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Public role in research oversight

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Rasmussen et al. (1) argue that "increasing oversight across virology or all microbe research would represent a misdirection of resources and would fail to provide a commensurate increase in safety or security" and "harm surveillance, antiviral discovery, monitoring for resistance to antivirals and vaccines, and other critical efforts." On the contrary, a strengthened version (2) of the recommendations of the National Science Advisory Board on Biosecurity (NSABB) is crucial for the success of microbiological science. Implementing these recommendations would reduce the risks of a deliberate or accidental pandemic, while using precious research resources efficiently, restoring trust in science, strengthening US leadership in biosecurity and biosafety, and safeguarding the biomedical research enterprise, as ASM itself has said (https://asm.org/press-releases/2023/january/asm-commends-nsabb-report).

The commentary by Rasmussen et al. conflates the alleged harms of the NSABB recommendations with those of recent NIH rules involving scrutiny of foreign collaborators. It argues based on a single newspaper article that virology as a whole has been widely chilled by even the possibility of increased safety measures. It elides the distinction between mouse-adapting a pathogen for study in an animal model, which most would support as low risk and high value (3), and deliberate efforts to confer a phenotype resembling human transmission (4, 5). It conflates controversy over the origin of SARS-CoV-2 with well-founded concern that began more than a decade ago (6) about laboratory accidents in high-level biosafety labs (7, 8). Its proposed solution of focusing on "observed outcomes" would imply waiting for high-consequence dangers to have been created, rather than anticipating and limiting such risks.

We note the philosophical/scientific defenses of experiments that increase the transmissibility of pathogens in the lab (9) but find no compelling refutation of arguments that alternative scientific approaches can (10) and do achieve the same goals of enhancing public health while being safer, cheaper, and more generalizable (11–13). Furthermore, vaccine and antimicrobial manufacturers are not claiming that creating more transmissible pandemic pathogens is essential for their work.

Everyone in society has a stake in spending scarce research dollars in ways that increase our preparedness and minimize the risk of pandemics. There is legitimate disagreement among scientists and policymakers about how to do that, but these are value-laden policy questions (14) on which ethicists, security experts, and especially the public have a legitimate voice (15). Extreme budget cuts to important areas of science and state bans on all gain-of-function work on potential pandemic pathogens have been proposed or enacted. We interpret these measures, at least in part, as harmful overreactions to what policymakers legitimately perceive as the scientific community's reluctance to address public concerns about the risks of a laboratory-associated pandemic. Calls for society to leave concerns about the creation of potential pandemic pathogens to self-regulation by experts (1, 16–18) have not proven convincing to the public and its elected representatives. Asilomar, as an example of self-regulation, has flaws (19). All

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microbiologists, scientists, and all those who benefit from scientific advances have an interest in addressing these issues promptly and seriously, together.

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REFERENCES

1. Rasmussen AL, Gronvall GK, Lowen AC, Goodrum F, Alwine J, Andersen KG, Anthony SJ, Baines J, Banerjee A, Broadbent AJ, et al. 2024. Virology—the path forward. J Virol 98:e01791-23. https://doi.org/10.1128/jvi.01791-23
2. Pannu J, Palmer MJ, Cicero A, Relman DA, Lipsitch M, Inglesby T. 2022. Strengthen oversight of risky research on pathogens. Science 378:1170–1172. https://doi.org/10.1126/science.adf6020
3. Evans NG, Lipsitch M, Levinson M. 2015. The ethics of biosafety considerations in gain-of-function research resulting in the creation of potential pandemic pathogens. J Med Ethics 41:901–908. https://doi.org/10.1136/medethics-2014-102619
4. Imai M, Herfst S, Sorrell EM, Schrauwen EJA, Linster M, De Graaf M, Fouchier RAM, Kawaoka Y. 2013. Transmission of influenza A/H5N1 viruses in mammals. Virus Res 178:15–20. https://doi.org/10.1016/j.virusres.2013.07.017
5. Linster M, van Boheemen S, de Graaf M, Schrauwen EJA, Lexmond P, Mänz B, Bestebroer TM, Baumann J, van Riel D, Rimmelzwaan GF, Osterhaus ADME, Matrosovich M, Fouchier RAM, Herfst S. 2014. Identification, characterization, and natural selection of mutations driving airborne transmission of A/H5N1 virus. Cell 157:329–339. https://doi.org/10.1016/j.cell.2014.02.040
6. Lipsitch M, Plotkin JB, Simonsen L, Bloom B. 2012. Evolution, safety, and highly pathogenic influenza viruses. Science 336:1529–1531. https://doi.org/10.1126/science.1223204
7. Byers KB, Harding L. 2017. Laboratory-associated infections. In Wooley D, Byers KB (ed), Biological safety: principles and practices, 5th Ed. ASM Press, Washington, DC.
8. Kimman TG, Smit E, Klein MR. 2008. Evidence-based biosafety: a review of the principles and effectiveness of microbiological containment measures. Clin Microbiol Rev 21:403–425. https://doi.org/10.1128/CMR.00014-08
9. Casadevall A, Fang FC, Imperiale MJ. 2023. The epistemic value of gain of function experiments. mSphere:e0071423. https://doi.org/10.1128/msphere.00714-23
10. Lipsitch M, Inglesby TV. 2014. Moratorium on research intended to create novel potential pandemic pathogens. mBio 5:e02366-14. https://doi.org/10.1128/mBio.02366-14
11. Lipsitch M. 2018. Why do exceptionally dangerous gain-of-function experiments in influenza? methods Mol Biol 1836:589–608. https://doi.org/10.1007/978-1-4939-8678-1
12. Lipsitch M, Galvani A. 2014. COMMENTARY: the case against 'gain-of-function' experiments: a reply to fouchier & kawaoka. Available from: http://wwwcidrapumnedu/news-perspective/2014/06/commentary-case-against-gain-function-experiments-reply-fouchier-kawaoka
13. Lipsitch M, Galvani AP. 2014. Ethical alternatives to experiments with novel potential pandemic pathogens. PLoS Med 11:e1001646. https://doi.org/10.1371/journal.pmed.1001646
14. Douglas HE. 2009. Science, policy, and the value-free ideal. University of Pittsburgh Press, Pittsburgh.
15. Pamuk Z. 2021. Politics and expertise. Princeton University Press, Princeton, NJ.
16. Lowen AC, Casadevall A, Alwine JC, Enquist LW, Goodrum FD, Imperiale MJ, Lakdawala SS. 2023. Oversight of pathogen research must be carefully calibrated and clearly defined. J Virol 14:e0017623. https://doi.org/10.1128/jvi.00176-23
17. Goodrum F, Lowen AC, Lakdawala S, Alwine J, Casadevall A, Imperiale MJ, Atwood W, Avgousti D, Baines J, Banfield B, et al. 2023. Virology under the microscope-a call for rational discourse. mSphere 8:e0003423. https://doi.org/10.1128/msphere.00034-23
18. Imperiale MJ, Casadevall A, Goodrum FD, Schultz-Cherry S. 2023. Virology in peril and the greater risk to science. mSphere 8:e0060722. https://doi.org/10.1128/msphere.00607-22

19. Palmer MJ, Fukuyama F, Relman DA. 2015. SCIENCE GOVERNANCE. A more systematic approach to biological risk. Science 350:1471–1473. https://doi.org/10.1126/science.aad8849