

1. Introduction and Executive Summary

2.A. Introduction:

An external review of the biosafety program at the University of Chicago was initiated by the Provost and Deans of the Biological Sciences Division following two unfortunate adverse incidents, one in 2009 and one in 2011. Although both incidents were reviewed by government agencies and did not result in adverse findings against the University, it was felt that an external review of 1) the biosafety programs and pathogen research labs, and 2) some evaluation of the significance, or not, of the two biosafety incidents that occurred in relation to biosafety practices would be useful to the academic community. The Chair of the Provost's External Biosafety Advisory Group was selected and invited to serve after consultation with diverse members of the community. The Chair, Virginia L. Miller, PhD then selected the remaining members of the committee and presented them to Dean Conrad Gilliam for approval (all were approved). The members of the committee were:

Virginia L. Miller, PhD [Chair]

Professor of Genetics, and Microbiology & Immunology
Associate Dean of Graduate Education
University of North Carolina, Chapel Hill

Paul Keim, PhD

Regents' Professor of Biology
The Cowden Endowed Chair in Microbiology
Director, The Pathogen Genomics Divisions, The Translational Genomics Research Institute
The Center for Microbial Genetics and Genomics
Northern Arizona University

Domenica (Dee) Zimmerman

Biosafety Officer
Environmental Health & Safety Consultant
Environmental Health and Safety
University of Texas Medical Branch, Galveston

David L. Wynes, PhD

Vice President for Research Administration
Emory University

Mark R. Denison, MD

Craig-Weaver Professor of Pediatrics
Professor of Pathology, Microbiology & Immunology
Vanderbilt University School of Medicine

The Biosafety Advisory Group had the full cooperation of the University in performing its review in terms of having access to documents, and scheduling interviews with people at all levels.

2.B. Executive Summary:

The University of Chicago is quite fortunate to have such a dedicated Biosafety Officer in Dr. Joseph Kanabrocki, as well as other staff from the Office of Biological Safety who are similarly committed to their work. Those at the University that interact regularly with these individuals – whether it be staff, administration, researchers, or the two IBCs – have nothing but praise for their expertise, dedication, and willingness to help them with their research program and biosafety needs. However, this staff is currently stretched thin and unable to cover all the needs of a full biosafety program for an institution such as the University of Chicago, as is discussed in more detail below. Similarly, there is a thorough review process by the Institutional Biosafety Committees (IBCs) of work deemed to involve biosafety risk. We would also like to highlight the efforts of Dean Gilliam to build bridges following the 2011 incident with the weekly town hall meetings. However, despite these strengths the two unfortunate incidents mentioned above revealed some weak links in the system. A detailed description of our perception of these weak links and some suggestions on how they might be addressed follow this summary.

It is our observation that the lingering misconceptions and distrust from the incidents, and *potential for future incidents* were influenced by the following:

- Poor communication to the university community (other than the Department of Microbiology) about the incidents, especially immediately following the incidents.
- Poor visibility one-on-one of personnel from the Office of Biological Safety (OBS) across campus as a partner in developing a safe research environment, and thus as a group to be trusted in the event of an incident.
- Under staffing of the OBS contributes to the inability of the OBS to achieve greater one-on-one visibility beyond labs working at BSL3, or to provide more hands on training and on-site risk evaluation.
- The reporting structure of the OBS with respect to Environmental Health and Safety (EHS) is different than at many universities, and although this many not need to be changed the university community would benefit from more communication between these groups.

Some key recommendations of the group are:

- Preparation of a response plan in advance; engage key stakeholders in preparing this plan and review the plan periodically to ensure it is up to date.
- Ensure that there are adequate resources for the OBS and that these resources come from the central administration. It is key for minimizing the potential for a future incident that the culture of responsibility achieved at the Ricketts Lab be achieved at all risk levels.
- Integration of IT systems across the IBCs, EHS and OBS will helps ensure worker training is up to date and tied in with lab protocols.
- Work towards greater integration/coordination of EHS and OBS services to the laboratory so that signage and contact information in buildings, waste pick up etc. are

kept up to date and done in a timely manner. This will also help maximize use of personnel resources.

2. Background and Concerns: Response to incidents

It was neither the charge nor the intent of the External Biosafety Advisory Group to investigate the details of the prior incidents. However these incidents, and to the response to them, has impacted the perceptions of the biosafety program and microbiology research, as well as affecting scientific interactions within the Cummings Building and general confidence and trust among investigators, staff, and administration. During our conversations with multiple staff, faculty, students, and administrators the incidents and the response continually arose as a central issue. Thus we queried people about: 1) awareness of the incidents; 2) adequacy of communication to determine risk for themselves and their students / workers / department / building / community; 3) where they obtained information; 4) sense of closure or continuing anxiety concerning the outcomes; 5) role and contributions of the Office of Biological Safety /Biological Safety Officer; 6) sense of satisfaction / trust in the outcome; 7) effect on research, collegiality and collaboration; 8) impact on trust in leadership and biosafety program. Several common themes emerged, as did some clear dichotomous impressions and continuing concerns. These are mostly based on the incident of August 2011, but these most likely had their roots in the earlier incident in 2009. We did not try specifically to ascertain the source or reliability of information, which in some cases may be based on data that was miscommunicated or misunderstood. Nevertheless, we feel that the background of communication and response is relevant and important for reviewing and augmenting a Biosafety Program and culture that is responsive to the needs of all investigators and members of the University of Chicago community.

2.A. Communication:

- Communication within the Department of Microbiology laboratories was current and rapid. Investigators, students and staff felt they had information that allowed them to make appropriate estimates of personal risk balanced with risk of offered prophylactic / presumptive antibiotic treatment.
- In contrast, communication outside of the Department of Microbiology was incomplete, late, or absent. The timing of communication was not current with events, and often information was obtained ex-vacuo from rumors or from news reports. There was an impression that Biological Safety was not advocating for all labs and workers in Cummings, and was not available or communicating effectively.
- The PI of the laboratory involved and Biological Safety Officer should have been allowed / encouraged / required to communicate their knowledge better beyond the Department of Microbiology.
- There is a perception that communication by the Biological Safety Officer or others was constrained or limited, or proscribed by the legal counsel office based on HIPAA regulations as well as potential legal risk to the University – *and that this potentially put them at risk.*

- There was a concern that the administration was not willing to communicate fully and in writing due to the risk of such communication being used in a legal action against the University.
- Lack of any communication led to a vacuum filled by rumors and possibly unwarranted concern.
- Lack of a very clear and timely summary to other Department Chairs or responsible leaders resulted in continued mis-impression of risk of organisms, of communicability, even of whether or not organisms were genetically engineered. Some of these misperceptions still exist today.
- Trust in the process would have been enhanced by communication, even by communication that was limited to information such as: “We may have a lab associated incident, we are not sure exactly what has happened yet but we are investigating. We do not believe there is any risk of transmission. We will keep you current. We have to protect the privacy of the individual investigators involved. Here is the best data we have at this time on possible causes.”
- An email to Cummings investigators later in the course of the incident with the general introduction something like “the events you are already aware of” was highly concerning because there was no general knowledge of events or understanding of risk to those who received the email. This engendered significant concern about breakdown in communication pathways and appropriate response.

2.B. Response to Incident:

- Decontamination of the 6th floor.
 - The decontamination of the 6th floor gave an increasing sense of confidence and safety to those working on that floor on an ongoing basis.
 - Decontamination of the 6th floor gave a sense of “hurry” or “cover-up” in the absence of detailed sampling or efforts to determine chronology or source of the infection.
 - The lack of sampling or decontamination of other floors left concerns - that persist – of possible contamination (albeit low) and risk associated with research in Cummings.
- Moving of research materials and investigators to HTRL.
 - The movement of research materials and investigators to HTRL was not predicated on a determination of increased risk or the investigation of the lab associated infection’s origin, but rather was determined by the PIs. It also appeared to be an effort to focus the work in one location for better control / regulation of risk, as well as the ability to completely decontaminate the 6th floor while maintaining an active research program.
 - Moving the lab programs influenced the perceptions of others at Cummings.
 - Many felt relief that materials and work was away from the main campus and in a more secure and “safe” environment.
 - Some came to the conclusion that the organism and work previously being performed in Cummings were more dangerous and risky than originally communicated, and that this move reflected part of a “cover up” to avoid a detailed investigation of how this occurred.

- Some had a general perception that all microbiology research is more dangerous and risky to both investigators and others in the building than has been acknowledged or communicated.
- There is a general sense that the move resulted in a loss of potential interactions among departments and possibilities for joint research – and loss of potential joint recruits.

2.C. Continuing Concerns and issues to be addressed in a Response Plan:

- Work with pathogens is performed in shared environments (open labs, in a hall, on a floor, in a building) at the University and, yet, there is no general awareness of which organisms are being worked on where. The need for such information should be shared. The level of detail, training and dissemination of information should be based on proximity and risk, but it also needs to be determined in advance of an incident.
- Chairs of other departments (in addition to Microbiology) sharing the Cummings Building, and responsible for many investigators / staff / trainees, should have pathways for clear and up-to-date communication in the event of an adverse incident. Even if the University deems it necessary to limit broad dissemination of incident information, focused and rapid communication to departmental leaders is crucial.
- The Biological Safety Officer needs to be viewed as independent and serving the needs of the entire University and Research Community.
- Administrative Leadership in consultation with the Biological Safety Officer need to assess the true need for withholding or limiting information prospectively, rather than react to non-specific concerns about legal liability.
- There is a need for current signage on floors / labs, as well as for current and updated contact information.

3. Planning for response to a future event

3.A. An institution of the size and complexity of the University of Chicago, and conducting important microbiological research must strive to minimize the risk of laboratory acquired infections, but at the same time prepare for such an eventuality. Despite the University's best efforts, the risk cannot be reduced to zero and it must plan for such health risks to its people, as well as the legal and public relations consequences. Multiple components must be considered in a crisis management plan that includes the immediate welfare of the victims, limitation of health risks for others, and the active management of information to control rumors and instill confidence in the actions of authorities striving to protect human welfare. A crisis management plan that leads to the appropriate response is essential and such a plan for future incidents may exist but was not clearly articulated to the review panel.

3.B. The plan's development process can be viewed as an important step in communication among the University's administration, occupational health personnel, biosafety personnel, faculty, staff and students. The development of the plan should include relevant stakeholders and should be viewed as a continuing process in that any plan should be viewed as a "living document" that is frequently revisited and revised. The current "gulf" that exists among

different components of the University's academic community might be ameliorated by active stakeholder participation in the response planning for future incidents. The stakeholders certainly include biosafety, occupational-health, departmental leaders, public relations, university legal, law enforcement, public health, etc., but also members of the academic community that would be in the same work environments as might be affected. Public and broader community representation might also be included in the development of a crisis management plan.

3.C. A plan should include general principles, specific strategies, and designated individuals for communication. We recognize that during the time of crisis, communication is a complex and difficult task but it is essential to protect health and safety by allowing the appropriate biosafety response, by enabling victims to seek necessary healthcare, but by also minimizing unnecessary public anxiety. It is clearly difficult given the many unknowns and rapidly changing conditions that occur during crises. A lack of information will always be filled by ill-informed rhetoric that is always counterproductive. Under communication leads to a mistrust of response authorities, unneeded public anxiety and potentially counterproductive public actions. False assurances or the overstatement of risks both lead to inappropriate responses.

4. Need to provide full service biosafety program from BSL1-BSL3

The role of biosafety in research is a resource and tool that must be made available for laboratorians that work at biosafety levels 1 through 3 with the corresponding agent risk groups. The level of risk is based on the modes of transmission, microbiological technique, personnel protective equipment and the facility design. The agents in use may be viruses, bacteria, parasites or fungi, with shared modes of transmission and protection factors. The greatest impact to any safety program is when risk is not evaluated and protection factors are not implemented in a timely manner. No department, division or person working with a biological agent is exempt from adhering to basic principles of biosafety.

The shift of parts of the Department of Microbiology laboratory to the Ricketts Laboratory in order to relieve the concern of building occupants has sent a message that is detrimental to interdepartmental relationships on many levels (see more on this below). *Any* breakdown in good biosafety practices has the potential to result in an increase in risk of exposure to the laboratorian and the community at large.

- Movement of research to BSL3 laboratories should not be considered as an appropriate default response for organisms the main campus does not want to deal with or is uncomfortable with. Square footage for BSL3 is limited and there will come a time when it will be needed for BSL3 not BSL2 work. In addition, this bypasses appropriate risk assessment and the need for communication and education of the University community.
- Dividing BSL2 researchers from the academic life of the main campus unnecessarily impacts the quality of interactions between departments over time, as well as having immediate effects for the Department of Microbiology. Although videoconferencing is available and in use, spontaneous interaction and a sense of belonging to the academic community has been and will continue to be impacted.

- BSL2 laboratories are numerous and dispersed across the University of Chicago main campus. These are the laboratories that are most underserved by the Office of Biological Safety (OBS), where the use of human pathogen research is being conducted in multiple departments and biosafety evaluation or knowledge may not be consistent with risk. In the absence of a close working relationship between BSL2 laboratories and OBS personnel this risk increases.
- Undertraining of those doing lentivirus work for example was cited during our discussions; however an understanding of the criticality of good biosafety, role of facility design in biological agent containment and microbiological practices would be advantageous for all BSL2 researchers and not just those working with lentiviruses.
- The strong culture of responsibility and biosafety that exists at HTRL should be the model to replicate in all the BSL2s. This will be more difficult to accomplish on the main campus. However a strong culture of biosafety will benefit the community at large and will foster an interactive academic community from faculty down to graduate student. This can be accomplished with daily interaction and awareness from the excellent base that currently exists in the Office of Biological Safety.

5. The isolation of the Department of Microbiology

In conversations with faculty, staff and students it appears that over time there has developed a 'silozation' effect for the Department of Microbiology creating the current situation where the Department of Microbiology is academically isolated. The microbiology graduate program, for example, withdrew from participation in programming with similar graduate programs on campus, and graduate students have been instructed to not 'borrow' or use equipment in other departments within the Cummings Building. Decisions such as these, although perhaps taken for good reason, reduce interactions between students and faculty between disciplines and reduce cross talk over time. This has contributed to a lack of understanding and knowledge by other groups about the type of research being done in the Department of Microbiology and contributed to the lack of communication during the incidents. It contributes to the suspicion that lingers even now. This is currently reinforced by the recent move of significant portions of the research programs of several prominent research groups within the department out to the HTRL.

This silo effect has contributed to an environment that reduces collaboration, will continue to inhibit collaboration between groups and will inhibit the research community's ability to recruit researchers in the future. We were told of one example where it already has done so. The isolation of the Department of Microbiology likely will impact the future competitiveness of the University as interdisciplinary research and team research programs are currently the top priority for NIH funding. It is our opinion that there needs to be leadership at multiple levels to aid in the re-integration of the Department of Microbiology into the greater University community.

6. Administrative structure

6.A Elements of the Biosafety program are located under multiple administrative units. Specifically:

Institutional Biosafety Committees (IBCs; traditional biosafety and select agents) and their support office fall within University Research Administration under the Office of the Vice President for Research. These committees meet the regulatory review requirements set forth by the federal government. The support office focuses on general IBC administrative support, administrative review of registration applications, and coordinating the registration process with the research community.

The **Office of Biological Safety (OBS)** is a component of the Office of the Dean in the Division of Biological Sciences, and the Director is also a faculty member in the Department of Microbiology. This unit provides biosafety training on campus, however the line of responsibilities between its training functions and those of Environmental Health and Safety are not clear. Staff in this unit also provides scientific review of IBC registration applications prior to sending them to the Committee(s) for review. The member of the OBS based at the Ricketts facility is also closely engaged in the day-to-day operation of the facility and the research that is conducted at that site.

The **Environmental Health and Safety Office** is in the Office of Risk Management, Audit, and Safety under the Vice President for Finance & Administration. EHS provides a variety of training programs such as the handling of bloodborne pathogens and use of biosafety cabinets. This office also maintains all waste manifests, including those for infectious and biological waste. EHS is much more engaged in programs such as radiation safety, industrial hygiene, and lab safety involving the use of hazardous chemicals. EHS also manages the collection and disposal of radioactive and chemical laboratory waste.

Stockroom clerks within the Facilities group under the Vice President for Finance & Administration collect infectious and other biological waste from individual laboratories.

We believe this structure for the “cradle to grave” management of a biosafety program in laboratories is substantially more fragmented than is common at academic institutions. This current structure results in a great deal of confusion among members of the research community. They report being “bounced around” when trying to address questions and concerns regarding their IBC paperwork as well as operations in the laboratory, and they frequently used the incorrect office name when discussing their interactions and frustrations. The end result is frustration and lack of clarity when seeking advice and assistance.

6.B. One option is for the University to consider a reorganization of their programs along the lines more commonly found at peer institutions which house biosafety and the administrative support for the IBC under the umbrella of the Environmental Health and Safety (EHS). An alternate approach is to charge the heads of these offices to develop a coordinated program with clear delegation of responsibilities. The roles and responsibilities regarding training need

to be clarified and formalized between the Office of Biological Safety and Environmental Health and Safety.

The goal should be a system that presents itself to the research community as a *unified* laboratory safety, or at least biosafety, program. The end result ought to include strategies to make understanding the organizational structure by research personnel unnecessary. One approach could be establishing a single point of contact/call center (suggested to be housed in EHS) where all calls and emails can be directed and the individuals staffing this function would then be responsible for assuring that the correct individual or office makes contact with the research personnel. Those individuals contacting this center would not be sent elsewhere, but the appropriate professional would contact them back directly and the call center would be accountable to assure that return contact was made. Finally, advice on web design should be sought to provide a clear and coordinated resource for both new and experienced investigators, staff and students working with biological materials in the laboratory.

7. Personnel and resources needed for the Office of Biosafety

The University of Chicago is a research intensive institution with a significant amount of research involving biosafety-related issues. Currently the Office of Biological Safety (OBS) is understaffed and unable meet its mandate of effectively serving these needs at all levels. The OBS has done an outstanding job of meeting the needs of those working at the BSL3 level and developing a face-to-face relationship with these investigators. However, for other laboratories doing other risk group/biosafety level work the OBS is more of an email/paperwork office that serves as an adjunct to the Institutional Biosafety Committee (IBC). Developing a face-to-face relationship where the OBS is a partner in developing a safe working environment and becomes the go-to unit for training when a lab brings in new protocols is critical for developing the trust needed when things go awry. More personnel are needed to get out into the labs regularly to do risk assessments/inspections. Specifically our assessment suggests a minimum of 2 additional biosafety officers will be required to meet the needs of the main campus.

Furthermore the OBS needs to be involved in mandatory training linked to IBC protocols. While much of this is likely to be done by some sort of online format, ideally there will be some in person contact as well. Some suggestions for this include:

- Developing a basic biosafety workshop for incoming graduate students.
- Having OBS personnel available to assist labs navigate through the logistics of new protocols to determine the biosafety risks and identify means to minimize them.
- Establish a “train the trainer program” where each lab identifies a lab biosafety coordinator that would participate in a basic biosafety workshop and be responsible for training new personnel that enter the lab. Including a practicum on good microbiological practices and facility design would enhance biosafety and further reduce risk resulting in a standardization of practice across all laboratories.

During our visit it appeared that some of the personnel in the OBS were directly supported by the Department of Microbiology. While we have complete confidence in the integrity of Dr. Kanabrocki, the Biosafety Officer, in our opinion, this has the potential to create a *perception* of

conflict of interest and possibly compromise his effectiveness with other units and potentially hinders his ability to build trust especially after the two incidents. Thus, we recommend that sufficient support for the OBS come from central administration resources.

8. Need to update and integrate IT systems

The IBC is currently operating an administrative system that is not in keeping with current technologies and likely requirements for documentation of protocols, training and ongoing assessment of safety. This results in a cumbersome process that also is lacking in ready access to essential information by its own staff as well as others on campus (Biosafety, Environmental Health and Safety, and Occupational Health). The application form is a writeable PDF document that requires double entry of any information that the IBC Office wishes to track. The Office, therefore, captures in its database only that information which is necessary for tracking protocols. This database is not the current generation of Access database and even its limited information is not accessible to other units

We were informed that there are current plans to update this system to use the Huron/Click Commerce software IBC module. We recommend that the University provide temporary additional resources to accelerate this planned implementation. This web-accessible module will not only address many of the information needs for the overall biosafety program, but should also provide smart form technology which will facilitate more complete and relevant information from investigators and, at the same time, reduce their frustration with the paperwork burden and process.

Those interviewed also communicated the need for cross integration of both training and occupational health records. This should be evaluated when implementing the Huron/Click software to determine whether or not it will meet these ancillary needs or if some other mechanism is necessary. What is clear is that several units have indicated that they cannot perform Q/A on critical matters with the current lack of a system given the number of labs and individuals engaged in research operating under BSL2 standards. As a specific example, the Occupational Health Office evaluates IBC protocols and recommends vaccinations and/or other prophylactic measures when needed. This information is provided to Principal Investigators with their IBC approval. However, there is no mechanism or process to follow up and determine whether or not a) this information was communicated to laboratory personnel, and b) those working in the labs follow through. There is, also, no integrated or coordinated mechanism to assure that required or recommended training is completed. With the frequent turnover of staff and students in a large number of laboratories working on an even larger number of protocols, better tracking of training needs and completions will improve the proper functioning of these programs.
