BIORISK MANAGEMENT CASE STUDY: AMERICAN SOCIETY FOR MICROBIOLOGY JOURNALS

AMERICAN SOCIETY FOR MICROBIOLOGY

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SUMMARY

The American Society for Microbiology (ASM) Journals are a collection of 16 influential microbiology publications, including the Journal of Virology, that screens submitted manuscripts for potential "dual-use" biosafety and biosafety concerns.

ASM Journals uses multiple parallel mechanisms for flagging potential concerns in manuscripts, and relies on extensive in-house expertise for its ultimate evaluations:

- Manuscripts are **automatically screened** for keywords and phrases of concern, including the presence of agents on the US Department of Health and Human Services' Select Agents and Toxins List (SATL).
- Manuscripts are **also manually reviewed** using a set of questions to evaluate their dual-use potential.
- **If flagged, manuscripts are further reviewed** by the editor-in-chief, and potentially also by a committee that contains current and former members of the United States National Science Advisory Board for Biosecurity (NSABB).
- ASM Journals has **never rejected or redacted** a manuscript over dual-use concerns, but has published manuscripts with accompanying editorials.

DISCLAIMER

Biosafety and biosecurity risk management practices can change over time. This case study represents one point in time and is a sample of an evolving set of risk management practices. For additional information on current practices please contact the organization directly.

THE VISIBILITY INITIATIVE FOR RESPONSIBLE SCIENCE (VIRS)

The goal of the Visibility Initiative for Responsible Science (VIRS) is to share information about the value of biorisk management and how life science stakeholder organizations approach the issue. VIRS was conceived by a multi-stakeholder group during an April 2019 working group meeting of the Biosecurity Innovation and Risk Reduction Initiative (BIRRI) program of NTI Global Biological Policy & Programs. With support from NTI, Stanford University Bio Policy & Leadership in Society VIRS produced a set of Case Studies in biorisk management, and The Biorisk Management Casebook that provides cross-cutting insights into contemporary practices.

THE BIORISK MANAGEMENT CASE STUDIES

The Biorisk Management Case Studies describes biorisk management processes for a diverse set of life science research stakeholders. The collection serves to evaluate the feasibility and value of knowledge sharing among both organizations that have similar roles and those that have different roles in managing research. Case studies were developed in consultation with organizations through a combination of research based on public sources, interviews, and providing a template with guiding questions for organizations to complete directly. Additional analysis can be found in The Biorisk Management Casebook: Insights into Contemporary Practices[1] in this collection. Project Directors: Megan Palmer, Stanford University; Sam Weiss Evans, Harvard University.

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ORGANIZATION BACKGROUND

The American Society for Microbiology (ASM) Journals are a collection of 16 influential microbiology journals whose stated mission is "to advance the microbiological sciences by disseminating the results of fundamental and applied research":

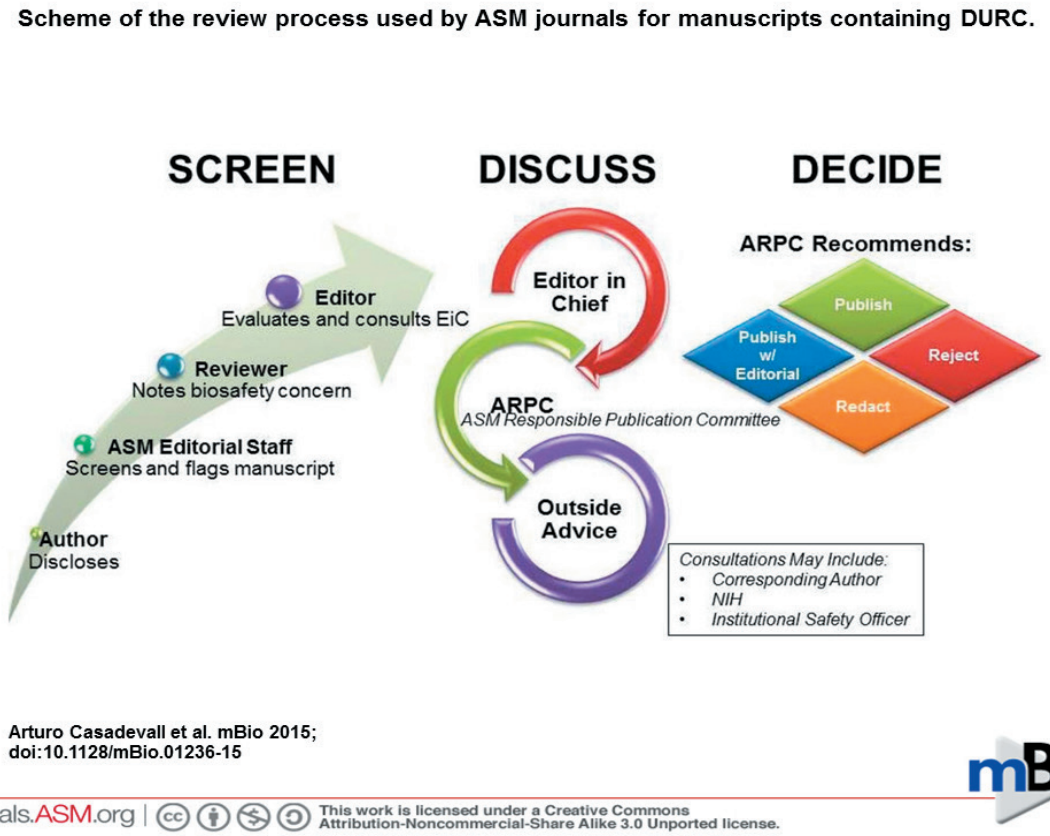
> *ASM journals publish high-quality research that has been rigorously peer reviewed by experts. Our academic editors are working scientists drawn from eminent institutions around the world. Known for the quality, rigor, and fairness of the review process, ASM Journals continue to provide current, influential coverage of basic and clinical microbial research.*
>
> *ASM Journals publish 15% of all microbiology articles and contribute 31% of all microbiology citations (per 2020 Web of Science data).*
>
> *Articles published in the ASM journals receive international media attention and have been featured in the New York Times, Science Magazine, Los Angeles Times, CNN, National Public Radio (NPR), CNBC, and dozens of other media outlets. —ASM "About" page*[2]

In 2007, the US National Science Advisory Board for Biosecurity issued a proposed framework for "minimizing the potential misuse of research information," which included a set of non-binding directives for publishers.[5] ASM Journals "responded to the NSABB directives by introducing a questionnaire in the manuscript referee review form used by its journals that asked reviewers to provide an assessment about whether the work involved experiments of concern."[4] Several ASM Journal Editors and Editors in Chief (EIC) are or have been NSABB members (including Arturo Casadevall, Michael Imperiale, and Rozanne Sandri-Goldin), which made ASM Journals particularly responsive to the NSABB's directives and particularly invested in biosafety and biosecurity.

Some ASM journals "have published papers that include potential DURC, and the ASM Journals Board has developed a process for evaluating such manuscripts prior to publication."[4] In 2011–2012, "ASM publications, and in particular the Journal of Virology, were [...] criticized for publishing a paper describing the adaptation of H7N1 HPAIV for transmission in ferrets without loss of virulence."[4,7,8,9] After this controversy, "the ASM instituted an ad hoc process of reviewing manuscripts with potential DURC content." An increase in MERS-related publications in 2012 was another contributing factor to the development of their process.

Overall sequence of steps

Figure 1: Schema of the ASM Journals DURC review process (Casadevall et al., 2015).[4]



PROCESS

Scope of risks considered

ASM Journals broadly evaluates manuscripts for potential dual-use biosafety and biosecurity risks. It bases its conceptions of these risks on the US government's definition of "dual-use research of concern" (DURC) and on the US department of Health and Human Services' Select Agents and Toxins List.[4,10,11] See "Risk assessment" below for details of screening questions.

Authors submitting to ASM Journals are expected to declare potential dual-use concerns in manuscript cover letters. From this point, there are three independent pathways by which a manuscript can be flagged for review by the editor in chief (EIC) of ASM Journals:

- ASM editorial staff screen all submissions for a set of dual-use related keywords and phrases, including the names of microbes and toxins on the HHS and USDA Select Agents and Toxins List (SATL), as well as phrases suggestive of DURC such as "increased pathogenesis or virulence," "increased transmission," "escape from antibody," and "cross-species transmission."
- Reviewers are also separately asked to manually review manuscripts for biosafety and biosecurity concerns using the question(s) described in the next section. Journal of Virology reviewers have a more extensive set of review questions.
- Individual journal editors also sometimes alert the EIC themselves.

"The screening phase is designed to be rapid and unobtrusive while at the same time identifying manuscripts that require discussion."[4]

Once alerted, the EIC reviews the manuscript and has discretion to approve the paper or to involve the ASM Responsible Publication Committee (ARPC) for additional review. Similarly, once alerted, the ARPC has final discretion to approve the manuscript, potentially recruiting outside support in the process. "When the paper under discussion comes from an ASM journal other than the Journal of Virology, mBio, and mSphere, which are represented on the ARPC by their editors in chief, that journal's editor in chief serves as an ad hoc member of the committee."[4]

RISK ASSESSMENT

For the Journal of Virology, reviewers are required to answer yes or no to all the following questions, any of which trigger further review by the editor in chief:

- Enhanced virulence?
- Generation of a pathogen that evades the immune response?
- Resistance to a clinically useful antimicrobial?
- Increased stability, transmissibility, or dissemination?
- A change in host range or tropism?
- Generation or reconstitution of an eradicated or extinct agent or toxin?
- Enhance the susceptibility of a host population to infection by a biological agent?

In addition, all Journal of Virology reviewers are provided the supplemental text included in Appendix A below.

For all other ASM journals, reviewers are required to answer only the following question:

- Does the work described in this study raise any concerns about biosafety or biosecurity that should be discussed prior to publication by the ASM Responsible Publication Committee?

If the EIC chooses to involve the ARPC, "Members of the ARPC read the manuscript and generally confer initially by e-mail, which may progress to a teleconference if there are issues that require more in-depth discussion."[4] The ARPC makes decisions verbally using a majority-vote process. ARPC members know each other well and frequently stand on different sides of a debate, and decisions are often not unanimous.

RISK MITIGATION

The EIC and ARPC consider four possible outcomes: "accept, reject, redact, or publish with an accompanying editorial explaining the decision to publish, describing the evaluation process, noting the biosafety and biosecurity risk mitigation in place, and highlighting the benefits of the research."[4] Thus far, the only options that have been chosen are full acceptance and publication with an accompanying editorial.

EXPERTISE REQUIRED

ASM Journals has exceptional access to biosafety and biosecurity expertise in the ARPC. In an article co-authored by the ARPC in 2015, the authors noted that "Very few journals have editors who are experienced with DURC-related issues, and until such expertise is available, it will be difficult, if not impossible, to carry out the type of analysis envisioned by the NSABB. The ASM is fortunate to have some expertise in-house, since three of the five members of the ARPC served on the NSABB and were intimately involved in drafting of DURC-related documents. However, other journals may not have access to this type of experience." They also noted that the ARPC sometimes solicits outside advice, "including reaching out to the National Institutes of Health Office of Biotechnology Activities, the funding agency, the authors of the paper, or biosafety officers at the institution at which the research was conducted."[4]

Initial manuscript reviewers are not given formal training or guidance on what constitutes DURC, beyond the instructions provided to Journal of Virology reviewers in Appendix A below, but ASM Journals has expressed potential interest in such training in the future.

IMPACT

ASM Journals considers their manuscript evaluation process to be relatively simple, but in their opinion, it has been highly effective and well accepted. They engaged in some internal debate regarding the use of more extended evaluation processes for their Journal of Virology (JVI), with some expressing concern that the processes would deter authors, but they ultimately felt that their processes were appropriate, and have so far not received any complaints from authors.

The frequency with which submissions reach the EIC varies significantly. Automatic flags for key words and phrases in Journal of Virology manuscripts can occur as often as weekly, and the majority of these are easily approved by the EIC. Less commonly, keywords related to DURC or gain-of-function concerns might prompt longer discussion (estimated to be roughly once per month, with high variance).

In the past five years (2016–2021) only six or seven submissions have reached the level of ARPC discussion; in each case the committee opted to publish with an editorial. No paper has yet been redacted or rejected by the ARPC, although several have been published with accompanying editorials.

SHARING

Thus far, ASM Journals have not been asked to share anything about their biorisk management processes among other journals. They also rarely need to collect additional outside information to inform their risk assessments. On one occasion, ASM did request supplementary information on a manuscript from three sources: the author, the institutional biosafety committee of the author's research institution, and the US National Institutes of Health (NIH).

REFLECTIONS

In an article co-authored by the ARPC in 2015, the authors noted that "Current manuscript review procedures are based on the NSABB DURC definition and on the SATL, both of which introduce significant limitations into the process." They consider the NSABB's DURC definition to be very broad and to require significant expertise to use effectively for risk assessment. Conversely, the SATL is relatively simple to apply, but incomplete: "Screening on the basis of the SATL can miss papers that potentially meet the DURC criteria if these involve organisms that are not usually considered potential biological weapons." ASM uses both approaches in parallel and is fortunate to have an internal committee with expertise to adjudicate cases of potential DURC that are not easily covered by the SATL.[4]

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APPENDIX A: TEXT PROVIDED TO JOURNAL OF VIROLOGY REVIEWERS

The ASM recognizes the importance of cutting-edge research on human, animal, and plant pathogens as well as our responsibility as scientists to minimize the likelihood that results of experiments with dangerous pathogens are misused or that these pathogens accidentally escape laboratory containment (https://www.asm.org/Articles/Policy/ASM-Statement-on-Recent-Biosafety-Lapses). In its commitment to responsible science, a goal of which is to protect our planet from infectious diseases, Journal of Virology is asking reviewers and editors to pay close attention to manuscripts that report agents with biological properties that are altered to enhance virulence in their natural hosts or allow them to cause disease in new hosts. Such results do not necessarily preclude the work from being published. Rather, we want to ensure that publication is accomplished in a responsible manner that clearly acknowledges the significance of the work and minimizes any undue risks associated with these agents.

Thinking about the organism in this study, do the experiments in this manuscript result in the following:

Enhanced virulence?

Enhancing the pathogenic consequences of an agent could increase the likelihood of disease and compromise the ability to treat the disease if current therapeutics are not effective. This includes making a nonpathogenic microbe pathogenic.

- Information likely to be of concern includes how to make a seasonal strain of influenza virus as deadly as the 1918 pandemic strain.
- Information unlikely to be of concern includes routine techniques for restoring the virulence of viral stocks by back-passage in animal hosts, identification of virulence factors through genome-wide screening or gene knockout techniques, or standard genetic manipulation to study the virulence of an organism.

Generation of a pathogen that evades the immune response?

Immunity is a key component of host defense against pathogens. Rendering an immunization ineffective could make a host population vulnerable to the pathogenic consequences of a microbe from which the host population would have otherwise been protected or for which protection, such as a vaccine, was available.

- Information that might be of concern includes insertion of an immunosuppressive cytokine into a viral genome to render the antiviral immune response less effective.
- Information unlikely to be of concern includes new findings about the immunosuppressive properties of chemotherapeutic drugs.

Resistance to a clinically useful antimicrobial?

Anything that might compromise the ability to prevent or treat disease (human or agricultural) caused by biological agents could result in a significant public health or economic burden.

- Information that might be of concern includes conferring antimicrobial resistance to pathogens of significance to humans, animals, or agriculture.

Increased stability, transmissibility, or dissemination?

Increasing the stability, host-to-host transmissibility, or capacity to disseminate within a population could increase the rate or ease by which an agent could spread, impeding attempts to contain a disease outbreak. This includes transmission between hosts of the same species or between hosts of differing species.

- Information that might be of concern includes changing genetic factors to increase transmissibility or altering the route of transmission to increase the ease and effectiveness of transmission of an agent.

A change in host range or tropism?

Altering the host range or tropism of a pathogenic agent could endanger a host population that normally would not be susceptible. Prophylactic or therapeutic measures for the newly vulnerable host population may not be available, possibly allowing uncontrolled spread of disease.

- Information that might be of concern includes converting nonzoonotic agents into zoonotic agents or altering the tropism of viruses.
- Information unlikely to be of concern includes development of animal models for infectious disease, which may involve alterations of the host range or tropism, e.g., the attenuation of viruses for vaccine development, whereby the attenuation procedure relies on a change in host range to reduce virulence.

Generation or reconstitution of an eradicated or extinct agent or toxin?

Host populations may not be immune to new agents and reconstituted eradicated agents. Diagnostics, prophylactics, and therapeutics may not be available for such agents.

- Information that might be of concern includes the de novo construction of a pathogen using wholly unique gene sequences or combinations of sequences that do not exist in nature or reconstitution of a pathogen that no longer exists in nature, such as the reconstruction of the 1918 pandemic influenza virus.
- Information not likely to be of concern includes standard experimentation that generates knockouts, mutants, reassortants, or infectious molecular clones of pathogens that are similar to naturally occurring agents.

Enhance the susceptibility of a host population to infection by a biological agent?

Information about rendering host populations more susceptible to pathogenic consequences of a virus could be used to compromise innate and adaptive immune responses and enable acquisition and spread of disease on an epidemic scale.

This list is not all-encompassing but describes the types of experiments that are most likely to lead to questions. For additional information, please go to: https://journals.asm.org/content/biosecurity. If you think that the results in the manuscript under consideration may lead scientists or others to question its publication, check the “yes” box below. Doing so will prompt referral of the manuscript to the ASM Responsible Publication Committee for additional review. The goal is to ensure that the manuscript is published in a responsible manner. We expect that the majority of such papers will be published if scientifically sound.