Institutional Biosafety Committees and the Public Stewardship of Bioscience Research: An Analysis of Community Membership

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by

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DEDICATION

To my daughter Kristen – a true scholar.

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ABSTRACT

Institutional Biosafety Committees and the Public Stewardship of Bioscience Research: An Analysis of Community Membership

Katherine Marie Wellman

Scientists continue to find new applications for recombinant or synthetic nucleic acid molecules, which are often used as biological tools that modify or construct living organisms. These molecules are used principally in the biosciences, in basic laboratory research relating to disease, drug discovery, and clinical applications, including gene therapy. The prospects and risks of moving this science forward, one experiment at a time, fall under the oversight of the Institutional Biosafety Committee (IBC). The role of the IBC community member is to represent the community's interests in health and environmental matters with respect to this research. This study established a baseline of knowledge about the composition and characteristics of IBC community members and the facilities conducting the research.

This research provided a glimpse of how citizens as stakeholders are involved in decision-making and provided insight for rethinking how oversight can move forward with science. Early motivation for the inclusion of outsiders on IBCs was primarily because NIH oversight and government investment in bioscience went hand in hand and public trust declined as oversight policies were not evolving as fast as the science. As we turn the corner with substantive justifications that provide a richer participatory infrastructure; the right mix of policies will open opportunities for public involvement.

Specifically, this was formative research that identified the occupational and educational characteristics of IBC community members, the ratio of outside members to inside members, and the types of facilities that conduct NIH regulated research and describes the biotechnology hub in Massachusetts. The study explored the influence of system-wide IBCs and local oversight ordinances on the committee composition and updates what we know about the outsiders appointed to IBCs to provide monitoring and their capacity to bring legitimacy and resources to the facility conducting recombinant or synthetic nucleic acid molecular research. Results indicate that stand-alone IBCs and facilities operating in areas without a local oversight ordinance are more likely to have IBCs with a higher composition of community members.

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INTRODUCTION AND OVERVIEW

The ever-increasing capability of scientists to manipulate biological systems at the molecular level continues to challenge the research oversight framework that aims to protect the public and the environment by ensuring safe research practices (Fogleman 1987; Patterson et al. 2013; Rodemeyer 2009). The best practices for working with recombinant or synthetic nucleic acid molecules are specified in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines* 2013). The *NIH Guidelines* were first issued in 1976, underwent a major revision in 1978 (Johnson 1982), and have been updated several times since then (*NIH Guidelines* 2013). The scope of oversight covered by the *NIH Guidelines* includes the formation and use of organisms and viruses containing recombinant or synthetic nucleic acid molecules.

Institutional Biosafety Committees (IBCs) are formed at the facility level as required by the *NIH Guidelines* to review research involving recombinant DNA and **s**ynthetic nucleic acid molecules. The facility IBC reviews research to guide its compliance with the *NIH Guidelines* and/or a local ordinance. IBCs are entrusted with decision-making at the facility-level that includes public health considerations and environmental concerns such as containment strategies and managing adverse events (*NIH Guidelines* 2013).

Not unexpectedly, the role of IBCs continues to evolve as the science advances. For example, the *NIH Guidelines'* most recent update expanded the scope of oversight to include synthetic nucleic acid molecules that are incorporated into biological systems. Thus, this new technology expanded the reach of IBCs beyond molecular biology to include physical sciences

(Corrigan-Curay and Fong 2012). The expertise required to evaluate risks in scientific research proposals will become more complex as science advances (Bereano 1984; Rodemeyer 2009).

Before we can assess whether the IBC structure functions adequately in representing the community and assessing the risks involved in recombinant or synthetic nucleic acid molecular research, we must do several things. We need to understand the composition and characteristics of IBCs and the types of organizations they serve. Then we move on to assemble evidence as to what types of facilities conform to community membership requirements, with and without local ordinances.

The NIH formalized transparency and public accountability through citizen participation at the local level by requiring two outsiders, or community members, on every IBC (*NIH Guidelines 2013*). Although the requirement to include community members was established in 1978, with a minimum of two community members at a 20% level little is known about its implementation (Bereano 1984).

All projects involving recombinant or synthetic nucleic acid molecules at a facility that receives National Institutes of Health (NIH) funding for conducting or sponsoring such research must follow the *NIH Guidelines.* Just over 800 facilities conduct research involving recombinant or synthetic nucleic acid molecules and receive NIH funding (Jambou 2013). In addition, compliance with the *NIH Guidelines* is often a condition of receiving funding from other federal agencies or other research funding entities (*NIH Guidelines FAQs* 2013). Most of the facilities conducting this research are clustered in areas with academic research laboratories, clinical facilities, and start-up biotechnology companies (Feldman and Lowe 2008).

Whether or not they receive NIH funding, facilities may also be subject to local ordinances that impose similar regulations (Lipson 2003). Often, the local public health

department has adopted the *NIH Guidelines* and requires compliance for all facilities within the city's jurisdiction (*Mass Bio BioReady® Communities* 2013). Local oversight greatly increased the number of facilities required to meet oversight regulations for research involving recombinant or synthetic nucleic acid molecules (Lipson 2013). For example, the Commonwealth of Massachusetts has 48 non-government facilities that receive NIH funding for research involving recombinant or synthetic nucleic acid molecules (Jambou 2013). In comparison, the city of Cambridge has a local ordinance that applies to nearly 100 facilities engaged in research involving recombinant or synthetic nucleic acid molecules (Lipson 2013).

Cambridge is a leading community in overseeing biotechnology research involving recombinant or synthetic nucleic acid molecules. Its oversight regulations are often used as a benchmark by other communities in the commonwealth and around the country that are planning to adopt local oversight laws (Lipson 2003). In 1977, Cambridge became the first community to regulate recombinant DNA research; it was also the first to establish direct public oversight over the research through the use of community members (Lipson 2003). Lipson affirms that officials from biotechnology businesses are attracted to Cambridge, in part, because of its established regulatory process for safe work practices. It is worth noting that Cambridge, a high-density biotechnology area, ranks first among all U.S. bioclusters in research and early-stage innovation (*Mass Bio BioReady® Communities* 2013).

The *NIH Guidelines* reflect the principles of agency theory and resource dependency theory as they authorize IBCs to monitor facility biosafety risks and provide the facility access to external resources through appointed community members. Outside members provide monitoring and a capacity to bring legitimacy and resources to an organization (Jensen and Meckling 1976; Pfeffer and Salancik 2003).

Agency theory suggests that choosing outside members is complex because candidate selection is based on a variety of considerations. Jensen and Meckling (1976) described the relationship between the principal and the agent as a contract where the key activity of the agent is monitoring the firm. Resource dependency theory suggests outside board members supply resources. In practice, outside board members monitor activities and provide resources, both though a network of ties to other organizations and their own experience, expertise, and reputation (Hillman and Dalziel 2003).

IBC community members in municipalities with local ordinances must meet the critetia in the local regulations in addtion to the *NIH Guidelines'* requirements. In this situation, the Public Health Commission often approved or appointed the IBC community members. It is unknown what impact the impementation of these requirements has on the community membership.

The NIH has recently recognized an alternative approach to stand-alone facility IBCs. It is a systems approach that involves a change in IBC structure to provide oversight to several facilites in response to fullfilling the IBC review requirements of the NIH regulations. This systems approach shares administrative overhead associated with using the IBC to oversee compliance. Some facilities that are affiliated through partnerships have joined to create and use multi-facility IBCs. It is unknown what impact this systems approach has on IBC composition with respect to the number of community member appointments in relatinship with insider appointments since so many facilities need representaiton with the IBC.

Community members are included on IBCs specifically to represent the community's safety interests in recombinant or synthetic nucleic acid molecular research. Previous studies conducted decades ago found that IBC community members were often scientists who were

reported as lacking the qualifications to represent the community interests with regard to the specific research concerned (Bereano 1984; Dutton and Hochheimer 1982; Jaggar et al. 1987). The potential for underrepresentation of the community's interests still exists today.

Statement of Purpose

The purpose of this investigative analysis was to identify compositional characteristics of the biosafety advisory boards with an emphasis on board participation by community members. There are strong theoretical underpinnings that support the role and function of community members serving on advisory and governing boards. This study examined the composition of the IBCs and selected characteristics of outside members. It also identifed facility factors that may affect the extent of community member participation on the advisory boards.

Public Administration Significance

Public administrators at the NIH Office of Science Policy stress the importance of public input as part of their mission statement. Yet scientists have long argued that restrictive oversight will suppress free inquiry in the application of recombinant DNA methods, thereby denying society the discoveries of unhindered research (Gilbert 1977). On the other hand, some scientists, politicians, regulators, and members of the public have disputed the rationale behind the free inquiry claim (Goggin 1986; Marris and Rose 2010). Marris and Rose (2010) say the scientific community and their funders have sought out public engagement in areas such as synthetic biology yet they caution "some scientific researchers may be wary of involving non-specialists" (2) especially in decisions about "the aims, motives, direction, funding, and regulation of scientific research" (2).

In the biotechnology sector, IBC community members are poised to play a key role as agents of the community with regard to the implementation of safe science practices at the

facility level. Local communities, especially in Massachusetts, have embraced regulations as a competitive advantage and used them to draw biotechnology facilities to their cities and towns (Feldman and Lowe 2008; Lowe and Feldman 2008). This shift in the perceived value of oversight has created more IBC structures in such communities, and the increase in IBCs is not limited to those institutions receiving NIH funding (Lipson 2013).

In addition to funding biomedical research that has enabled innovative health solutions, the NIH is important to the U.S. economy in its own right by being a steward of a major public investment in research (Reichard 2012). The volume of research supported by the NIH involving recombinant or synthetic nucleic acid molecules is not specifically known. Research grants account for 53% of the $30.7 billion annual NIH budget (NIH 2013). The NIH awards grants to various types of organizations that include higher education, hospitals, research, and other nonprofit institutions and—in recent times—an increasing number of for-profit firms (NIH 2013).

For-profit biotechnology companies have turned to NIH funding as private funding becomes ever more difficult to obtain (Gollin et al. 2006). The Biotechnology Industry Organization (BIO) addressed the needs of its membership in navigating public funding by providing a session at an annual conference (Gollin et al. 2006). There is little information for biotechnology companies about how to manage public funding, including the requirements the granting agency imposes on the company (Gollin et al. 2006).

Public administrators are concerned about public funding used to support research and development and the resulting economic impact (Reichard 2012). According to the American Association for the Advancement of Science (AAAS), the total publicly funded research and development budget equals around 1% of U.S. Gross Domestic Product (GDP). Biological

research is the largest government-supported area of research, with more than 20 agencies supporting biological sciences committing 27% of the research budget to this area (*Committee on Science and Technology - 21st Century Biology* 2010).

A recently ended campaign to double the total NIH budget over a five-year period boosted the NIH research and development budget (Lambright 2008). According to Lambright, the success of The Human Genome Project largely influenced this increase. The human genome was sequenced using advanced sequencing technologies involving recombinant DNA methods, among other analytical tools and technologies. The Human Genome Project spurred a genomic revolution, with a $3.8 billion investment over 13 years creating $796 billion in U.S. economic impact and 310,000 jobs (Battelle 2011).

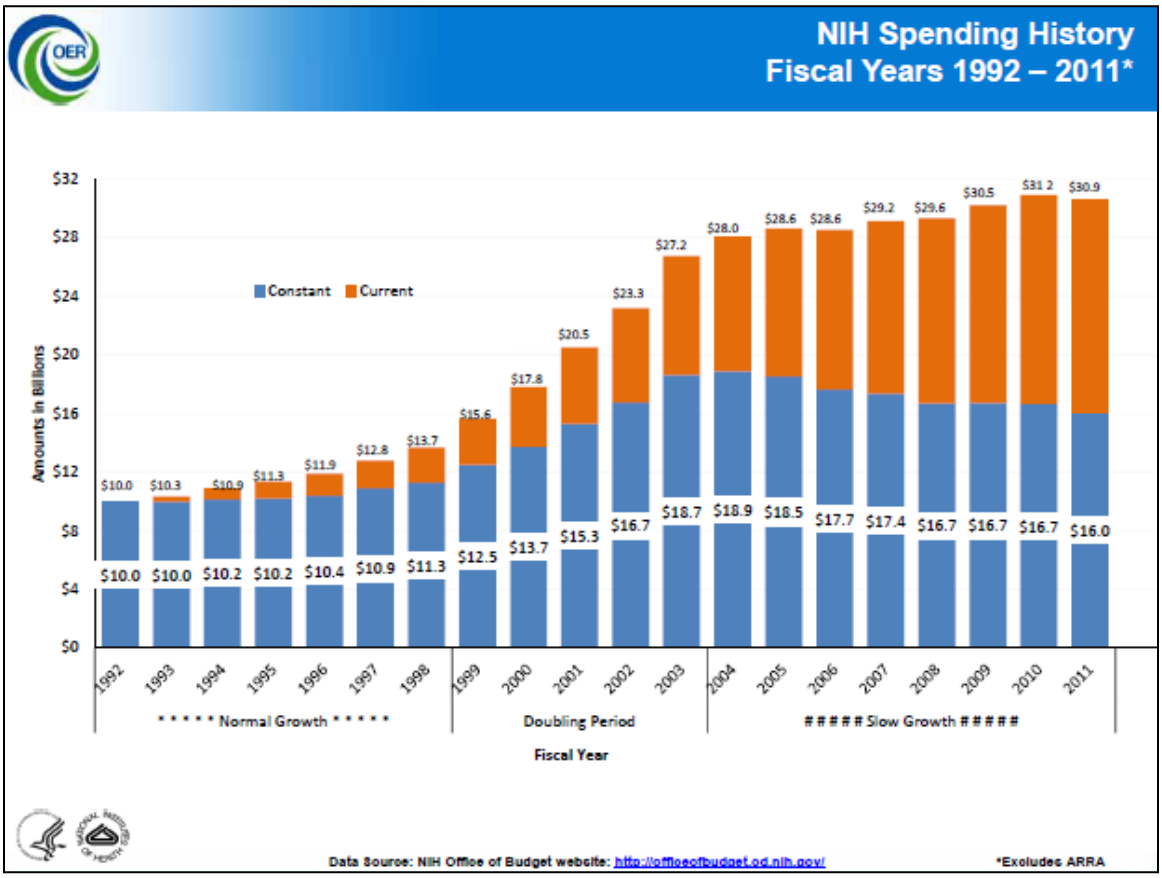

Figure 1. NIH Spending History and Budget 1992–2011

Source: NIH Office of Extramural Research
http://www.airi.org/washington/2013%20washington%20files/06-moore.pdf

Summary

The trajectories of bioscience research and subsequent discoveries are driven by NIH-funded research priorities. Emerging technologies will inescapably require public administrators to "take a hard look at the capacity of public organizations to be effective in dealing with the large issues ahead" (Lambright 2008, 15). This study investigated one such organization that has linked the public with science and government in research risk decision-making that involves recombinant or synthetic nucleic acid molecules.

Little is known about the appointed community members that engage with scientists on the frontline. These scientists must seek approval from their facility IBC in order to proceed with their research proposal if it falls under the *NIH Guidelines*. This was an exploratory study which examined the governance, organization and location characteristics of NIH registered IBCs in Massachusetts. The study determined the relationships between IBCs composition and organizational and local area characteristics.

LITERATURE REVIEW

This chapter is organized in sections that provide justification for the research questions that first profile the NIH registered IBCs in Massachusetts including governance, organizational and location characteristics. Then the research shows what organizations are more likely to develop boards with at least 20% outside members.

The first section provides a background explaining how recombinant or synthetic nucleic acid molecules are regulated in the United States. It includes a brief overview of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (*NIH Guidelines* 2013) and local ordinances, with an emphasis on IBCs and the community member. The next section examines why the *NIH Guidelines* are necessary and explains the significance of the issue of science and society as it relates to recombinant or synthetic nucleic acid molecules. The last section reviews relevant research on IBCs.

Oversight of Recombinant or Synthetic Nucleic Acid Research

The purpose of the *NIH Guidelines* is "to specify the practices for constructing and handling: (i) recombinant nucleic acid molecules, (ii) synthetic nucleic acid molecules, including those that are chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, and (iii) cells, organisms, and viruses containing such molecules" (*NIH Guidelines* 2013, 10). IBCs "are the cornerstone of institutional systems of oversight of recombinant DNA research" (Shipp 2003, 4) and serve as the interface for other "committees that review the science, safety, and ethics of experimentation from bench, through animal models, to the clinic" (4–5). According to Shipp, "transparency, which has served to inform the

public and to provide assurance of adequate oversight" (4) is a key public value of the *NIH Guidelines*.

The *NIH Guidelines* outline six catagories of experiments requiring various levels of review and oversight. First, experiments that could hamper the ability to control human, animal, and plant diseases by deliberately transfering a drug-resistant trait to a microorganism are classified as major actions. These experiments require approval of the NIH Director and the Recombinant DNA Advisory Committee (RAC) in addtion to the local facility IBC.

The second level consists of experiments that involve cloning highly lethal toxin molecules. These require both NIH approval and IBC approval before initiation.

The third level of experiments includes those involving transfering recombinant or synthetic nucleic acid molecules into human subjects. These experiments require RAC review and Institutional Review Board (IRB) approvals in addition to IBC approval before participant enrollment.

The fourth tier of experiments comprises those that require only IBC approval before initiation because of the risks associated with the agent. Infectious agents are categorized by the *NIH Guidelines* into risk groups based on pathogenicity, mode of transmission, preventative measures and effective treatment. Risk Groups (RGs) range from a low RG1 to a high RG4. For example, the bacterial agent *Bacillus anthracis* can cause disease in humans but is rarely serious in a laboratory setting as preventive or therapeutic remedies are typically available so it is classified in the *NIH Guidelines* as RG2. The viral agent Ebola is classified as RG4 as it is likely to cause death as preventative or therapeutic remedies are not available. IBC approval is required before initiating the experiment for agents classifed in RG2 through RG4 and other specific restricted agents such as pox viruses.

IBC approval is also required for experiments that include nucleic acid molecules derived from infectious viruses, including influenza viruses. Experiments involving whole animals and whole plants also require IBC approval before initiation. As do large scale (more that 10 liters) uses of organisms.

Experiments in the fifth level require IBC approval simultaneously with initiation. This group includes those experiments that can be conducted with Biosafety Level 1 (BSL 1) practices. Biosafety containment levels range from Biosafety Level 1 (BSL 1) to Biosafety Level 4 (BSL 4). The levels designate the standard microbiological practices for the agents to protect the workers the environment and the community from risks associated with handling the agents. The protection level is from lowest (BSL 1) to highest (BSL 4). Experiments requiring IBC approval simultaneously with initiation are those in the lowest BSL 1. These include certain experiments involving the development of recombinant or synthetic nucleic acid molecules with no more than two-thirds of the genome of a virus, certain plant experiments, and certain experiments involving transgenic rodents.

Additionally, some experiments in the sixth and final level do not require full IBC review because they have been determined to not be a significant risk to health or the environment. The *NIH Guidelines* are revised as science changes and the understanding of the risks change (Shipp 2003).

Roles and Responsibilities

Each facility that conducts or sponsors recombinant or synthetic nucleic acid molecule research funded by the NIH is responsible for compliance with the *NIH Guidelines* (*NIH Guidelines* 2013). Specifically, the facility must establish safety policies and create an IBC with at least five members, at least two of whom must represent the community with the remainder

being internal experts. The internally appointed members should have the expertise to conduct risk assessments and develop safety practices based on the types of experiments being conducted at the facility. For example, these individuals may have expertise in biosafety, plant containment, animal containment, and human gene transfer.

The focus of this study was on the two remaining members, identifed as community members, who are defined in the *NIH Guidelines* as "not be affiliated with the institution (apart from their membership on the Institutional Biosafety Committee) and who represent the interest of the surrounding community with respect to health and protection of the environment (e.g., officials of state or local public health or environmental protection agencies, members of other local governmental bodies, or persons active in medical, occupational health, or environmental concerns in the community)" (*NIH Guidelines* 2013, 26).

The IBC reviews recombinant or synthetic nucleic acid molecule research and determines the risk category, containment level, access to the laboratory facility, training requirements, policies, and procedures. The IBC also notifies the NIH when required to based on the experiment's risk level or whether the experiment involves new techniques that have not been included in the *NIH Guidelines*. The IBC communicates the outcome of the IBCs determination based on the proposal presented by the Principal Investigator. The IBC is also responsible for overseeing the facility with internal audits to ensure conformance with *NIH Guidelines* and reporting significant adverse events to the NIH.

Application of the NIH Guidelines

The *NIH Guidelines* apply to recombinant or synthetic nucleic acid research that occurs when it is within any of these classifications: 1) conducted at an institution that receives funding for recombinant or synthetic acid research from NIH, 2) sponsored by an institution that receives

funding for recombinant or synthetic nucleic acid molecule research from NIH, 3) involves using human subjects to research materials developed with NIH funding. The *NIH Guidelines* apply to recombinant or synthetic nucleic acid molecule research that occurs in foreign countries as well, but the institution can follow the host country's rules if they are consistent with the *NIH Guidelines.*

The *NIH Guidelines* apply to all NIH-funded and non–NIH-funded research involving recombinant or synthetic nucleic acid molecules conducted at or sponsored by a facility that is funded by the NIH for these types of experiments. Noncompliance can result in the deferment or termination of NIH funding. The *NIH Guidelines* are far-reaching at the facility level once the facilty accepts an award where the *NIH Guidelines* apply. More than 800 facilities have IBCs registered with the NIH (Jambou 2013).

Federal-Level Oversight

Facilities that do not receive awards from the NIH or other federal agencies that require compliance with the *NIH Guidelines* for research involving recombinant or synthetic nucleic acid molecules do not need to comply with the *NIH Guidelines,* but they can elect to voluntarily comply (*NIH Guidelines FAQs* 2013). Scientific research with recombinant or synthetic nucleic acid molecule experiments is not regulated at the federal level, despite several attempts to pass legislation (Dickson 1988; Fogleman 1987; Krimsky and Ozonoff 1979; Talbot 1983). In reality, many facilities that conduct this type of research do comply with the *NIH Guidelines,* either because other federal agencies require self-certification of compliance under certain conditions, or because the facility complies voluntarily (*NIH Guidelines FAQs* 2013). Since these facilities are not registered with the NIH, the number of facilities having IBCs that conform with the *NIH Guidelines* at the federal level is unknown.

Research Involving Recombinant or Synthetic Nucleic Acid Molecules

The advent of recombinant DNA research methods in the 1970s was an important achievement. However, more than once the potential risks of these experiments have caused scientists to cease work, come together, and recommend safety precautions and methods to censor their work (Kaiser and Moreno 2012). In 1974, the journal *Science* published a letter written by prominent scientists recommending a voluntary moratorium on recombinant DNA experiments until the risks could be evaluated (Berg et al. 1974).

The following year, more than 100 molecular biologists met at the Asilomar Conference center near Monterey, California to debate the risks involved in the then-emerging field of recombinant DNA technology (Watson et al. 1992). At that time, scientists were concerned about the risks of using the new techniques that permit isolating DNA from one organism and inserting it in a vector to create a recombinant DNA molecule that is then inserted into a host cell to be replicated (Watson et al. 1992). Scientists were especially concerned about public health risks and biosecurity issues. They worried about causing harm to themselves and others by transmitting DNA from tumor cells that could inadvertently cause cancer or by unintentionally creating a weaponized pathogen (Watson et al. 1992). Many of these early issues initially raised by scientists have been resolved (Wright 1982).

The self-censorship meeting of scientists simply referred to as "Asilomar" was called an "expert town meeting" (Dworkin 1978, 1471) that ironically excluded the public. Asilomar provided the framework that led to the establishment of the *NIH Guidelines* in 1976 to provide institutional and NIH oversight (Dworkin 1978; Shipp 2003; Watson et al. 1992; Wright 1982). Asilomar is a touchstone for scientists whenever they are shaping governance of emerging technologies (Kaiser and Moreno 2012; Petsko 2002).

Concerns about the potential risks of new technology to health and the environment continue today, as achieving the right mix of "policies to maximize benefits while minimizing risks is not an easy task" (Rodemeyer 2009, 11). Advances in recombinant DNA techniques have progressed in many areas, including synthetic biology, gene therapy, and research with a potential for misuse referred to as dual-use research. As these areas of biotechnology continue to progress, the public—and scientists themselves—continue to raise concerns about the risks and benefits of applying the same recombinant DNA regulatory framework to these next-generation recombinant or synthetic nucleic acid molecular technologies during the research phase (Rodemeyer 2009).

The *NIH Guidelines* were recently amended in a major way to cover synthetic nucleic acid research that has equivalent risks to those of recombinant DNA research (*NIH Guidelines* 2013). Once synthetic nucleic acids are placed in a biological system, they may be subject to the *NIH Guidelines* if they pose the same risks as recombinant DNA that is subject to the rules.

The *NIH Guidelines* also recently underwent minor amendments after NIH-funded research engineered a highly pathogenetic H5N1 avian flu virus that became transmissible to mammals (Kaiser and Moreno 2012). In 2012, a publishing debate ensued, and researchers imposed a voluntary moratorium on H5N1 research that increases pathogenicity, transmissibility, or extended range of hosts, especially humans. This debate about dual-use research that can benefit public health or be used for destructive purposes has been called "a shining example of scientists' ability to act responsibility when unfettered" (Kaiser and Moreno 2012, 345).

Local Communities

At the same time that the *NIH Guidelines* evolved, some communities with recombinant DNA laboratories within their jurisdictions conducted public meetings with a variety of

stakeholders to discuss the risks and oversight of recombinant DNA experiments (Krimsky 1982). In 1977 Cambridge, Massachusetts became the first city to regulate recombinant DNA with a public health ordinance that includes a mechanism for community member participation (Lipson 2003). Since then, several jurisdictions in the Commonwealth of Massachusetts, including Boston, have enacted local recombinant or synthetic nucleic acid molecule laws largely modeled after what was done in Cambridge (Feldman and Lowe 2008).

The Cambridge effort to regulate was criticized by some as an impediment to scientific freedom and a barrier to attracting commercial biotechnology (Feldman and Lowe 2008). These reservations have proven to be unfounded as the consensus-building within the Cambridge community has created a biotechnology-business-friendly area that is thriving (Feldman and Lowe 2008). Massachusetts has actively supported the adoption of local public health ordinances to regulate recombinant or synthetic nucleic acid molecules with a BioReady® Community Campaign (*Mass Bio BioReady® Communities* 2013). However, Massachusetts has not been successful in enacting a similar law to cover the entire commonwealth.

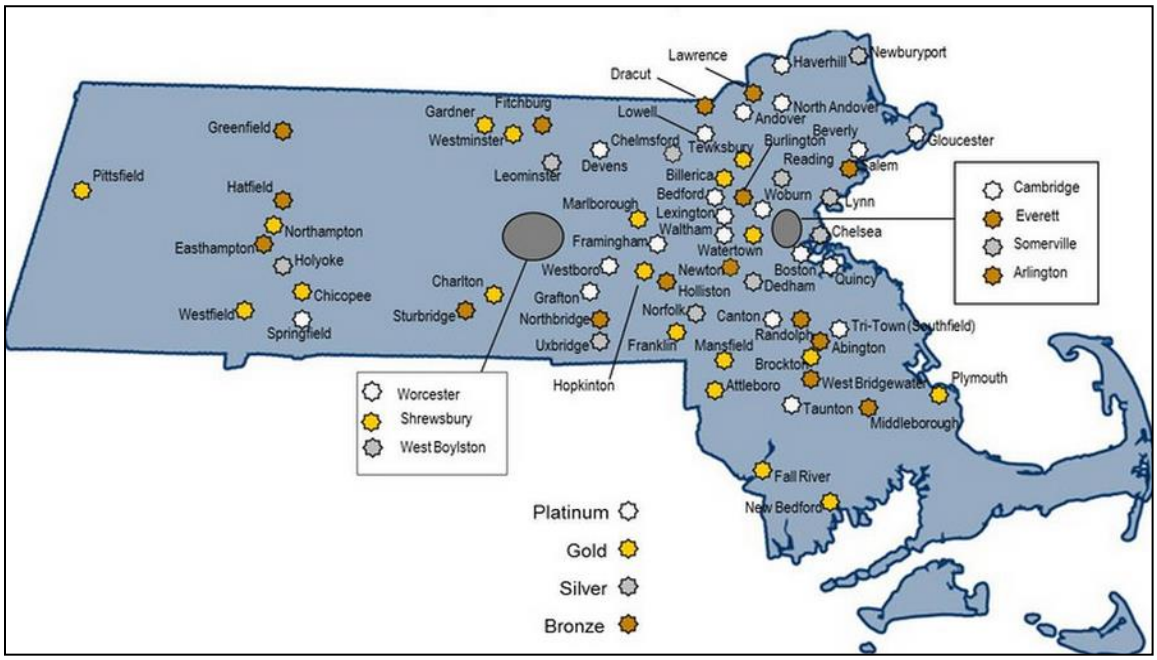

Figure 2. Locations of Massachusetts BioReady® Communities

Source: Mass Bio BioReady® Communities. 2013. http://www.massbio.org/economic_development/bioready_communities (accessed April 15, 2013).

Protecting the public health and the environment is important in Massachusetts because it houses 48 non-governmental NIH registered facilities (Jambou 2013). Massachusetts is the leading life sciences research and development state, employing nearly 30,000 people in this field (*MassBio* 2013). Without local ordinances, many facilities would not be regulated with respect to recombinant or synthetic nucleic acid molecules, as no federal or commonwealth laws regulating recombinant DNA or synthetic nucleic acid molecules exist.

Several Massachusetts communities have followed Cambridge in adopting local health ordinances that aim to promote research while protecting public safety and the environment (*Mass Bio BioReady® Communities* 2013). The local boards of health have the authority to implement their own biological laboratory recombinant DNA technology ordinances. Many

communities have slowly promulgated these ordinances to provide oversight as facilities, especially those with high-containment biological research laboratories, are being built in their jurisdictions.

Such an ordinance gives the local community the opportunity to involve citizens by including residents and the local board of health as appointed IBC community members for the facilities in its jurisdiction. Some communities have enacted ordinances that include restrictions on facilities requiring BSL 3 and BSL 4 standard microbiological practices, or they have imposed limitations on batch volumes of live culture in an effort to reduce the potential risks from accidental releases into the community that might cause a threat to public health if an incident occurred.

Just to demonstrate the reach of these local ordinances, nearly 100 IBCs are registered with the Cambridge Department of Health (Lipson 2013), yet fewer than 10 facilities located in Cambridge are registered with the NIH. This is because the former do not receive NIH funding for recombinant DNA or synthetic nucleic acid research that has equivalent risks to those of recombinant DNA research. The concept of local ordinances has not taken hold much outside of Massachusetts (Krimsky and Ozonoff 1979); therefore, Massachusetts provides an ideal environment for studying what impact these local ordinances have on compliance with NIH rules for IBC community members who also serve on NIH-regulated IBCs.

Public Involvement in Science

Public involvement in governance is defined as "activities initiated by government to encourage citizen participation" (Yang and Callahan 2007, 249). The motivation for seeking public input arises from a variety of reasons including normative, instrumental, and substantive justifications (Fiorino 1990). Normative justifications maintain that the public is in the best

position to judge their interests, especially if the research is funded by taxes. Instrumental justification addresses a lack of trust in the concept that public involvement legitimizes decision-making about risk factors, leading to better outcomes. A substantive justification affirms the usefulness of public involvement in decision-making where there is uncertainty. Fiorino (1990) contends that public involvement improves the decision-making outcome, particularly concerning social and political consequences.

Normative justification provided the basis to include community members on IBCs (Bereano 1984; Jennings 1986). The stewardship of public funds was emphasized by Berenao (1984), who testified at an NIH hearing in September 1978 and advocated IBC community members. He said, "much, if not most, of this research is supported by tax dollars paid by the general citizenry: risks to health, safety and the environment would be widely shared, and the benefits which have been suggested for such research would affect many sectors of society" (Bereano 1984, 23).

Instrumental justification was also described as a primary motivator for including community members on IBCs (Dickson 1988; Goggin 1986). The "exchange relationship" (Goggin 1986, 13) between science and society evolved in the 1970s as public trust declined, creating a legitimacy problem (Goggin 1986). Goggin (1986) maintained that governments became willing to include limited public involvement in science decision-making because of the legitimacy problem. Goggin (1986) further described structures for participation as "ceremonial–window dressing" (24) aimed at advancing public support. Furthermore, Goggin (1986) also believed society's standing has moved from "patron to partner and finally to servant of science" (13).

Substantive justifications were endorsed by participatory governance researchers who claim that community member involvement on IBCs created a competitive advantage for the community (Feldman and Lowe 2008; Lowe and Feldman 2008). A richer participatory infrastructure included the community in decision-making by creating an environment where emerging technology combines with local regulations to produce "socially and economically optimal outcomes by widening the public dialogue through participatory democracy and open decision-making process" (Lowe and Feldman 2008, 266). These authors show how Cambridge created support for the biotechnology industry while protecting public interests.

Factors for including IBC community members vary, and the reasons why particular members of the public become engaged in IBCs is not well understood. Scientific institutions that include citizen participation are seldom studied, even though it is widely accepted as a good practice to include the public in decision-making that affects the community (Yang and Callahan 2007; Fiorino 1990). In Massachusetts, facilities are required to establish IBCs in accordance with the *NIH Guidelines* if they receive NIH funding. If the facilities are located in a community with an applicable local ordinance, they are required to establish IBCs regardless of their NIH funding status.

Review of Relevant Research

This section reviews relevant research that examined IBCs. So far, research on the composition of IBCs is limited to a review of NIH files conducted before the creation of the community member requirement (Bereano1984), a 1980 survey involving 19 California IBCs (Dutton and Hochheimer 1982), and a 1987 national survey by the Government Accounting Office (Jaggar et al. 1987).

Prior to the community member requirement, a review of NIH files that looked at IBC composition found that 70% of IBCs had no community members (Bereano 1984). In 1984, Bereano indicated that this cursory IBC composition review demonstrated that IBCs had failed to give adequate consideration to personal and professional characteristics of IBC membership. The author also concluded that IBCs at that time were not representative of the communities in which they operate.

After the *NIH Guidelines* were revised in 1978 to include community members on IBCs, two published studies surveyed IBC composition (Dutton and Hochheimer 1982; Jaggar et al. 1987). Dutton and Hochheimer (1982) called the IBC community member requirement an "experiment in public participation in science policy" (11). The Dutton and Hochheimer (1982) study was a National Science Foundation–funded project investigating biomedical innovation and public policy. The Jaggar, et al. (1987) study was initiated by the U.S. House of Representatives Committee on Science, Space and Technology to review the capabilities of IBCs in overseeing recombinant DNA responsibilities, with an emphasis on containment of genetically engineered organisms. The committee asked the researchers to address four issues, including IBC membership. These studies provide data describing IBC community members at the time the *NIH Guidelines* were first put into action.

Both studies had high response rates. Dutton and Hochheimer (1982) sent separate surveys to all the chairpersons and all the unaffiliated community members of the 20 IBCs registered in California, and 19 chairpersons responded (95% response rate). In addition, 45 of the 48 community members responded (94% response rate). In 1987, the government initiated a new study that involved 1) a review of IBC records on file at NIH, 2) a survey sent to the 312

chairpersons of NIH-registered IBCs, and, 3) interviews with 20 federal officials (Jaggar et al. 1987). The survey had an 84% response rate.

In the first study, Dutton and Hochheimer (1982) found that all 19 California IBCs surveyed had at least 2 community members, as required by the *NIH Guidelines*. Although the researchers did not specifically report on the ratio of outsiders to insiders, they did report that the IBCs ranged from 7–16 members, with a range of 2–4 community members.

The Jaggar, et al. (1987) study did not verify the presence of community members, nor did it review the ratio of outsiders to insiders; however, they did report that 12% of the chairpersons affiliated with public facilities indicated that they probably would not retain community members on their IBCs if it were not an NIH requirement. Similarly, 7% of IBC chairpersons affiliated with private facilities indicated that they probably would not retain community members, and 2% said they definitely would not do so, if it were not an NIH requirement. These findings were in alignment with the Dutton and Hochheimer (1982) study that reported over 80% of chairpersons and just over 90% of community members holding a favorable opinion of the NIH requirements surrounding IBC structure and member roles.

The studies characterized community members and found them to be similar in education and occupation with insiders appointed to the facility IBCs. Many were engaged in recombinant DNA research or genetic engineering themselves, only at another facility. This classification calls into question whether the community members met the qualifications for representing the community interests in accordance with the *NIH Guidelines.* Dutton and Hochheimer's (1982) study found that 25% of community members were scientists, and Jaggar, et al. (1987) found through a records review that 50% of IBCs had at least one member classified as a scientist—more specifically, a genetic engineer.

Dutton and Hochheimer's (1982) data were based on the surveys completed by the IBC chairpersons and community members, along with a review of *curricula vitae* to clarify responses related to occupation and community affiliation. Jaggar, et al. (1987) reviewed NIH records to determine the occupations of community members, surveyed IBC chairpersons for occupational preferences, and reported on the percentage of IBCs having one or more community members with an occupation targeted in the *NIH Guidelines*.

Dutton and Hochheimer (1982) found that 33% of community members were public health or other government officials and 31% were classified as local citizens. The researchers noted that a quarter of all California IBC community members were scientists, with the majority of them engaged in recombinant DNA research at another facility. The researchers further concluded, after reviewing the *curricula vitae* of the community members, that they did not meet the qualifications to represent the community interests in accordance with the *NIH Guidelines*.

Likewise, Jaggar, et al. (1987) found 25% of the IBCs had at least one member with an occupation classified as public health, and 40% had at least one member classified as working in a medical occupation. The IBC chairpersons had a high preference for appointing community members in public health (70%) and medicine (50%). Interestingly, the IBC chairpersons indicated that they least valued the genetic engineering occupation for a community member (25%), yet more than 50% of IBCs had one or more community members who were classified as genetic engineers.

Dutton and Hochheimer (1982) conclude that the approach to implementing the community interests requirement was ambiguous and decentralized, inviting varying degrees of conformity with regard to the appointments of unaffiliated community members. Dutton and Hochheimer (1982) also conclude that differences in IBCs vary with local circumstances, and

"given a chance, public participation seemed to work fairly well" (15), but "without mechanisms for assuring accountability to community interests, public participation in biosafety committees has not been fully tested" (15), as is proven by the appointments of scientists who show no evidence of representing community interests. Jaggar, et al. (1987) concluded that there was a lack of occupational diversity in IBC members, with both affiliated and unaffiliated community members being mostly genetic engineers.

Shortly after the *NIH Guidelines* were revised to include community members in IBCs specifically to serve the community's interests, a high number of scientists served in that capacity. Therefore, it is reasonable to speculate that scientists remain prevalent in this role in current practice. Dutton and Hochheimer (1982) pointed out, decision-making dominated by scientists does not fulfill the *NIH Guidelines'* intent with respect to a "direct public voice in decisions at the local level" (11).

Deficiencies in the Studies

The limited nature of the reviews of IBCs provokes questions about the mechanisms that the NIH and local government bodies have put in place to provide recombinant DNA oversight at the local level. The committees' expanded decision-making, along with public policy mandating that two community members serve on every IBC in a representational capacity for the community, merits research to further explore factors associated with the composition of IBCs.

Summary

The IBC is on the front line of protecting the public interests with respect to scientific advancements involving recombinant or synthetic nucleic acid molecules, including human gene transfer, dual-use research, and synthetic genomics. No federal regulations cover recombinant or

synthetic nucleic acid molecule research, but the NIH opted for quasi–self-regulation at the facility level with IBCs. In 1978, a major revision of the *NIH Guidelines* included the requirement for two community members (20% of the participants) on IBCs. The current *NIH Guidelines* just stipulate two community members with no percentage requirement. Facilities that receive federal funding for recombinant or synthetic nucleic acid molecule research are required to follow the *NIH Guidelines*.

In 1977, Cambridge, Massachusetts became the first community to enact a local ordinance establishing IBCs that included community members to oversee recombinant DNA research (Lipson 2003). Since then, several other Massachusetts cities and towns have enacted local regulations governing recombinant or synthetic nucleic acid molecule research. This trend is being stimulated by the BioReady Communities campaign that started in 2008 (*Mass Bio BioReady® Communities* 2013). The number of facilities conducting recombinant or synthetic nucleic acid molecule experiments has grown, and NIH funding of for-profit facilities has increased.

IBCs and their community members are not well characterized. It is uncertain how IBCs are composed. Therefore, the present study characterized facilities by ownership type, administration type and local areas and ordinances. It also determined the composition of IBCs with respect to the percentage of community members and characterized IBC community members by education and occupation. The results of this study are useful to public health administrators involved in recombinant or synthetic nucleic acid molecule policy implementation.

THEORETICAL BACKGROUND AND CONCEPTUAL FRAMEWORKS RELATED TO GOVERNANCE

The literature identified board composition as a key influential governance characteristic that affects the board's ability to monitor management and leadership as well as make policies in the best interests of stakeholders (Dalton et al. 1998; Zahra and Pearce II 1989). This chapter provides a review of the theoretical underpinnings of governing boards that often serve to monitor leadership to ensure policies are serving the owner's interests. The first section is a review of the oversight framework in the *NIH Guidelines* and how they support community monitoring through IBCs. The next section reviews agency theory that advocates the power and control of organizational leaders need to be monitored by external board members (outsiders) to ensure that policies serve the best interests of owners or stakeholders. Then the concept of governance is reviewed followed by the conceptual framework for this study and the proposed research questions.

NIH Guidelines

Because of NIH's Office of Science Policy's role to monitor and provide oversight to NIH supported research, many of its guidelines and practices reflect the tenets of agency theory. This is demonstrated in terms of who should serve on the governing biosafety board at the facility level. The NIH has emphasized the importance of monitoring for IBCs as the nation's medical research agency is in a uniquely weak position of assuring the *NIH Guidelines* are being followed by NIH funded facilities the absence of the IBCs.

The primary role of IBCs is to ensure that the laboratory and clinical research involving recombinant or synthetic nucleic acid molecules is appropriately reviewed for conformance to

the *NIH Guidelines* and report violations and significant adverse events related to the research to the NIH Office of Biotechnology Activities (OBA). IBCs act on behalf of key stakeholders to ensure the safeguards prescribed in *NIH Guidelines* meet their needs and interests. Key internal stakeholders include laboratory workers, principal investigators and management. Key external stakeholders vary from gene therapy research participants to federal agencies including the NIH and local agencies including health departments. They also include research partners, clients and peer organizations.

The community where a NIH registered facility operates is a key external stakeholder that is especially concerned about containment procedures designed to protect the public and the environment from serious adverse events. Another key external stakeholder, the public at large, is concerned about risks associated with this emerging area of science including research participant safety and societal implications in general. Agency theory provides sound reasons for NIH's requirements that IBCs ensure implementation of the at the facility level.

The National Institutes for Health developed protocols within the *NIH Guidelines* that specify who ought to serve on biosafety review boards. In 1978, the importance of community participation on the biosafety review board was recognized with a required 20% level of outsiders as a means to control agency problems. The current version of the *NIH Guidelines* has IBC composition requirements that dictate a minimum of 5 total members with a minimum of 2 of those being external board members. However, the proportion of external board representation can vary depending on number of internal members as no proportion level of outside members is currently required.

In addition to the number of external advisory board members serving on IBCs, then *NIH Guidelines* require the biosafety review board's members have needed scientific and community

expertise to ensure appropriate oversight and monitoring of research conducted at the facility. These guidelines also suggest specific occupations for external members that include: officials from local or state health or environmental protection agencies; members of local government bodies; and those active in medical, occupational health, or environmental concerns (*NIH Guideline* 2013, 26).

Agency Theory

Agency theory is the dominant theoretical framework of corporate governance (Dalton et al. 2007; Durisin and Puzone 2009; Raelin and Bondy 2013). In publicly traded corporations, management is expected to make decisions in the best interests of investors and owners. An underlying tenet of agency theory is that agents (management) of the organization who are separate from their principals (owners or shareholders) will pursue their own self-interests rather than those of owners because of asymmetric information in which owners rely on management's institutional knowledge (Dalton et al. 1998). This "potential for mischief" (Dalton et al. 2007, 1) has confronted early scholars of management including Jensen and Meckling (1976) who defined the control based agency theory. Jensen and Meckling (1976) define the agency relationship as "a contract under which on one or more persons (the principal(s)) engage another person (the agent) to perform some service on their behalf that involves delegating some decision-making authority to the agent" (308).

Shleifer and Vishny's (1997) review of research on corporate governance mechanisms focus on the contractual nature of the relationship between the principal and agent that is formed to reduce managerial opportunism. Shleifer and Vishny (1997) discuss the notion of reputation building as a plausible cause of why agents deliver on agreed terms to cultivate their credibility as being a "good risks" (737) in order to bring future rewards even if the contracts are weak. The

conjecture that self-interest is the exclusive motivating factor behind agency risks is limiting. Agency risks are often stirred by incongruent goals or additional factors that escalate conflicts of interests (Buchanan 1996). In fact, Buchanan (1996) states, "All that is necessary is that there be conflicts of interests" (421).

Agency theory research was largely focused on corporate governance structures that protect the value of the firm and thus serves interests of shareholders. Now a "second layer" (Raelin and Bondy 2013, 422) of agency theory that benefits not only the firm, but benefits society as well demonstrates the significance of agency theory for governance studies. This notion that has been gaining traction creates a relationship between maximizing value and doing good (Thomsen and Pedersen 2000).

Governance

The term governance has no uniform definition in the literature. To put this in perspective; "It [governance] means what I choose it to mean- neither more or less" (Rhodes 2007, 1246). Traditionally governance has been a synonym for government yet it has a diverse application from corporations to public administration as an organizing framework for understanding the governing process (Stoker 1998). Governance has been described as "steering" (Kjær 2011, 103) or setting and enforcing a set of rules. Regardless of how governance is described or applied, it often is used to characterize the research covering board composition and structure. In fact, boards have been called "instruments of corporate governance" (Zahra and Pearce II 1989, 291). The idea that governance is a mechanism helps define the concept.

Board Composition and Characteristics

Because the role and contributions of community members is multifaceted this study of board composition and other characteristics will draw on agency theory from a monitoring perspective and resource dependency theory from an external resource perspective. Meta-analytic reviews show that board composition is well researched especially the proportion of outside board participation to control agency conflicts for publically traded firms (Dalton et al. 1998; Durisin and Puzone 2009; Finegold, Benson, and Hecht 2007). Agency theorists Fama and Jensen (1983) claim that governing boards act as a mechanism for the "separation of decision and risk-bearing functions" (301) that applies not only to public-traded corporations, but organizations with different ownership types such as non-profits and non-corporate partnerships.

Agency theory has been applied to board research in the non-profit and public sectors (Eisenhardt 1989; Wincent, Anokhin, and Örtqvist 2013). However, board characteristics and outside community representation are "understudied" (610) in nonprofit and public sectors (Gazley, Chang, and Bingham 2010). These sectors are similar to the corporate sector except legislators or regulators act as the principals and the board serves the public interests (Buchanan 1996; Gazley, Chang, and Bingham 2010). For example, in the case of IBCs, outside board members act as agents of the community in making decisions and policies about research involving recombinant or synthetic nucleic acid molecules.

Fama (1980) argued that increasing the proportion of outside directors will increase board independence and in turn enhance the firm's financial viability. Boards with an increased percentage of outsiders have been found to be beneficial where successful board intervention has been linked to a governance process (Durisin and Puzone 2009). Applied to modern good governance oversight boards provide another layer to oversee society interests (Raelin and

Bondy 2013). It is reasoned the role of outsider board participation makes the IBC more independent from management and thus better able to act as community or stakeholder agents.

In certain situations effective board monitoring required specialized knowledge to effectively exercise monitoring and oversight. Outside board members often influence through advice and counsel or "human capital" (Hillman and Dalziel 2003, 383) and thus help the board to act on behalf of stakeholder. Recent studies have reviewed the external board members' advisor function as an important role claiming that expert knowledge improved their monitoring vigilance that, in turn, improved firm performance (Krause, Semadeni, and Cannella 2013; Kroll, Walters, and Wright 2008; McDonald, Westphal, and Graebner 2008).

This aligns with the theory of Fama and Jensen (1983) that claims the agency problem, namely, insider board members not acting as agent for stakeholders or community is mitigated with knowledgeable outsider board members who can actively monitor board decisions and address asymmetric information held by insiders. In fact, board outsiders with expertise provide an information advantage to boards. Therefore, the presence of relevant expertise at the governance level enhances the control mechanism of the board.

Organizational Factors Affecting Governance

A stream of research has shown that ownership structure has consequences for governance among various organizational types (Shleifer and Vishny 1997; Short 1994; Thomsen and Pedersen 2000). Firms, non-profits, universities, hospitals and most other organizations are 'legal fictions which serve as a nexus for a set of contracting relationships among individuals" (Jensen and Meckling 1976, 310) with organizational types needing different sets of contracts. Jensen and Meckling (1976) go so far to say "contractual relations are the

essence of the firm" (310). Ownership structure matters in formulating risk perceptions and social goals among other organizational strategies (Thomsen and Pedersen 2000).

Resource Dependency Framework

An alternate view of agency theory is resource dependency theory which provides insight to outside board composition. Resource dependency theory views the organization as an open system where the governing board has a role in attracting resources more so than monitoring. The idea of expertise is in alignment with other theorists that view boards through a relationships lens where networks are formed by board members with other individuals in organizations the community and government that often involve a resource exchange (Mizruchi and Koening 1991; Pfeffer and Salancik 2003).

For example, Pfeffer (1973) shows that effective hospital board members are selected based on the resources they can provide to organization. These influential board members help the organization network with other organizations and source needed resources. According to Pfeffer (1973), it was common to have bankers serve on hospital boards to help hospital secure funds and bonds to finance projects and operations. In practice, outside board members no matter the organization type or level monitor activities and provide resources, both though a network of ties to other organizations and their own experience, expertise, and reputation (Hillman and Dalziel 2003). Hence, agency theory and resource dependency theory are useful frameworks to understand and examine the composition of governing boards such as the IBC.

Conceptual Framework

This section presents board attributes and methods of measuring local governance mechanisms in laboratory and clinical research involving recombinant or synthetic nucleic acid molecules that operationalize the board attributes as they relate to IBCs. The board attributes

reviewed in this study includes board composition, characteristics, and structure. Composition refers to the proportion of outside members as compared to inside members. Characteristics refer to the members' scientific background and outsiders' occupation conformance with *NIH Guidelines*. The scientific background is measured by the proportion of insiders and outsiders with scientific expertise measured by occupation and the presence of a doctorate degree. Structure refers to the organization of the board as it relates to the presences of a system-wide IBC.

Other descriptive factors about the facilities and the environment where they operate will also be determined to have a better description of those facilities and determining if these factors have relationships with governance attributes. These factors include facility ownership, located in the Boston metro area and located in a municipality that regulates biosafety.

The conceptual framework used to formulate this exploratory study of NIH registered IBCs follows these core factors:

1. The NIH relies on both for- profit and not-for- profit organizations in conjunction with governmental research laboratories to meet research goals based on public value.
2. The *NIH Guidelines* gives the authority to IBCs to monitor facility biosafety risks associated with the NIH funded research involving recombinant or synthetic nucleic acid molecules.
3. Because the *NIH Guidelines* require two outside members be appointed to every IBC, these members serve as outsiders monitoring the facilities conformance to the *NIH Guidelines*.
4. The percentage of outsiders to total members captures board composition. Community members are independent board members, thus free from management influence. Their role in safeguarding the community interests conforms to the underlying monitoring principles.

5. Community members provide an outsider perspective with expertise and counsel on matters in safeguarding the community. The *NIH Guidelines* require certain experts on the IBC. Insights that show the science expertise and education attributes of board members as a facet of the role of expert will need to be explored.
6. Community members provide a means to facilitate linkages to the community and legitimacy to the facility from a community perspective.
7. System-wide IBCs are accepted by the NIH as a structure that combines the members of more than one IBC in practice yet registers the IBCs separately.
8. Local ordinances provide and additional layer of oversight. This is not widely implemented; in fact, local biosafety ordinances are unique to Massachusetts.
9. Life science research facilities are typically located in biotechnology clusters such as Boston.

Proposed Research Questions

1. What is the profile of NIH registered IBCs in Massachusetts?
    a. Governance - percentage of community members, and expertise defined by occupation and education
    b. Organization - ownership type, IBC administration type
    c. Location - Boston Metro area location, local ordinance
2. What are the relationships between IBCs composition at or above and below 20% community member participation and organizational and local area characteristics?

MATERIALS AND METHODS

This section outlines the methods used to accomplish the research objectives. The focus of this study are the biosafety advisory boards of registered biotechnology facilities that conduct laboratory and clinical research involving recombinant or synthetic nucleic acid molecules. These facilities receive NIH funding for research and are required by NIH to have biosafety advisory boards with community member participation to oversee this research. These advisory boards are referred to as IBCs – which stands for Institutional Biosafety Committees. The intent of this investigative study is to examine all IBC advisory boards in a geographic area. The Commonwealth of Massachusetts was selected because it has a disproportionately high number of biotechnology research facilities as compared to the rest of the country and therefore is considered active biotechnology hub worthy of examination. The purpose of this section is to, define the study population, clarify the study design, describe the data sources and data management procedures, identify the variables and values, and explain how the data were categorized and examined to address the research question.

The Study Population

This is investigative research for several reasons: 1) there is no public information available re: IBCs and their advisory board members, 2) even though the NIH requires community board member participation on IBCs that receive NIH funding, these data have not been systematically collected. Because biotechnology facilities are influenced by local and state regulations, the decision was made to select a state with an active biotechnology industry that would enable examination of the state's population of NIH funded biotechnology facilities and their advisory boards.

Another important reason to study Massachusetts is that it is a leader in early-stage biotechnology research and development and adopter of local biosafety ordinances to oversee compliance of this research. The examination of IBCs in the Commonwealth of Massachusetts provides data about numerous NIH funded facilities that operate in a defined area where local ordinances can influence the structure and policies of IBCs. The unit of analysis in this exploratory study is NIH-registered IBCs in Massachusetts.

Massachusetts is a clear leader in early-stage biotechnology research and development, where recombinant or synthetic nucleic acid molecules can be incorporated in experiments that require IBC review. The early adoption of local ordinances, coupled with the role this biotechnology cluster played in sparking public involvement in recombinant DNA research, further strengthens the rationale for selecting this location for this study. The effectiveness of local ordinances in regulating biosafety and creating an environment that embraces biotechnology is not well understood. Massachusetts is unique in that it was the first state to have a local ordinance adopted (in Cambridge), and also because it has actively supported the adoption of local public health ordinances to regulate recombinant or synthetic nucleic acid molecules.

Massachusetts also offers the opportunity to examine IBCs that are part of a system when two or more facilities operate their IBCs jointly. This is an emerging trend that provides administrative productivity enhancements. Given that three system-wide IBCs operate in Massachusetts, the influence this is phenomenon has on IBC governance can be explored.

Massachusetts ranks first in early-stage research and development employment with 27,883 employees working in biotechnology research and development (*MassBio* 2013).

Massachusetts continues to grow in this sector and ranks second in biotechnology research and development job growth with just over 3,000 jobs added in the last six years (*MassBio* 2013).

The profile of facilities located in Massachusetts that received NIH funding in fiscal year 2012 was constructed (Table 1) to show that the NIH is an important funding source for all organization types. Massachusetts ranks second as an NIH award recipient, accounting for 4,897 awards collectively valued at $2,559,628,069 in fiscal year 2012 (*NIH RePORTer* 2013). In total, 50,929 awards were given to U. S. facilities in 2012 totaling $23,812,931,760 according to a query of total 2012 NIH awards by state in RePORTer. Only California exceeded Massachusetts in the number (7,768) and amount of awards ($3,474,569,212) in 2012.

Table 1. Massachusetts NIH award recipients by organization type[a] 2012

Facility Type	Number of Facilities	Total Awards	Funding
Higher Education	23	1,900	$955,916,990
Hospitals	13	2,432	$1,193,521,362
For-Profits	119	209	$108,184,427
Research Institutions	28	356	$302,005,290
Total	183	4,897	$2,559,628,069

A limited number of the 183 facilities in Massachusetts that received NIH funding during the study year conduct experiments that fall under the *NIH Guidelines* or maintain a NIH-registered IBC. Table 2 provides an overview of organizations by type with registered IBCs in Massachusetts. Because a condition of NIH funding is compliance with *NIH Guidelines* for the facilities that do research involving recombinant or synthetic nucleic acid molecules, those facilities that must comply could put their funding at risk if they fail to follow the *NIH*

[a] See http://report.nih.gov/award/index.cfm

Guidelines. Audit records obtained from the NIH Office of Biotechnology Activities (OBA) show that NIH compliance reviews have recently occurred in Massachusetts. The facilities selected for the audits include Tufts University, Tufts Medical Center, Harvard Medical School, and the University of Massachusetts Medical School.

Table 2. Massachusetts NIH registered IBCs by organization type 2012

Facility Type	Number of IBC Registered Facilities
Higher Education	16
Hospitals	12
For-Profits	11
Research Institutions	9
Total	48

The study population for this study consists of all NIH registered IBCs serving 48 nongovernmental facilities that are located in Massachusetts. This group was not randomly selected; rather, Massachusetts was chosen for this study because of the rational described in this section. Therefore, while examining the population of IBCs in the Commonwealth of Massachusetts makes data collection manageable, this population also provides a rich landscape to view the composition of the biosafety advisory boards to assess their ability to monitor and oversee cutting edge biotechnology research.

Study Design

A fact-finding approach is an appropriate way to move forward when identifying preliminary details about a topic (McNabb 2013). The literature review showed that there is a clear lack of current information and research about IBCs. The literature review also provided the contextual factors for data assembly, defining variables and developing a research question. New concerns about the topic were identified to establish the importance of studying the issues surrounding IBCs.

Previous studies about IBCs provided information about how they were reviewed by the researchers and what those researchers discovered, what they overlooked, and what was deemed important during the time of the review. This study is a first step to systematically identify the structural profile of facilities with NIH-registered IBCs referred to as facility variables. Then examine the composition and selected characteristics of outsiders that serve on IBCs referred to as governance variables. Once the descriptive characteristics are identified and correlated, binary logistic regression will show which facility variables may be appropriate predictors of board composition.

Agency theory, the dominant governance theory (Dalton et al. 2007, 1; Raelin and Bondy 2013) offered the conceptual framework used to examine the features of the *NIH Guidelines* requiring outsider board participation. The NIH relies on both for- profit and not-for- profit organizations in conjunction with governmental research laboratories to meet research goals based on public value. The *NIH Guidelines* gives the authority to IBCs to monitor the risks associated with the NIH funded research involving recombinant or synthetic nucleic acid molecules.

Because the current *NIH Guidelines* require two outside members be appointed to every IBC, these members serve as outside agents monitoring the facilities conformance to the *NIH Guidelines*. Community members are important to the IBC because they provide an independent perspective that reflects the interests of the community. As outsiders, community members serve to monitor actions of the IBC to ensure that community interests are safeguarded. Outsiders' role in safeguarding the community interests is consistent with the underlying principles of agency theory as described by Fama and Jensen (1983). In addition to two outside members, the 1978 version of the *NIH Guidelines* also stipulated that at least 20% of the membership be

outside members (Bereano 1984, 16-34). It is unknown what impact the elimination of this composition percentage requirement has had on the composition of insiders and outsiders.

Institutional Review Board

The proposal for this study was submitted to the University of Baltimore Institutional Review Board. The study was classified as exempt because the data for this study are publically available and no personal identifiers were included in the coding of data. The study was reviewed and approved prior to data collection.

Data Sources

This analysis focuses only on the IBCs registered with the NIH OBA for facilities that are located in Massachusetts. The number of such IBCs in the United States and in foreign countries has grown from nearly 250 in 1984 (Bereano 1984) to 873 in 2012 (Jambou 2013). Table 3 shows that of the 873 registered IBCs, 768 are in the United States. California has 90 registered IBCs the only state with appreciably more registered IBCs than Massachusetts.

Table 3. Top 10 states with most NIH registered IBCs in US 2012 (N=768)

State	Total
California	90
Texas	52
New York	51
Massachusetts	50
Florida	43
Pennsylvania	34
Illinois	30
Maryland	27
Washington	24
Louisiana	20
All other states	374

A facility with an NIH-registered IBC is required to submit an IBC roster annually to the NIH OBA (*NIH Guidelines* 2013). Data about the NIH- registered facilities and their IBCs were

primarily collected from the most recent IBC rosters reported by IBC administrators located in Massachusetts to the NIH OBA. Data were also obtained from an IBC facility list provided by the NIH OBA and the NIH Research Portfolio Online Reporting Tools (RePORT). Additional data about local ordinances and limited community member information were obtained from online sources not affiliated with the NIH.

Records obtained from the NIH OBA were used to identify all the facilities with registered IBCs. This NIH Office oversees compliance with the *NIH Guidelines* and maintains the records associated with IBCs. Facilities that receive NIH funding for projects that employ research methods that fall under the *NIH Guidelines* must register with this office annually by providing a roster of their IBC. The population of registered IBCs located in Massachusetts was drawn from these NIH OBA records.

IBC Rosters

The IBC rosters provide the dimensions of interests to this study about the facility and IBC. In summary, facility officials are required to provide specific information about the facility and the membership annually. This information is sufficiently detailed to cover the variables about the facility itself and the IBC. Annually, the facility official must submit a signed IBC roster identifying the facility, system-wide affiliations, the facility address, and IBC administrators' contact information to the NIH. In addition to the facility information, the roster must list all IBC members, with specific information about each member. A biographical sketch for every member must also be included with the submission. Table 4 depicts the member information that must be included to comply with this submission requirement as specified by the NIH Office of Biotechnology Activities.

Table 4. IBC member information required in the Annual Facility Report

Name
Title
Business mailing address
Phone number
Fax number
E-mail address
The role of the member: e.g., chairperson, contact person, non-institutional community member, special expert as relevant (biosafety officer, expert in plant research involving recombinant DNA, plant expert, expert in animal research involving recombinant DNA, animal expert, etc.)

The year the IBC roster was submitted was reviewed to determine if facilities are meeting the IBC annual registration requirement. A submission date in 2011 -2012 was defined as a current submittal for the purposes of this study since the registration must be completed within 12 months of the last registration. An annual submittal due date for all facilities is not imposed by NIH.

The NIH OBA provided rosters for all 48 non-governmental facilities with registered IBCs. Most of the facilities had current IBC rosters on file with the NIH OBA. Of those facilities with registered IBCs, 37 (77%) had current registrations based on a (2011-2012) submission date on their roster. Closer examination reveals that 21 facilities (44%) registered in 2012 and 16 (33%) registered in 2011. In addition, 11 facilities (23%) had older rosters on file with submission dates between 2010 - 2004. Of these 11 facilities with older rosters, 5 had not received NIH funding in 2011 or 2012, so these 5 facilities are classified as voluntarily registering their IBC.

Once the facility official submits the annual registration, the IBC administration coordinator at the NIH OBA completes a facility report that includes a checklist to assure that the roster is complete and fulfills the IBC membership requirements including two community members. Once the quality review is complete, the submitting facility receives a confirming letter from a representative of the NIH OBA indicting that the facility is in compliance with this requirement or is otherwise not compliant. Therefore, the 2012 roster data were regarded as accurately reported by the IBC administrator and checked by the NIH OBA office.

List of Current IBCs

NIH OBA provided a list with 873 facilities with registered IBCs identifying the name and address of the facility. This 2012 list was used as an indirect check to affirm that rosters were provided for all NIH-registered facilities in Massachusetts. Errors in addresses on this list where facilities were coded in Massachusetts but actually were not were identified then verified before eliminating the facility from the list. Once these facilities were eliminated the list was in total alignment with the rosters. The lists also provided the total number of facilities in the population and their facility name and address.

NIH Research Portfolio Online Reporting Tools (RePORT)

Information about the facility type was verified by a query on the NIH RePORT Awards tool. The NIH RePORT website provides access to data about NIH research. For the purposes of this study, data were sorted based on geographic region and organization type. Data about NIH-funded research important to this study was queried by using the "Awards by Location and Organization" tool on NIH RePORT. The fiscal year 2012 was used because the most current rosters provided by the NIH OBA were also from 2012, and the data were frozen at the end of each fiscal year. RePORT freezes at the end of the fiscal year, thus the data should not vary and should provide consistency.

Data Collection Approach

To obtain NIH records under the Freedom of Information Act (FOIA), a written request was sent to the NIH Freedom of Information Officer in January 2013 requesting: 1) a list of all current registered IBCs with their organizations' names, addresses, and contact information; 2) all the most current IBC rosters, listing their membership, submitted by organizations per *NIH Guidelines* Section IV-B-2-a-(3), which requires institutions to register their IBCs with the NIH OBA and update their registrations annually (*NIH Guidelines* 2013); 3) biographical sketches (e.g., curricula vitae or résumés) of community members located in Massachusetts; and, 4) audit records for reviews performed in Massachusetts.

The list of IBCs was provided by the NIH OBA in an Excel (Microsoft Corporation, 2010) file before the rosters were sent. The request for IBC rosters and community member biographical sketches was deemed voluminous by the NIH Freedom of Information Officer, and it was determined that the information would not be forthcoming in the near future unless the request was substantially modified. The request was then modified to include the most recent

IBC rosters of the membership submitted by organizations per *NIH Guidelines* for Massachusetts. This information was received in a Portable Document Format (PDF) file in August, 2013. The request for biographical sketches was withdrawn.

Developing the Data Set

First the Excel list of all 873 registered IBCs was sorted by state or foreign nation in Excel. After this the population, defined as the facilities located in Massachusetts, was copied and pasted into a new Excel spreadsheet. Only the facility name and city were copied into the columns as the starting point for this data set.

The new data set was checked to make sure all of the facilities met the inclusion criteria: for-profit and not-for-profit facilities located in Massachusetts with IBCs registered with NIH OBA during the study period. First, the facilities' cities, identified in the addresses provided in the original Excel spreadsheet, were cross-checked by searching for the facilities' addresses in NIH RePORT to verify the facilities' location. Then the data set was compared with the 50 IBC rosters.

Facilities that were not located in the geographic area of the study were deleted from the data set. Of the 57 facilities in the data set, 7 were excluded because they were not located in the geographic area of the study or because they were no longer registered with the NIH OBA. In addition, 2 government facilities were omitted from this study because they did not represent the facility ownership types under review. Consequently, there are 48 facilities in this study population.

Components that make up the data set were collected and first combined in an Excel file to standardize data analysis. The data set was formed by sorting the information provided in the Excel spreadsheet from NIH. The information on the spreadsheet that was important for the

research was the facility name and city location. Each column represented a variable, and all variables were assigned abbreviated names by placing the name in the top row. The variables were ordered on the basis of the organized level of collection, including facility, IBC, and IBC community member.

The facility-level variables' names were listed in the columns just after the facility identification number. These variables included ownership type, whether there was a local ordinance at the location and if the facility IBC has a system-wide affiliation.
Variables about the IBC characteristics followed. The IBC roster identification number was included as a reference point to ensure that the values were taken from the correct roster associated with the facility. The next column showed the IBC registration year. Further columns held the total number of members, then number of voting internal members, and then the number of voting community members.

Columns to collect values about community members were developed at two levels on the spread sheet, since each facility had a maximum of three community members and the data to be recorded was associated with both the member and the facility. Because the maximum number of community members on any IBC was three, the variables at the community member level were captured for each member in columns named "Community Member 1," "Community Member 2," and "Community Member 3." A column was added in the row below each community member to add a distinct community member number. This was followed by additional columns for each community member, to which were added the variable labels for community members, including occupation, education level, and system-wide membership.

Populating the Data Range

The data set was formed by listing the names of the facilities in alphabetical order along with the facility identification number and the city where the facility was located. First the actual data were entered in a column next to the variable value in a prescribed order to optimize the records review. Then the value labels were determined using the chart summarizing study variables, which identified the variable label, variable name, value labels, and research question.

Observations gathered from records were assigned numeric codes. Observations for each variable were systematically added to the spread sheet by inputting the value code that matched the observation. After the spreadsheet was given a quality-control check, the Excel file was transferred into the Statistical Package for the Social Sciences (SPSS),Version 20.0, (IBM Corporation 2011) for data analysis. The values in SPSS were then rechecked for missing data and accuracy. Dichotomous categorical variables were coded where the value of 1 was assigned if the observation was affirmative and 0 was assigned otherwise.

IBC Roster

Paper copies of the IBC rosters were reviewed and pertinent information was highlighted in a prescribed order to optimize the records review and minimize errors in transferring the values to Excel. First, each IBC roster was assigned an identification number in the order they were reviewed. Key information was highlighted; it included year IBC submitted by facility to NIH OBA, facility name, system-wide name, community member name, community member doctorate distinctions, and community member job title. Then the total number of people listed on the record was counted and noted on the record. This was followed by a count and notation of all voting members, then voting insider members, and finally voting community members.

The names of community members for every facility were listed in a column as it appeared on the rosters. Once all the names were listed, the column was sorted in alphabetical order and the community member was assigned a unique number based on the sorted order. This number was transferred to the master spreadsheet based on IBC affiliation(s) so that each community member had a unique identification number.

NIH RePORT

The NIH web-based tool, RePORT, was accessed to determine the facilities' organization and ownership type. Each facility that receives NIH funding is classified in NIH RePORT as one of the following organization types: 1) domestic higher education, 2) research institutes, 3) independent hospitals, 4) domestic for-profits, and 5) other domestic not-for-profits. For purposes of this study, research institutes and other domestic non-profits were later combined into one category, not-for-profit/research institute. This data were then recoded to categorical dichotomous variables not-for-profits and for-profits.

Data can be filtered by fiscal year and by many other parameters on the NIH Awards by Location & Organization page in RePORT. Those that were important considerations for this study included the state where the recipient organization was located, the type of recipient organization, and the name and contact information of the recipient organization.

The information of primary concern was how NIH categorizes award recipients by organization type. To explore organization type, the "Fiscal Year" in RePORT was set at 2012 and the "Institute/Center" was set at "All," as was the "Funding Mechanism." Massachusetts was selected as the location, and then each organization type was selected and submitted separately to create a report that was downloaded into Excel.

Internet Search

A municipality where a particular facility was located was already listed on the spreadsheet. The municipality column was sorted alphabetically in Excel. Census.gov was accessed to determine what cities and towns are included in The New England City and Town Area (NECTA) Division number 71654 Boston-Cambridge-Quincy, Massachusetts. In the preliminary analysis this list was compared to the facilities in the study population to determine if they were within the boundaries of this biotechnology hub.

An Internet query of local ordinances was conducted. Since municipalities vary in how they describe recombinant DNA regulatory requirements, the applicable public health department list of regulations was scanned or searched using key phrases including the following: 1) recombinant DNA technology, 2) biosafety committees, 3) regulated biological agents, and 4) biological laboratory regulations. Regulations that were identified were further scanned for IBC mandates, including community membership requirements. A list of cities and towns with local ordinances was developed from this search. This list was compared to the facilities in the study population to determine if they were within the boundaries of a municipality with a local ordinance.

Community member data were also drawn from other sources on rare occasions when the job title or occupation of the community member was not on the roster. This situation typically occurred when the community member was listed by his or her home address because they did not hold a position at another facility. The home address was redacted from the roster by the NIH OBA. Other sources of information included facility web pages and searches on LinkedIn in attempt to verify the community member without a job title was not an oversight by the IBC administrator.

Potential Data Collection Problems and Solutions

This section provides an overview of how data collection can affect the accuracy of the study results. Some records provided by NIH needed to be augmented with data from other sources when the records were incomplete or redacted. The reliability and consistency of data sourced from IBC membership rosters submitted by organizations was high because the *NIH Guidelines'* Section IV-B-2-a-(3) requires institutions to register their IBCs with the NIH OBA and update their registrations annually.

The consistency of data on IBC rosters was high because the IBC administrators are required to include the facility's name and address and the name, job title, business mailing address, fax number, e-mail address, and role of each member. Since the request for biographical sketches (e.g., curricula vitae or résumés) of community members was deemed voluminous by the Freedom of Information Officer, that secondary source of data was not available for this study. Therefore, other data collection modes used to collect data about a limited number of community members may increase the source of error in community member variables.

In a few cases, the community member information was redacted from the record if a home address were on the record. Such community members are typically retired or not working; therefore, their contact information is listed as a home address, which requires the agency to redact the information to protect this personal information. In these cases, LinkedIn and the facility web page was accessed to verify that the community member's job status was retired and the member did not hold a job title. If a job title was absent from the roster and the individual's job title was not identified by another means, or the member was listed as retired on the roster the occupation was coded as "community member."

Although it is customary to include an earned doctoral degree after a name if appropriate, it is impossible to be certain whether this information was included. This potential quality problem was dealt with by looking for a pattern of including terminal degrees on the IBC roster for members, and then checking an alternate source for this distinction. It is most likely that the target group is highly educated. If terminal degrees were included for some members, it was most likely that they were included for all members who held an earned doctorate.

The year the roster was submitted was based on the receiving agency's date stamp. If a stamp was not present, the year used was based on the date provided by the IBC administrator as listed on the roster. In some rare cases where neither existed, the year used was based on the date the agency uploaded the file into a PDF record.

Bias is defined as the difference between the real values of variables and the observed values generated (Czaja and Blair 2005). The problems that lead to bias should be minimized by gathering data from official NIH documents and submittals as a first choice in data collection rather than using a survey or interview.

The data gathered for this study was classified as similar or different based on the categories of the variable. Numbers were assigned to characteristics with a set of pre-determined numerical codes. For example, a characteristic was given a number 1 if it was present and if the characteristic was missing 0 was assigned. Steps were taken to minimize data entry error by integrating a coding scheme into the Excel spreadsheet by pre-coding values and placing numerical codes for values on the data source and in each Excel field to facilitate data entry (Babbie 2007). The data entry process was designed in such a way as to avoid confusion and skipping. Clear headings on columns and rows and fixed reference points were provided in Excel to minimize missed codes or key stroke errors.

Cleaning procedures checked for coding entry errors before and after the data were transferred from Excel into SPSS. Data were reviewed at the time of entry. Error codes were developed, and all identified errors received an error code to track the types and frequency of errors. A review for errors was conducted for each variable after all the data had been entered. A frequency distribution of all variables was conducted to identify missing data. If an error was found or suspected, the original data source was accessed and a correction was made if necessary.

Data recodes were needed before data analysis when data categories were combined to simplify analysis or provide another view of the variables. In addition, composite measures were developed to provide a more complete analysis. These recoded data and composite measures are identified in the table below along with the all the variables.

Once all the values were coded on the Excel spreadsheet all identifiers—with the exceptions of assigned facility number, IBC roster numbers, and community member identification numbers—were removed. All of the values were coded and checked, and then the Excel spreadsheet was uploaded into SPSS.

In summary, value codes were entered into Excel in the following order: 1) facility attributes, 2) IBC attributes; and 3) community member attributes. The IBC roster was the primary document used in collecting data, with the exception of facility organization type; the NIH RePORT database was accessed to determine the latter category. Organizing the data and coding it in a specific order streamlined the data collection process. Because data were generated specifically for this study there were no missing values.

Facility Variables

A profile of the facilities in Massachusetts that have NIH-registered IBCs was constructed from NIH records. The facility characteristics summarized in Table 5 include ownership, system affiliation, Boston metro and local ordinance. The structural variables of IBCs that include ownership and system affiliation are expected to influence the composition of the IBCs; the presence of a local ordinance is also likely to affect the composition of the IBC. These dichotomous categorical variables will serve as predictor variables for the binary logistic regression model.

Ownership Type

Because the NIH has external resource dependency on facilities with different facility types; for profit and not for profit, both were analyzed to determine if there are differences in IBC board composition based on ownership type. Facilities that are of the same ownership type are likely to have similar reactions to external factors, according to DiMaggio and Powell (1983).

Categories of ownership included in this study are not-for-profit facilities and for-profit facilities as identified by the Internal Revenue Code. Government facilities were not included in this study. Facilities that qualify for tax exempt status and are not established to make a profit are classified as not-for-profit. Facilities that pay taxes and operate to make a profit are classified as for-profit facilities. Ownership type was derived from the facility organization and ownership types assigned in NIH RePORT.

Administration Type

There has been a recent movement toward the systems approach to IBCs. "System-wide IBCs" may be said to occur when two or more facilities form one IBC in practice but register this IBC separately with the NIH OBA. This system-wide IBC oversees research that is subject to

the *NIH Guidelines* for all entities joined together. In effect, it functions as one system-wide IBC. This joint IBC may be externally administered. Each facility performing the research that is subject to the *NIH Guidelines* has the responsibility for registering the multi-facility jointly formed IBC with the NIH OBA. Some facilities located in Massachusetts have actively supported the adoption of System-wide IBCs. Four distinct systems were identified by reviewing the IBC rosters:

1. Harvard Committee on Microbiological Safety (COMS),
2. Partners Institutional Biosafety Committee (PIBC),
3. Tufts Medical Center and Tufts University (Tufts), and
4. Western IBC

Boston Metro Area

The New England City and Town Area (NECTA) Division number 71654 Boston-Cambridge-Quincy, Massachusetts was used to determine if the facilities with NIH-registered IBCs were located in this biotechnology hub.

Local Ordinance Oversight

Massachusetts uniquely has several municipalities with local ordinances. Frequently the local ordinances are harmonized with the *NIH Guidelines*, by adopting of them. While local ordinances have become commonplace in Massachusetts, other states have not followed. It has been argued that local ordinances provide stability to the biotechnology industry (Feldman and Lowe 2008). Yet the effect of local ordinances on IBC composition is unknown.

Often local ordinances include a stipulation that the health commission has control over community member appointments to IBCs. This control is implemented differently in the various municipalities, which may exercise appointment powers, the authority to approve the

appointments, or—in some cases—community member training requirements. Some ordinances require a board of health agent or his or her designee to be on the IBC.

Table 5. Summary of facility variables Massachusetts non-governmental facilities with NIH Registered IBCs 2012 (n=48)

Variable	Variable Label	Values	Nature of Variable	Mode of Inquiry
Facility Ownership Type	FACOWN	Is the facility a not-for-profit ownership type? 1= Yes 0= No	Discrete/ Nominal	Univariate Frequency Median Percentage Bivariate Correlation matrix Binary Logistic Regression
Facility IBC Administration Type	IBCSYSB	Is the IBC administered as a system- wide IBC? 1= Yes 0= No	Discrete/ Nominal	Univariate Frequency Median Percentage Bivariate Correlation matrix Multivariate Binary Logistic Regression
Boston Metro Area	BOSTON METRO	Is the facility located in The New England City and Town Area (NECTA) Division number 71654 Boston-Cambridge-Quincy, Massachusetts (Boston Metro area)? 1= Yes 0= No	Discrete/ Nominal	Univariate Frequency Median Percentage Bivariate Correlation matrix Multivariate Binary Logistic Regression
Facility Local Oversight	FACORDIN	Is the facility located in an area where the Municipality's Board of Health or other local government agency is regulating rDNA (typically by adopting the *NIH Guidelines*) as part of its regulations? 1=Yes 0= No	Discrete/ Nominal	Univariate Frequency Median Percentage Bivariate Correlation matrix Multivariate Binary Logistic Regression

Governance Variables

The literature review provided the rationale for examining the composition and characteristics of IBCs. The governance variables are outlined in Table 6. Community members, often referred to as outsiders, nonaffiliated members or external members should not have any relationship with the facility other than their participation in the IBC according to the *NIH Guidelines*. Their role is to represent their communities' interests at the IBC meetings.

Composition of IBC

The *NIH Guidelines* require a minimum of five members, with two being community members that are not affiliated with the facility other than serving on the IBC (*NIH Guidelines* 2013). Local ordinances have similar requirements stipulating two, and sometimes three, community members. As far as the ratio of insiders to outsiders is concerned, the town of Grafton has a requirement based on ratio, with no less than 10% of the membership to be unaffiliated community members. The *NIH Guidelines* do not include any restrictions on the number of insiders appointed therefore the outsiders appointed can be diluted by more insider appointments.

The *NIH Guidelines* once required that at least 20% of the membership be outside members (Bereano 1984). Currently no percentage requirement exists and the composition of outsiders to insiders is unknown. The 20% level was selected as the operational definition of outsider participation, the outcome variable in the binary logistic regression.

Because expertise and knowledge of the community member is important, this study examines expertise and knowledge in various ways to capture the community members' public official role, scientific occupations and education level.

Occupation of Community IBC Members

Job titles and employer identification serve as indicators of IBC board members' expertise and background required to help IBC make sound decisions. The *NIH Guidelines* suggest several occupations for community members. Possibilities include officials from local or state health or environmental protection agencies; members of local government bodies; and those active in medical, occupational health, or environmental concerns. This study determined if IBCs appointed outside members with these preferred qualifications. According to Fischer (2009) policy expertise related to governance is becoming more important along with professional expertise as society becomes more complex and expects more from citizen participation in matters of public responsibility.

This study reviewed community board member credentials of science expertise. An expert is defined as "a widely acknowledged source of reliable knowledge, skill or technique that is accorded status and authority by the peers of the person who holds it and is accepted by member[s] of the larger public" (Fischer 2009, 17), expertise gained through formal training calls for the expert to act as a "social trustee" (22).

The scientific scope required to participate on IBCs can be beyond that of most citizens, thus expertise is an important element to consider. Yet purely scientific justifications to move forward with bioscience research can be co-opted by the facility's other interests. Community members are thought to safeguard the interests of the community. Fischer (2009) validates embedding local knowledge into technocratic decision-making such as IBCs. This study fills a gap in our understanding of IBCs as science becomes more complex so does the role of the potentially novice community member.

Variables concerning the expertise of outside members were primarily determined by job titles with employer identification and doctorate as a secondary source of information. For example, job titles with "scientist", "investigator", and "laboratory manager" clearly denote scientific expertise. Other individuals holding job titles such as "professor" were classified as science experts if their position or background was associated with the sciences. Often professors have both academic and principle investigator duties therefore professors in the sciences were classified as science experts. Medical doctors and veterinarians were classified as science experts if they were associated with basic or clinical research. This variable is an indicator for the science expertise of outside board members.

Education of Community IBC Members

Education level is a representative measure of expertise. This variable identifies the percentages of community members holding terminal degrees (i.e., Ph.D., M.D., D.V.M.). This variable is an indicator if community members are more or less novices or they hold similar educational distinctions as the internal counterparts.

Table 6. Summary of governance variables Massachusetts non-governmental facilities with NIH Registered IBCs 2012 (n=48)

Variable	Variable Label	Values	Nature of Variable	Mode of Inquiry
Outsider monitoring/ participation	GOVPER20	Does the IBC have at least 20% of the members as outside members 1= Yes 0= No	Discrete Nominal	Univariate Frequency Median Percentage Bivariate correlation matrix Multivariate Binary Logistic Regression
Outsider NIH preferred community member occupations	GOVNIH50	Does the IBC have at least 50% of the outside members with NIH preferred community member occupations listed in the *NIH Guidelines*? 1= Yes 0= No	Discrete Nominal	Univariate Frequency Median Percentage
Outsider science expertise	GOVDOC50	Does the IBC have at least 50% of the outside members with science expertise on the IBC? (doctorate degree serves as a proxy for science expertise) 1= Yes 0= No	Discrete Nominal	Univariate Frequency Median Percentage

Study Objectives

The goal of this study is to have a better understanding of IBCs that serve as the oversight mechanism governing laboratory or clinical research involving recombinant or synthetic nucleic acid molecules at the facility level. The objectives are: 1) to determine the composition and select characteristic attributes of IBCs referred to as governance variables, 2) to determine facility characteristics of the organizations that have NIH registered IBCs, and 3) to determine local characteristics of areas where the facilities are located. This is followed by a research objective that determines the existence or lack of an association between the facility variables and the percentage of outsiders at or above 20%, the level previously required by the *NIH Guidelines*. This will determine if facility variables are associated with the differences in this IBC governance variable. For example, board composition and the existence of a system-wide IBC partnership was analyzed to determine if this emerging administration process has affected independent monitoring.

Research Questions

1. What is the profile of NIH registered IBCs in Massachusetts?
    a. Governance - percentage of community members, and expertise defined by occupation and education
    b. Organization - ownership type, IBC administration type
    c. Location - Boston Metro area location, local ordinance
2. What are the relationships between IBCs composition and organizational and local area characteristics?

Data Analysis Plan

Since facilities with NIH registered IBCs must adopt board monitoring to oversee research, the study was conceptualized using the tenants of agency theory. Public administration research often uses descriptive research methods to summarize a data set and explore relationships among variables (McNabb 2013). According to McNabb (2013) this affords the researcher an opportunity to find information and patterns about the data and such exploration may reveal further questions where confirmatory data analysis may subsequently be used.

This study is an exploratory examination, guided by agency theory and resource dependency theory, of an innovative model for managing oversight for science that can at times be complex and controversial. It is not a confirmatory analysis of a specific research hypothesis rather it makes observations about IBCs in the study population to guide practitioners and future research. After these observations are made and the data are described, a comparison is made to determine if facilities with various characteristics systematically differ in their outside IBC board member participation: ≥20% community members. Experimental design related terminology was used to describe the variables and guide the study. For all procedures that involve significance testing, the result is considered statistically significant if the p-value is less than .05.

Before the data were analyzed, values for each variable were entered into the Statistical Package for the Social Sciences (SPSS), Version 20.0 (IBM Corporation 2011). Each value was reviewed for consistency and potential missing data. There was no missing information so all the values were complete for the data set.

Summary

The methodology delineated in this section provides a comprehensive account of the study design including data gathering used to accomplish the research objectives. The data sources and analytical methods used to create a structural profile of IBCs located in Massachusetts and registered with the NIH OBA are identified. The analytical strategies used to examine the composition and characteristics of IBCs' board membership and the differences in IBC board composition with selected structural characteristics of the facilities are described. The presence of a disproportionate number of inside members as compared to outside members was reviewed in association with facility attributes as board studies often include a descriptive analysis of representation.

ANALYSIS AND FINDINGS

The preceding chapter explained how this study is exploratory yet ground-breaking because this social inquiry about IBCs organizational profiles (facility and area) and IBC governance attributes are not well characterized. This chapter reviews the analytical methods and reports the findings about the association between board composition and selected facility and location variables. First, it provides a profile of NIH registered IBCs in Massachusetts. The composition and characteristic attributes (occupational and scientific expertise of outsider members), described as governance variables, and the structural profile (ownership type, administration type) and local area characteristics (Boston Metro area and local oversight ordinance).

Data Analysis Strategies

After identifying the population, determining the study, defining the variables, gathering data from the study population, and recording and recoding the values for the variables in SPSS, the analysis was accomplished in multiple stages. The data analyses are based on the research questions outlined in the previous chapter. The first question requires univariate analysis to profile NIH registered IBCs in Massachusetts. The second question requires bivariate and multivariate analyses to determine the association between board with ≥ 20% community members and selected facility and location variables.

The first step, univariate (descriptive statistics) summarized the study population. Bivariate (cross tabulation and correlation matrix) were used to determine cell frequencies and multicollinearity. Multivariate (binary logistic regression) was used to understand the complexities of associations between the outcome variable, board composition and multiple

predictor variables. Operations used for each variable are specified in the variable Table 5 and 6 in the previous chapter.

Descriptive statistics summarized the data and provided an opportunity to assess the distributional features of continuous quantitative variables. This process also provided an opportunity to identify and correct data errors by checking for invalid and missing values.

A contingency table compared the outcome variable with the three predictor variables to identify the frequencies in each cell. A correlation matrix was developed to identify strong multicollinearity among the predictor variables identified to be included in the binary logistic regression.

Binary logistic regression models were developed to assess the associations between IBCs board composition at or above 20% community member participation and organizational and local area characteristics. Key SPSS output includes generation of cell frequencies, assessment of model fit, and the contribution and statistical significance of the predictor variables in the change in odds.

Specification of Study Population

The study population consists of all 48 non-governmental facilities in Massachusetts with NIH registered IBCs. The strategy as reviewed in the previous chapter outlined how and why Massachusetts IBCs were selected for this study. The findings of this study are based on 2012 NIH records, the most recently completed record year when the study was commenced.

The study population was not randomly drawn for several reasons including the access and time constraints in data gathering. However, Massachusetts is considered the top biotechnology hub for early stage biosciences research so it is sensible to start with this area.

The study population size for this initial investigation (n=48) is small but exceeds the minimum study population size recommended (Corder and Foreman 2009).

In addition, local oversight ordinances are generally restricted to Massachusetts and another emerging trend in system-wide IBCs has started in this area. Because of this distinctiveness, NIH registered IBCs in other locations will not have these early adopter characteristics to study.

Profile of NIH Registered IBCs in Massachusetts

Descriptive Characteristics Ownership Type, Administration Type

The majority of the facilities, 36 (75%) were classified as not for profit while the remaining 12 (25%) were for profit facilities. The IBC review of research is the responsibility of the facility; however, some affiliated institutions have joined forces to combine this review and their oversight activity on behalf of the facility. These special member models are referred to in this study as system-wide IBCs. Most of the facilities in the research study population 35 (73%) were not members of a systems-wide IBC. However, a total of 13 facilities (27%) are members of system-wide IBCs.

Table 7. Study measures and descriptive statistics -organizational characteristics for Massachusetts non-governmental facilities with NIH registered IBCs 2012 (n=48)

Variable	Description	Frequency	Percentage
Ownership Type	For-profit	12	25
	Not-for-profit	36	75
	Total	48	100
Administration Type	Stand-alone IBC	35	72.9
	System-wide IBC	13	27.1
	Total	48	100

The largest system-wide IBC included a total of 7 facilities that were affiliated with the Harvard Committee on Microbiological Safety (COMS). These members include Harvard

University, Harvard University School of Public Health, Harvard University Medical School, and Harvard Medical School teaching hospitals, Beth Israel Deaconess and Massachusetts Eye and Ear Infirmary and Harvard Medical School Affiliates, Joslin Diabetes Center and Schepens Eye Research Institute.

Then three facilities were affiliated with Partners Institutional Biosafety Committee (PIBC), Massachusetts General Hospital, Brigham and Women's Hospital and McLean Hospital. The PIBC is the IBC for Partners HealthCare, a nonprofit integrated health care system founded by Brigham and Women's Hospital and Massachusetts General Hospital.

Tufts University and Tufts Medical Center are the last 2 facilities with a systems-wide IBC. Tufts Cumming School of Veterinary Medicine has a stand-alone IBC and was not a part of the Tufts systems wide IBC.

Another IBC administration practice worth noting is an IBC that is externally administered by an entity other than the facility performing the research subject to the *NIH Guidelines*. One facility from the study group administers their IBC through the Western Institutional Review Board. This review board is a for profit service provider for IBC outsourcing.

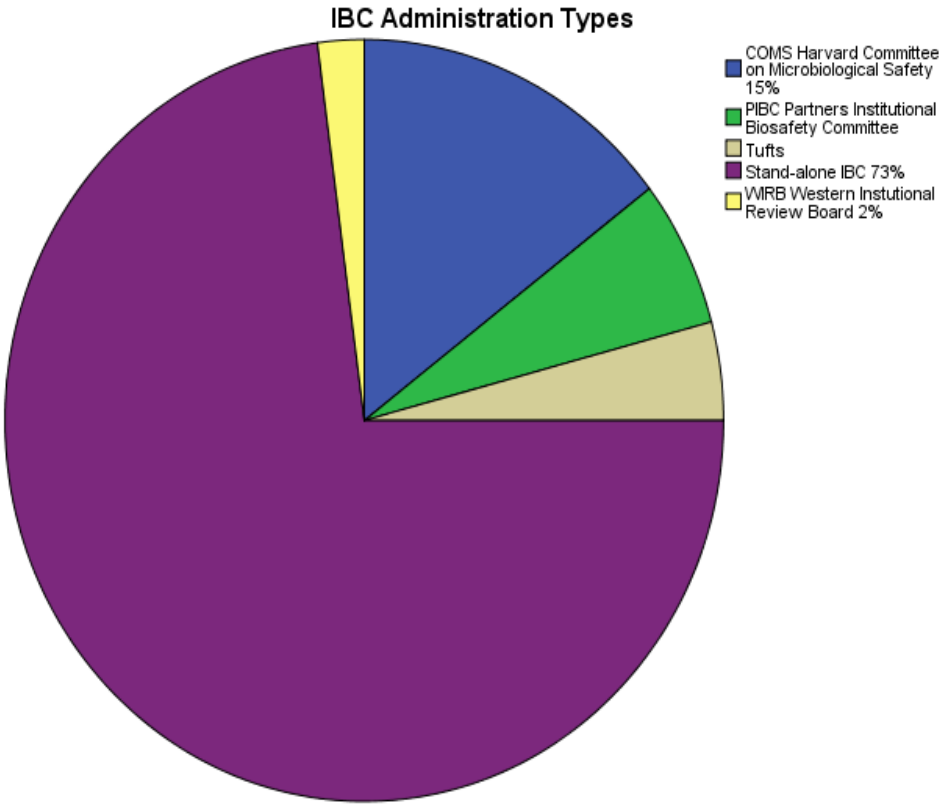

Figure 3. Percentage distribution by IBC administration types for NIH registered IBCs in Massachusetts 2012 (n=48)

Descriptive Characteristics Boston Metro Area Location, Local Ordinance

A total of 30 facilities (62%) were located in municipalities with local oversight ordinances that regulate research involving recombinant or synthetic nucleic acid molecules at the local level. This requires all facilities within the municipality with local oversight to comply with safety regulations no matter the source of funding. The remaining 18 (38%) are located in areas without local oversight. The geographic distribution of the facilities was predominately the Boston Metro area with 39 (81%) of the IBC registered facilities located there. The remaining 9 (19%) of the facilities were located elsewhere in Massachusetts.

Table 8. Study measures and descriptive statistics -area characteristics for Massachusetts non-governmental facilities with NIH registered IBCs 2012 (n=48)

Variable	Description	Frequency	Percentage
Facility Ordinance	No local ordinance	18	37.5
	Local ordinance	30	62.5
	Total	48	100
BostonMetro	Not in Boston metro	9	18.8
	In Boston metro	39	81.3
	Total	48	100

Descriptive Characteristics Governance: Percentage of Community Members, and Expertise Defined by Occupation and Education

A total of 28 (58%) of IBCs had at least 20% of their membership as community members while 20 (42%) did not meet the 20% level of outsiders participating. This shows the outcome variable (IBC composition ≥ 20% community members) has a normal distribution.

The mandated minimum number of community members is two and the mandated minimum number of IBC members is 5. The voting membership on IBCs ranged in size from 5 to 22. Only 3 (6%) of the IBCs did not meet the mandated minimum number of community members. In addition, 16 (33%) exceed the requirement with 3 community members while 29 (61%) had the required number of 2 community members.

The *NIH Guidelines* indicate appropriate occupations for community members, such as officials of state or local public health or environmental protection agencies, members of other local governmental bodies, or persons active in medical, occupational health, or environmental concerns in the community (*NIH Guidelines* 2013, 26). A total of 14 (29%) of IBCs had at least 50% of their community members with an NIH suggested occupation while 34 (71%) did not have at least 50% of their community members with an NIH suggested occupation. A total of 12

(25%) of IBCs had at least 50% of their community members with science related occupations and 36 (75%) had less than 50% of their membership with science related occupations. A total of 15 (31%) of IBCs had at least 50% of their community members with a doctorate degree and 33 (69%) had less than 50% of their membership with a doctorate degree.

Table 9. Study measures and descriptive statistics: Governance characteristics for Massachusetts non-governmental facilities with NIH registered IBCs 2012 (n=48)

Variable	Description	Frequency	Percentage
IBC composition	Outsiders < 20%	20	41.7
	Outsiders ≥20%	28	58.3
	Total	48	100
NIH occupation	Not preferred	34	70.8
	Preferred ≥50%	14	29.2
	Total	48	100
Science expertise	No expertise	36	75
	Expertise ≥50%	12	25
	Total	48	100
Doctorate degree	No doctorate	33	68.8
	Has doctorate≥50%	15	31.3
	Total	48	100

IBC Composition and Facility and Area Variables

Cross Classification of Variables

To get a better understanding about the data, relationships among variables were examined and compared with cross tabulations and correlation analysis. This comparison of variables was primarily conducted to identify significant correlation between and among predictor and the outcome variables. Significant correlations among predictor variables may cause the variables to compete thus the findings may not be significant. If predictor variables were highly correlated, those with strong multicollinearity were dropped from the binary logistic regression.

The variables were cross classified to observe the responses in a contingency table comparing the outcome variable with the three predictor variables. This table shows that three cells, one for each predictor variable had frequencies below 5.

Table 10. Cross tabulations (frequencies) by composition ≥ 20% outsiders and facility ownership, administration and ordinance type NIH registered IBCs 2012 (n=48)

IBC composition	Facility ownership type NFP 1=Yes		Total	System-wide IBC 1=Yes		Total	Facility ordinance 1=Yes		Total
	No	Yes		No	Yes		No	Yes	
No	2	18	20	10	10	20	3	17	20
	.167	.5	.417	.286	.769	.417	.167	.567	.417
Yes	10	18	28	25	3	28	15	13	28
	.833	.5	.583	.714	.231	.583	.833	.433	.583
Total	12	36	48	35	13	48	18	30	48
	1	1	1	1	1	1	1	1	1

Pearson's product moment (Pearsons *r*') is appropriate when one or both variable types are categorical and are true dichotomies (Warner 2013). The author shows how Pearsons r, though parametric and point biseral *r*, the nonparametric procedure, provide comparable results. Variables in this analysis either have an attribute or not, therefore they are classified as true dichotomies. This is an important distinction as they can be used in binary logistic regression.

The correlation co-efficient is generated when two variables are compared (Corder and Foreman 2009). Results can vary in value from -1 to +1 indicating the direction and strength of the association between two variables. A direct relationship is a positive correlation with a value ranging from 0 to +1.0. This means as one variable increases so does the other variable. An indirect relationship is a negative relationship with a value ranging from -1.0 to 0. This means as one variable increases the other decreases. Corder and Foreman (2009) further describe values closer to -1.0 or +1.0 as stronger and those closer to 0 as weaker. Correlation strengths are not linear and the interpretation of strength varies.

The result of Pearson's r shown in Table 11 provides evidence for the construction of the binary logistical regression model. Correlation coefficient (r) values were computed and a critical values table was examined to determine the level required to achieve statistical significance between variables (Corder and Foreman 2009, 239). The critical value to achieve statistical significance shown was .279 for an n=48 and a two-tailed $\leq .05$ (Corder and Foreman 2009, 240).

There was a strong positive correlation between the predictor variables Boston metro area and local oversight ordinance with an r value of .400. This was the only case where predictor variables were highly correlated. Also there was not a correlation between Boston metro area and the outcome variable, IBC composition (.027). Boston metro was excluded from the binary logistic regression model. The more important predictor of the two is if the facility is located in an area where the municipality's Board of Health or other local government agency is regulating recombinant DNA.

All of the three remaining predictor variables were negatively correlated with the outcome variable regarding IBCs that have a higher level (20% or more) of community member participation. Ownership type was negatively correlated with an r value of -.293. IBC administration type was negatively correlated with an r value of -.436. Local ordinance oversight was negatively correlated with an r value of -.393. These inverse relationships indicate IBCs with any of the characteristics, not-for-profit ownership type, system-wide administration type and in an area with a local ordinance have a moderate indirect relationship with IBCs that have at least 20% of the membership as community members.

Table 11. Correlation of facility and area variables with IBC composition (n=48)

Variables	1	2	3	4	5
1.Ownership type	1	.244	.149	.216	-.293*
2. Administration type	.244	1	.085	.173	-.436*
3. Ordinance	.149	.085	1	.400*	-.393*
4. BostonMetro	.216	.173	.400*	1	.027
5. IBC composition	-.293*	-.436*	-.393*	.027	1

*Correlation is significant at the .05 level (2-tailed).

Associations between IBC Board Composition and Organizational Characteristics

Binary Logistic Regression Assumption

Since the outcome of interest and the predictor variables are categorical and dichotomous and the predictor variables are not evenly distributed, binary logistic regression was used to understand how IBC composition was influenced by facility variables. Binary logistic regression is a statistical method used to "predict membership in a target group" (1007) with one or more predictor variables and statistically independent dichotomous outcome variables (Warner 2013).

Design decisions about the binary logistic regression model were based on the factors obtained in the preliminary analysis of the potential variables pre-selected for this analysis that can impact statistical power. For this study the following factors were taken into account in building the model equations for each outcome;

1. The outcome variable is dichotomous
2. There are three predictor variables
5. The predictor variables are dichotomous
6. The predictor variables are not evenly distributed
7. The study population size is small

Model Specification

The logistic regression model equation with multiple predictor variables is as follows (Warner 2013, 1015):

$Li= B_0+B_1X_1+….+B_kX_k$

The logit (Li) or ratio of odds is the value of the outcome variable

B_0 is the intercept (constant) predicted score on Y when X=0

$B_1…B_k$ are the coefficients for predictor variables X

$X_1…X_k$ are the predictor variables or covariates

L_i (Outsider Composition ≥20%) $= B_0 + B_1$ x (local ordinance)+ B_2 x (ownership) + B_3 x (system-wide)

Table 12. Logits implied by predictor variables in model Li= B0+B1X1+….+BkXk

Ownership (For-profit)	Administration (Stand alone)	Ordinace (No local ordinance)	Logit	Model
1	1	1	$B_0+B_1+B_2+B_3$	Model 1 (Full Model)
0	1	1	$B_0+B_2+B_3$	Model 2
0	1	0	B_0+B_2	Model 3
0	0	1	B_0+B_3	Model 4
0	0	0	B_0	Model 5 (Null Model)

Comparison of Observed and Expected Frequencies

It was important to check the distribution of values in a contingency table particularly since the study population size is small. According to Warner (2013) frequencies for each cell in the classification table should not be less than five for each predictor variable and if more than 20% of the cells are below 5 the model needs revisions. However other authors report the "sparseness" (Khamis 2011, 2) of data issue has been relaxed allowing for more predictor variables for small data sets such as this one. Warner (2013) also reports the minimum study

population size should be 10 times the number of independent variables. Agresti (2007) suggests a minimum of ten outcomes for every predictor variable. The models for this study were built to maximize the model with the given data set yet avoid multicollinearity issues.

SPSS provides a number of ways to check the fit of the model and provides ways to check the significance of each predictor by comparing models. The – 2 Log likelihood measures how poorly the model fits. A smaller number in the full model summary than in the null only model indicates a better fit. The L^2 measure is the -2 Log likelihood of the full model minus the -2 Log likelihood null only models. This provides the Chi-square with associated degrees of freedom representing the number of predictor variables in the full model. A larger Chi-square value that exceeds the critical values for chi-square statistics with a significance below .05 shows that the full model is a better predictor that the null model.

The model fit can also be assessed by reviewing the pseudo r values reported in SPSS. R^2 equivalents such as Cox and Snell's R^2 that is typically less than 1 with a value closer to 1 indicating the model is a better fit than if it were closer to 0. Likewise the more widely used Nagelkerke R^2 is similar yet the goodness of fit range includes 1(Warner 2013).

Table 13 shows that all models while significant, the models with multiple predictors are similar in their fit. The test of the full model compared to the null model was statistically significant, X^2 (3) = 18.908, p ≤.05. The strength of association between the outcome and predictor variables was Cox & Snell R^2 .326 Nagelkerke R^2 .438.

Likewise, Model 2, the selected model for this study, was statistically significant, X^2 = 17.48, p ≤ .05. The strength of association between the outcome and predictor variables was Cox & Snell R^2 .305 Nagelkerke R^2 .411.

Table 13. Goodness of fit for models 1-4

Model	X^2	df	Sig	L^2	Cox & Snell R^2	NagelkerkeR^2
1 (Full)	18.908	3	0	46.294	.326	.438
2	17.48	2	0	47.723	.305	.411
3	9.278	1	.002	55.924	.176	.237
4	7.928	1	.005	57.274	.152	.205
5 (null)				65.203		

Model Inputs

The outcome variable board composition was coded 0= less than 20% of the IBC voting members are community members and 1= 20% or more of the IBC voting members are community members. SPSS reported the odds on the value of 1= 20% or more of the IBC voting members are community members.

Three predictor variables were included in the full model: (i) ownership type, (ii) administration type, and (iii) local oversight ordinance. In SPSS, 1 was the reference group for the predictor variables; facility ownership, 1= not for profit facility, 0= for profit facility; IBC administration, 1= system-wide IBC, 0=stand-alone IBC; and local oversight ordinance, 1= local oversight ordinance, 0= no local oversight ordinance. Because the reference category for the ratio of odds was on the SPSS default setting, "last" it means SPSS will use 1 as the reference group.

The value for Exp(B) are the odds of 20% or more of the IBC voting members are community members for the comparison group of predictor variable that are coded 0 as depicted in Table 14.

Table 14. Binary logistic regression reference group

Coding	Facility ownership	IBC administration	Local ordinance
1= Yes	Not for profit	System-wide	Local oversight
0= No*	For profit	Stand-alone	No local oversight

* reference category "last" instructs SPSS to use 1=Yes as the reference group

Summary of Logistic Regression Results

The logistic regression results indicated that both administration type and local oversight ordinance were significant covariates for board composition. Stand-alone IBCs were significantly more likely than system-wide IBCs to have 20% or more outsiders appointed on their boards. IBCs not serving facilities located in a municipality with a local ordinance were also significantly more likely to have 20% or more outsiders appointed to the board. Ownership was not a contributing predictor with a p value > .05. These findings are shown in detail in the following section.

Table 15. Summary of binary logistic regression results for IBC board composition odds ratio outsiders ≥ 20% (95%CI)

Predictor variables	Ownership	Administration	Ordinance
Compare group = 0	For-profit	Stand-alone IBC	No local ordinance
Model 1	2.833 (.47-16.90)	9.712(1.57-60.21)	8.31(1.47-47.14)
p	>.05	<.05	<.05
Model 2*		11.538 (1.96- 68.11)	9.069 (1.60-51.31)
p		<.05	<.05
Model 3		8.333 (1.89-36.76)	
p		<.05	
Model 4			6.538 (1.56-27.45)
p			<.05

* selected final model

Model 1 Full Model

The full model built for this study first compares a single predictor variable then produces all predictions in a stepwise manner. In this study, the default setting “enter” was used for the full model. Contributions of individual predictor variables are shown no matter how the data are

entered. According to Warner (2013) when the model is found significant, the individual predictor variables are then assessed for individual contributions to the outcome. The odds Exp(B) that 20% or more of the IBC voting members are community members are tested with three covariates: (i) ownership type, (ii) administration type, and (iii) local ordinance.

The Wald Chi-Square statistic tested the contribution of each predictor variable while holding constant other predictors. The binary logistic regression results (Table 16) for the full model shows the predictor variable, ownership type has a p> .05, and therefore it is non-significant. This variable was eliminated from the model and Model 2 was determined to be the most acceptable model for this study.

Table 16. Model 1 coefficients ownership, administration, ordinance types for binary logistical regression of the odds of ≥ 20% outsiders on IBC

Variables in the equation		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1a	FACOWNNFP(1)	1.041	.911	1.306	1	.253	2.833	.475	16.897
	IBCSYSB(1)	2.273	.931	5.964	1	.015	9.712	1.567	60.211
	FACORDIN(1)	2.117	.886	5.718	1	.017	8.31	1.465	47.137
	Constant	-2.234	.904	6.103	1	.013	.107		

Model 2 Administration Type and Local Ordinance

Both administration type and local ordinance are significant at the p .05 level. Recall that SPSS reported the odds on the value of 1= 20% or more of the IBC voting members are community members and 1 was the reference group for the predictor variables; IBC administration, 1= system-wide IBC; and local oversight ordinance, 1= has local oversight ordinance. Therefore, IBC administration 0= stand-alone IBC and local ordinance 0= no local oversight ordinance are the values for Exp(B) or change in odds.

The logistic regression results (Table 17) for the odds of community member participation at or above 20% for the comparison group of predictor variables stand-alone IBC

and no local oversight ordinance are described below. Specifically, stand-alone IBCs were 11.6 times more likely to have 20% or more outsiders appointed on their boards than system-wide IBCs, with a 95% confidence interval between 1.955 and 68.113. This spread in the confidents limit demonstrates the statistically significant elevation of the odds ratio, but less precise quantification due to the small study population size and variability of the data.

IBCs located in municipalities without a local ordinance were 9.1 times more likely to have 20% or more outsiders appointed on their boards than IBCs located in municipalities with local ordinances, with a 95% confidence interval between 1.603 and 51.314.

Table 17. Model 2 coefficients, administration, ordinance types for binary logistical regression of the odds of $\geq$ 20% outsiders on IBC

Variables in the equation		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1a	IBCSYSB(1)	2.446	.906	7.289	1	.007	11.538	1.955	68.113
	FACORDIN(1)	2.205	.884	6.218	1	.013	9.069	1.603	51.314
	Constant	-2.147	.879	5.964	1	.015	.117		

a Variable(s) entered on step 1: IBCSYSB, FACORDIN.

Models 3 and 4 Individual Variables

Models 3 administration type and Model 4 local oversight ordinance are significant at the p .05 level. The logistic regression results (Table 17) for the odds of community member participation at or above 20% for the comparison group of predictor variables stand-alone IBC are shown below. Specifically, stand-alone IBCs were 8.3 times more likely to have 20% or more outsiders appointed on their boards than system-wide IBCs, with a 95% confidence interval between 1.889 and 36.757. Recall that in Model 2, stand-alone IBCs were 11.6 times more likely to have 20% or more outsiders appointed on their boards than system-wide IBCs, with a 95% confidence interval between 1.955 and 68.113.

Table 18. Model 3 coefficient, administration type for binary logistical regression of the odds of ≥ 20% outsiders on IBC

Variables in the equation		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1a	IBCSYSB(1)	2.12	.757	7.841	1	.005	8.333	1.889	36.757
	Constant	-1.204	.658	3.345	1	.067	.3		

a Variable(s) entered on step 1: IBCSYSB.

The logistic regression results (Table 19) for the odds of community member participation at or above 20% for the comparison group of predictor variables no facility oversight ordinance are described below. Specifically, IBCs with no oversight ordinance were 6.5 times more likely to have 20% or more outsiders appointed on their boards than system-wide IBCs, with a 95% confidence interval between 1.558 and 27.448. Recall that in Model 2, IBCs without a local ordinance were 9.1 times more likely to have 20% or more outsiders appointed on their boards than IBCs located in municipalities with local ordinances, with a 95% confidence interval between 1.603 and 51.314.

Table 19. Model 4 coefficient, ordinance type for binary logistical regression of the odds of ≥ 20% outsiders on IBC

Variables in the equation		B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
								Lower	Upper
Step 1a	FACORDIN(1)	1.878	.732	6.581	1	.01	6.538	1.558	27.448
	Constant	-.268	.368	.53	1	.467	.765		

a Variable(s) entered on step 1: FACORDIN.

Summary

A review of NIH registered IBCs in Massachusetts shows that both administration type and local oversight ordinances are associated with the composition of the IBC Specifically IBCs administered as stand-alone were more likely to be composed of ≥20% or community members. Likewise, IBCs not associated to facilities located in a municipality with a local ordinance were

also significantly more likely to have 20% or more outsiders appointed to the board. Ownership was not a contributing predictor to board composition.

The findings also answered the first research question about IBC governance characteristics and the organizational profiles (facility and area). This univariate analyses showed that the outcome variable, board composition, was evenly distributed with 28 (58%) of IBCs with at least 20% of their membership as community members and 20 (42%) did not meet the 20% level of outsiders participating.

The bivariate analysis provided an opportunity to review the data before the multivariate analysis. One of the predictor variables, Boston metro area was eliminated from the study because there was a strong positive correlation with the predictor variables local oversight ordinance with an r value of .400. The next chapter provides a discussion about the findings.

DISCUSSION AND CONCLUSIONS

Research has shown that boards with an increased percentage of outsiders are more effective at monitoring. However, there are other known benefits to appointing outside board members besides monitoring. Outside board members also bring resources such as expertise and community linkages to the organization.

The NIH first issued the *NIH Guidelines* in 1976 in response to concerns about the risks associated with recombinant DNA. In 1977 Cambridge became the first city to regulate recombinant DNA with a public health ordinance that included a mechanism for community member participation. The *NIH Guidelines* were revised in 1978 to include public representation with at least two community members (no less than 20% of the IBC membership). The current *NIH Guidelines* (2013) still require two community members but no longer requires 20% of the voting membership to be outsiders.

This study primarily utilized a review of NIH records to assess the structural profile of facilities with NIH registered IBCs and the characteristics of these boards with particular emphasis on the community members. The purpose of this study was to summarize features of IBCs and determine if relationships exist between board composition and organization and location factors.

Review of Findings

The overall number of inside board members has grown disproportionality to outside community members. This is due, in part, because the *NIH Guidelines* no longer specify that the board must have at least 20% participation by outside members. It could also be driven by external forces such as the complexity of decision-making requiring more internal members to

cover the range of expertise needed as science advances. It even could be because of the difficulty in recruiting, training and retaining community members. Consequently, it is reasoned that the governance process involving the IBC as an independent organization may be weakened when community or stakeholder agents have a lower participation rate.

This study examined system-wide IBCs, a structure that combines the members of more than one IBC in practice yet registers the IBCs separately with the NIH. This study suggests that stand-alone IBCs are positively associated with 20% or more outsider membership on these boards. As research organizations, hospitals, educational institutions and for-profits grow and re-structure to remain viable; they are looking for opportunities to become more efficient. System-wide IBCs by their nature are one such mechanism that can improve efficiency while increasing consistency in decision-making across the system members. This study suggests this highly coordinated approach can have a negative effect on outsider participation.

Contrary to expectations, IBCs that serve facilities located in areas that do not have a local oversight ordinance were positively associated with at least 20% outsider board membership. Most local ordinances required at least two community members but may have further requirements that involve the local public health department in recruiting, approving and training IBC community members. This suggests the local government is more concerned with quality of the community member rather than quantity.

Comparison with other Studies

Voting membership on IBCs has increased with a range of 5–22 members including 1–3 community members. The Dutton and Hochheimer (1982) study found a range from 7–16 members, with a range of 2–4 community members on California IBCs. Since the regression results indicate that stand-alone IBCs were more likely to have at least 20% of the voting

members as community members, the policy implications for IBC community membership needs further review. Under present conditions, attention needs to be directed towards the unintended consequences of system-wide IBCs in particular.

It is not surprising that the facilities in support of these systems require more members to assure all affiliations are represented. Cost efficiencies in health systems and academia could be the driver that has moved the trend in joint operating arrangements of IBCs with affiliates. The risks and benefits of these systems affiliations have not been fully realized. The 13 NIH registered IBCs in Massachusetts that have adopted a systems approach have greatly changed the profiles of IBC voting members. The ratio of voting insiders to outsiders is as high as 19:2.

Limitations and Future Research

Limitations

Even though this research indicates that the facility administration types and local oversight ordinances were found to be associated with board composition, the positive and negative implications of these outcomes have not been measured. Future research could address this deficiency.

The study population is a limitation because it was small and unique. Given the early adoption of local ordinances and system-wide IBCs, Massachusetts is a distinctive area that may limit the generalizability of the findings. While this is a weakness of the study, it also can serve as an early review of what could be trending in other bio-clusters.

IBC Composition

The proportion of outside members as compared to inside members is a measure of the monitoring function. The guiding principle of agency theory focused this study on the community member's role in safeguarding the community interests. Further research using the

tenants of resource dependency theory, particularly as it relates to external resources and interlocking relationships could provide a richer analysis if coupled with agency theory. Studies on linking organizations with resources and expertise have shown consequences both good and bad including "collusion, cooptation and monitoring, legitimacy, career advancement and social cohesion" (Mizruchi 1996, 273).

Future research with a larger sample population could help validate the associations and explore additional associations of other governance variables described in this study. This is recommended before policy changes are considered. This research could be easily replicated by drawing on data from all NIH registered IBCs.

Implications

Local Oversight Ordinances

Local oversight ordinances may expand into other bioclusters beyond Massachusetts. The biotechnology trade association that provides support to the industry in Massachusetts, MassBio, has developed a successful BioReady® campaign. This campaign supports biotechnology friendly public policies to attract biotechnology organizations to the area. Support of local oversight ordinances is one component of this campaign. Perhaps biotechnology trade associations in other states will adopt a similar strategy.

It was unexpected that the biotechnology industry would embrace a local oversight ordinance yet they did partly because the rules are known and the community is biotechnology business friendly (Feldman and Lowe 2008). This finding indicates that the concentration of the biotechnology industry is not only resource centric, but also may have a social cohesiveness.

The finding that facilities in areas without local ordinances are more likely to have an IBC with 20% or more outsiders provides an incomplete understanding of how local oversight

ordinances influence community membership. The boards of health get involved in recruiting strategies and training for IBC community members in areas where there are local ordinances.

On the surface, it seems the benefits of the local oversight ordinances are in the best interests of the industry and the public. Regulatory capture theory cautions us to not just assume public good rather "is regulation simply an arena in which special interests contend for the right to use government power for narrow advantage?" (Levine and Forrence 1990, 172). It is difficult to disagree with the public value of local ordinances when the regulatory systems have standards, structures and training processes that all facilities must follow regardless of funding. However, the effectiveness of local ordinances should be monitored to support staying true to public value.

System-wide IBCs

System-wide IBCs can provide a competitive advantage though shared resources and consistency in oversight. Movement in shared IBC resources can expand beyond academic institutions and hospitals as the science moves from research laboratories to clinical settings on to early stage commercial operations. Private companies may be a little wary about sharing insider information in an IBC joint review process. Perhaps another model where the local biotechnology trade association provides external monitors would be more appealing. These external monitors would have the capacity to provide technical biosafety expertise to the IBC as an *ad hoc* IBC member. This model could provide similar advantages to small start-ups that system-wide IBCs provide to large universities and hospitals.

Governance Factors

These findings show that the recommended occupations for community members listed in the *NIH Guidelines* are not being adhered to by the facilities. Recruiting, training and

retaining community members can be challenging (Lipson 2013). In comparison to previous studies, this research shows that community members have more diverse backgrounds and are less likely to be scientists. A fresh look at recommended occupations for community members should be considered.

For example, science, technology, engineering and mathematics (STEM) teachers are located in every community. STEM teachers need support in professional development (Desimone et al. 2002). One way a community can support the development of STEM teachers is to appoint them to local facility IBCs. This would enhance their science content knowledge and give them an abundant supply of real-world examples to bring back to the classroom. Active learning opportunities with leadership roles and collective participation have had positive outcomes on teaching according to a three year study of STEM teachers (Desimone et al. 2002).

Summary

This formative research adds to our limited understanding of the composition and characteristics associated with IBCs. The study was further enhanced with semi-structured interviews and reviews of published materials from NIH and local policy leaders to augment what was learned though a records review. As the industry moves towards shared resources and a changing IBC infrastructure, the NIH should revisit the *NIH Guidelines* to assure that the community member can maintain their monitoring role with clear guidance on the ratio of insiders to outsiders.

Experiments requiring IBC review and approval often require a separate review by another board. For example, clinical trials that involve gene transfer in human subjects are also reviewed and approved by the Institutional Review Board (IRB). Research involving animals requires Institutional Animal Care and Use Committees (IACUC) oversight. These separate yet

often coordinated reviews all involve internal and external resources including unaffiliated outsiders on the various facility level review boards.

The IBC is the most obvious starting point to review the oversight decision-making processes for bioscience research. Because bioscience is advancing rapidly and IBCs play a prominent role, the timing of this study is important to draw attention to this oversight system established long ago for transparency and accountability in lieu of federal regulations.

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IRB CONSENT LETTER

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February 13, 2013

Katherine M. Wellman
Johns Hopkins University
Gilchrist Hall
9601 Medical Center Drive
Rockville, MD 20850

Dear Ms. Wellman:

This letter serves as official confirmation of the Institutional Review Board's review of your protocol for a study entitled "Institutional Biosafety Committees and the Public Stewardship of Recombinant DNA Scientific Research: An Exploratory Analysis of Community Member Characteristics," submitted for review on January 24, 2013.

The Institutional Review Board considered your request and concluded that your protocol poses no more than minimal risk to participants. In addition, research involving the use of widely acceptable interview procedures where the results are kept confidential and the questions pose minimal discomfort to participants is exempt from IRB full-committee review per 45 CFR 46.101 (b) (2). As a result, the Institutional Review Board has designated your proposal as exempt.

Investigators are responsible for reporting in writing to the IRB any changes to the human subject research protocol, measures, or in the informed consent documents. This includes changes to the research design or procedures that could introduce new or increased risks to human subjects and thereby change the nature of the research. In addition, you must report any adverse events or unanticipated problems to the IRB for review.

If you have any questions, please do not hesitate to contact me directly by phone or via email.

As authorized by Eric B. Easton, J.D., Ph.D.
Chair, Institutional Review Board

Marc P. Lennon

Marc P. Lennon
Coordinator, Institutional Review Board

cc: Dr. C. Spencer

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