic engineering (Singer and Soll, 1973). The concern was based upon the conjecture that the new techniques could accidently produce a recombinant molecule with hazardous characteristics (Hellman, 1973). It was speculated that an inadvertent modification of DNA in a previously harmless organism might enhance the organism's capability of producing a highly infectious disease (Singer and Soll, 1973). After extensive deliberation, the session's participants voted in favor of sending a letter to the National Academy of Sciences (NAS) suggesting that the academy consider the risks associated with genetic engineering and "recommend specific actions or guidelines" (Berg, Baltimore et al., 1974). In response to the Gordon Conference

letter, NAS appointed a panel of experts to study the risk question (Johnson). The risk question was to be addressed at a conference near Asilomar State Beach in California (Paul Berg, 1975).

Asilomar Conference

Prior to the Asilomar Conference in February, 1975, a call was issued by leading basic research scientists for a voluntary moratorium on life sciences research using rDNA technology in July, 1974 (Berg and Singer, 1995). For the moratorium, scientists agreed new rDNA technology created the potential for novel approaches in medicine, agriculture and industry, but also could result in unforeseen and damaging effects to human health and the environment. The moratorium would only be lifted after a conference was held to evaluate and regulate the risks associated with rDNA technology (Berg, Baltimore et al. 1974).

The conference, held at the Asilomar Conference Center in Monterey, California included scientists, lawyers, media, and U.S. government representatives. The primary goal of the meeting was whether to lift the moratorium, and if so, under which prescribed conditions rDNA research could be conducted in a safe and prudent manner. While little data beyond Berg's experiment existed at the time, despite opposition, the Conference ended with the understanding rDNA research should proceed but under strict guidelines (Berg, Baltimore et al., 1975). Such guidelines were collected and drafted into the 1976 Federal Register as the NIH Guidelines for Research Involving Recombinant DNA Molecules (NIH Guidelines, 1976), and were revised multiple times immediately after and in the subsequent years, most recently in March 2013, with a slight modification of the title to become the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acids (National Institutes of Health, 2013). The rationale for prompt action by scientists and the government from 1973 to 1976 was to protect laboratory personnel, the general public, and the environment from unintended or intended harm rDNA research with replicating organisms could potentially cause (Berg and Singer, 1995). In order to facilitate local protection with rDNA, the concept of the Institutional Biosafety Committee (IBC) was formed as a requirement for local review of biological materials for institutions upon receipt of federal funding in the NIH Guidelines. This Committee was and is today a community represented group of scientific peers with oversight at each individual entity, on research with rDNA molecules at each institution (National Institutes of Health 2013).

Definition and Applications of Recombinant DNA Technology

An overview of rDNA and rDNA technology is provided followed by background on the evolution of the IBC. The NIH Guidelines define rDNA as "molecules that are constructed outside living cells by joining natural or synthetic DNA segments to DNA molecules that can replicate in a living cell, or molecules that result from the replication of those described above" (National Institutes of Health, 2013). Recently, changes to the NIH Guidelines now specify rDNA to also include synthetic nucleic acid research, due to advances in synthetic biology, and for the purposes of this document, research involving recombinant and synthetic nucleic acids will be referred to as rsNA (National Institutes of Health, 2013).

Recombinant and synthetic nucleic acids as a technology can be used because all organisms share the same chemical structure, with the only difference being the actual sequence of nucleotides (Lodish, 2000). Thus, when DNA from a foreign source is introduced into host sequences that can drive DNA replication and introduced into a host organism, the foreign DNA is replicated along with the host DNA (Brown, 2010). Consequently, the biological functions, and therefore applications and uses of rsNA are theoretically nearly limitless (Brown, 2010).

The most common application of rsNA is in basic life sciences research, where it is important to most current work in the biological and biomedical sciences (Brown, 2010). Recombinant DNA is used to identify, map and sequence genes, and to determine their function (Boyle, 2008). Recombinant DNA probes are employed in analyzing gene expression within individual cells, and throughout the tissues of whole organisms (Boyle, 2008). Recombinant proteins are widely used as reagents in laboratory experiments and to generate antibody probes for examining protein synthesis within cells and organisms (Alberts, 2008). While promising, rsNA is not without potential risk when manipulating the components of genetic heredity (Werkmeister and Ramshaw, 2012).

Risks of Recombinant DNA and Biological Materials

The history and use of recombinant DNA in biological organisms has a history of controversy, and no one understood the controversy more than Dr. Donald Frederickson. (Frederickson, 2000). Dr. Frederickson was the Director of the NIH in the mid-1970's and oversaw the rDNA technology controversy from start to finish with the issuance of the NIH Guidelines. While the possibilities and potential of rDNA seemed endless, researchers involved in rDNA experiments feared that they might produce unpredictable occupational and environmental hazards. For example, one risk was by increasing the virulence of viruses or the resistance of bacteria to treatment with antibiotics. The fear that gene splicing could produce epidemic pathogens was heightened by the fact that biologists were using microorganisms in their recombinant DNA research that have human hosts, most notably the bacterium E. coli.

The task to develop the principles formulated at Asilomar into a detailed set of technical guidelines on containment facilities and safety procedures in rDNA research fell to Dr. Frederickson (Frederickson). As the Director of the main funding agency for rDNA research, and the leading biomedical research facility in the country, NIH and Dr. Frederickson had both the institutional resources and the scientific authority to set laboratory standards in the United States, and by extension, for the rest of the research world.

Some scientists, including biochemist Erwin Chargaff, warned against regulation by NIH (Chargaff, 1977). In his eyes, it was an irreconcilable conflict of interest and an encroachment on the freedom of scientific inquiry for the agency that funded most rDNA research to also be the agency that regulated such research (Chargaff and Simring, 1976, Davis, Chargaff et al., 1977). Other scientists, including Nobel laureates James D. Watson, David Baltimore, and Stanley N. Cohen, called upon NIH in Science to devise guidelines for the containment of rDNA molecules so that researchers around the country could adhere to a common, predictable standard in conducting their experiments (Berg, Baltimore et al. 1974).

The controversy soon involved local citizens, public organizations, and politicians. In the summer of 1977, the city council of Cambridge, Massachusetts, held contentious hearings on rDNA research conducted at the city's universities, (Culliton 1976, 1977). It created the Cambridge Biohazards Committee to conduct site visits and review containment measures for all proposed experiments, in the name of protecting residents from potential health risks (1976, 1977). Similar measures were urged by Science for the People, an organization of community health activists in Ann Arbor, Michigan, home of the University of Michigan (SSG 1977). The environmental organization Friends of the Earth brought suit demanding that rDNA research proceed only after NIH issued a comprehensive Environmental Impact Statement, a time-consuming and complex task (Frederickson 1982). Other critics opposed rDNA research on ethical grounds, arguing that it amounted to an attempt to upset the order of nature by manipulating DNA, the code of life (Frederickson).

Congress was as divided over the issue of regulating rDNA research as well as American society at large, with some members favoring strong legislation and penalties, while others trusted scientists to regulate their own work, or deferred to local jurisdiction. As a result of these divisions, no law was enacted (Teichmann 1983).

In addition to the biological concerns, secondly, Fredrickson was convinced that no new regulatory machinery, other than RAC, was needed to supervise rDNA research (Frederickson). Scientists, he was convinced, were familiar with and supportive of centralized decision-making by panels of NIH experts. Third, he concluded that in order to gain public support for genetic research and avoid charges of secrecy, RAC deliberations were to be open to the public and their transcripts to be published in Recombinant DNA Research, a multi-volume compilation of correspondence, legislative bills, drafts, and media accounts of the rDNA controversy. Fourth, Fredrickson prevailed upon President Gerald Ford to establish a Federal Interagency Committee on Recombinant DNA Research, with the goal of replacing the uncoordinated approaches of various departments that sponsored rDNA research with a single set of guidelines. Fifth, judging that it was most urgent to allow rDNA research to proceed, Fredrickson decided to issue the guidelines before completion of an Environmental Impact Statement (Frederickson 1982).

The NIH Guidelines were released by Fredrickson on June 23, 1976, an event that made for front-page news, followed in October 1977 by a draft Environmental Impact Statement (Frederickson). Canada and several western European nations agreed to adhere to the guidelines as well (Zilinskas and Zimmerman 1986). Using their regulatory powers, the Food and Drug Administration and other federal agencies compelled the small number of private laboratories then using rDNA technology to abide by the NIH guidelines (Zilinskas and Zimmerman 1986).

A revised set of Guidelines took effect on January 1979, in particular easing containment requirements for rDNA experiments with E. coli after no such experiments had produced harmful side-effects (National Institutes of Health 2013). The revised Guidelines also laid out procedures for ongoing revision, and shifted responsibility for interpretation and enforcement to researchers' home institutions.

The NIH Guidelines remain in force today, and the most controversial research continues to be reviewed by the RAC. No new epidemic pathogen has been inadvertently produced in the course of three decades of rDNA research (National Institutes of Health 2013). The struggle of the participants in the rDNA controversy to find a compromise that would at once preserve scientific freedom, the public's health, and ethical values lays the groundwork to understand the oversight in place today (Frederickson). Genetic manipulation with recombinant and synthetic nucleic acids remain at the center of today's debate over stem cell research, genetic cloning, and genetically modified foods, with the Institutional Biosafety Committee center in the middle of the discussion.

The Role of the Institutional Biosafety Committee and Risk Assessment

The NIH, Office of Biotechnology Activities (OBA) oversees the implementation of the NIH Guidelines through registration, annual updates, and periodic on-site audits of local IBCs (National Institutes of Health 2013). The role of the IBC is to ensure adequate containment of potentially hazardous biological agents; add a level of expert review and monitoring of potentially hazardous experiments; to inform the public about experimental plans that have a potential to be hazardous; and to provide a means of communication among researchers and healthcare provides about potentially hazardous protocols (NIH-OBA 2010).

The fundamental core of IBC review is the concept of a risk assessment of work with biological materials, highlighted in Section IV-B-2-b of the NIH Guidelines (National Institutes of Health 2013). The risk assessment is initiated by a Principal Investigator conducting the research and subsequently reviewed, modified, and subsequently accepted or rejected by the entity's local IBC. The International Biological Threat Reduction Program of Sandia National Laboratories elaborates the biological risk assessment should clearly define the biological risk being assessed and mitigated (Caskey, 2010). Assessment and mitigation methods are a combination of engineering controls, procedure and administrative controls, and the use of personal protective equipment (Caskey, 2010). The NIH Guidelines directly reference the CDC biosafety resource and guidance document, the BMBL 5th edition, in elaborating on the concept of risk assessment (DHHS, 2009) (National Institutes of Health, 2013). The CDC BMBL defines risk assessment as the process used to "identify the hazardous characteristics of a known infectious or potentially infectious agent or material, the activities that can result in exposure to an agent, the likelihood that such exposure will cause a laboratory acquired infection, and the probable consequences of such an infection" (U.S. Department of Health and Human Services, 2009).

The NIH Guidelines outline the risk assessment must take into consideration "virulence, pathogenicity, infectious dose, environmental stability, route of spread, communicability, operations, quantity, availability of vaccine or treatment, and gene product effects such as toxicity, physiological activity, and allergenicity" (National Institutes of Health, 2013). Additional factors such as advances in synthetic biology and genetics may introduce new variables to the assessment of the Risk Group, characteristics, and proposed containment (National Institutes of Health, 2013).

The Institutional Biosafety Committee system and process is not without public criticism. A study by Race and Hammond, highlighted "serious ongoing problems with IBCs' adherence to NIH Guidelines" and called for the abolition of the voluntary governance framework the Institutional Biosafety Committee uses. Race and Hammond argue the current system requires improvement or replacement, citing a survey of institutional practices (Race and Hammond, 2008).

In terms of age as a compliance committee, the non-profit organization, Public Responsibility in Medicine and Research recognizes the three "I"s in research: the Institutional Review Board, or IRB, the Institutional Animal Care and Use Committee, or IACUC, and the IBC (PRIMR, 2010). As far as entity funding and support, PRIM&R recognizes IBCs lacks the support and resources that are in place for IRBs and to some extent IACUCs around the country. The NIH-OBA office through on-site audits and outreach has assisted in bringing awareness of the IBC up to level of awareness by the institution to the IRB and IACUC (Shipp and Patterson, 2003).

To date, surveys by Hackney, et al and others have raised awareness on the current review structure and capabilities of IBCs (Hackney, 2011). The qualitative data obtained from several surveys provides insight into the selected aspects of IBC burdens, including staffing and review process of biological materials, and training.

The Hackney, et al surveys found improvements in IBC management, staffing, and compliance observed over the course of the surveys. For example, Hackney reports that NIH OBA has, since 2001, increased efforts to offer educational conferences and courses for IBC members and those responsible for IBC oversight (Raymond W. Hackney 2011). Because of these efforts, the research compliance workforce is likely to be slightly more educated on the Guidelines than in the past. Second, the NIH OBA established the site visit program, which allows for an in-depth review of the rDNA research oversight structure and practice for an institution. The program review can also reveal a need for additional staff in order to fulfill the IBC responsibilities. Of those respondents to the 2010 survey, 22% of those who reported that they had a site visit at their institution indicated that they had increased funding or staffing as a result of the site visit (Hackney, 2011). Unfortunately, the number of institutions having been through an NIH-OBA site is estimated to be a small percentage from the actual list of registered IBCs with NIH-OBA. Finally, incidents in the news and public scrutiny drew attention to weaknesses in IBC compliance with the Guidelines (Cook-Deegan, Berkelman et al. 2005, Field 2005).

However, the prior surveys by Hackney et al lacks quantitative data on the increasing registration and policy burdens of IBCs over time, as well as on the number of protocol reviews, administrative, resources, and financial support. Other research by Dolgitser on Dual Use, Muller on IBC Quality Improvement, and research by Shine and Chamberlain touch on aspects of Institutional Biosafety Committee and biological materials oversight, but none attempt to address the issue of quantitative burden over time (Muller, Stewart et al., Dolgitser 2007, Chamberlain, Burnett et al. 2009, Shine and St. Onge 2009).

Thus, no other data exists in the scientific literature addressing IBC oversight, burden, and trends. The goal is to obtain data via a cross-sectional survey aspects of IBC composition,

review, support, and administration to provide further knowledge into biological safety and regulatory oversight in relation to biosecurity and public health for entities working with biological materials.

United States Regulatory Oversight of Biological Materials in Research

An extensive federal review of biological materials took place and concluded in 2009, entitled "Report of the Trans Federal Task Force on Optimizing Biosafety and Biocontainment Oversight provides an in-depth review of the current regulatory climate for biological materials (USDA, 2009). The regulatory environment for biological materials research oversight is a patchwork composite from different federal, state, and even local or municipal agencies and organizations (USDA 2009). High containment laboratories at BSL-3 in particular have received increased scrutiny due to their work with Risk Group 3 agents (Kingsbury, 2013). The dominant agencies with oversight over biological materials are the NIH Guidelines for entities receiving NIH funding for rsNA research, and the CDC and USDA for high consequence pathogens and importation concerns, as well as others (USDA 2009). A visual example of biological materials oversight is provided in Figure 1:

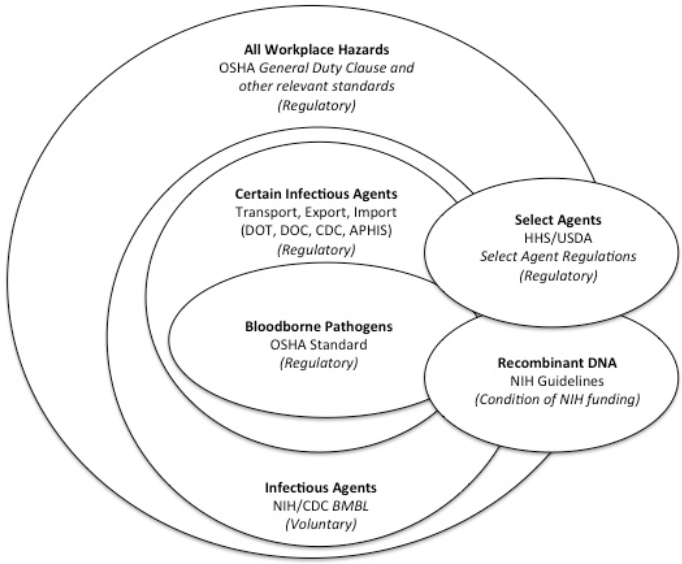

Figure 1. Biosafety/Biocontainment Regulations, Standards, and Guidelines Pertinent to High Containment and Maximum Containment Research (USDA 2009)

As noted in Figure 1, a variety of agencies and regulations touch on various aspects of biological materials oversight in research. The next sections will highlight the major federal regulations and guidelines for biological materials oversight in research.

National Institutes of Health

The Institutional Biosafety Committee is required to be formed and conducts risk assessments for review of rsNA molecule research, if the entity or product given to human subjects receives or received NIH funding for rsNA research in the life sciences (National Institutes of Health, 2013). Otherwise, an institution is not required under any Federal regulation to conduct a risk assessment by a committee of scientific peers on recombinant or wildtype biological materials unless an entity chooses to work with viable organisms on the CDC/USDA Select Agent list, or specific state and municipal are triggered (National Institutes of Health, 2013).

Covered under Section III of the NIH Guidelines are the specific requirements of experiments requiring IBC review (National Institutes of Health, 2013). The experiments range from major actions such as Section III-a-1 where review by the NIH, RAC, and the local IBC is required for research involving the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally (National Institutes of Health, 2013). With advances in gene therapy, IBC reviews of human gene therapy utilizing rDNA and rsNA is increasing (National Institutes of Health, 2013). Most research reviewed by the IBC falls under the categories of Section III-D, III-E, and III-F, which involve IBC review prospective of the research, concurrently with the research, or through exemptions by the NIH, exempted from Committee review but registered with the IBC (National Institutes of Health, 2013).

Given the growing threat of the misuse of biomedical research by terrorists or others, entities are likely to encounter research protocols that raise dual-use issues. The National Science Advisory Board for Biosecurity (NSABB) released in 2012 the United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (National Institutes of Health, 2012). 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). This policy was enacted specifically to mitigate risks where appropriate, and collect information needed to inform the development of an updated policy, as needed, for the oversight of DURC (National Institutes of Health, 2012).

The challenge with DURC is that all life sciences research can be considered dual use, and thus the policy aimed to pinpoint certain types of experiments where additional conduct and review is warranted (Fauci, 2012). A dual-use committee (DUC), institutional biosafety committee (IBC), or other committee should handle this task and convey its findings and recommendations to institutional officials (Resnik, 2010).

Oversight of human gene transfer research ("gene therapy") presents an important model with potential application to oversight of nanobiology research on human participants (Wolf, Gupta et al. 2009). Gene therapy oversight adds centralized federal review at the National Institutes of Health's Office of Biotechnology Activities and its Recombinant DNA Advisory Committee to standard oversight of human subjects research at the researcher's institution (by the Institutional Review Board and, for some research, the Institutional Biosafety Committee) and at the federal level by the Office for Human Research Protections (National Institutes

of Health, 2013). The Food and Drug Administration's Center for Biologics Evaluation and Research oversees human gene transfer research in parallel, including approval of protocols and regulation of products (Wolf, Gupta et al., 2009).

CDC and USDA/APHIS Select Agent Program

The Centers of Disease Control and United States Department of Agriculture, Agriculture and Health Plant Inspection Service, regulate a list of high-consequence pathogens deemed to possess bioterror weapon characteristics, such as high mortality rate, low LD50, or highly infectious nature (CDC, 2011) (USDA 2011) (USDA 2011). The Federal Select Agent Program is jointly comprised of the Centers for Disease Control and Prevention/Division of Select Agents and Toxins and the Animal and Plant Health Inspection Services/Agricultural Select Agent Program (Pastel, Demmin et al., 2006). The Federal Select Agent Program oversees the possession, use and transfer of biological select agents and toxins, which have the potential to pose a severe threat to public, animal or plant health or to animal or plant products (CDC/USDA, 2013).

The Select Agent Program aims to enhance United States oversight of the safety and security of Select Agents by developing, implementing, and enforcing the Select Agent Regulation, maintaining a national database, inspecting entities that possess, use, or transfer select agents (USDA, 2009). In addition the Program seeks to ensure that all individuals who work with these agents undergo a security risk assessment performed by the Federal Bureau of Investigation/ Criminal Justice Information Service, provide guidance to regulated entities on achieving compliance to the regulations through the development of guidance documents, conducting workshops and webinars, and to investigate any incidents in which non-compliance may have occurred (CDC/USDA, 2013).

The Select Agent regulations are located in found at 42 CFR Part 73, 9 CFR Part 121, and 7 CFR Part 331 (2011, 2011, 2011). The Select Agent Regulations implement the Subtitle A and Subtitle B (also known as the Agricultural Bioterrorism Protection Act of 2002) of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, setting forth the requirements for the possession, use, and transfer of select agents and toxins (2002). The Centers for Disease Control and Preventions' (CDC) Division of Select Agents and Toxins (DSAT) and the Animal and Plant Health Inspection Services' (APHIS) Agricultural Select Agent Program (ASAP) jointly constitute the Federal Select Agent Program (USDA 2009).

A subset of select agents and toxins have been designated as Tier 1 because these biological agents and toxins present the greatest risk of deliberate misuse with significant potential for mass casualties or devastating effect to the economy, critical infrastructure, or public confidence, and pose a severe threat to public health and safety (Obama 2010, Avalos 2012).

In determining whether to include an agent or toxin on the HHS select agent list, the Public Health Security and Bioterrorism Preparedness and Response Act requires several criteria be considered, including the effect on human health of exposure to the agent or toxin, the degree of contagiousness of the agent or toxin and the methods by which the agent or toxin is transferred

to humans and the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent any illness resulting from infection by the agent or toxin (DHHS, 2002). In addition, other criteria, including the needs of children and other vulnerable populations is also considered (DHHS, 2002).

For the USDA determinations, in determining whether to include an agent or toxin on the USDA list, the Agricultural Bioterrorism Protection Act of 2002 requires consideration of the effect of exposure to the agent or the toxin on animal and plant health, and on the production and marketability of animal or plant products, the pathogenicity of the agent or the toxin and the methods by which the agent or toxin is transferred to animals or plants, and the availability and effectiveness of pharmacotherapies and prophylaxis to treat and prevent any illness or disease caused by the agent or toxin (Avalos 2012). In addition, any other criteria that the Secretary considers appropriate to protect animal or plant health, or animal or plant products (2005). The lists are required to be reviewed and republished every 2 years, or revised as necessary (Avalos 2012).

The Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC) is an inter-agency workgroup of subject matter experts from Federal government Departments and Agencies constituted by the CDC Director to provide recommendations to the Select Agents and Toxins in the following three technical areas: (1) review of requests for the exclusion of attenuated strains, (2) review of requests to conduct restricted experiments, and (3) review of the select agents and toxins listed in Part 73 (National Academies, 2009).

Administrative penalties under the Federal Select Agent Program have the authority to deny, suspend, or revoke registration to use, possess, or transfer select agents and toxins (Preparedness Act, 2002). In addition, the Federal Select Agent Program has the authority to deny an individual access to Select Agents and Toxins to protect public health and safety (Preparedness Act, 2002).

In addition to any other penalties that may apply under law, any person who violates any provision of Select Agent regulations shall be subject to the United States for a civil money penalty in an amount not exceeding $250,000 in the case of an individual and $500,000 in the case of any entity (Preparedness Act, 2002).

Violations of 18 USC 175b, a "restricted person" that possesses a select agent or toxin, or transfers select agent or toxin in interstate or foreign commerce, (and is not excluded or exempted under select agent regulations) is subject to a criminal fine, imprisoned not more than 10 years, or both (Preparedness Act, 2002).

Whoever transfers a Select Agent or Toxin to a person who the transfer or knows or has reasonable cause to believe is not registered with the Federal Select Agent Program in accordance with the Select Agent regulations is subject to a criminal fine or imprisoned for not more than 5 years, or both (Preparedness Act, 2002). Whoever knowingly possesses a Select Agent or Toxin when that person is not registered with the Federal Select Agent Program in accordance with the Select Agent regulations is subject to a criminal fine and/or imprisoned for not more than 5 years (Preparedness Act, 2002).

Occupational Safety and Health Administration

More than 500,000 workers are employed in laboratories in the U.S. Laboratory workers exposed to numerous potential hazards including chemical, biological, physical and radioactive hazards, as well as musculoskeletal stresses fall under various oversight by OSHA (Roy 2000). Laboratory safety is governed by numerous local, state and federal regulations (Azmi Mohd and Norafneeza). Over the years, OSHA has promulgated rules and published guidance to make laboratories increasingly safe for personnel (Krienitz). There are several primary OSHA standards that apply to laboratories as well as other OSHA standards that apply to various aspects of laboratory activities, including OSHA Bloodborne Pathogens and OSHA Hazard Communication (Kuruvilla 2010, 2011, Traynor 2012).

Additional OSHA standards provide rules that protect workers in laboratories from chemical hazards as well as biological, physical and safety hazards. Occupational Exposure to Hazardous Chemicals in Laboratories standard was created specifically for non-production laboratories (Kenison 1994) For those hazards that are not covered by a specific OSHA standard, OSHA often provides guidance on protecting workers from these hazards under the Hazard Communication Standard (Traynor 2012).

Although the OSHA standards discussed deal specifically with laboratories within the jurisdiction of Federal OSHA, there are twenty-five states and two U.S. Territories (Puerto Rico and the Virgin Islands) that have their own OSHA-approved occupational safety and health standards, which may be different from federal standards, but must be at least "as effective as" the federal standards These state-OSHA plans must meet the minimum criteria laid out in the Federal OSHA standard, and typically are more stringent than the Federal OSHA (USDA 2009) (USDA 2009).

In addition, the OSHA Bloodborne pathogens are infectious microorganisms in human blood that can cause disease in humans (Cuny and Fredekind 2002). These pathogens include, but are not limited to, hepatitis B (HBV), hepatitis C (HCV) and human immunodeficiency virus (HIV) (Narin, Gedik et al. 2012). Needlesticks and other sharps-related injuries may expose workers to bloodborne pathogens (Marini, Giangregorio et al. 2004). Workers in many occupations, including research laboratories and support staff, may be at risk of exposure to bloodborne pathogens (Buesching, Neff et al. 1989).

Food and Drug Administration, Center for Biologics Evaluation and Research

The Center for Biologics Evaluation and Research (CBER) regulates cellular therapy products, human gene therapy products, and certain devices related to cell and gene therapy (Gruber 2011). CBER uses both the Public Health Service Act and the Federal Food Drug and Cosmetic Act as enabling statutes for oversight (Theresa, 2007, Gruber 2011).

Cellular therapy products include cellular immunotherapies, and other types of both autologous and allogeneic cells for certain therapeutic indications, including adult and embryonic stem cells (Mason, Brindley et al. 2011). Human gene therapy refers to products that introduce

genetic material into a person's DNA to replace faulty or missing genetic material, thus treating a disease or abnormal medical condition (Friedmann 1972).

Although some cellular therapy products have been approved, CBER has not yet approved any human gene therapy product for sale in the United States, although the first therapy was approved in Europe in early 2013 (Wirth, Parker et al. 2013). However, the amount of cellular and gene therapy-related research and development occurring in the United States continues to grow at a fast rate (2009). CBER has received many requests from medical researchers and manufacturers to study cellular and gene therapies and to develop cellular and gene therapy products. In addition to regulatory oversight of clinical studies, CBER provides proactive scientific and regulatory advice to medical researchers and manufacturers in the area of novel product development.

Other Regulatory Oversight of Biological Materials and Summary

In addition to the NIH, CDC/USDA Select Agent Program, OSHA, and FDA, other federal organizations may peripherally regulate aspects of biological materials. Figure 2 provides the framework of United States biosafety and biocontainment oversight for biological materials starting with the Principal Investigator.

The Department of Transportation and Federal Aviation Administration regulate the packaging and transport within the United States (USDA 2009). The Office of Export Controls oversees the transactions of biological to entities beyond U.S. borders. The CDC and USDA have additional divisions to inspect and regulate facilities seeking inter-state or international transport of biological materials into the United States. Municipalities and state legislature

Figure 2. Biosafety and Biocontainment Oversight

such as Cambridge, Massachusetts and the State of California may enact additional regulation on biological materials in life sciences research. A current list of oversight with biological materials is provided as Appendix C from the USDA Report of the Trans-Federal Task Force on Optimizing Biosafety.

Based on the literature review and current described above, this research hypothesizes a survey of current biological materials oversight and regulatory review will highlight gaps in United States federal and local oversight. Next, a review of the methodology to assess this hypothesis is provided.

Materials and Methods

As required by the NIH Guidelines, all institutions are required to register with the NIH Office of Biotechnology Activities for the creation of the IBC. Based off prior research by Hackney and others, assistance of NIH-OBA, and a lack of quantitative data on IBCs, a cross-sectional survey was deemed through the development phase with the scientific dissertation committee to be the appropriate method for approaching the topic of biological materials oversight.

The survey consisted of 28 questions regarding administration of IBC responsibilities, Committee membership and support, and oversight of biological materials, and is listed as Appendix A for the Pilot Survey and Appendix B for the full survey. In order to recruit institutions for a survey on IBC practices, support, and review parameters, two Freedom of Information Act requests by the researcher to the NIH/OBA office was issued. The first FOIA request in August, 2012 under FOIA #40395, resulted in the receipt of an electronic spreadsheet detailing IBC contact information for IBC institutional representatives and biosafety officers (National Institutes of Health, 2012). As of September, 2012, a total of 857 Institutional Biosafety Committees existed in the NIH/OBA records, with 1157 institutional contacts and listed biosafety officers. The data range of the survey begins with the initiation of IBCs in 1976 (coinciding with the inception of the NIH Guidelines) through February 15, 2013; a period spanning close to forty years for some IBCs. After the survey was disseminated, a second FOIA request, #41253 was issued in April, 2013, and a response from NIH-OBA was received in May, 2013, with a spreadsheet total of 866 Institutional Biosafety Committees in the NIH-OBA records (National Institutes of Health, 2013).

In consultation with the researcher's IRB, a human subject's review was determined to be unnecessary as the research focus was institutions and not human subjects.

A pilot study survey was initially distributed to 5% of registered IBCs, followed by an analysis of data for meaningful results, and then distribution of the survey to the remaining 95% of registered IBCs. The Dissertation Committee and literature review of survey responses aimed for a 20% participant response rate for the main survey in order to obtain valid data for statistical analysis. The pilot survey was open for two weeks in December, 2012. Upon

survey closure, interviews were conducted with selected recipients and analysis of the pilot data commenced. The main survey was released January 15th, 2013 to February 15th, 2013. Survey distribution was conducted using Qualtrics© survey software available for the School of Public Health at Saint Louis University Graduate School (Qualtrics, Provo, UT) via e-mail. Reminders to survey recipients were sent via e-mail at the two week and four week intervals. For both the pilot and main surveys, institutional responses were kept confidential, and the survey results reported only in aggregate, as the population of institutions that responded to the survey. The statistical analysis package used was SPSS 19 (IBM).

Institutional Recruitment

In FOIA request #40395, NIH-OBA provided the institution name, first and last name of the primary IBC contact, phone number, and e-mail address as required for registering the IBC with NIH-OBA. In addition, for institutions with rsNA research requiring a Biosafety Officer, contact information in the same format was provided. From FOIA #40395, the initial pilot survey institutions were chosen randomly using the SPSS 19 software package. Of the 40 pilot survey institutions, 7 of the pilot institutions contact e-mail addresses were unable to be delivered, due to incorrect contact information provided by NIH-OBA.

Due to the size and ease for which contact information, the remaining 817 institutions listed under the NIH-OBA FOIA request #40395 were contacted with a survey request by electronic mail on January 15th, 2013. Another 43 institutions from the NIH-OBA list did not have correct contact information from the entity in order for the survey to reach the institutional representatives for the IBC. FOIA request #41253 in May, 2013 noted an increase in IBCS by 9 IBCs.

Demographics of the Population

Most entities receiving NIH funding tend to be academic in nature, although other entities include private commercial ventures, non-profit research institutions, government entities, and other bodies including hospitals and clinics. A lack of identifiable information by NIH-OBA from the FOIA requests did not allow for a pre-survey assessment of the demographics of the types of entities registered with NIH-OBA. In addition, while many entities do not receive NIH funding for rDNA or rsNA research, NIH-OBA encourages and entities voluntarily register an IBC with NIH-OBA if work is conducted with rDNA or rsNA as a life sciences industry best practice.

The survey itself sought to establish the demographics of the entities registered in order to ascertain support inferences from additional information on practices and institutional support, in addition to the type of biological materials research under review at the institution.

For the purposes of the survey, an institution is an entity that is distinct to require a registered IBC.

Results

Initial Results

Upon closure of the survey February 15, 2013, main survey resulted in responses from 181/817 institutions, for a total of 21.2% response rate, including 49 partially completed surveys. Another 49 surveys were started but were not submitted. This is in addition to 13/40 out of the initial pilot survey, for a 32.5% response rate for a total of 194/857 complete responses, and 22.6% response rate overall. For the purposes of the tabulated research results, the main survey consists of 181 responses, 132 responses with all questions answers and the 49 partially completed surveys, were used for cross-tabulation and statistical analysis.

Biological Materials Oversight

From the main survey, 172/173 (99.4%) Institutional Biosafety Committees who registered with the NIH-OBA review rsNA. 109/173 IBCs review whole microorganisms, 103/173 review work with OSHA Bloodborne Pathogens, 94/173 work with biological toxins, 56/173 Dual Use Research of Concern (DURC), and 20/173 indicated other, for field releases. This information is presented in Table 1.

	Small University	Medium University	Large University	Research Institute	Private Industry	Government	Non-Profit	Other	Total
rsNA	18	35	59	17	11	8	13	11	172
Microorganisms	11	24	43	8	2	5	8	8	109
OSHA BBP	10	22	37	13	3	5	5	8	103
Biological Toxins	8	18	41	9	2	6	3	7	94
Select Agents	10	20	40	7	2	5	2	7	93
DURC	2	9	30	5	0	2	3	5	56
Other	1	4	9	1	1	1	0	3	20
Total	18	35	59	17	11	9	13	11	173
Chi-Square: 53.18	Df: 28	p-value: 0.00							

Table 1. IBC Survey Cross-Tab - Institution Type by Type of Biological Materials Research

Of the 172 entities reviewing rsNA, 156/172 (91%) review laboratory benchtop projects, 124/172 (72%) animal research with rsNA, 67/172 (39%) review rsNA with plant materials, 58/172 (34%) review gene therapy or pre-clinical vaccine work, and 10/172 (6%) indicated other categories not asked in the survey question. This information is presented in Table 2.

	Small University	Medium University	Large University	Research Institute	Private Industry	Govern ment	Non-Profit	Other	Total
Lab Benchtop	18	31	60	15	7	7	10	8	156
Animal	13	26	51	14	3	3	6	8	124
Plant	7	11	42	2	2	0	2	1	67
Gene Therapy	6	12	15	3	3	3	3	9	54
Other	0	2	4	0	1	0	2	1	10
Total	18	34	60	17	11	8	13	11	172
Chi-Square: 53.18	Df: 28	p-value: 0.00							

Table 2. IBC Survey Cross-Tab - Institution Type by Categories of Recombinant DNA Review

Also of interest is the frequency for which entities review biological materials, and the length of time of IBC Protocol duration are addressed in Tables 3 and 4, respectively. The most common meeting schedules were monthly, 69/174 (40%), and as needed, 51/174 (31%). The most frequenty type of protocol review schedule was annually, with 69/174 (40%) institutions, and triannually 66/174 (38%).

	Small University	Medium University	Large University	Research Institute	Private Industry	Govern ment	Non-Profit	Other	Total
As needed	5	11	14	5	7	3	5	1	51
Annually	1	4	4	1	4	0	1	1	16
Quarterly	3	6	3	3	0	3	6	1	25
Bi-monthly	1	1	3	2	0	0	1	1	9
Monthly	7	10	35	6	0	3	3	5	69
Other	4	7	2	2	0	1	0	2	18
Total	17	35	60	17	11	9	14	11	174
Chi-Square: 43.02	Df: 28	p-value: 0.03							

Table 3. Institution Type by IBC Meeting Frequency

	Small University	Medium University	Large University	Research Institute	Private Industry	Govern ment	Non-Profit	Other	Total
Annual (Every Year) Renewal	10	14	14	2	8	6	9	6	69
Bi-Annual (Every 2 Years) Renewal	1	0	3	0	0	0	0	0	4
Tri-Annual (Every 3 years) Renewal	4	15	29	10	0	2	2	4	66
One-time with approval indefinite	1	2	5	1	2	1	0	0	12
Other	6	4	14	4	1	0	3	2	34
Total	18	34	60	17	11	9	14	11	174
Chi-Square: 43.02	Df: 28	p-value: 0.03							

Table 4. Institution Type by IBC Protocol Duration

Institutional Support

162/173 (94%) of the entities internally reviewed and administered the IBC to review work with rsNA, with 11/173 (6%) of institutions electing to utilize external sources for IBC administration. Most entities elected to staff with the minimally required two community members (160/173), although several entities indicated a need to have additional members on the Committee in case quorum could not be reached (13/173). 33/139 (24%) of IBCs compensated the IBC Chair for time spent running the Committee, and 7/128 (5%) compensated IBC members for time spent on the Committee. These items are addressed in Tables 5 and 6.

	Small University	Medium University	Large University	Research Institute	Private Industry	Govern ment	Non-Profit	Other	Total
Yes	2	7	14	1	1	3	1	4	33
No	14	21	36	10	8	4	9	4	106
Total	16	28	50	11	9	7	10	8	139
Chi-Square: 17.71	Df: 14	p-value: 0.22							

Table 5. IBC Survey Cross-Tab - Institution Type by IBC Chair Compensation

	Small University	Medium University	Large University	Research Institute	Private Industry	Government	Non-Profit	Other	Total
Yes	1	0	2	1	0	1	2	0	7
No	15	25	43	12	7	6	6	7	121
Total	16	25	45	13	7	7	8	7	128
Chi-Square: 9.45	Df: 7	p-value: 0.22							

Table 6. IBC Survey Cross-Tab - Institution Type by IBC Members Compensation

Review and Approval Process

The next set of questions dealt with the review and approval process. Respondents approached the survey question on "Estimated Time for Review per Protocol) in two different methods. One method calculated the actual time spent reviewing the project in minutes. The other method saw responses from initial receipt of the project, to actual time of IBC review of approval in days.

The average length of time for 105 responses in hours of review by the biosafety officer and administrative support, starting with receipt of the IBC protocol from a researcher to a convened meeting, involving pre-review, inspection, and back-and-forth feedback to a PI, was 5.2 hours per protocol. Several respondents noted two types of review, human gene transfer and high containment reviews at BSL-3/BSL-4, would require significantly more time and should not be included. 49 responses indicated the length of time from receipt to IBC approval in days, to be an average of 29 days, with a minimum of 7 days to a maximum of 90 days for IBC review.

Case Studies of Research by Year

Twenty-two entities provided a year by year summary of IBC registered protocols and research. This data is represented in Figure 3.

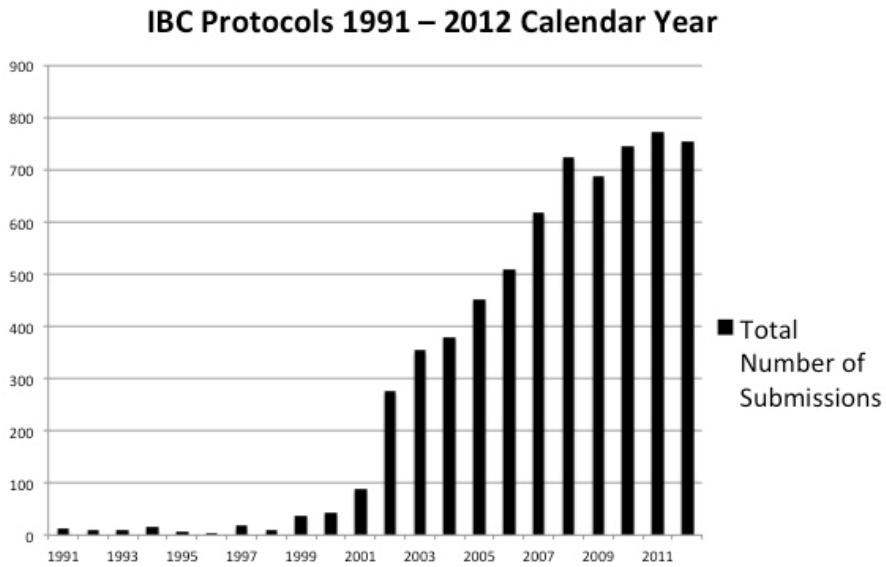

Figure 3. IBC Protocals 1991-2012 Calendar Year Case Study

In addition, data obtained from the two FOIA requests in addition to data from previous FOIA requests show the increase in the number of registered IBCs started with 56 in 1976, to 886 in 2013. This is shown in Figure 4.

Responder Comments

The survey provided an opportunity for biosafety professionals to raise concerns concerning the field of biological materials oversight. These anecdotal responses help to shed light on the current state of support for the IBC and biological safety program at the entity.

Responses indicated a lack of institutional support for both financial support as well as staffing in order to even maintain a database of past and current IBC protocols. Other statements in free form from responders commented on recombinant DNA being remarkably safe, and the real issues of biological materials oversight with whole microorganisms at Biosafety Level 1 and Biosafety Level 2. Another area of expressed concern was over the implementation of the Dual Use Research of Concern and how that would be accomplished at the local entity level.

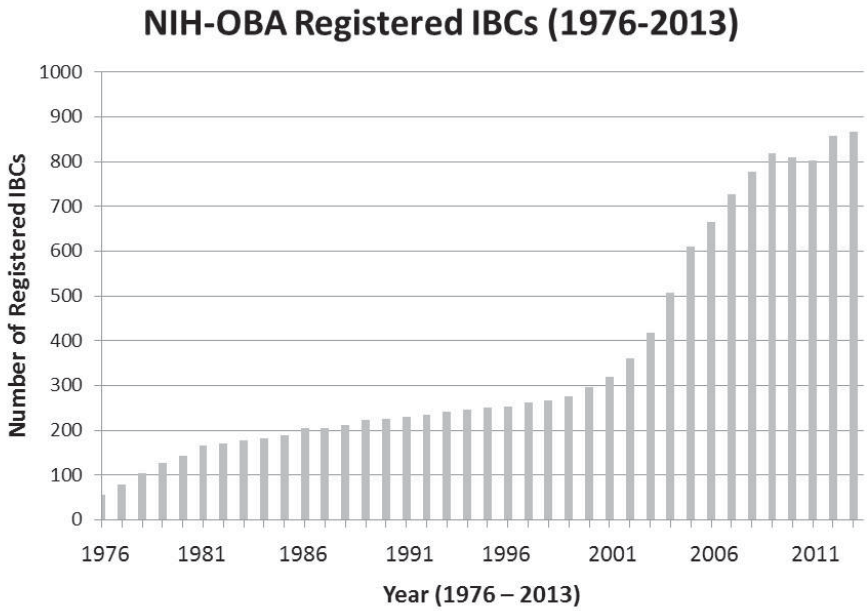

Figure 4. Number of Institutional Biosafety Committees Registered By Year

Discussion

Observed Trends in Biological Materials Oversight and IBCs

Several items regarding biological materials review and support can be inferred from the results of the survey. First, basic research in the life sciences involving biological materials is increasing. This is evidenced by the increasing number of registered IBCs from the Hackney surveys to this cross-sectional survey, and the case-studies of protocols reviewed by year. Second, the IBC is not currently supported with resources for the IBC to function. As currently structured at the majority of institutions, financial and staffing resources are little to non-existent. The most common support is financial compensation for the IBC chair, and a quarter of time allotment for an administrative staff member to assist the Biosafety Officer in running the IBC.

Another finding is institutions are expanding the role of the IBC to include oversight beyond recombinant materials only, to also include review of whole microorganisms, blood borne pathogens, and biological toxins. In addition, IBCs are tasked with fulfilling federal requirements for the review of new DURC requirements, essentially asking institutions to conduct an analysis of whether a research project should ethically be allowed to proceed.

Another finding of note is multiple institutions have on record more than one IBC to cover different aspects of research. The rationale and actual numbers for doing so are unclear at this time, although the researcher hypothesizes entities segment aspects of research for internal

review and external review by registering multiple IBCs. One example is a mid-size academic entity with a hospital system employing one IBC to conduct biosafety assessments of rsNA laboratory, animal, and plant research, and the other IBC to conduct research of rsNA into human subjects.

Recent deaths from biological materials from a Yersinia *pestis* attenuated strain wild-type Neisseria *meningitis*, and other biological materials highlight the importance of institutional risk assessment on manipulations with biological materials (2011, Erin 2013). Little data exists on laboratory acquired infections, but are believed to be underreported by as much as 80% (Pike 1979). For the safety of the growing field of life sciences, it is imperative institutions and regulators work together to assure safety of staff and the environment against unintended release and exposures.

Of the entities with IBCs, 172/173 reviewed rsNA. This is evidence entities such as small colleges and universities, pharmaceutical companies and non-profits, view developing an IBC as an afterthought due to the lack of regulatory stimulus to create and maintain an IBC.

Until now, this information has not been made public, and is of interest to the biosafety community, regulators, and research scientists to see the increase in biological materials oversight through IBC Registrations.

The Future of United States Biological Materials Oversight in Research

As of this writing, current amendments to the NIH Guidelines for research involving human gene transfer are in the process of public comment and review by NIH-OBA. In addition, the recent H5N1 research highlighted concerns from NSABB into issuing requirements for the review of Dual Use Research of Concern. The CDC and USDA Select Agent Program review additions and subtractions to the Select Agent List on a two-year cycle, and have recently implemented a higher level of regulation with 11 agents known as Tier 1 agents. The list is currently in between review cycles for additions or subtractions.

An interesting developing is the American Biological Safety Association's (ABSA) continued efforts since 2008 to establish a BSL-3 accreditation program, to eventually become a self-sustaining accrediting body. The ABSA Laboratory Accreditation program was developed for United States Biosafety Level (BSL) 3 and animal biosafety level (ABSL)-3 laboratories (ABSA, 2012). The purpose of the ABSA accreditation program is to ensure that biocontainment facilities have in place the necessary practices, procedures, personnel, and equipment to protect people, animals, plants, and the environment and minimize the potential of laboratory associated infections and laboratory accidents (ABSA, 2008). Key factors in the ABSA accreditation process are an objective assessment of the technical competence and quality system of an organization or laboratory as it relates to biohazard management, including personnel training and experience (ABSA, 2011). Accreditation, using relevant local, national and international guidelines, regulations and standards is an effective way of ensuring competence in a comprehensive and uniform manner in laboratories working with biohazards. The accreditation program is voluntary, and an agreement between the entity and the ABSA Accreditation Board will define the scope of the review (ABSA, 2012).

Key components assessed by the accreditation program include components of reviewing the biosafety expertise and training of personnel managing and conducting the research, assessing the adequacy and function of the biosafety management structure supporting the research activities, and determining the adequacy and function of biocontainment measures, including facilities, equipment, practices, and record-keeping systems, in place at the facility that is evaluated (ABSA, 2011).

ABSA accreditation will provide entities recognition of excellence and compliance with high standards that will be important among their peers as well as their organization's management (ABSA, 2012). The ABSA accreditation standards will help facilities that need guidance in generating processes and policies to create a safer environment for their organization, its employees, and for the community (ABSA, 2012). Achieving accreditation will be verification to the organization, the employees, and the community that the organization is taking extra steps to create a safer environment. The ABSA Laboratory Accreditation Program does not supplant any required regulatory inspections (ABSA, 2012).

Limitations of the Study

The study has several limitations. First, most institutions lacked the ability to accurately report prior reviews of biological materials in order to determine changes over time. Of the 183 institutions who responded to the survey request, only 22 (12% of respondents in the 2013 survey) institutions were able to provide yearly totals of protocol reviews. The main reason reported by responders is due to a lack of institutional administrative and information technology support for Institutional Biosafety Committees. Few responders had access to information on whether IBC support lacked, matched or surpassed other research compliance committees such as the IRB and IACUC.

Second, responses were skewed towards academic institutions, with medical institutions under represented. In previous research by Hackney there has a very low response rate (5% in the 2013 survey) to the survey from hospitals and non-profits, an institution type that has increased dramatically in the NIH IBC database population over the last fifteen years (Hackney, et al). Fifty-five hospitals and clinics were registered IBCs in 2002 as compared with 303 in 2010. One of the reasons that may have contributed to the lack of response from these organizations was that a handful of commercial organizations that manage IBCs for the vast majority of registered clinics and hospitals did not respond to the surveys. Many of these hospitals and clinics that are registered with NIH may have a very small number of clinical trials being conducted at their sites that require IBC review. The lack of response from clinics and hospitals and the high response rate from academic institutions (71% of the IBCs that participated in the 2010 survey were from academic institutions compared with 42% in the actual IBC population registered with NIH) suggests that the survey results are more representative of academic IBCs than the IBCs from other types of institutions.

A third limitation is that cross-sectional surveys are known to be the weakest method of capturing data to make inferences on a population. Survey data is generally weak on validity but strong on reliability.

There is a lack of data on the true number of accidents with biological materials, and as detailed by Pike earlier, it is well documented for lab accidents to be under reported (Pike, 1979). The current data set is also difficult to determine the difference between Select Agent incidents and recombinant DNA incidents, and a lack of willingness from institutions to disclose non-recombinant accidents with biological materials.

Conclusion

This survey and previous literature on IBCs registered IBCs operate under an unfunded mandate with little institutional support for conducting risk assessments on biological materials. IBCs only provide a snapshot of all biological materials research reference due to the requirement of NIH funding, and institutions who do not receive NIH funding have no incentive or requirements to register and conduct risk assessments on the handling of whole microorganisms, toxins, and human materials. In addition, the survey highlights the disparities between institutions, and highlights the need for additional staffing, training, and support from institutions and at the federal level. The results suggest that while IBCs at larger institutions and well-funded private entities are following many of the practices required by the NIH-OBA, smaller entities may struggle for funding and administrative support. The results indicate that there may be many IBCs that lack adequate staffing and oversight. Thus, future recommendations are aimed at enhancing biological materials oversight through an expansion of NIH-OBA oversight of the IBC, and expansion of the laboratory reporting requirements to the CDC/USDA, through expansion of the NIH Guidelines applicability beyond NIH funded entities.

Author Information

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Appendix

Institution Type
- Small University (student enrollment of 1-4,999 students)
- Medium University (student enrollment 5,000 to 14,999 students)
- Large University (student enrollment of 15,000 and above)
- Research Institute
- Private Industry
- Government
- Non-Profit
- Other

Type of Biological Materials Research Reviewed by the IBC
- Recombinant DNA (Yes/No)
- Whole Microorganism (non-recombinant) (Yes/No)
- OSHA Bloodborne Pathogens (Yes/No)
- Biological Toxins (Yes/No)
- Select Agents (Yes/No)
- Dual Use Research (Yes/No)

Is your IBC administered internally (support staff on location) or externally? (third-party) (Internal/External)

Number of protocols reviewed over IBC active date range (1976 to 2012)
- At BSL-1
- At BSL-2
- At BSL-3
- At BSL-4

Estimated Time for Review per Protocol (from receipt, processing, inspection, IBC meeting, and follow-up items, approval) (0 hours to indefinite)

What type of renewal strategy is employed upon approval?
- Annual renewal
- Bi-annual renewal
- Tri-annual renewal
- One-time with approval indefinite
- Other

Number of Investigators with Approved Protocols

By year from the inception of the IBC, how many initial protocols are approved each year? (1976 to 2012)

If yes to Recombinant DNA Research, what categories of rDNA research have been reviewed? (Select all that apply)

- Laboratory Benchtop
- Animal
- Plant
- Human Gene Therapy

How often are IBC meetings held?

- As needed
- Annually
- Quarterly
- Bi-monthly
- Monthly
- Other

How many Full-Time Employees support the Institutional Biosafety Committee? (0 to indefinite)

How much financial support does the IBC receive from the Office of Research? ($0 to indefinite)

If yes, is the IBC Chair Compensated for time spent? (Yes/No/N/A)

If yes, are other Committee members compensated for time spent serving on the IBC?

How much financial support does the IRB receive from the Office of Research? ($0 to indefinite)

How much financial support does the IACUC receive from the Office of Research? ($0 to indefinite)

Committee Composition (NIH Roster and Function Support)

Number of scientific members

Number of biological safety professionals

Number of external (public) members

Number of administrative staff

Other members (include title and number)

If known, the number of NIH reported laboratory accidents involving recombinant DNA at the entity from 1976-2012.

Appendix B – Full Survey Questions

Institution Type
- Small University (student enrollment of 1-4,999 students)
- Medium University (student enrollment 5,000 to 14,999 students)
- Large University (student enrollment of 15,000 and above)
- Research Institute
- Private Industry
- Government
- Non-Profit
- Other

Type of Biological Materials Research Reviewed by the IBC
- Recombinant DNA (Yes/No)
- Whole Microorganism (non-recombinant) (Yes/No)
- OSHA Bloodborne Pathogens (Yes/No)
- Biological Toxins (Yes/No)
- Select Agents (Yes/No)
- Dual Use Research (Yes/No)

Is your IBC administered internally (support staff on location) or externally? (third-party) (Internal/External)

Number of protocols reviewed over IBC active date range (1976 to 2012)
- At BSL-1
- At BSL-2
- At BSL-3
- At BSL-4

Estimated Time for Review per Protocol (from receipt, processing, inspection, IBC meeting, and follow-up items, approval) (0 hours to indefinite)

What type of renewal strategy is employed upon approval?
- Annual renewal
- Bi-annual renewal
- Tri-annual renewal
- One-time with approval indefinite
- Other

Number of Investigators with Approved Protocols

By year from the inception of the IBC, how many initial protocols are approved each year? (1976 to 2012)

If yes to Recombinant DNA Research, what categories of rDNA research have been reviewed? (Select all that apply)

- Laboratory Benchtop
- Animal
- Plant
- Human Gene Therapy

How often are IBC meetings held?

- As needed
- Annually
- Quarterly
- Bi-monthly
- Monthly
- Other

How many Full-Time Employees support the Institutional Biosafety Committee? (0 to indefinite)

How much financial support does the IBC receive from the Office of Research? ($0 to indefinite)

If yes, is the IBC Chair Compensated for time spent? (Yes/No/N/A)

If yes, are other Committee members compensated for time spent serving on the IBC?

How much financial support does the IRB receive from the Office of Research? ($0 to indefinite)

How much financial support does the IACUC receive from the Office of Research? ($0 to indefinite)

Committee Composition (NIH Roster and Function Support)

Number of scientific members

Number of biological safety professionals

Number of external (public) members

Number of administrative staff

Other members (include title and number)

If known, the number of NIH reported laboratory accidents involving recombinant DNA at the entity from 1976-2012.