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Select agent program impact on the IBC

10

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Introduction and background

The classical role of the IBC

The role of the Institutional Biosafety Committee (IBC) has not been universally defined, and each Institute creates a unique charter for this oversight committee. There are specific IBC guidelines promulgated by the National Institutes of Health (NIH) involving work with recombinant DNA [1]. There have also been recent guidelines issued by the National Biodefense working groups and others on “gain of function” (GoF) experiments and the NIH on Dual use Research of Concern (DURC) [2]. The IBC may be directly involved in approving or referring these experiments to the NIH for approval. Other traditional roles for the IBC include review and approval of all work with infectious agents, work with biologics including nanoparticles, infection

of animals or plants and/or microbiological work including projects in the classroom laboratory. Broadly, the IBC serves to ensure that biological experiments conducted within their Institute are within regulatory guidelines to protect the Institute from financial and/or legal liabilities and also that laboratory workers conduct these activities as safely as is reasonable in line with current safety recommendations. In other words the primary questions the IBC should ask when reviewing protocols are “Is it safe?” and “Is it legal?” A review of the regulatory requirements of the IBC is covered in Chapters 2, 4, and 5 of this text.

Select agent program

Beginning in 2003 with the expansion of the national biocontainment capabilities in both facilities and personnel, more IBCs had to address new regulations on the so-called select agents [3,4]. Select agents are those bacteria, viruses, and toxins deemed dangerous enough that they require special biosafety and biosecurity precautions and facilities. For instance, they require extra safety training and procedures and background checks to vet the persons working with or with access to these agents. Because of these additional requirements, IBC committees had to expand their capabilities and expertise to adequately address review of protocols involving select agent research. Not all biosafety level 3 (BSL-3) or 4 (BSL-4) pathogens or toxins are select agents but in most cases all select agents require containment in the appropriate BSL3/4 laboratory. When infectious work involves animal models of disease, most select agent studies must be performed in animal biosafety level 3, 3-Ag, or 4 facilities (ABSL-3/3-Ag/4). These studies pose a challenge for IBC oversight as they are not strictly the purview of the Institute of Animal Care and Use Committee (IACUC/ACUC). The purpose of this chapter is to highlight approaches and strategies the IBC can employ to best meet its obligation to review select agent, GoF, and DURC research and ensure the work is properly reviewed so that it is both safe and legal.

Challenges and options

Expanding roles of IBCs: select agent program requirements outside of (or in addition to) NIH OBA

The IBC, and in particular the Biological Safety Officer (BSO), has a myriad of new regulatory compliance issues and other challenges to consider when reviewing/approving microbiological research involving select agents. In addition to its mandated role in ensuring compliance with the NIH *Guidelines* for research involving recombinant and synthetic nucleic acids, the IBC traditionally reviews microbiological protocols for biological safety, for compliance with CDC guidelines for select agent research, for dual use research of concern (DURC), and for gain-of-function (GoF) research projects. When presented with research protocols involving select agents the IBC must be particularly diligent in assessing whether the work also falls under DURC policies or GoF guidelines [5].

Gain-of-function research

A current area of emphasis for IBCs is to identify and closely monitor biological GoF research. There is interest at the highest levels of government in controlling or regulating this type of research activity. The National Academy of Sciences has recently published a report on GoF research. This report was issued following at least two federally directed research stoppages on GoF agents of concern [6]. Categorically, one could debate the wisdom of these moratoriums on on-going research. However, clearly this needs to be resolved quickly as the negative impacts on acquiring knowledge during a time when these emerging viruses are causing human infections are substantial. While it is important to maintain oversight on this type of research, many believe that the benefits outweigh the risks. While this debate is outside the scope of this chapter, it is clear that IBCs will be increasingly drawn in on the subject of managing GoF research. Currently, the GoF agents of concern include respiratory viruses such as highly pathogenic avian influenza (HPAI), and the corona viruses that cause Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS). Although there is currently no specific regulatory requirement for the IBC to report GoF research activities, other than those experiments which are classified under current NIH guidelines as “Major Actions,” there is an institutional interest in identifying GoF research, in particular for respiratory pathogens. Additionally, specific regulatory guidelines on influenza, SARS, and MERS will likely be promulgated by the federal government in the near future and the list of gain-of-function restricted agents may expand [6]. The underlying concern is that GoF research needs unique biosafety and biosecurity solutions because it leads to the creation of specific pathogens with increased virulence, capability to thwart the immune response or defeat medical countermeasures or that the published knowledge from these studies will enable a terrorist or nation to create biological weapons transmissible through aerosols. Obviously, not all GoF experiments involve this subset of respiratory viruses or other select agents but those that do pose difficult issues for the IBC to manage. Most GoF research in select agents requires approval by not only the institution IBC but also the NIH Recombinant DNA Advisory Committee (RAC). The regulatory concerns may become more complex when a GoF project is also Dual Use Research of Concern (DURC) such as those involving certain noncontemporary or HPAI strains of influenza virus. For a more complete discussion of research that qualifies as DURC, the reader is referred to Chapter 6. The IBC can best serve its institution, the research staff, and itself by articulating clear policies for identifying and reviewing GoF/DURC projects early and streamlining their review. This is optimally done during grant preparation. The PI and IBC would first identify whether a grant contains GoF or DURC research, and develop a risk-mitigation strategy which would be included in both the grant and the IBC protocol. A rubric to illustrate this review process is included in [Figure 10.1](#). To better explain how this process should work from the perspective of the IBC, specific examples of GoF research are highlighted in the following case studies.

Mouse pox

In 2001, a paper was published as a result of studies with an altered ectromelia virus, which is the causative agent of mouse pox [7]. Mouse pox is not a select agent or

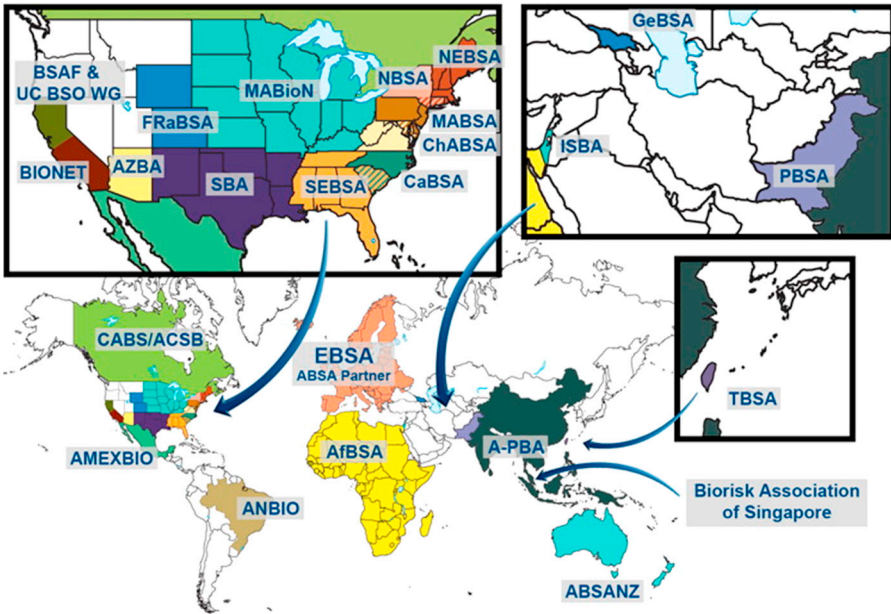


Figure 10.1 Regional and International Biosafety Organizations (<http://www.absa.org/trainingtools.html>). The American Biological Safety Association was established as a US-based organization but over time has formed international relationships with common goal of improving biosafety. Asian-Pacific Biological Safety Association (A-PBA), Association of Biosafety for Australia and New Zealand (ABSANZ), African Biological Safety Association (AfBSA), Association of Mexican Biosafety (AMEXBIO), Association of National Biosafety (ANBIO), Arizona Biological Safety Association (AZBA), Biological Safety Information Network (BIONET), Carolinas Biological Safety Association (CaBSA), Chesapeake Area Biological Safety Association (ChABSAs), Canadian Association for Biological Safety (CABS/ACSB), Front Range Biological Safety Association (FRaBSA), Georgian Biological Safety Association (GeBSA), Israeli Biological Safety Association (ISBA), Midwest Area Biological Safety Association (MABioN), Mid-Atlantic Biological Safety Association (MABSA), Northeast Biological Safety Association (NBSA), New England Biological Safety Association (NEBSA), Pakistani Biological Safety Association (PBSA), Southern Biosafety Association (SBA), South East Biological Safety Association (SEBSA), Taiwanese Biological Safety Association (TBSA). Colors denote the relative respective geographical areas in which these organizations function.

DURC agent, however because it is a model for human pox virus in the mouse, research with this agent might raise scientific concerns, especially GoF concerns [8]. The intended purpose of the research was to develop and study a virally vectored contraceptive vaccine construct including the gene for targeted *zaona pellucida* glycoprotein 3 (ZP3) which had been previously developed with the addition of the mouse IL-4 gene. The concept was that IL-4 expression would delay viral clearance and thus

enhance the formation of antibodies and memory cells to the ZP3, leading to an extension of the period of infertility previously observed in ectromelia-ZP3 vaccine studies. However, the observed effect was to make the construct lethal in susceptible mice, and in previously ectromelia-resistant mice. Therefore, this was an unintended GoF experiment. The authors attributed these results to the immunosuppressive effects on cytotoxic T lymphocytes (CTL) and natural killer (NK) cells. Following publication of this manuscript, there was concern that this paper was a road map to creation of weaponized smallpox virus (*Variola major*). While there is ample room to debate this conclusion, the bigger issue is whether either the authors or their IBC should have predicted this result. There was previously published work similar to the Jackson study using vaccinia virus [9,10,11]. These studies did generate data that indicated IL-4 coexpression led to measurable reduction in Th1 cytokines, which are critical for antiviral CTL and NK cell responses. Therefore, a case could be made that the results reported by Jackson should have been foreseen. However, given the differences in pathogenesis of vaccinia and ectromelia in the mouse model, a counter-argument could be made that the highly immunosuppressive results could not have been predicted in the ectromelia study. For the purposes of this discussion it is not important to find fault or assign blame. What is important is to determine what, if any, actions an average IBC could or should take when presented with a similar proposal. Looking at Figure 10.2 we can determine that the Jackson study is not DURC. However, it does appear to fall under what we would now call GoF. Therefore the PI and the IBC would likely need to address these concerns formally before the studies are approved. The authors would then need to create a rationale of why the benefits of the proposed study outweigh the perceived risks. The IBC should be able to articulate their specific concerns perhaps citing the previous studies in vaccinia. Finally, a risk mitigation plan that includes the anticipated results of the study should be proposed, given the legitimate concern over how the information could be misused for altering other pox viruses. The IBC should communicate with the NIH-OBA to determine whether the risk mitigation plan adequately addresses any perceived risk in the proposed studies. This case study may or may not be covered explicitly in new federal GoF regulations but it likely represents the more common type of GoF problem for IBCs. Each institution will likely need to develop its own policy on what constitutes a GoF concern and communicate this policy to their investigators. Additional examples of case studies of this type can be found on the websites for the Federation of American Scientists (FAS) [12] and National Institutes of Health (NIH) [5,13].

Influenza

Future GoF research efforts on influenza virus, particularly highly pathogenic influenza virus, are likely to be affected by new federal oversight, select agent and DURC regulations. Highly pathogenic avian influenza strains are select agents, DURC agents and in some cases GoF agents if they are noncontemporary strains. The initial concern about influenza virus in particular was a result of a published study on creation of an H5NI virus that gained the ability to become transmissible by air between ferrets [15]. The observed increased transmissibility did not lead to increased pathogenicity (though the latter could not have been precisely predicted). The newly created virus

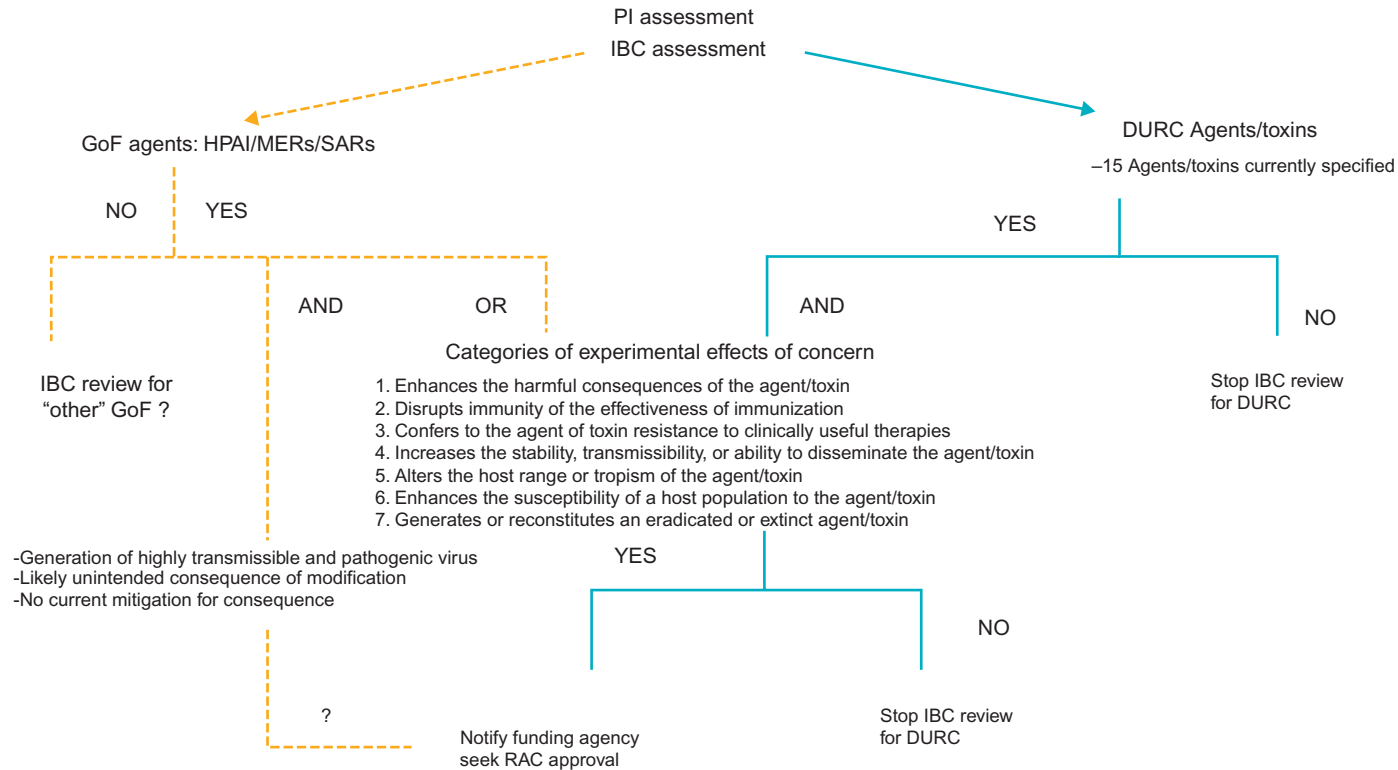


Figure 10.2 Integrated IBC Assessment Methodology for GoF/DURC Grants/Protocols. Categories of experimental effects of concern are specified for DURC protocols. The DURC agent list is available at Ref. [14]. Blue line, current regulatory requirement; yellow, possible regulatory/IBC approach.

was susceptible to both the currently recommended influenza vaccine and the licensed neurominidase inhibitor Oseltamivir. It appears that the authors of this paper and their respective IBCs exerted more than due diligence in reviewing, approving and monitoring this research project [2]. The concerns raised as a result of this research were initially focused on the inadvertent creation of an influenza strain with pandemic potential. This concern then became more global: creating pathogens that are transmissible via the aerosol route and thus more contagious or able to infect new hosts. The IBC must weigh the value of the information derived from the research study against these and other potential risks. In the case of the Imai study the balance of the equation of risk versus reward seems tilted towards support for the research. The information gained from the Imai study does improve our basic understanding of the influenza virus and in particular key amino acids that affect transmissibility. This information may actually help the public health community better respond to a potential future high-pathogenic avian influenza epidemic. In cases such as this, where the IBC lacks sufficient in-house expertise to address the risk–benefit ratio of a specific protocol or study, they should identify and consult with pathogen-specific experts outside the committee and/or seek additional guidance from NIH-OBA [16].

NIH major action

The NIH currently defines a Major Action as “the deliberate transfer of a drug resistance trait to microorganisms that are not known to acquire the trait naturally, if such acquisition could compromise the ability to control disease agents in humans, veterinary medicine, or agriculture” [1]. Because many recombinant strains are constructed using antibiotic resistance as a selectable marker, the IBC must pay close attention to protocols that propose such developmental experiments. Sometimes the IBC’s role in studies is to help avoid having a proposal fall in the Major Action category. Two common methods include demonstration that the antibiotic resistance marker is already present in environmental isolates, or with qualified help, make the argument that a resistance marker is not clinically relevant. In the first case, if a researcher or the IBC can demonstrate that a strain can naturally acquire a resistance marker, then the proposed work may be deemed to not be a “major action.” In the latter case the IBC may work with the researcher to prove that there is no resistance to clinically useful drugs. As an example, if a researcher proposes to use kanamycin as a marker in *Burkholderia* studies, a current tier 1 select agent, they could demonstrate that the aminoglycoside kanamycin does not confer resistance to commonly employed aminoglycoside drugs such as gentamicin or streptomycin. This evidence could be obtained from the literature or *de novo* research. If such evidence could be provided for this proposal the research would not be classified as a major action. If, however, the research is deemed to be a major action, the IBC must refer the protocol to NIH-OBA for review and approval.

Responsible officials: dual-duty biosafety officers and responsible officials (biosafety and biosecurity)

In the United States, the CDC and USDA administer current regulations for select agent research, and discussions covering these issues are included in Chapters 1 and 2.

The overarching guidance for biocontainment-based select agent research comes from the manual *Biosafety in Microbiological and Biomedical Laboratories (BMBL)* [17], currently in its fifth edition [17]. This text should be considered a primary guidance document for the IBC when addressing questions related to select agent protocol biosafety review and approval. Elsewhere the WHO guidelines on microbiological research are followed [18]. The institutional BSO is responsible for overseeing biosafety operations in the laboratory and the Responsible Official (RO) is responsible for the security of select agent inventories and overall compliance with the select agent program inclusive of biosafety. These two individuals should be members of the IBC as either voting or nonvoting members. Their primary function during the review is to identify specific issues for consideration by the IBC that are unique to select agent research. These issues may include compliance of laboratory facilities, security concerns, or safety concerns for the intended research. These roles may also be performed by other experienced and knowledgeable IBC members when the RO or BSO are not present or lack the requisite knowledge. The IBC should not rely on an appointed BSO/RO who does not have relevant biosafety experience, including containment laboratory operations and regulatory compliance for select agent research. As an example, in many institutions, BSO duties are often assigned to someone in the Environmental Health and Safety (EH&S) office as an additional duty. Often this might be a chemical hygiene or occupational health expert. However, EH&S professionals will likely lack the requisite biosafety competencies required of the BSO. In such a circumstance, the IBC should seek outside expertise to supplement the committee's review of protocols involving select agent research. Examples of this supplementation are discussed below.

Institutional oversight and IBC quality improvement of select agent research-related issues

Membership and use of subcommittees

Collectively, most would agree that the ideal IBC would consist of highly motivated properly trained and/or experienced individuals that have a mindset focused on assisting the research efforts for safe and compliant research while protecting their institutions from bad publicity, fines, and possible lawsuits. There is no single accepted approach that leads to the development of the right IBC mindset. However, when the IBC focuses on what is optimal for the applicant as distinct from what is optimal for the IBC unnecessary conflicts and delays can be avoided. IBCs that are the most successful at implementing this approach often have direct support from their institutions. This support may include financial assets or direct support in the form of administrators that can implement or assist the IBC members with "best practices." These may include IT-based solutions such as websites with protocols, information products, and/or templates to help the investigator submit their proposal in a timely fashion and identify and address regulatory issues.

A good IBC can often have significant impact and shorten times for IBC approval by becoming involved in research projects, which fall under their oversight as early

as possible. Often that time would be during the preparation of the grant proposal. When most grants are prepared, the PI recognizes the need for IBC approval for certain aspects of their work. However, IBC protocol applications are often deferred pending a firm grant award. The IBC may be able to contribute to the substance of a proposal by identifying potential biosafety and biosecurity issues early on, limiting risk to the institution should the grant be funded, and also likely shorten the time-line for IBC approval of the formal protocol. The IBC may form a subcommittee that works closely with their Office of Research to identify and prereview protocols that have identified IBC compliance or select agent research issues as components of the submitted proposal. This subcommittee should work directly with the PI to identify and mitigate issues associated with select agent research.

A second subcommittee that IBC may find useful is one focused on occupational health and worker safety [19]. This committee could consist of one or more members of the occupational health program (OHP), an institute clinical representative, a representative from human resources, and/or an institute legal representative. A health and safety program provides a means to ensure that the risks associated with laboratory activities can be mitigated to best protect the scientific staff and the community. Thus, input from OHP can be a valuable part of the IBC protocol review process. A medical monitoring program, if appropriate, can also help establish inclusion and exclusion criteria for lab staff based on perceived risks and medical conditions of employees for potentially hazardous research. The IBC should work closely with OHP at their institute to recommend specific medical countermeasures matched to the risk involved in each procedure/laboratory. These countermeasures may include vaccinations or plans for provision of therapeutic treatments, such as oseltamivir or ciprofloxacin, should there be a high level of suspicion of the possibility of exposure. This committee may also be charged with helping to prepare agent-specific information documents for the PI, the biocontainment lab's biosafety and incidence response plans and/or for institute or private clinicians or healthcare providers. Finally, this committee can also develop recommendations for initial and/or on-going assessment (physical and/or emotional) of select agent workers in concert with the RO. This final task is often performed outside the purview of the IBC but inclusion of an IBC subcommittee often closes the loop on several issues including communication of requirements, fostering understanding of the IBC on the rigorous oversight of select agent researchers, and understanding the nature and extent of time and training which is required to obtain select agent clearance from both the federal and institute regulators.

Additional support is available in the form of professional and academic outreach, fellowships, and mentorships. The IBC should ideally have one or more biosafety professionals on the committee. This expertise will help identify and address unique challenges when studies involve select agents or biocontainment activities. If such experience is not available, there are experts in the field and different geographical areas that can be called on for assistance. To ensure successful recruitment of *ad hoc* experts, the IBC should join and/or support regional biosafety organizations. A representation of the ABSA affiliate organizations is shown in [Figure 10.2](#). ABSA and its regional affiliate's membership include a large number of biological safety experts with nationally recognized credentials whose expertise can be brought to

bear on problems ranging from regulatory compliance to protocol-specific biosafety/biosecurity concerns.

Biosafety, biosecurity, and surety expertise are gained by recruiting and utilizing staff and committee members with specialized backgrounds and expertise. In general, the IBC is responsible for ensuring that the committee membership includes individuals with the requisite technical expertise to properly assess the risk involved in proposed studies and whether proposed facilities and procedures are adequate to mitigate these perceived risks. One area which is often overlooked is the inclusion of persons with expertise in biosecurity. These responsibilities are often assigned to the Biological Safety Officer (BSO). However, not all assigned BSOs have either training or practical knowledge to properly perform biosecurity duties for the IBC. A person with nationally recognized credentials, such as a Registered Biosafety Professional (RBP) or Certified Biosafety Professional (CBSP), will usually meet the requisite requirements. The IBC should develop procedures to assess the expertise of their appointed biosafety officer or seek outside expertise to supplement the committee as needed. In addition to the basic requirements in biosafety and biosecurity, two additional areas of knowledge must be covered by the IBC: biological surety and gain-of-function (GoF) research. These areas may be the purview of the BSO or may be covered by other IBC members.

Special surety requirements

Just as NIH regulates rDNA research and requires the IBC to implement policies and oversight to ensure their guidelines are met, other federal agencies such as the Department of Defense (DoD) have special compliance rules. The IBC has a role in compliance of these DoD rules. Institutions that accept grant funding from DoD for research involving select agents must implement a biological surety program. Biosurety is described in Army Regulation 50-1 and DoD directives 5210.88 and 5210.59 [20,21]. These documents describe personal reliability or surety requirements beyond those required by CDC or USDA. The IBC must ensure that these directives are met, for example by establishing working groups or subcommittees with members from the relevant working groups including *inter alia*, the institute research office, human resources, legal, IBC, IACUC, and IRB.

Lack of appropriate biocontainment experience on the IBC

It is not uncommon for members of the IBC to be unfamiliar with noncontainment laboratory space and procedures in their institute and even more likely the case for biocontainment work. An example of a common issue in the nonbiocontainment space that affects safety includes issues such as access to autoclaves. If a laboratory worker has to travel through heavily trafficked public corridors, up or down public elevators, and then has to stage waste outside of the autoclave in a public area, this represents a potential increased biosafety and biosecurity risk as compared to an in-lab autoclave. IBC members unfamiliar with the laboratory layout may not perceive this risk. The same is true for biocontainment operations. Interestingly, a retrospective study which examined the effect of NIH site visits on improving oversight and

regulatory compliance for rDNA research by IBCs [22] has not yet been extended to work on biocontainment operations. The IBC can seek one of many outside experts to evaluate their containment laboratory operations and facilities and provide feedback to the IBC. Often IBCs may be hesitant to pursue this route through government regulatory agencies as findings can impact on-going laboratory operations and/or be construed as punitive, given the nature of the findings. There are also professional consultants available for hire to perform this type of assessment but this may be cost-prohibitive. The American Biological Safety Association (ABSA) has proposed a site-visit-based accreditation program [23]. The role of the IBC in the accreditation program is not specified but it would be reasonable to assume they should play a role in compliance and problem resolution following accreditation visits. Because ABSA is not a government regulatory agency and their findings are confidential, this may be a reasonable way to educate the IBC, identify and remedy shortcomings and improve the safety and security of biocontainment laboratories, especially those which conduct select agent research.

Complex projects involving animals

The IBC should establish procedures to address biosafety and biosecurity risks associated with all aspects of select agent work in animal studies. These include, but are not limited to, examination of the waste stream, ensuring the animal room is properly posted with biohazard signage, determination of the infectious risks from animals to humans and if select agents are involved special precautions to prevent theft or misuse. The IBC should develop a pathogen road map to ensure that all biosafety and biosecurity concerns involving select agents are addressed by the PI. An example of this road map is shown in [Figure 10.3](#). In this figure we see the traditional roles of the IBC and IACUC and the areas of new or expanded emphasis the IBC should expect to evaluate for new research proposals involving select agents or select agent studies in animals. The IBC should use the roadmap or a similar template or checklist to determine whether the PI has addressed all critical steps in their protocol. The CDC and USDA often request this type of information from the PI at the time application is made for permission to work with a select agent. Often, the BSO or RO can bring this information directly to the IBC and the IBC should then ascertain whether those procedures are present in sufficient detail to mitigate the identified risks. The institutional Biosafety Officer can help identify and address biosafety and biosecurity gaps for both select and nonselect agents. An effective way to ensure this occurs is to assign the BSO as a member of both the IBC and IACUC committees.

As is often the case in infectious disease research there is significant overlap for safety concerns when animals are intentionally exposed to infectious agents. Both the IBC and the IACUC committees may only perceive portions of the risks associated with such work. Members who have served on both the IBC and IACUC are invaluable in identifying these overlap risks. Risks include biosafety-related procedures for propagating and manipulating select agent cultures, security of select agents, sharps management, animal exposure methods, animal-to-human transmission risks, and overall waste management. A risk commonly overlooked by the IBC and IACUC

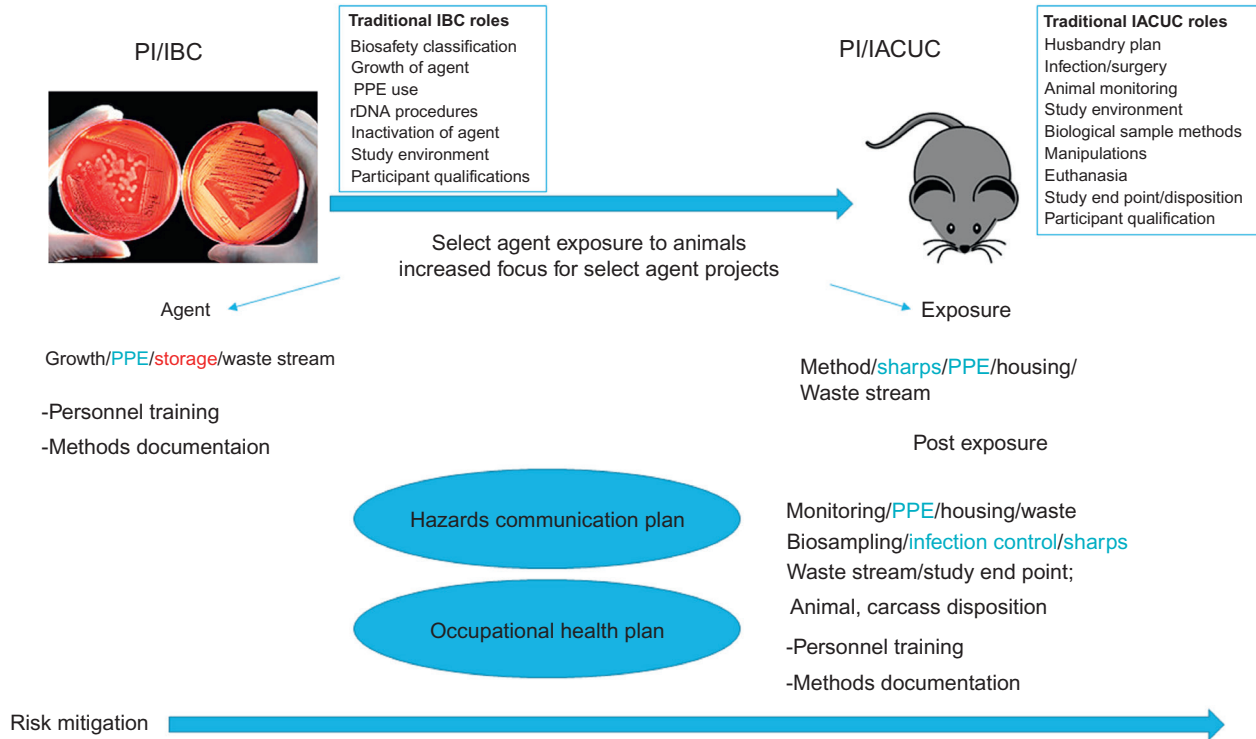


Figure 10.3 Pathogen road map. The traditional roles of the IBC and IACUC are shown as insets. These roles are expanded in scope when overseeing select agent research projects and are more complex when animals are involved. Risk is mitigated by implementing review for all items shown in the graphic, including the development and use of hazards communication tools and enrollment of affected persons in an active occupational health program. Font colors indicate issues involving both biosafety and biosecurity aspects (black), principally biosafety (blue) and biosecurity (red).

is management of animal waste and bedding. If infectious agents are present in the animal waste they pose a biosafety risk that the IBC and/or IACUC may not perceive or address as they may think the other committee will address the hazard. The IACUC considers allergens a primary exposure of concern, and the issue of animal bedding is often neglected altogether by the IBC. When an animal is infected with a select agent that animal, its biological samples, and often animal waste are classified as select agents. If a select agent can be shed in animal secretions the disposition of contaminated materials must be addressed in the IBC protocol and should also be addressed in the IACUC protocol.

Figure 10.3 also highlights additional risk mitigation tools. First, is the role of an effective occupational health program, enrollment in this program is not required for work with non-tier 1 select agents but is required for tier 1 select agents. Often, the best practice is to enroll all select agent research staff in the occupational health program to fully cover management of occupational exposure to select agents. A second useful tool is the development of a hazards communication plan or tools. Essentially, this tool can be tailored to include the entire laboratory, separate research spaces, or even individuals. The components of this tool/plan include hazard identification methods (e.g., labels, room placards), communications methods (e.g., in person meetings or text messages such as “Anthrax in use in room XX on these dates”), and what needs to happen if something goes wrong (e.g., Incident Response Plan). Finally, it is important to note that it is not the primary role of the IBC to dictate how the PI establishes proper safety and security protocols *per se* but rather to evaluate the adequacy of the procedures to meet the intended purpose, the guidelines established by NIH or the *BMBL* [17] or other specific institutional regulation or best practice. In general, the PI and IBC should work together to identify areas of risk in the research proposal, define appropriate methods and evaluate these methods for adequacy in terms of both biosafety and biosecurity and, finally, propose risk mitigation strategies in cases where the hazard may not be fully understood.

Infrastructure and resource challenges

IBCs develop and implement detailed procedures and policies for users. However, they often overlook the burdens, sometimes unnecessary, that these procedures place on the research community. Often the retort to complaints by PIs about overly onerous requirements is “that’s the policy,” a response that may create frustration and tension amongst the research staff that in turn may lead to noncompliance. When the IBC takes a different approach and seeks to improve and streamline application procedures, there is often more buy-in from researchers and better compliance. An important factor in compliance is protocol turnaround times. Many laboratory protocols are time-consuming to write and researchers frequently find themselves facing deadlines. Anything the IBC can do to reduce turnaround times on reviews is highly valued and appreciated by the research staff. Recognizing this key item, the Biohazard Compliance Office (BHC) at the University of New Mexico implemented internal procedural changes that reduced their turnaround times from 14.3 to 0.9 days [24]. Almost any IBC can reduce review and turnaround times for IBC protocols with

such an introspective approach that values the PI as their customer versus someone who needs to be “regulated.” The IBC itself, or the Institute Official, may also wish to use processing times as a measure of efficiency or responsiveness or an indirect measure of workload for the IBC. This may be useful in discussions on administrative or resource support for the IBC.

Biocontainment facilities are unique

The IBC plays a role in not only the initial design and modification of containment laboratories but also in the safe continuing operations of the facility. Therefore, the IBC must have a detailed understanding of their biocontainment facility design and operation. When the IBC is not involved in design or modification discussions a knowledge gap is created. No two biocontainment laboratories are the same in layout though many are similar in function or capabilities. This happens for a number of reasons including architectural design, budget, user input, building restrictions and most importantly the various interpretation of standards for construction. Standards affecting construction of the facilities themselves are often drawn from multiple sources including local building codes, state building codes, and guidelines such as those in the NIH *Guidelines* for construction [25], USDA facility design guidelines [26], *Biosafety in Microbiological and Biomedical Laboratories (BMBL)* [17] or American Society of Heating, Refrigerating and Air Conditioning Engineers (ASHRE) [27]. Another recent standard that affects air handling within biocontainment facilities is ANZI Z9.14 [28] and the IBC can rely on the results of the tests as set forth in this standard as proof that the facility design is safe. As an example of design variations two different architects will read the BMBL requirement “Floors must be slip resistant, impervious to liquids and resistant to chemicals. Consideration should be given to the installation of seamless, sealed, resilient or poured floors, with integral cove bases.” These two architects will in turn design two different solutions after consideration of a number of variable factors including cost, durability, and maintenance. This same scenario plays out for all aspects of the laboratories’ design including but not limited to doors, anterooms, autoclaves, shower facilities, etc. Consequently, this poses unique challenges and opportunities to managing risk in the facility both for the staff and the IBC. The IBC should add the Biocontainment Facility Director or Manager to the membership of the committee to address facility-related questions. This person can best address the capabilities and limitations of the facility in general or as it pertains to a particular research proposal. This subject is addressed in greater detail in Chapter 4.

Additional importance of time on biocontainment studies

Biocontainment studies are often scheduled well in advance or are scheduled in a tight window for completion at the biocontainment facility. Biocontainment laboratory spaces are often not assigned to single users or even single pathogens. These spaces often must be decontaminated, and reconfigured to support individual research protocols. Therefore, unexpected delays in beginning work are often critical to completion of planned studies, facilities utilization, and reporting to granting agencies. These considerations impact labor and costs beyond the individual PI. The IBC should be aware of these special biocontainment limitations and establish a fast-track approach

to review of biocontainment studies or other procedures which will expedite the process. This is not to say that protocol reviews should be rushed or that due process is skipped to accommodate poor planning on the part of the PI. If the IBC publishes their standing committee review schedule and submission deadlines this greatly aids PI compliance. Additionally, if the IBC identifies the need for biocontainment work at the time of grant submission they can work with the PI to identify their expectations on issues for which the PI must prepare information to support an IBC submission.

Select agent PIs as IBC members

Because select agent or biocontainment research in general is more complex than research at lower biosafety levels, the best and most experienced IBC members have often performed research in biocontainment facilities. This experience provides insights into both risk areas as well as reasonable solutions to biocontainment research. If biocontainment researchers have a positive perception of the IBC process and can be convinced of the need for their expertise they are often more willing to participate as an IBC member. These select agent PI members often know and are familiar with other select agent research occurring in the biocontainment lab and can mentor new or junior faculty in meeting IBC expectations for protocols and procedures.

Summary remarks

Work with select agents often engenders an unreasonable amount of fear and apprehension both in the public and within the scientific community. A knowledgeable and well-run IBC is a key asset in allaying worries about research conducted with select agents. In particular, the IBC can institute sound reviews and implement policies that mitigate risk both to the research staff and the community. Additionally, with capable community members as part of the IBC more effective communication with the public can help educate the community on the benefits of select agent research. Staffing the IBC with the “correct” persons can dramatically streamline select agent research, improve biological safety and security and ensure regulatory compliance by answering the two basic questions: Is it safe? And is it legal?

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