

Title:

Making Security Viral: Shifting engineering biology culture and publishing

Authors: Rebecca Mackelprang¹, Katarzyna P. Adamala², Emily R. Aurand¹, James C. Diggans³, Andrew D. Ellington⁴, Sam Weiss Evans⁵, J. L. "Clem" Fortman¹, Nathan J. Hillson^{6,7,8,9}, Albert W. Hinman¹, Farren J. Isaacs¹⁰, Medford I. June¹¹, Shadi Mamaghani¹², Tae Seok Moon^{13,14}, Megan J. Palmer^{15,16}, Jean Peccoud¹⁷, Elizabeth A. Vitalis¹⁸, India Hook-Barnard¹, Douglas C. Friedman^{1*}

Affiliations:

¹Engineering Biology Research Consortium, Emeryville, CA 94608, USA

²Department of Genetics, Cell Biology and Development, University of Minnesota, 420 Washington Ave SE, Minneapolis, MN 55455 USA

³Twist Bioscience, 681 Gateway Blvd, South San Francisco, CA 94080 USA

⁴Center for Systems and Synthetic Biology, University of Texas at Austin, Austin, TX, 78712 USA

⁵Program on Science, Technology & Society, Harvard Kennedy School, 79 JFK St, mailbox 38, Cambridge, MA 02139 USA

⁶Biological Systems & Engineering Division, Berkeley National Lab, 1 Cyclotron Road, Berkeley, CA 94720 USA

⁷DOE Agile BioFoundry, 1 Cyclotron Road, Berkeley, CA 94720 USA

⁸DOE Joint Genome Institute, 1 Cyclotron Road, Berkeley, CA 94720 USA

⁹DOE Joint BioEnergy Institute, 1 Cyclotron Road, Berkeley, CA 94720 USA

¹⁰Department of Molecular, Cellular & Developmental Biology, Department of Biomedical Engineering, Systems Biology Institute, Yale University, New Haven, CT, 06520, USA

¹¹Department of Biology, Colorado State University, Collins, CO 90523-1878, USA

¹²AAAS Science and Technology Policy Fellowship, 1200 NW New York Avenue, Washington DC, 20005 USA

¹³Department of Energy, Environmental and Chemical Engineering, Washington University in St. Louis, One Brookings Dr. Box 1180, St. Louis, MO 63130

¹⁴Division of Biology and Biomedical Sciences, Washington University in St. Louis, One Brookings Dr. Box 1180, St. Louis, MO 63130

¹⁵Department of Bioengineering, Stanford University, Stanford, CA 94305, USA

¹⁶Center for International Security and Cooperation, Freeman Spogli Institute for International Studies, Stanford University, Stanford, CA 94305, USA

¹⁷Department of Chemical & Biological Engineering, Colorado State University, Fort Collins CO 80523-1370 USA

¹⁸Inscripta, 5500 Central Ave Boulder, CO 80301 USA

*Corresponding email: dcf@ebrc.org

Keywords:

Biosecurity, biosafety, SARS-CoV-2, synthetic biology, engineering biology

Abstract:

The ability to construct, synthesize, and edit genes and genomes at scale and with speed enables, in synergy with other tools of engineering biology, breakthrough applications with far-reaching implications for society. As SARS-CoV-2 spread around the world in early spring of 2020, researchers rapidly mobilized, using these tools in the development of diagnostics, therapeutics, and vaccines for COVID-19. The sharing of knowledge was crucial to making rapid progress. Several publications described the use of reverse genetics for the *de novo* construction of SARS-CoV-2 in the laboratory, one in the form of a protocol. Given the demonstrable harm caused by the virus, the unequal distribution of mitigating vaccines and therapeutics, their unknown efficacy against variants, and the interest in this research by laboratories unaccustomed to working with highly transmissible pandemic pathogens, there are risks associated with such publications, particularly as protocols. We describe considerations and offer suggestions for enhancing security in the publication of synthetic biology research and techniques. We present three recommendations: 1) protocol manuscripts for the *de novo* synthesis of certain pathogenic viruses undergo a mandatory safety and security review; 2) if published, such papers include descriptions of the discussions or review processes that occurred regarding security considerations in the main text; and 3) the development of a governance framework for the inclusion of basic security screening during the publication process of engineering biology / synthetic biology manuscripts to build and support a safe and secure research enterprise that is able to maximize its positive impacts and minimize any negative outcomes.

Introduction

Engineering biology research is accelerating advances in health & medicine, food & agriculture, environmental sustainability, and the bioeconomy (1). With the ability to build and

1 engineer complex biological pathways, circuitry, and organisms comes an imperative to grapple
2 with the potential negative uses and outcomes in addition to celebrating and sharing the good.
3 The biological research community has long recognized the need to consider the safety and
4 security aspects of research and innovation in publishing, however, addressing security while
5 ensuring the fundamental values of open science and knowledge sharing has proved
6 challenging. This issue came into focus during debates over publication of papers describing
7 H5N1 variants with enhanced transmissibility (2-7). There are currently no widely implemented
8 guidelines for attending to security concerns in publishing (8).

9 We, as members of the Engineering Biology Research Consortium (EBRC), offer the
10 perspective of researchers working to build a scientific culture that supports the proactive
11 identification and management of security issues emerging from biological research while
12 recognizing and upholding the value of open science and the free flow of information as a driver
13 of progress and innovation. Rarely, information or knowledge shared widely can pose significant
14 risks. Evaluating the risks relative to the benefits of publication of some types of research or
15 techniques—such as the *de novo* synthesis of viruses—is difficult and often subjective, and
16 processes for doing so have not been widely adopted. Informed authors, editors, reviewers,
17 researchers, and other stakeholders may, and do, reasonably come to different conclusions as
18 to the levels of risk posed by research and how best to address and mitigate those risks (9).

19 The publication in early 2021 of “Engineering SARS-CoV-2 using a reverse genetic
20 system” in *Nature Protocols* (10) is a clear example of the need for such evaluative processes to
21 be established, made transparent, and consistently implemented. The detailed, step-by-step
22 guide for the *de novo* construction of SARS-CoV-2 in the laboratory makes it feasible for
23 individuals with minimal molecular biology or virology training, without access to appropriate
24 biosafety facilities, and/or with ill-intent, to build and generate live virus from scratch along with
25 variants with potentially higher transmissibility, decreased vaccine efficacy, and/or greater
26 disease severity (11,12).

1 Protocol papers explicitly lower the barriers for non-experts to engage in new areas of
2 research and are generally a great asset to the scientific community. However, in addition to the
3 technical information provided in protocols, scientists new to an area of research or attempting a
4 new method or approach need similarly detailed relevant safety and security information,
5 particularly when the stakes associated with successfully completing the protocol are so high.
6 Future iterations of security governance processes, standards, or guidelines should at a
7 minimum identify protocol papers describing the synthesis and modification of viruses that
8 cause serious disease as warranting further security review.

9 To initiate meaningful discussion that yields actionable, widely adoptable guidelines, we
10 offer preliminary recommendations for the publication of manuscripts with security implications
11 in engineering biology. We call on researchers, journals, reviewers, and funders to
12 collaboratively iterate upon these recommendations through further discussion with thoughtful
13 input from stakeholders across the field (13).

14 We recommend that: 1) protocol manuscripts for the *de novo* synthesis of certain
15 pathogenic viruses undergo a mandatory safety and security review; 2) if published, such
16 papers include descriptions of the discussions or review processes that occurred around
17 security considerations in the main text; and 3) the development of a governance framework for
18 the inclusion of basic security screening during the publication process of engineering biology /
19 synthetic biology research to build and support a safe and secure research enterprise that is
20 able to maximize its positive impacts and minimize any negative outcomes. We conclude by
21 discussing potential processes for the adoption and implementation of these recommendations.

22 **Recommendation 1: Review of protocols for *de novo* viral synthesis**

23 Protocols describing the *de novo* synthesis of human, animal, or plant viruses that are
24 likely to be highly transmissible and have high mortality or morbidity (e.g., biosafety level 3 and
25 4 viruses) raise unique security concerns that deserve consideration in advance of publication. .
26 We recommend that editors incorporate security expertise into the peer review process before

1 such protocols are published. Editors often invite peer review from individuals qualified to
2 evaluate different aspects of a manuscript. Here, editors should invite security experts to review
3 the manuscript in addition to technical reviewers or could find individuals with technical
4 expertise who demonstrably incorporate security into their research and/or professional
5 activities. We suggest the inclusion of three to five reviewers qualified to evaluate security
6 considerations because experts often disagree about the extent of biological threats, so it is
7 important that publication decisions that could have global implications not be made based on
8 the views of one or two individuals (9). There is, of course, a procedural burden of finding
9 additional reviewers; however, the number of protocol papers describing synthesis of agents
10 with transmissibility and high mortality or morbidity is low enough that this standard can be met
11 if journals that publish protocols agree to do so.

12 In this review process, parties involved should consider the risks and the benefits of
13 publishing the detailed protocol compared to letting previously published methods sections
14 stand (generally, protocol papers elaborate on approaches previously published in research
15 papers). Reviewers should incorporate mitigating factors into their review considerations,
16 including 1) a globally available vaccine with high efficacy against circulating variants and/or 2)
17 established regulatory constraints around the distribution and availability of associated physical
18 materials. At the time of publication of “Engineering SARS-CoV-2 using a reverse genetic
19 system,” vaccines were available only to the highest risk groups in the United States and widely
20 inaccessible on a global scale. And, early evidence in a preprint about Omicron (B.1.1.529)
21 suggests they are less efficacious against some variants (14). Efficacious therapeutics are now
22 being approved but were unavailable even a few months ago. SARS-CoV-2 is not a Federal
23 Select Agent, so its possession, use, and transfer are not regulated in the United States,
24 although in November 2021, the CDC announced an Interim Final Rule placing SARS-CoV-2 /
25 SARS-CoV chimeras on the Federal Select Agent list (15). If a nefarious actor was unable to
26 access associated plasmids due to regulation or security practices of the repositories that might

1 distribute them, that actor might be able to reconstruct the virus by ordering and assembling
2 synthetic DNA. Some DNA synthesis companies screen for SARS-CoV-2 sequences, but they
3 are not required to do so and, especially on an international scale, many do not. Those that do
4 screen for SARS-CoV-2 sequences still fulfill orders absent any other indicators of potential
5 misuse.

6 *Biodefense in the Age of Synthetic Biology*, a 2018 consensus study report from the
7 National Academies of Sciences, Engineering, and Medicine, provides a useful framework for
8 evaluating research and capabilities for general usability, usability as a weapon, expertise and
9 infrastructure required, and the potential for mitigation (16). Derivatives of this framework that
10 are expanded to evaluate safety and additional security considerations, developed through
11 deliberation and consultation with the research community, journal editors, government
12 agencies, and security experts, may be useful for security reviewers. If security reviews were
13 divergent, a conversation between security reviewers and editorial staff should be considered to
14 work toward a safe and secure outcome.

15 The most likely outcome of a review process that includes security-minded reviewers is
16 that the authors be asked to make some revisions to their manuscript, e.g. to incorporate explicit
17 safety and security cautions in their paper and/or describe the necessity of appropriate
18 laboratory conditions such as locked doors and freezers, appropriate air flow control, and
19 biosafety cabinets. They may also be asked to provide a description of the security review
20 process (see below). It's also possible that security reviewers might recommend that the journal
21 should decline to publish the protocol article or that it should wait until the risks of doing so are
22 decreased by greater availability of diagnostics, therapeutics, and/or vaccines, in which case
23 previously published methods sections would still stand and enable direct communication
24 between researchers as appropriate. Editors make decisions all the time about how manuscripts
25 can be improved during review and whether or not manuscripts are appropriate for publication in

1 their journal. Adding these reviewers to the process will better position editor(s) to make fully
2 informed decisions about publication.

3 **Recommendation 2: Publication of security review process alongside manuscripts**

4 Publications describing the reconstruction of highly transmissible pathogenic viruses with
5 high mortality or morbidity should be accompanied by a description of the safety and security
6 review it underwent in advance of publication, including all efforts to engage with, understand,
7 and mitigate security risks. Within the paper text itself, authors should briefly describe risks
8 inherent in the research, detailed precautions that anyone using the protocol should take,
9 mitigating actions, and any discourse undertaken with relevant experts or authorities during
10 research or publication.

11 Journals could publish short commentaries accompanying such pieces describing how
12 the security issues came to their attention, what (if any) steps they took to address these issues
13 or to discuss the issues with the authors, and the journal's assessment of why the benefits of
14 publication outweigh identified risks. While such statements may draw the attention of those
15 wishing to cause harm, they can also draw the attention of relevant authorities positioned to
16 monitor and intervene in nefarious activities. Protocols journals in particular often include
17 concrete warnings about the safety risks of individual chemicals used in each protocol. These
18 warnings show the journals take their role seriously in keeping practitioners safe, and we
19 suggest that they extend this same attention to the security implications of published papers.

20 Security statements within a manuscript or accompanying articles with security
21 implications may be seen as platitudes or boilerplate; however, their value is four-fold as they:
22 1) indicate that the authors have considered security issues associated with their work; 2)
23 encourage authors to implement security best practices throughout the research lifecycle, as
24 they know publishers will require a description of these practices; 3) help inform readers that
25 evaluating the security implications of research is an important part of the scientific process;

and, 4) provide an empirical basis for future improvements of the security assessment process itself.

Recommendation 3: Broader pre-publication security evaluation

The above recommendations pertain specifically to protocol papers describing the synthesis of highly transmissible viruses with high mortality or morbidity. There is, however, a broader scope to consider, including how security concerns can be identified and addressed more broadly in engineering biology publication. More than other life science disciplines, engineering biology can be used to produce pathogenic biological agents, synthesize drugs and toxins, and have considerable environmental effects. Journals publishing engineering biology research should implement a standardized questionnaire or survey addressing security as part of the submission process. Some preliminary suggestions of information journals should consider, include: 1) whether or not the authors identified any security concerns associated with the work they have submitted; 2) what, if any, security evaluation was done within the author's institution, the relevant funding organization, or a government-supported panel or review board; 3) whether the authors can cogently summarize whether (or, importantly, not) publication of the work poses substantive risk; 4) what mitigations they considered around this risk; 5) whether the submitted work has been previously rejected by any other journal due to security concerns; and, 6) whether and how they plan to restrict access to materials required to reproduce their research, particularly for research involving recently emerged viruses or organisms for which regulation on possession is still in development. Journals should make public the authors' answers to these questions in the same way and for the same reasons as answers to ethical and safety questionnaires are currently made public: to maximize transparency and opportunity for debate as to the boundaries of the publication of such research.

Questions for editors and reviewers should prompt them to consider if the work poses obvious security concerns, for example if it involves engineering of human or agricultural pathogens, synthesis of toxic compounds or narcotics, or could have serious environmental

1 implications. Editors and reviewers should also be asked if the work has less obvious security
2 implications, such as making an entire class of compounds significantly easier to synthesize
3 (particularly if that class includes toxic chemicals or other controlled substances) or facilitating
4 easier assembly of long DNA fragments. Given the limited security expertise and unpaid nature
5 of journal editing and reviewing, questions for editors and reviewers should not be onerous.
6 The outcomes of author, reviewer, and editor surveys should be used as a basis for discussion
7 on minimizing publication risks. In extreme cases, it may be valuable for authors to discuss
8 security concerns that may result from publication with appropriate governmental officials (e.g.,
9 in the United States, FBI WMD Coordinators).

10 **Implementation**

11 Decisions as to when and how to publish research and protocols that pose safety and
12 security concerns have caused debate in the past (e.g., 17-19). Moving beyond debate to the
13 development of standards and practices that systematize biosecurity governance will take active
14 participation and commitment from diverse members of the biological sciences research
15 community. The vastness and diversity of this community make governance efforts by any
16 single government difficult to develop and to implement and could not address the international
17 nature of the field. The National Science Advisory Board for Biosecurity (NSABB) in the United
18 States was formed to provide guidance and recommendations on biosecurity and dual use
19 issues but has only met once since May 2017, and the US Department of Health and Human
20 Service's Potential Pandemic Pathogens (PPP) Care and Oversight Review Group reviews
21 funding decisions on proposed PPP research (20). International efforts, including those of The
22 World Health Organization and the Nuclear Threat Initiative's Visibility Initiative for Responsible
23 Science (21), are developing experiments in the governance of security concerns across the
24 research lifecycle, from funding to publication and beyond (22). As universal implementation
25 and international enforcement mechanisms are not feasible, this paper's recommendations are
26 geared to journals that individually, or in concert with one another, can take steps to increase

1 security. With the high number of biosecurity stakeholders with different experience and
2 expertise, reaching consensus on governance is difficult. We suggest the development of a pilot
3 governance mechanism, producing real-world data for iteration and broader implementation. A
4 pilot program at one or more journals could be implemented at relatively low cost and the
5 lessons learned from its outcomes may catalyze further NGO, philanthropic, and/or government
6 investment.

7 A successful end state might have parallels with the practices of DNA synthesis
8 providers. Government guidance has significantly impacted the screening practices of many
9 DNA synthesis providers in the United States. Even without formal regulation, many companies
10 still follow the Department of Health and Human Services “Screening Framework for Providers
11 of Synthetic Double-Stranded DNA” to screen sequences and customers before filling orders.
12 Similarly, government guidance could help journals implement appropriate publication standards
13 for manuscripts with potential security concerns. And similar to how DNA synthesis companies
14 developed and have grown the International Gene Synthesis Consortium, which brings
15 companies together to design and apply such screening steps, a consortium of journals could
16 similarly come together to discuss security best practices. Of course, there are important ways
17 that publication differs from gene synthesis; one significant challenge would be defining which
18 journals ought to implement such processes, and how journals that publish research across a
19 range of disciplines would determine when to implement security protocols. Implementing these
20 changes will support the development of a stronger culture of security in engineering biology
21 research and publication. Other strategies for effecting such a cultural shift may draw on the
22 findings of previous reports (e.g., 23). Adequate security training for undergraduate, graduate,
23 and postdoctoral researchers can build a generation of community leaders equipped to
24 incorporate security considerations into their work. Emphasis of the ethical, social, safety, and
25 security issues in scientific research can be incorporated into undergraduate education,
26 normalizing these as part of the research process and even highlighting career opportunities in

1 these areas (24). EBRC directly supports such training for graduate students and postdocs in
2 engineering biology research through its “Malice Analysis” workshops ([https://ebrc.org/malice-](https://ebrc.org/malice-analysis)
3 [analysis](https://ebrc.org/malice-analysis)). The workshops have been free to attend and have facilitated the assessment of
4 security considerations by trainees of their own work using a framework based on one
5 developed by the National Academies of Sciences, Engineering, and Medicine in *Biodefense in*
6 *the Age of Synthetic Biology* (16).

7 Funders can also encourage a culture of security by requesting that proposers include
8 precautions and/or mitigation strategies for work with security implications, and by tracking
9 potential risks through the project lifecycle via progress reports for funded projects. They could
10 incentivize or require publication of synthetic biology research or techniques in journals that
11 have security screening. Additional fora for teaching and reinforcing security awareness should
12 be identified, or built, and supported and should facilitate the building of professional networks
13 such that researchers know with whom they can consult or collaborate when security issues
14 arise.

15 Because EBRC advocates for and supports engineering biology, it also has an obligation
16 to engage in discussions and development around security and responsible researcher conduct
17 in the field. We took the publication of a detailed protocol for reconstructing SARS-CoV-2 as a
18 call to catalyze dialogue around the guardrails for research with serious security and/or safety
19 implications. As capabilities within life science research grow, so too does the need for a culture
20 that recognizes the concomitant security risks accompanying rapid development and
21 dissemination. Despite discussion around security in publishing, little concrete progress has
22 been made toward establishing best practices across journals. We recommend the
23 development of standards that give concrete guidance for authors and editors when evaluating
24 whether to publish findings with safety and security implications. Such standards would need to
25 be iterated upon and revisited over time but should be shaped by consensus built between the
26 research community, the security community, publishers, and other important stakeholders. We

offer preliminary recommendations that can be built upon to support a research enterprise that incorporates security into its research, development, and publication practices.

Acknowledgments: The authors gratefully acknowledge the contribution of the members of the Engineering Biology Research Consortium who provided direction and feedback. **Funding:** RM & JLF were supported by the Department of Homeland Security* under award #19STFRG00011-01-00. RM, ERA & JLF were supported by the National Science Foundation (NSF) under award #1818248. KPA was supported by National Science Foundation awards #1807461 and #1935372. ADE was supported by Welch Foundation, F-1654. SWE was supported by Schmidt Futures "Ethics in the Lab" grant. NJH was supported by the U. S. Department of Energy, Energy Efficiency and Renewable Energy, Bioenergy Technologies Office, and the Office of Science, through contract DE-AC02-05CH11231 between Lawrence Berkeley National Laboratory and the U.S. Department of Energy. FJI was supported by NSF #EF-1935120 and DOE #2011882. TSM was supported by the National Science Foundation under MCB-1714352 and MCB-2001743. MJP was supported by the Open Philanthropy Project; Nuclear Threat Initiative. JP was supported by the National Science Foundation Award DBI-1934573.

*The views and conclusions contained in this document are those of the authors and should not be interpreted as necessarily representing the official policies, either expressed or implied, of the U.S. Department of Homeland Security.

Author contributions: Authors, excepting the first and senior authors, are listed in alphabetical order.

References and Notes

1. Engineering Biology Research Consortium. Engineering Biology: A Research Roadmap for the Next-Generation Bioeconomy. (2019). DOI: 10.25498/E4159B.

2. Ledford H. Call to censor flu studies draws fire. (2012). *Nature*. 481, 9–10.
<https://doi.org/10.1038/481009a>
3. The fight over flu. (2012). *Nature*. 481, 257–259. <https://doi.org/10.1038/481257a>
4. Imai M, Watanabe T, Hatta M, et al. Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets. (2012). *Nature*. 486, 420–428. <https://doi.org/10.1038/nature10831>
5. Herfst S, Schrauwen EJ, Linster M, Chutinimitkul S, de Wit E, Munster VJ, Sorrell EM, Bestebroer TM, Burke DF, Smith DJ, Rimmelzwaan GF, Osterhaus AD, Fouchier RA. Airborne transmission of influenza A/H5N1 virus between ferrets. (2012). *Science*. 336(6088):1534–41. doi: 10.1126/science.1213362
6. National Academies of Science, Engineering, and Medicine (NASEM). Gain-of-Function Research: Summary of the Second Symposium, March 10–11, 2016. (2016)
<https://www.nap.edu/catalog/23484/gain-of-function-research-summary-of-the-second-symposium-march>
7. National Academies of Science, Engineering, and Medicine (NASEM). Potential Risks and Benefits of Gain-of-Function Research: Summary of a Workshop. (2014).
<https://www.nationalacademies.org/our-work/gain-of-function-research-a-symposium>
8. Journal Editors, Authors Group. Statement on Scientific Publication and Security. (2003). *Science*. 299, 1149.
9. Boddie C, Watson M, Ackerman G, Gronvall GK. Assessing the bioweapons threat. (2015). *Science*. 349, 792–793.
10. Xie X, Lokugamage KG, Zhang X, Vu MN, Muruato AE, Menachery VD, Shi P-Y. Engineering SARS-CoV-2 using a reverse genetic system. (2021). *Nat. Protoc.* 16, 1761–1784.
11. Centers for Disease Control and Prevention (CDC). About Variants (2021).
<https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html>

12. Mahase E. Delta variant: What is happening with transmission, hospital admissions, and restrictions? (2021). *BMJ*. 2021;373:n1513.
13. Palmer M. J. Learning to deal with dual use. (2020). *Science*. 367, 1057.
14. Wilhelm A, Widera M, Grikscheit K, Toptan T, Schenk B, Pallas C, Metzler M, Kohmer N, Hoehl S, Helfritz FA, Wolf T, Goetsch U, Ciesek S. Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and Monoclonal Antibodies. (2020, PREPRINT). *medRxiv*. <https://doi.org/10.1101/2021.12.07.21267432>
15. Possession, Use, and Transfer of Select Agents and Toxins-Addition of SARS-CoV/SARS-CoV-2 Chimeric Viruses Resulting From Any Deliberate Manipulation of SARS-CoV-2 To Incorporate Nucleic Acids Coding for SARS-CoV Virulence Factors to the HHS List of Select Agents and Toxins; 86 Fed. Reg. 64075; (November 17, 2021).
16. National Academies of Sciences, Engineering, and Medicine. Biodefense in the Age of Synthetic Biology. (2018). *Washington, DC: The National Academies Press*. <https://doi.org/10.17226/24890>.
17. Patrone D, Resnik D, Chin L. Biosecurity and the Review and Publication of Dual-Use Research of Concern. (2012). *Biosecurity Bioterrorism Biodefense Strategy Pract. Sci.* 10, 290–298.
18. Koblentz GD. The De Novo Synthesis of Horsepox Virus: Implications for Biosecurity and Recommendations for Preventing the Reemergence of Smallpox. (2017). *Health Secur.* 15, 620–628.
19. DiEuliis D, Berger K, Gronvall G. Biosecurity Implications for the Synthesis of Horsepox, an Orthopoxvirus. (2017). *Health Secur.* 15, 629–637.
20. U.S. Department of Health and Human Services. Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens. (2017).

- 1 21. Palmer MJ, Hurtley S. M, Evans SW. Visibility Initiative for Responsible Science, NTI
2 Biosecurity Innovation and Risk Reduction Initiative Meeting, October 15, 2019, Paper 3.
3 (2019).
- 4 22. Evans SW, Beal J, Berger K, Bleijs DA, Cagnetti A, Ceroni F, Epstein GL, Garcia-
5 Reyero N, Gillum DR, Harkess G, Hillson NJ, Hogervorst PAM, Jordan JL, Lacroix G,
6 Moritz R, ÓhÉigearthaigh SS, Palmer MJ, van Passel MWJ. Embrace experimentation in
7 biosecurity governance. (2020). *Science*. 368, 138–140.
- 8 23. National Research Council. Safe Science: Promoting a Culture of Safety in Academic
9 Chemical Research. (2014). *Washington, DC: The National Academies Press*.
- 10 24. Moritz RL, Berger KM, Owen BR, Gillum DR. Promoting biosecurity by professionalizing
11 biosecurity. (2020). *Science*. 367, 856–858.