VISIBILITY INITIATIVE FOR RESPONSIBLE SCIENCE

Megan J. Palmer, Stanford University, Stella M. Hurtley, Science,
and Sam Weiss Evans, Tufts University

In April 2019 NTI | bio convened a working group meeting of the Biosecurity Innovation and Risk Reduction Initiative. At this meeting a group[1] conceived and created a pilot project concept aimed to improve the performance and recording of risk-benefit assessments before, during and at publication of biological research. This paper describes and builds upon the concept created by this group with specific recommendations to demonstrate proof of principle over a 12-16-month period.

Problem

There is a lack of transparency and information sharing about the *presence* and *process* of risk assessment and management throughout the research lifecycle.

At this time, biosecurity risk assessment and management is not consistently conducted for research projects at the funding stage, within research institutions, or by journals. Even in cases where risk assessment and management *is* conducted, it is not necessarily documented or shared with other stakeholders in the research lifecycle. Moreover, such assessments and management plans are often made without standard or specific methods for comparison, and they typically rely on narrowly defined categories of risk rather than considering new forms of risk beyond traditionally recognized areas of concern.

The lack of transparency and sharing leaves stakeholders and decision makers in research (e.g., practitioners, research institutions, funders, publishers) both reinventing the wheel in conducting independent assessments and management plans and in the dark about whether and how they have been done at other stages in the research lifecycle. A dearth of public information about risk assessment and management processes is an impediment to the normalization of practice and to others learning about and improving existing practices.

The ability to learn about and adapt risk assessment and management is especially important in an era of rapidly emerging tools and technologies. Traditional approaches may no longer prove useful to forecast potential unintended consequences and hazards for cross-disciplinary or nascent scientific areas. Furthermore, growth in global research capacity and capability enables life science research by individuals trained in new disciplines and at institutions where life science research may not have been conducted previously. To standardize assessment and management processes and publicize them would be a tremendous benefit for both groups who may not otherwise have access to a local expert.

---

[1] Working group participants: *Megan J. Palmer, Stanford University; *Sam Weiss Evans, University of Cambridge & Tufts University; *Stella M. Hurtley, Science; Ritu Dhand, Nature; Katherine Bowman, The US National Academies; Mark Perkins, World Health Organization; Nahoko Shindo, World Health Organization; Nusblat Leonora, UOCCB-ANLIS; Christopher Wallace, Australian Reinsurance Pool Corporation; Deborah Rosenblum, NTI; Jaime Yassif, NTI
* prepared this paper

Goals

(1) To promote the widespread performance of risk analysis through the promotion of the sharing of the *presence* and *process* of analyses across the research lifecycle – from funding, through study design, research performance, peer review, and eventual publication. Documentation should travel with the research from the proposal stage through peer review and into publication.
(2) To enable learning and adaptation in risk assessment and management processes.

Benefits

It is anticipated, though not assumed, that more transparent and regular risk assessment and management processes, and standardized ways by which this can be reported, will support researchers and their institutions. Similarly, such processes will benefit the entire decision-making process—from research proposal to manuscript submission for publication e.g., by enabling a more informed, robust review process. Furthermore, such an approach should promote informed management of research (e.g., by encouraging risk management plans to be developed early in the research lifecycle when it is most cost-effective). Over time, sharing should enable collective learning about how and when risks emerge, which risks should be prioritized, and how they might be managed. This visibility initiative will also support a growing field in the science and practice of risk analysis, and encourage reflection by researchers and research stakeholders on the ways that risk is related to research design, conduct, and dissemination. Taken together, this initiative should then create a basis for learning, accountability, and shared responsibility. require a clear and standardized biosecurity framework through which biotechnology funders can commit to reducing biological risks, coordinate their risk reduction activities, and facilitate horizon scanning activities to identify emerging risks.

Existing Initiatives

There are a number of initiatives aimed at developing processes for risk assessment and management and ways in which to share these processes, and in some cases, their outcomes (see Appendix for detailed listing). These initiatives include research organizations conducting risk assessments above and beyond what is required as a result of anticipated risks outside of traditional areas of concern (e.g., involving pathogens). We also describe efforts aimed at promoting reproducibility, transparency and accountability in research. These initiatives may provide templates and models that can be expanded or combined.

One notable initiative is a publisher-led effort to develop minimum reporting standards related to methods and study design (see 'MDAR framework' in the Appendix). Their framework for sharing core information about research materials, study design, experimental design, data and analysis builds on many complementary efforts in the life sciences, including EQUATOR Network, MIBBI, STAR, and ARRIVE.

The most recent Sept 22 2019 version of recommendations for use of the MDAR framework includes a reporting requirement on disclosing whether work is subject to dual use research of concern (DURC) risk management. However, there is relatively little general understanding of what information would be most useful and important to include in this reporting, compared to other aspects of minimal reporting framework (e.g., experimental design for statistical analysis). Moreover, these frameworks are not designed to promote detailed reporting of risk assessment

and management strategies nor go beyond the confines of existing DURC implementation. A pilot study, however, could explore the value of leveraging and informing these reporting systems.

Pilot/Feasibility Study

One pilot approach would be for groups involved in research management from ~3 universities to conduct a feasibility study for creating and implementing a simple and regular risk assessment and reporting process. This pilot could involve a small but diverse portfolio of life sciences research at each institution (e.g., in areas such as genomics, synthetic biology, and microbiology). The pilot would focus initially on the design and performance stages of research, where principal investigators have the most authority to implement changes. Ideally these university groups would work with another researcher, likely in the social sciences, who would co-design the pilot to generate robust and generalizable insights. The purpose of this pilot should be to:

(1) Develop a risk assessment and management reporting process based on input and involvement from institutional biosafety and biosecurity officials, principal investigators, risk analysis experts, funders, and publishers. This process would specify the role of different groups, and what information would be recorded and shared with the goals of holding the research to account and enabling communication and learning.
(2) Evaluate the ease, utility, and benefit of implementing the process over the course of a 12-16-month period.
(3) Develop a report with recommendations and lessons learned to improve upon the process and inform funders, publishers, and other researchers of important considerations to facilitate global use.

A second pilot approach, that could be conducted independently or in conjunction with the above pilot, would involve a major funder (or consortia of funders) that would provide incentives for conducting and sharing risk analysis and management processes. For example, the funder-led pilot would require that new proposals in an emerging technology area or applying a newly developed biotechnology tool include a statement summarizing the initial risk assessment performed prior to proposal submission. The funder(s) would further require that the researcher(s) conduct reviews of the analysis throughout the project, and include a statement of the process of the risk assessment and mitigation strategies in any final publications. Ideally the funder would provide additional resources, on top of normal research funding, to support these additional risk assessment and management tasks (and potentially also the research on risk management described above). Conducted over a 12-16-month period, this pilot project would inform the funder(s) of potential unforeseen risks in research as well as best practices to recommend for all awardees working in a certain technology area.

Like the first pilot approach described, a key output from this small-scale proof of concept would be lessons learned regarding the benefits and burdens created by instituting this requirement. Additionally, it will be important to confirm that the requirements do not disadvantage any type of research proposed based on size, geography, or other criteria.

These two pilot approaches could leverage the MDAR framework reporting requirements as a starting point. A separate study could look at the value of information conveyed through this broadly collected but lower resolution reporting as compared to the more detailed reporting that might be generated by the two pilots described above.

Questions the Pilot(s) Should Seek to Answer

- What are the current practices, if any, for risk assessment and management at different stages of research?
- What are possible organizational structures and formats for reporting? How could reports travel with the research?
- What information is used in designing and conducting risk assessment and management (i.e. what parts of the reporting are useful for others in informing their processes)?

Incentives

Funders (and other stakeholders) want to protect the research enterprise from reputational risk.

Journals would benefit from access to information about previous decisions regarding risk assessment as part of their commitment to assess security concerns in research.

If *required* by funders or publishers, researchers and research institutions will be incentivized to participate. If also r*esourced* by a funder on top of normal funding, then institutions will be much more likely to be engaged.

Research institutions want to develop more effective, scalable and streamlined approaches for safety and security management and the scale and scope of life science research increases. *Institutional biosafety and biosecurity officers* may benefit from learning about approaches at other institutions. Members of institutional biosafety (and biosecurity) committees (ICBBCs) may have an easier job if their researchers they are overseeing are engaged in risk management and greater visibility of their role in the research process. IBBC members and biosafety professionals could be incentivized further by thanking them in the acknowledgement section of the publication, or even adding them as co-authors if the risk assessments ended up significantly adapting the research design.

For *biological investigators*, this initiative could provide support for conducting risk management by putting them in contact with groups with expertise, especially if these tasks are funded or otherwise rewarded. By revising the reporting process based on early pilots, a more streamlined and useful structure could emerge that would be less burdensome and more informative for all communities.

Investigators in the social sciences may be compelled to be involved in a rich study of what processes are effective in risk assessment, and in promoting increased attention to and mitigation of risk in research.

For both the social and biological researchers, this may also spur new lines of applied biosafety and biosecurity research.

Potential for Global Adoption and Scale

Commitment to this idea by a major research funder and/or group of major publishers would significantly advance global reach of the concept. Assuming the inclusion of requirements for risk analysis was well received, government funding agencies would be likely to follow suit.

This model could help to provide a framework that could be expanded for use in research settings globally. This could iteratively go on to improve the system itself by, for example, sharing templates for risk assessments and by providing models of the types of questions asked between different stakeholders. By highlighting the need for risk assessments, and providing visibility and credit for conducting those assessments, it would help make a case for more funding in applied biosafety and biosecurity research.

APPENDIX – List of Existing Initiatives

MDAR - minimal reporting standards for life scientists

A group of journal editors and experts in reproducibility and transparent reporting is developing an initiative on scientific reporting standards. Initial steps laid a foundation for the TOP (Transparency and Openness Promotion) guidelines published in Science in 2015. Following subsequent discussions based on the TOP statement, a working group was formed to establish a "minimal standards" framework and checklist for transparency in reporting research. The MDAR (Materials, Design, Analysis, and Reporting) framework is meant to advance normative best practices in publishing experimental studies in the life sciences. They are developing a minimal standards checklist to facilitate compliance by scientific authors, as well as a tool for editors and reviewers to assess reporting and compliance. This initiative is mainly aimed at increasing reproducibility, but also focuses on reporting governance of research -- which would dovetail very well with VIRS. The checklist already collects information on materials (including animals, model organisms, etc.), protocols, ethics, DURC, statistics, and reporting guidelines.

BBSRC, MRC, Wellcome Trust position statement

The position statement jointly released by the BBSRC, MRC, and Wellcome Trust describes a possible shared approach to managing risk in Dual-Use Research of Concern (DURC) from the funder perspective. This statement focuses on the life sciences and wrestles with balancing the significant risk that DURC poses and preventing excessive restrictions on responsibly conducted research. Autonomy was a key value outlined by the statement and a primary suggestion was to organize self-governance within the scientific community that draws on inputs of key stakeholders to provide the most effective risk management. In this plan, the community should take active steps to develop mechanisms of self-governance that do not hinder responsible research. Steps towards this goal include risk assessment on application forms, developing guidance for funding committees, and requiring notification of risk status adjustments. These actions are meant to heighten awareness and identify risks at an early stage by focusing on motives of the scientific community. As a whole, this initiative presents a similar funder-driven concept that focuses on risk assessment while placing stronger emphasis on not hindering responsible research.

Joint Journal Editors Statement of Scientific Publication and Security

In 2003, editors from many top journals made a joint statement about their commitment to creating risk assessment and management processes at the publication stage of research. Nature has a prominent and public statement of their process of assessing ethical and security concerns in articles. Satisfying this commitment is one reason for the MDAR initiative, noted above.

Research Institutions Going Beyond Compliance

A number of research institutions review research beyond what is required as a function of their funding. At a September 25-27 2017 "Stakeholder Engagement Workshop on the Implementation of the *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern* (DURC)*"* a number of biosafety professionals at research institutions described their processes. For instance, investigators at the University of Wisconsin (US) review research for potential dual use beyond what is required; they do not limit their review to the 15 agents and recently have gone beyond the 7 experimental effects required in the *United States Government Policy.*

DOE Joint Genomics Institute Review

The U.S. Department of Energy Joint Genome Institute (JGI) is a user facility that offers a variety of capabilities to the scientific community, including DNA sequencing, single cell genomics, metabolomics, and DNA synthesis/engineering biology approaches. Since 2013, synthetic biology proposals submitted to the JGI have been assessed, beyond technical feasibility and scientific merit, for the broader aspects and implications of the research. At JGI this process primarily concerns biosafety, biosecurity, biocontainment/environmental aspects and implications, but it can also include social justice, legal, ethical, and other concerns. Broader aspects and implications review is performed for each proposal by 3 external reviewers with complementary expertise. Reviewers can elect to approve proposals after discussion, request proposal modifications, or reject proposals. To date (September 2019), 118 proposals have been reviewed by a set of 28 reviewers, who have made 539 comments across (General, Biosafety, Biosecurity, Ethical, Legal, Social, Environmental) categories. Roughly 55% of proposals are approved without further discussion, 10% are approved after discussion, and 35% are approved after modification. The process has not rejected any proposal to date. The process has proven to be very valuable to the JGI, in that it serves as a time-stamped paper trail of (external reviewer) concerns expressed over proposed research that the JGI has (or will) enable, is very reassuring to the JGI community and broader publics that research is being conducted in a responsible manner, and has also added significant value to downstream biosecurity screening processes (e.g. those implementing the U.S. Department of Health and Human Services guidelines for providers of synthetic double stranded DNA). A publication describing the JGI process in detail, along with distilled review outcomes, is anticipated for 2020. This model may provide a good prototype for reporting structure and requirements, and provide data/lessons on how concerns emerge.

MIT-Broad Foundry Self-Assessment Tool

The MIT-Broad Foundry has developed a biosecurity risk self-assessment tool. The goal is to enable researchers to identify risks in their work (to enable proactive mitigation measures), to raise the team's biosafety/biosecurity awareness, and to develop skills around identifying concerns. The tool is a single slide template designed to be simple and easy enough to use to not detract from compliance and interest (so far at 100%). The tool asks research teams to identify potential technological risks of their work within different categories (e.g., public health, weaponization, economic etc), for elements in progress and complete, and also for both products and enabling capabilities. It also identifies potential ways the work could be compromised through physical or digital means. The tool is used to facilitate regular discussions, at every 6 months, when the Broad also gathers biosecurity experts outside of their team and institute to receive an overview of their experimental design and progress, which also inform their strategies moving forward. So far there has been 100% participation, although they have observed very different assessments between team members. The Foundry funders at DARPA have shared this tool with others as an example that could be used more broadly.

iGEM Safety and Security Risk Analysis Tools

iGEM is an international student competition to develop novel genetic constructs, which gathers around 6000 students and community lab members from 40+ countries each year to compete for prizes and awards. It has a dedicated Safety and Security Program, which reviews all the projects and genetic parts used in the competition. All iGEM teams are required to fill in safety and security forms at multiple points in their yearly projects, and when they propose work that is within set of areas for which iGEM requires special review and permission. The team forms are publicly

accessible. The processes and policies for the program are revised yearly and all iterations are publicly available.

Currently, external contractors assess whether relevant risks have been identified and appropriate measures in place to manage them. Substantive issues are elevated to the competition's own Safety and Security Committee (SSC), comprised of regulators (present and past), biosafety and biosecurity professionals, bioethicists, and animal use professionals from every inhabited continent. The committee members then bring to bare their expertise from their home institutions to work with teams to resolve concerns. iGEM has sanctioned teams, including disqualification, for shortcomings. It also rewards and encourages excellence. Each year, the program undergoes a self-evaluation through its committee and has significantly more ability to iterate on its design than state-based oversight processes. The Safety and Security Program is supported in part by a grant from the Open Philanthropy Project. Open Philanthropy Project has also supported a complementary research project to derive insights from the Safety and Security Program.

Clinical Trial Transparency

Initiatives to foster transparency and reporting in clinical trials provides potential models and lessons for designing a system for disclosing information about the governance/management of research. The funding mechanisms behind clinical trials also provide examples of how reporting requirements might be structured. Transparency has been a critical issue for the progress of clinical trials as efforts to make accessible information about trial progress, impactful results, and raw trial data have been limited in effectiveness. New initiatives such as the ISRCTN registry (supported by the Wellcome Trust) and WHO requirements for the International Clinical Trials Registry Platform (ICTRP) aim to address this problem by standardizing and normalizing reporting requirements before, during, and after trials. Such requirements include obtaining relevant ethical approvals, proper management protocols, continued governance and data monitoring, publishing results, and making clinical trial data accessible. To push towards a normalization of transparency, a focus on the accountability aspect of public disclosure is necessary. This emphasis on accountability could be integrated into efforts to normalize reporting on risk management in DURC as well.