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To: UW-Madison Institutional Biosafety Committee (IBC)

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RE: Recommendations to improve the biosafety protocol process

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Introduction

OBS is the administrative home of the IBC. Primary support for the IBC is provided by members of the IBC and Laboratory Operations team under direction of the BSO and ABSO - IBC and Laboratory Operations. Additional support for the IBC is provided by other units within OBS (Animal Research Safety, Select Agent Program, and Biosafety Cabinet Program), which also report through the BSO.

In 2009, the Huron Consulting Group was engaged to assess the biosafety program at UW-Madison. A number of recommendations were made to improve the biosafety protocol process that were subsequently implemented. These include:

- Hiring of additional OBS staff
- Implementation of the electronic "Click Commerce" system (i.e., ARROW) for biosafety protocols
- Creation of a campus biosafety manual (i.e., UW-Madison Researchers' Biosafety Manual)
- Modifications to the review process such as developing clear procedures for protocols approved with contingencies, assigning "ownership" of incoming protocols to individual OBS staff members, defining criteria for when protocols may be approved without IBC review, removing chemical use from biosafety protocols, and creating a process to update personnel listed on protocols

These measures, most notably the increase in staffing and the conversion from "paper" biosafety protocols to Bio-ARROW, have significantly improved oversight and compliance for biological research. Nonetheless, a number of challenges currently exist, including increased regulatory and administrative burdens for researchers, an expanded scope of responsibility for EH&S and OBS, and limited resources and budgetary constraints, all of which have been exacerbated by the ongoing COVID-19 pandemic.

In the spirit of continuous programmatic improvement, in 2020-2021 we conducted a comprehensive review of the biosafety protocol process. We thank Carrie Ensrud (ABSO - Animal Research Safety) and Christina Pier (Select Agent Responsible Official) for providing helpful input. This report summarizes our analysis and presents recommendations for improvement that were developed in collaboration with the IBC.

Goal: To develop recommendations that will improve the biosafety protocol experience by:

- Identifying and eliminating or mitigating common pain points
- Reducing processing time by streamlining the review process
- Increasing transparency of deadlines and process workflow
- Improving collaboration between OBS staff and investigators

Approach: Each step in the protocol process, from pre-submission to post-approval, was evaluated from the perspectives of the principal investigator (PI) and research team, the IBC, and OBS staff. Questions that were considered included:

- What outcomes are desired, and are the desired outcomes being achieved? For example:
    - Are appropriate risk assessments being performed and documented?
    - Are all regulatory and policy requirements being met?

- Are the established processes meeting operational goals? How can these processes be improved? For example:
    - Are there any redundant or unnecessary steps that can be eliminated?
    - Are there common points of confusion that could be prevented through better instruction or guidance?
    - Is the process flexible enough to work well for all common situations?
- Are there any unintended outcomes of the process? If so, are they beneficial or harmful?
- What constraints exist, and have these constraints changed since the process was developed?
- What improvements have already been implemented? Have they been effective?

Guiding principles

The mission of EH&S is to protect and promote the health and safety of people, buildings, spaces, and the natural environment at UW-Madison, its affiliates, and surrounding community. We accomplish our mission through professional services, technical expertise, strong partnerships, and regulatory oversight.

The vision of OBS is that our team members work in collaboration with campus partners to provide knowledge, resources, and exceptional service to help them create a safe and compliant research and educational environment at UW-Madison.

In alignment with our mission and vision, OBS is committed to:

- Supporting the research and educational mission of UW-Madison
- Promoting the health and safety of our campus and community
- Helping investigators achieve full compliance with University, local, state, and federal requirements
- Providing timely and efficient service to the research community

The IBC is charged with the responsibility for oversight of research using biological materials that entail a potential risk to humans, animals, plants, or the environment. Whereas the Institutional Review Boards (IRBs) and Animal Care and Use Committees (IACUCs) protect the welfare of human and animal research subjects, respectively, the IBC seeks to protect research personnel, members of the public, and the local environment. The IBC does this through risk assessment of biohazardous materials, research activities and locations, engineering controls, personal protective equipment, SOPs, and training. It is worth emphasizing that IBC oversight is not intended to obstruct research, but rather to ensure that it is conducted in a manner that is as safe as reasonably achievable. This review of the protocol process was therefore conducted with the following tenets:

- Research is central to the core mission of UW-Madison
- Research carries inherent risks
- Responsibility for safety and compliance within a laboratory ultimately lies with the PI
- The regulatory and administrative burden of research can be substantial and has increased over time

Thus, we sought to identify ways to reduce PI burden and increase the efficiency of OBS operations without compromising safety, compliance, or service.

Analysis of the biosafety protocol process

To provide a context for our recommendations, here we provide an overview and analysis of the scope, compliance mandates, committee size and composition, OBS staff, process workflow, Bio-ARROW, and connections to other compliance committees. Key strengths and areas of opportunity are highlighted at the end of this section.

Research portfolio and scope

Approximately 550 PIs have an active biosafety protocol. Roughly 85% of biosafety protocols include work at BSL2 and more than two dozen PIs are approved for work at BSL3. While less than 10% of biosafety protocols involve research with plants, more than half include work with animals. Additionally, one-fifth of biosafety protocols include work with biological toxins, two-thirds include work with human-derived materials, and more than 80% include work with microbes or infectious agents (i.e., bacteria, viruses, fungi, parasites, or prions).

In addition to UW-Madison investigators, the UW-Madison IBC serves a number of affiliates, including the William S. Middleton Memorial Veterans Hospital, Morgridge Research Institute, and United States Department of Agriculture (USDA) Agricultural Research Services facilities located on the UW-Madison campus. The IBC/OBS also provide oversight and biosafety support for diagnostic laboratories at the Wisconsin State Laboratory of Hygiene and Wisconsin Veterinary Diagnostic Laboratory.

At this time, teaching laboratories not involved in the conduct of research are not required to have a biosafety protocol. Biosafety is incorporated into laboratory-based courses at the direction and discretion of instructors, with involvement from OBS only upon request (which is rare). There is no institutional policy framework or oversight body that reviews laboratory-based coursework and curricula for biosafety and compliance. Although this may be an area of opportunity for UW-Madison, we do not explore it further here as it is beyond the scope of this review.

Compliance mandates

Biosafety protocols provide a mechanism for ensuring compliance with federal, state, local, and University policies and regulations for biological materials, including but not limited to:

- As an institution that receives federal funding, UW-Madison is subject to the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acids (NIH Guidelines)*.
- UW-Madison is subject to the *U.S. Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC)*. The DURC subcommittee of the IBC serves as the Institutional Review Entity under this policy.
- Biological agents declared by the Department of Health and Human Services (HHS) or USDA to have the potential to pose a severe threat to public health and safety (7 CFR part 331, 9 CFR part 121, and 42 CFR part 73) are subject to Select Agent Regulations.
- Work involving human blood, cell lines, or other potentially infectious materials falls under the federal Occupational Safety and Health Standard 29 CFR 1910.1030, *Toxic and Hazardous Substances, Bloodborne pathogens*.
- The Wisconsin Department of Natural Resources has established regulations for the decontamination and elimination of infectious and medical wastes.

More than 80% of biosafety protocols include work with recombinant or synthetic nucleic acids. Thus, one of the primary compliance functions of the IBC/OBS is ensuring UW-Madison research follows requirements defined by the *NIH Guidelines*. Violations of these requirements must be reported to the NIH Office of Science Policy. In spring 2018, after receiving clarifications of several points in the *NIH Guidelines* from the NIH, OBS performed an internal audit of all active biosafety protocols that contain work falling under Section III-D (requiring IBC approval prior to initiation). Of 308 total protocols audited, only one minor violation was identified. In total, four incidents of non-compliance with the *NIH Guidelines* were reported in FY18; one was later determined to be exempt and therefore not a violation. No instances of non-compliance with the *NIH Guidelines* were identified in FY19 or FY20.

In 2019, we conducted an IBC program review using the *Self-Assessment Tool for Institutional Biosafety Committees and Programs of Oversight for Recombinant or Synthetic Nucleic Acid Research* from the NIH Office of Science Policy. This self-assessment tool is designed to evaluate the IBC and institutional biosafety program in regard to the expectations, standards, and requirements of the *NIH Guidelines*. No program or policy deficiencies were identified. A similar review had last been performed in 2015, at which time several corrective actions had been identified and successfully implemented.

Committee size and composition

The IBC is composed of faculty, laboratorians, *ex officio* and community members in accordance with the *NIH Guidelines* Section IV-B-2. The IBC typically has 16-18 voting members, including two *ex officio* members (the BSO and the Chief Campus Veterinarian) and two non-affiliated community members. The current roster has 17 voting members. The *ex officio* members each have designated alternates that can attend in their place if they are unavailable.

Quorum is defined as one more than half of the voting members (currently 9 of 17). IBC meetings are scheduled for two hours but may run over on occasion if business is not complete and quorum is maintained. In the past four years, the IBC lost quorum one time when the meeting ran long and needed to schedule a second meeting to complete the review of all protocols that month; the IBC has not had to reschedule a meeting due to failure to reach quorum.

In 2019-2020, between 10 and 34 protocols were assigned to IBC members for full review each month, with both an average and median of approximately 19 protocols. On average IBC members are expected to review 3-4 protocols per IBC meeting, though this number is often higher for individual members when the volume of protocols assigned to a particular meeting is high, some IBC members are unable to review due to conflicts or absences, or several protocols require their specific expertise (e.g., SARS-CoV-2 protocols requiring expertise in virology).

IBC members have expertise in one or more of the following areas: recombinant techniques; plant, plant pathogen, or plant pest containment; animal containment; microbiology (virology, bacteriology, or mycology); pharmacology; and infectious disease. In addition, the IBC has more than a dozen designated consultants that provide expertise in human subjects research, occupational health and medicine, containment equipment, laboratory facilities and building systems, select agents and DURC, biological toxins, chemical safety, and the law.

The *ex officio* members serve on the committee as long as they hold their position. Non-affiliated community members serve an indefinite term for as long as they are willing and able. Other IBC members are asked to commit to serving a three-year term, which is renewable. As of April 2021, current members had served between three months and 11 years. The average length of service of current members was 4.5 years and the median was 3.7 years.

As of April 2021, ten committee members had left the committee in the preceding four years, including three community members. Nine of these were replaced by new members with similar areas of expertise. In order to fill these open positions, 27 invitations were extended and 18 were declined. Those that declined mostly cited other commitments as the reason. We have thus far failed to recruit a replacement for one IBC member (Dr. Noelle LoConte) that stepped down in spring 2020, who provided expertise for human clinical trial protocols. This may be attributable to the COVID-19 pandemic, as many physician scientists that would be well qualified to fill this role have higher than normal clinical commitments during this time. We are grateful that Dr. LoConte has agreed to continue reviewing human clinical trial protocols as an *ad hoc* IBC consultant until this role can be filled by a full-time member.

OBS staff

Currently, the IBC and Laboratory Operations team is composed of five biosafety specialists under the direction of the ABSO - IBC and Laboratory Operations (Stephanie Kutz). Members of this team hold degrees in the biological sciences and have professional laboratory experience. Three members of this team hold the Registered Biosafety Professional credential from the American Biological Safety Association International (ABSA). All OBS staff receive general and specialized biosafety training through in-person and online courses offered through UW-Madison, ABSA, and other safety organizations.

At any given time, each IBC and Laboratory Operations team member may be handling anywhere from a handful to 20 or more biosafety protocols or amendments in various stages of the review process. In addition to processing and reviewing biosafety protocols and amendments, members of the IBC and Laboratory Operations team also conduct laboratory audits, participate in incident investigations, create guidance and tools (e.g., fillable templates and signage), assist with import/export permits for biological materials, facilitate laboratory cleanouts and closures, consult on laboratory renovation and building projects, and collaborate with other members of OBS, EH&S, and campus partners on a variety of safety-related projects.

It is worth noting that while current staffing levels meet the recommendations of the 2009 Huron report, at that time OBS did not perform many of these other functions. For example, OBS did not dedicate time to assist laboratories with permits until 2017; in FY20, the OBS Import/Export Liaison helped researchers with nearly 50 permit inquiries or incidents. The transition of biosafety protocols to the Bio-ARROW system introduced many process efficiencies to the protocol review process; however, these have not freed up work hours equivalent to those now devoted to these additional functions. The identification of additional process efficiencies is therefore critical to create more "bandwidth" for OBS to effectively provide these additional services to the research community.

Process workflow

UW-Madison requires that biosafety protocols undergo renewal every three years. OBS receives and processes all new biosafety protocols, renewals, and amendments, and conducts a pre-review prior to review by the IBC (*Figure 1*). A research protocol/amendment is assigned to an OBS staff member in the IBC and Laboratory Operations group ("owner"), who processes the protocol, conducts a primary review, and acts as a point of contact for the research team and IBC. During the primary review, the OBS owner will look for compliance with the *NIH Guidelines*, IBC policies and requirements, and standard biosafety practices as outlined in the UW-Madison Researchers' Biosafety Manual and *Biosafety in Microbiological and Biomedical Laboratories (BMBL)*. If human-derived materials are used, the protocol/amendment is also reviewed by the BBP Program Manager (Carrie Ensrud) for compliance with the OSHA bloodborne pathogens standard. If vertebrate animals are used, a member of the OBS Animal Research Safety team conducts a congruency check against the PI's animal protocol(s). BBP and animal reviews are conducted concurrently with the OBS primary review. The established expectation for turnaround of primary review (including BBP and animal reviews) is no more than five business days. When the primary review is complete, the OBS owner assigns a secondary reviewer, typically the ABSO - IBC and Laboratory Operations. The primary purpose of the secondary review is quality control, to ensure consistency across protocols assigned to different primary reviewers and provide a second set of eyes for complex research projects; the expected turnaround for secondary review is two business days.

Figure 1. Flow chart of the biosafety protocol review process

During the OBS pre-review, if information is missing, unclear, incongruent, or deviates from established standards, the protocol/amendment is returned to the research team for revision. There is no set turnaround time for the research team to respond, though slow resubmission of the revised protocol/amendment can delay approval and therefore initiation of new research.

OBS also determines whether IBC review is required during the pre-review. Protocols and amendments that fall under Sections III-D (experiments requiring IBC approval prior to initiation) and III-E (experiments requiring IBC notification) of the *NIH Guidelines* must be reviewed by the IBC. The NIH Office of Science Policy stipulates that official IBC business (including review and approval of protocols subject to the *NIH Guidelines*) be conducted at a convened meeting (i.e., interactive and in real-time). Electronic exchanges such as email are not deemed acceptable, prohibiting a "designated review" model such as that used by the IACUCs. However, protocols that are not subject to the *NIH Guidelines*, grant and personnel changes, and certain amendments deemed similar enough to previously approved work may be reviewed and approved by OBS on behalf of the IBC; these account for more than half of all protocols and amendments (*Table 1*). Grant and personnel changes can be processed and approved by an assigned OBS staff member without secondary review and are usually registered the same day.

Table 1. Biosafety protocol and IBC administrative functions for Fiscal Year 2019-2020

Activity	Number
IBC meetings organized	12
Principal Investigators (PIs) with active biosafety protocols (as of 06/30/20)	548
Total number of active biosafety protocols (as of 06/30/20)	576
Protocols and amendments that underwent full review (i.e., OBS followed by IBC review)	252
Total new protocols, renewals, and research amendments reviewed and registered by OBS	548
Total grant/personnel amendments reviewed and registered by OBS	1051

When a protocol requires IBC review, it is assigned to a minimum of two IBC members (a primary and a secondary reviewer); additional IBC members or IBC consultants are sometimes assigned as tertiary reviewers to weigh in on specific aspects of a protocol (e.g., toxins, specialized containment equipment, occupational health considerations). IBC review assignments are made two weeks prior to the IBC meeting. The cutoff for protocols being assigned to a meeting is the Friday before meeting materials are sent out to allow three business days for processing. This is not a hard deadline, however, and late additions by OBS are permitted for extenuating circumstances up to one week prior to the meeting; additions made less than one week prior to the meeting are allowed only with approval from the IBC Chair.

When a protocol/amendment is reviewed by the IBC, there are five possible outcomes:

- Approval
- Approval with contingencies
- Approval with contingencies – must go back to reviewers
- Table
- Reject

When approved, a protocol/amendment is registered by OBS. If approved with contingencies, the protocol/amendment is returned to the research team for revision. Upon resubmission, OBS determines whether the contingencies have been met; if they have the protocol is registered, and if not, the protocol is returned to the research team for further revision. If approved with contingencies – must go back to reviewers (previously known as "select committee review"), the protocol/amendment is returned to the IBC reviewers to determine whether the contingencies have been met. Protocols/amendments are tabled if the IBC decides that there is insufficient information to conduct the risk assessment. While rare, protocols/amendments may be rejected by the IBC if deemed unacceptable.

Approval with contingencies is the most common outcome of IBC review (*Figure 2*). Most contingencies are minor requests for additional details or clarifications. Approval is the second-most common outcome (20-25% of protocols and amendments). Approximately 12% of protocols/amendments were approved with contingencies – must go back to reviewers in FY18 and FY19, though this dropped to 7% in FY20. Likewise, about 5% of protocols/amendments were tabled in FY18 and FY19 but dropped to 2% in FY20. Although this downward trend represents a single year, this dip corresponds to the renewal of protocols that transitioned into Bio-ARROW in

2016-2017 and may reflect improvements in the overall state of protocols compared to earlier paper versions. There was only one rejection during FY18 through FY20.

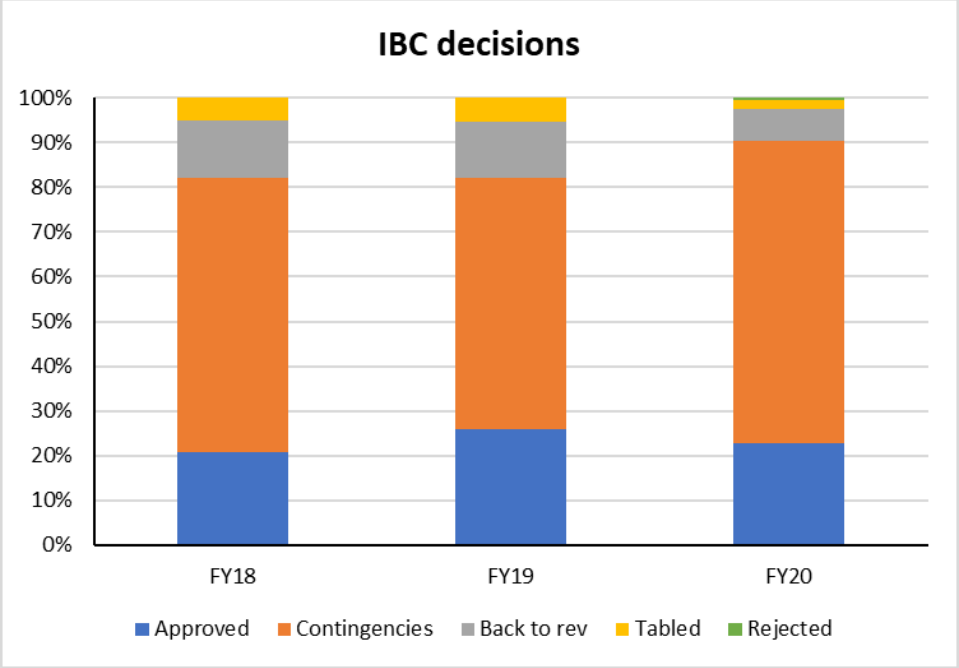

Figure 2. Breakdown of decisions for biosafety protocols reviewed by the IBC

To evaluate the timeliness of different stages of the review process, the average and median days in each of the following states was evaluated for the last three fiscal years (*Table 2*):

- OBS assignment: state when a protocol/amendment is submitted, before it is assigned to an OBS staff member for primary review
- In-house review: state when a protocol/amendment is undergoing in-house review by OBS; this includes pre-review (primary and secondary) before IBC meeting and post-IBC review (e.g., evaluating if contingencies have been met)
- Changes requested: state when the protocol/amendment has been returned to the research team to revise the protocol (before or after IBC review)
- Assigned to meeting: state the protocol/amendment is in when it is ready for IBC review
- Back to reviewers/select committee review: state when a protocol/amendment is being re-reviewed by IBC members when it has been "approved by the IBC with contingencies - must go back to reviewers"

Table 2. Days in state for new protocols, renewals, and research amendments FY18 to FY20

State	Average days	Median days
OBS assignment	0.28	0.08
In-house review	2.62	1.01
Changes requested	5.26	1.41
Assigned to meeting	16.46	15.10
Back to reviewers	no data	no data

Notably, if these data are separated by year a downward trend is observed in the time spent in the "Changes requested" state. In FY18, protocols/amendments spent an average of 6.06 days in the "Changes requested" state (median = 1.88 days), but this dropped to 5.50 days in FY19 (median = 1.86 days) and to 4.14 days in FY20 (median = 1.13 days). This trend may suggest that protocols/amendments require less revision, or that PIs are becoming more comfortable with Bio-ARROW. The time spent in the "In-house review" state has remained relatively steady at less than three days on average, approximately half the time the protocols are with the research team. These data suggest overall efficiency in turnaround by OBS, though the number of times protocols/amendments go "back and forth" between OBS staff and the research team is not captured here.

The average and median time spent in the "Assigned to meeting" state is just over two weeks, which corresponds to the cutoff time for an upcoming IBC meeting. This suggests that on average protocols and amendments are not languishing in this state longer than necessary; however, shortening this time through a change in the cutoff could provide researchers more time to refine their protocols before IBC review or allow submission closer to the IBC meeting date.

Using existing reports in Bio-ARROW, data is currently not available for the time spent in the "Back to reviewers" state. Anecdotally, many protocols/amendments remain in this state until a few days before the next IBC meeting, perhaps because IBC members complete these reviews when doing their new meeting review assignments.

Under the *NIH Guidelines*, a small number of protocols require approval from both the IBC and the NIH Office of Science Policy. The most common reason for NIH approval is a request to lower containment as a Minor Action under section IV-C-1-b-(2). If the IBC supports a Minor Action, the request is prepared and submitted to the NIH by the BSO. Between March 2018 and April 2021, six downgrade requests were made to the NIH, all of which were approved. The time to prepare these requests (which includes writing a justification, redacting the biosafety protocol, and review by UW Legal) ranged from two to eight business days, with an average of four days and median of three days. Time in which approval was received from the NIH ranged from one to 17 business days, with an average and median of six days.

Bio-ARROW

Biosafety protocols were transitioned from "paper" protocols to Bio-ARROW between 2015 and 2017. With this conversion, the biosafety protocol was redesigned to better capture information for risk assessment and for ease of use. OBS has a designated Bio-ARROW Liaison (Tara Schnell), who works with the IBC and Laboratory Operations team and the OVCRGE IT team to prioritize and implement changes to Bio-ARROW. Since its adoption, Bio-ARROW has undergone continuous improvements. These include, but are not limited to:

- In 2017, ARROW underwent a software upgrade and redesign
- In collaboration with the IRBs, IACUCs, and Stem Cell Research Oversight Committee (SCRO), a combined "Request for PI Status" form was created
- The BBP personnel page was redesigned to remove individual vaccination information, simplifying completion and providing better protection for personal medical information

- The PPE section has been redesigned to better capture information about PPE that is worn for specific locations, agents, or activities

In addition to modifications of the Bio-ARROW protocol itself, a number of tools are available to aid protocol completion and review. Some examples include:

- To help researchers navigate Bio-ARROW, help pages in the UW-Madison KnowledgeBase (KB) are reviewed and updated at least annually
    - Of particular note, at the request of the IBC OBS updated and expanded guidance for the Research Description including things to consider and examples of different types of projects
- To help researchers address specific topics in their biosafety protocols, guidance documents and tools have been created and are available on the EH&S website, such as:
    - Guidance for adding flow cytometry to a Bio-ARROW protocol
    - Guidance for adding CRISPR to a Bio-ARROW protocol
    - Guidance for Core Facility biosafety protocols
    - Guidance and customizable templates for biological spill protocols
    - Guidance, FAQs, signage, and occupational health plan templates for COVID-19 pandemic research
- To help make sure researchers renew their protocols in a timely manner, in addition to the automatic email notifications from Bio-ARROW OBS proactively tracks protocols with upcoming expiration dates and contacts PIs to share cutoff dates and offer assistance
- For quality assurance, the IBC and Laboratory Operations team maintains a "consistency document" that contains standard questions and notes on IBC decisions for use during OBS pre-review; this document is continuously updated and undergoes a full review at least annually
- Guidance is available for IBC members on topics such as:
    - Using the "View Differences" feature in Bio-ARROW
    - Reviewing select agent protocols in Box
    - Recombinant Human Clinical Trials in Bio-ARROW
    - Reviewing CRISPR in a Bio-ARROW protocol
    - Guidance on Minor Actions under the *NIH Guidelines*

Connection with other compliance committees

Research covered under the biosafety protocol may require approval from other campus compliance committees. The IBC/OBS have connections with the IACUCs, IRBs, and SCRO for research involving vertebrate animals, human subjects, and human stem cells, respectively.

Research involving vertebrate animals that have been administered recombinant or synthetic nucleic acids, administered cells or microbes that have been recombinantly modified, administered pathogens or biological toxins, or genetically modified using recombinant techniques must be approved by both the IBC and the appropriate IACUC. As mentioned above, during OBS pre-review protocols and amendments that involve vertebrate animals are assigned to a member of the Animal Research Safety team to check congruency against the investigator's animal protocol(s). Animal Research Safety team members also check for congruency with the biosafety protocol when performing safety reviews of animal protocols and amendments. In addition, the Chief Campus

Veterinarian (who is an *ex officio* voting member of the IBC) is a member of the UW-Madison All Campus Animal Planning and Advisory Committee (ACAPAC), as is the OBS Animal Research Safety Manager (Carrie Ensrud).

Under Section III-C of the *NIH Guidelines*, experiments involving the deliberate transfer of recombinant or synthetic nucleic acids, recombinant microbes or cells into human research participants require IBC approval prior to initiation. There are currently approximately 20 approved protocols for human gene transfer studies. A member of the Human Subjects Office (John Cejka) serves as an IBC Consultant, attends meetings when III-C protocols are discussed, and communicates relevant safety concerns of the IBC to the appropriate IRB. Some human gene transfer studies may not be reviewed by an IRB at UW-Madison as changes to the Common Rule made in 2019 mandate that multi-site human clinical trials use a centralized IRB; however, under the *NIH Guidelines* IBC review must be performed at each local site. In addition to IRB review, many clinical trials require review and approval from the UW Health Research Safety Committee. The BSO and the OBS Human Subjects Research Liaison (Kathy Krasny) are voting members on this committee.

Under the OSHA bloodborne pathogen standard, an exposure control plan (BBP plan) is required for work with human-derived cells; for research, the BBP plan is incorporated into the Bio-ARROW protocol. Thus, all work that would require oversight by the SCRO should also be covered in an approved biosafety protocol. To allow the SCRO to identify researchers that need SCRO protocols, the OBS secondary reviewer sends an email to the SCRO Manager (Heather McFadden) when human stem cells are listed on a biosafety protocol. Information provided includes the PI name, protocol number, protocol type (new, amendment, renewal), and a snapshot of the "Cells, Organs, Tissues, or Biological Specimens" page. In addition, a Bio-ARROW query for human stem cells is performed every four months and the resulting report is sent to the SCRO Manager.

Summary of strengths and areas of opportunity

Many notable strengths were identified during this analysis, including:

- High rate of compliance with *NIH Guidelines*
- Expertise of IBC members and consultants
- Knowledge and experience of OBS staff members
- Low rate of protocols being tabled or needing to go back to reviewers
- Efficient turnaround of protocols by OBS
- Improved design of electronic protocol and continuous improvements of Bio-ARROW
- Established connections between the IBC/OBS and other compliance committees

Nonetheless, there is room for improvement in a number of areas. Some of these will be difficult to address, such as challenges with IBC member recruitment and OBS service capacity. Other areas of opportunity, such as streamlining the review process workflow and increasing transparency, should be well within reach. Specific recommendations for these are captured in the next section.

While some committee turnover is healthy, with long-standing members providing continuity and new members providing fresh viewpoints, recruiting new IBC members has been challenging. In general, Assistant Professors that have not yet attained tenure are not invited to join the

committee as it is viewed as unduly burdensome, yet more senior faculty members often cite other service obligations as a reason to decline. In the last four years, two-thirds of invitations were declined. The development of additional incentives for IBC service might help recruit and retain busy members, but it is unclear how this could be accomplished as uncompensated service is an expectation of academic faculty and staff and the IBC must compete with other campus committees that may be similarly challenged.

OBS staffing levels are anticipated to remain the same. It is worth emphasizing that IBC support is considered an essential role of OBS, and so the biosafety protocol review process, IBC meeting administration, and associated tasks are prioritized during periods of heavy workload or staff turnover. Other biosafety service areas may be curtailed during temporary staffing shortages to maintain IBC support. Other programmatic areas are undergoing internal review as well, with the hope that in combination with the recommendations in this report process efficiencies can be implemented that increase the OBS service capacity.

Recommendations

Below we outline our recommendations to improve the review process, the biosafety protocol and Bio-ARROW, as well as our proposed communication plan and next steps.

The review process

1. **Reduce back-and-forth with investigators during OBS pre-review**
   Ideally, during OBS pre-review a protocol or amendment is sent back to the research team for revision no more than a single time. When a protocol/amendment is sent back to the research team for revision multiple times it can be a source of significant frustration and can delay IBC review or initiation of research. To reduce the back-and-forth between OBS and investigators, we propose the following modifications to the OBS pre-review process:

   - Do not request changes from the research team prior to IBC review if all revisions are deemed to be minor (i.e., "housekeeping")
     - This is already done for protocols that are submitted very close to the cutoff for assignment to a meeting
     - This may result in fewer protocols/amendments being approved without contingencies
   - If a single round of revisions by the research team likely will not address all potential issues with a protocol/amendment (e.g., more information is needed before specific changes can be requested), the OBS owner will proactively contact the PI or designated point of contact for the protocol via phone to gather information needed to make specific requests

2. **Reduce the time protocols/amendments wait in the "Assigned to meeting" state**
   As noted above, a change in the cutoff for assignment of a protocol/amendment to an IBC meeting could provide researchers more time to refine their protocols before IBC review or allow submission closer to the IBC meeting date. The current cutoff is the Friday before meeting materials are sent out, which is the Wednesday two weeks prior to the IBC meeting. We propose the following change:

- Send meeting materials out on the Wednesday one week before the IBC meeting instead of two weeks before the meeting, and keep the cutoff as the Friday before the meeting materials are sent out: this would give researchers an additional week to prepare their submissions and IBC members would have one week to complete their review assignments

3. **Reduce the time protocols/amendments spend in "Back to reviewers" state**
   The time that protocols and amendments spend in re-review varies but may last until just before the next IBC meeting. This can be weeks in cases where researchers quickly resubmit revisions. Currently, IBC members that have a protocol sent back for re-review receive an email reminder from Bio-ARROW every 7 days. To improve transparency and facilitate timely review, we recommend:

   - Establish an expected turnaround time for IBC reviewers of 7 days
   - Modify the email sent to IBC members from Bio-ARROW to more clearly distinguish between a protocol/amendment being sent back for re-review and a new review assignment for the next IBC meeting

4. **Increase visibility of process and deadlines**
   Although IBC meeting dates are posted on the OBS website, researchers are often unaware of the cutoff dates for submission to specific meetings. Furthermore, new PIs and PIs that have transferred to UW-Madison from elsewhere may be unfamiliar with the OBS pre-review process and how it may affect the timing of IBC review. To improve the transparency of our process, we propose the following:

   - Update the IBC page on the OBS website annually to include a calendar graphic with IBC meeting dates, cutoffs, and suggested submission targets for the year
   - Update renewal email notifications from Bio-ARROW to include a link to the IBC webpage that would show them meeting dates and cutoffs
   - Develop an optional online or virtual "Introduction to Bio-ARROW" training for new PIs and read-write personnel

5. **Implement a biennial review of all IBC policies**
   IBC policies may be updated at the request of the committee, or updates may be proposed to the IBC by OBS. Policies that are commonly invoked are frequently reviewed and updated, whereas less used policies may go years without review. We propose that a biennial review schedule be established for review of the IBC policies by OBS to help ensure all policies reflect the current regulatory requirements and perspectives of the committee.

6. **Implement a biennial review of Bio-ARROW guidance documents**
   As noted above, in addition to help pages in the KB, OBS has created several guidance documents for researchers and IBC members. We propose that a biennial review schedule be established for review of these guidance documents by OBS to help ensure they reflect the current state of Bio-ARROW and perspectives of the committee.

The biosafety protocol and Bio-ARROW

1. **Update and customize the biosafety protocol**
   Since its inception, Bio-ARROW has undergone continuous improvements. During the last several months, OBS has been working with the IBC to identify larger changes that will make the protocols easier for researchers to fill out while better capturing and presenting information needed by OBS and the IBC for risk assessment. Proposed changes include:

   - Updating the "Genome Editing" section
     OBS has developed a plan; redesign of this section is pending review of by the IBC. Proposed changes will:
     - Capture details about targets, delivery vehicles and methods not currently found in this section
     - Use branching logic to tailor questions based on use (e.g., only ask gene drive questions when genome editing is performed in animals, plants, or germline cells)
   - Creation of a new "Nanoparticles" page
     Nanoparticle research is a growing field, but there is currently no place in the Bio-ARROW protocol specifically designed to capture information about nanoparticles. In collaboration with the IBC and other units within EH&S (i.e., Occupational Medicine and Chemical Safety), OBS has begun development of a "Nanoparticles" page. This page will:
     - Let investigators know what kind of information is needed for work with nanoparticles and provide a central location to enter that information in the protocol
     - Help OBS owners, IBC reviewers and consultants perform more comprehensive risk assessments for research involving nanoparticles
   - Creation of a separate "Viral Vectors" section
     Currently viral vectors are listed in the "Viruses" section on the "Microbes and Disease-Causing Agents" page; however, the experimental use and risks associated with viral vectors often differ from those of intact viruses. With input from virologists on the IBC, OBS has begun development of a separate "Viral Vectors" section that will have questions customized for risk assessment of viral vectors. The existing "Viruses" section will remain for viruses not being used as vectors.
   - Customize the biosafety protocol template for human clinical trials
     Human clinical trials (e.g., human gene transfer studies) differ substantially from other types of research projects. OBS has developed a plan to customize pages within the Bio-ARROW protocol for human clinical trials; this has been reviewed by the IBC and is ready for development with the IT team.

2. **Create new Bio-ARROW reports to track additional metrics**
   To expand our ability to assess the impact of changes to the review process and compare trends over time, we propose that OBS work with the OVCRGE IT team to create or refine reports in Bio-ARROW to track additional metrics, such as:

   - Number of times protocols go back-and-forth between OBS and the research team

- Compare days in state for different types of protocols (e.g., separate data for III-C or BSL3 protocols) or at different stages in the protocol review process (e.g., separate before and after IBC review)

3. **Create new activities in Bio-ARROW**
   During our review, we identified a couple of additional options that may offer value to the PI/research team. These are:

   - Add "Request a Video Visit" activity to all states of the protocol
     This would supplement the existing "Request assistance" activity and provide an additional way for investigators to connect with OBS.
   - Add "Archive upon expiration/Do not renew" activity
     This activity could be run by PIs when they do not intend to renew their biosafety protocol (e.g., project ending, PI retiring, PI leaving UW-Madison). When run, this activity would send a notification to OBS that the PI does not intend to renew the protocol and turn off renewal notifications to the PI.

Communication plan and next steps

We conducted this review based on our own analysis and available metrics. To create opportunity for the research community to provide feedback, we propose the following:

1. **Post this report on the OBS website**
   This will provide transparency regarding the process, performance, challenges, and proposed changes.

2. **Offer a public comment period**
   We propose that once the report is posted, a public comment period be established and advertised. A web form could be created for submission of comments, which could remain anonymous. OBS would consolidate these comments for review by the IBC at the end of the comment period. Unforeseen challenges could be addressed, and new ideas be incorporated into the implementation plan.

3. **Develop a timeline for implementation**
   Once the action items have been finalized, we will develop a projected timeline for implementation of each recommendation. While some changes can be implemented immediately, some will take time (e.g., those involving programming changes by the OVCRGE IT team).

4. **Establish a schedule for progress reports to the IBC**
   Once the timeline has been established, we will provide regular status updates to the IBC on a schedule to be determined by the committee. We suggest progress reports occur at least quarterly (i.e., every three months) until implementation is completed.

5. **Develop a strategy for communicating changes to the research community**
   OBS will work with the FP&M Communications team to develop a strategy for communicating proposed and adopted changes to the UW-Madison research community. Elements may include webpages, email blasts, newsletters, articles, or town hall meetings.

Please let us know if you have any questions. Thank you for your consideration, and for your continued dedication to biosafety at UW-Madison.