A more systematic approach to biological risk

Management of emerging risks in life science and technology requires new leadership and a sober assessment of the legacy of Asilomar

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On 29 October 2015, the White House issued a memorandum to agencies with its plans to enhance U.S. biosafety and biosecurity. This memo identifies important gaps and constructive steps, but it grafts recommendations onto inadequate institutional structures and fails to address underlying systemic needs.

The memorandum was a response to a series of events, including U.S. laboratories' mishandling of pathogens. In the summer of 2014, U.S. labs were in the spotlight over mishandling of anthrax, smallpox, and avian flu. In 2015, live anthrax shipments from U.S. defense labs and an investigative report revealed pervasive and long-standing gaps in oversight of work with deadly pathogens, including inadequate systems of reporting and accountability for lab accidents (*1*–*5*). Meanwhile, "gain-of-function" experiments with viral pathogens are back at the center of an international debate over whether certain research poses unjustifiable public safety and security risks (*6*, *7*). The Ebola outbreak drove home the potential public health consequences of infectious agents, irrespective of whether they originate inside or outside the lab. The debate has widened as other dual-use experiments and technologies, such as gene drives, are pursued (*8*, *9*).

POLICY

The nature of these events varied, but the responses to them were all similarly reactive and shortsighted: temporarily stop research and shut down labs, as well as conduct narrow reviews of specific programs and standard protocols. The White House laudably recognized the need for a more systematic approach to biological safety and security. However, its recommendations again place additional oversight responsibilities onto existing institutional structures (*10*). Inadequate processes for assessing the significance of risks have hindered efforts to develop sustained and coordinated plans. The default response has been a narrow treatment of individual incidents rather than a proper diagnosis and a more expansive and proactive approach to a systemic problem.

Our strategies and institutions for managing biological risk in emerging technologies have not matured much in the last 40 years. With the advent of recombinant DNA technology, scientific leaders resorted to halting research when confronted with uncertainty and public alarm about the risks of their work. To determine a framework for managing risk, they gathered at the now-fabled 1975 Asilomar meeting. Their conclusions led to the recombinant DNA guidelines still used today, and Asilomar is often invoked as a successful model for scientific self-governance.

However, Asilomar's legacy has some negative aspects. Like most scientists today, participants at Asilomar had little expertise in and appreciation for institutions that manage risk. Some scientists were shocked to discover the liabilities of their work and their wide disagreements on how to assess risk (*11*, *12*). Organizers focused on safety and sidelined what they deemed to be social, ethical, and political topics, such as security and human modification issues. Asilomar created risky expectations: that leading biological scientists are best-suited for and wholly capable of designing their own systems of governance and that emerging issues can be treated as primarily technical matters.

The world has changed since 1975. The challenges remain just as much social as they are technical in nature but the scope and scale of biological science and technology have changed dramatically. Strategies for balancing benefits and risks must now reach a practitioner community proliferating globally. The increased ease of reading and writing genetic information means that securing materials in a handful of established labs is not feasible.

Unfortunately, today's leadership on biological risk reflects Asilomar's risky legacy: prioritizing scientific and technical expertise over expertise in governance, risk management, and organizational behavior. Political leaders have largely ceded a strategic leadership role, with the analysis of emerging issues of biological risk captured by the largest scientific funding agency for biological research: the U.S. National Institutes of Health. For example, NIH is now leading the U.S. federal risk-benefit analysis of so-called gain-of-function research. It is a one-off study, with very limited scope and timelines, conducted through a process that is tightly controlled by an institution with a clear conflict of interest (*13*, *14*). This and other related studies on emerging biotechnology risks, such as the National Academies of Science investigations of gene editing and gene drives, underrepresent expertise on governance in favor of technical expertise.

This is a worrisome precedent for such

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studies, the purpose of which, in part, is to offer conceptual approaches to risk management (*15*, *16*). Leadership biased toward those that conduct the work in question can promote a culture dismissive of outside criticism and embolden a culture of invincibility. We need to develop leadership that represents and integrates technical and social expertise. Leaders must instill safety and security as core missions driving the work of scientific and political institutions. By supporting work to identify and mitigate risks, acknowledging failure and uncertainties, and facilitating participation of diverse experts, they can empower organizations to respond to new challenges.

Although enlightened leadership is vital, regulatory oversight is critical to modifying behavior. Effective oversight institutions must have the expertise to assess and adapt performance metrics, the incentives (requirements and rewards) for reporting, and the authority to impose meaningful penalties when standards are not met. Institutional Biosafety Committees currently provide some local oversight but have limited expertise in biosecurity and risk. The Recombinant DNA Advisory Committee and National Science Advisory Board for Biosecurity (NSABB) lack the independence and authority to enforce rules. Embedding these boards within NIH also creates conflicts of interest that can lead to disenfranchisement when problems arise such as occurred following the NSABB's initial recommendations on publication of avian influenza gain-of-function research (*16*). The Office of Science and Technology Policy (OSTP) and the Presidential Commission for the Study of Bioethical Issues (PCSBI) have a great deal of expertise but no authority to regulate behavior. Currently, oversight relies on few enforcement mechanisms outside of revoking or creating barriers to public funding—an indirect and limited approach that does not apply to private entities. Fines can be effective, but only if enforced and tied to specific performance expectations. Reputation is also an important motivator; public reporting of performance (good and bad) is an underutilized tool to improve behavior and enhance accountability.

Unfortunately, metrics and processes for monitoring the performance of our biological safety and security regimes are currently underdeveloped. Mere collection of accident data is not sufficient—at present, lack of errors is considered proof of success, and little forecasting is done to predict future failures. Recognizing a long-standing gap, the U.S. Government Accountability Office (GAO) has suggested that a single federal entity oversee high-containment labs and perform periodic strategic assessment. In order to scale its efforts and adapt over time, such an entity must prioritize public reporting. A lack of transparency in risk-management processes undermines the ability to evaluate substantive claims and solicit input and expertise to inform the design of improved strategies. The current review by the U.S. Federal Select Agent Program, although commendable in emphasizing transparency, does not provide a compelling management plan.

Expertise and precedents across other high-risk, high-consequence activities may suggest lessons for institutions that manage biological risk. In transportation, the Interstate Commerce Commission (ICC) was created to regulate railroads; when trucking needed to be regulated, responsibility was also given to the ICC with the rationale that both crossed state lines. This was a mistake, since there were conflicts of interest between the rail and trucking industries. It thus made sense with the advent of aviation for Congress to give authority to a new, independent regulator, the Federal Aviation Administration (FAA). The National Transportation Safety Board (NTSB) was also created to provide independent investigative functions. The FAA and NTSB were able to design mechanisms through which pilots and controllers could note unsafe conditions, near misses, and accidents, and were able to protect those who reported unsafe conditions.

"to mature and learn, oversight institutions must approach governance as a long-term strategic challenge"

In the nuclear power industry, the Nuclear Regulatory Commission (NRC) was created as an independent and powerful authority, and the industry also formed the Institute of Nuclear Power Operations (INPO) as an independent nonprofit organization to provide standards for, and assessment of, the safety of nuclear plants. Although issues remain, the shared oversight structure between INPO and NRC evolved to resolve conflicting interests and to enhance communication and expertise as compared with the predecessor, the Atomic Energy Commission.

To respond to today's challenges and to prepare for the future, scientific and political leaders must work together to cultivate social expertise alongside technical know-how. A key step is for scientific and political leaders (i) to acknowledge the insufficiencies in our current institutions and risk-management strategies, (ii) to position public safety and security as drivers of ongoing research, and (iii) to create institutional structures that can anticipate and adapt. In the United States, the reviews of biosafety and biosecurity systems conducted by the Federal Expert Security Advisory Panel and the National Science and Technology Council highlight the unnecessary complexity of the process require to reconcile and enforce recommendations. The White House memo clarified some immediate responsibilities but did not resolve long-term issues with overlapping jurisdictions. Although competing perspectives are critical to exposing emerging issues, centralized facilitation is needed. Our consultations with colleagues in other countries indicate that they face similar problems with multiple chains of command. Agreements, such as the Biological Weapons Convention, rely on state-based programs to ensure compliance and updating of safety and security standards, so effective national leadership is essential.

In terms of organization, countries should create permanent, credible national-level oversight and standard-setting bodies that work in partnership through international entities. The International Civil Aviation Organization of the United Nations is an example of the latter; it coordinates state-based programs and adopts standards for global civil aviation. In biotechnology, the mandate should extend beyond health to recognize significant drivers in other domains, such as the production of chemicals, materials, and food. In the United States, the Executive Office of the President could create a high-ranking government official position, such as a special assistant to the president, and a coordinating committee, responsible for anticipating and managing risks associated with biotechnology (*17*). This committee would be independent from, but work in partnership with, funding bodies like NIH and organizations with overlapping roles in biological risk management, including the Department of Homeland Security, Department of Health and Human Services (DHHS), U.S. Department of Agriculture, and Department of Defense (DOD). Rather than acting as a command-and-control czar, this official and committee should facilitate information-sharing and build processes for accountability and harmonization across agencies. This should include assessing the creation of entities like the NTSB that can provide independent performance reporting and the complementary removal of unnecessary or duplicative functions from other agencies. There is precedent for the role of special adviser (*17*), but such a role and a single lead for oversight and strategy have since been rebuked by OSTP and national security staff (*5*). We believe such responses indicate a lack of appetite for acknowledging and ad-

dressing underlying issues. Alternatives, such as creating a new position within OSTP, are insufficient to navigate complex interagency chains of command.

Last, to mature and learn, oversight institutions must approach governance as a long-term strategic challenge in need of management and research, as well as the involvement of the general public. Investing in interdisciplinary research centers is one way to bring focus to critical risk governance topics like leadership, organization, and learning in a future of distributed biological knowledge and technology. If we do not address the foundational challenge of emergent technologies and biological risk properly, we should expect reactive and poorly conceived restrictions on potentially beneficial research, as well as many more normal "accidents" with increasingly consequential risks to people and the environment, as biotechnology proliferates globally. ■

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ACKNOWLEDGMENTS

The authors thank S. Falkow, D. Endy, A. Zegart, S. Sagan, K. Bernard, K. Oye, S. Weiss-Evans, C. Perrow, S. Hecker, and L. Eden for helpful discussions. D.A.R. is a former member of the NSABB. F.F. was a member of the President's Council on Bioethics.

10.1126/science.aad8849

Where next? Survival and reproduction of wolves in the Northern Rockies have declined.

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CONSERVATION POLICY

Questionable policy for large carnivore hunting

U.S. wolf-hunting policies do not align with ecological theory or data

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Terrestrial large carnivores are in rapid global decline, with consequences for ecosystem structure and function. Among drivers of these declines, legal hunting is unique because it is intentional and thus relatively easily controlled. Although regulated carnivore hunting potentially reduces conflict and provides revenue for conservation, it can also drive population declines (*1*–*5*).

POLICY Some policies regulating carnivore hunting address negative effects on demography and population dynamics, but others do not. Here, we use wolf harvesting in the western United States to illustrate four aspects of policy that do not align well with ecological theory and data, and we suggest resolutions.

Policies regulating human effects on lions, cougars, leopards, and tigers have responded to research by moving to better evaluate and mitigate demographic costs (*1*, *2*, *5*, *6*). For example, policies for lions (*Panthera leo*) include temporary hunting closures to allow population recovery (*5*) and reduced quotas with sex- and age-limited harvesting (*2*). Nonetheless, hunting policies for large carnivores still often suffer from a lack of science-based guidance. For example, policies for harvest of wolves (*Canis lupus)* in the Northern Rocky Mountains Distinct Population Segment (NRM DPS) suggest that annual harvest of up to 50% of the population has little or no effect on dynamics. Wolves were reintroduced in the mid-1990s, and the NRM DPS grew steadily until 2009 (see the chart, part A). Legal hunting began immediately after removal of the Endangered Species Act (ESA)