United States Senate

Committee on Homeland Security and Government Affairs

Origins of COVID-19: An Examination of the Available Evidence

Prepared Statement of

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June 18, 2024

Chairman Peters and Ranking Member Paul and other members of the Committee, thank you for the chance to speak with you today about the origin of the COVID-19 pandemic and its implications for biodefense. My name is Gregory Koblentz, and I am an associate professor and director of the Biodefense Graduate Program at the Schar School of Policy and Government at George Mason University. I am also a member of the Scientists Working Group on Biological and Chemical Security at the Center for Arms Control and Non-Proliferation and the Security Working Group of the Engineering Biology Research Consortium. The opinions expressed herein are my own and do not necessarily reflect the views of George Mason University or the other organizations with which I am affiliated.

Origin of SARS-CoV-2 and the COVID-19 Pandemic

More than four years after the start of the COVID-19 pandemic, the origin of the SARS-CoV-2 virus remains debated, despite a desire for a more precise conclusion. There are two pandemic pathways that have been widely discussed to explain how SARS-CoV-2 emerged in Wuhan in 2019: a natural spillover event from animals to humans or an accidental release from a laboratory. The possibility that SARS-CoV-2 was developed as a biological weapon has been unanimously rejected by the U.S. intelligence community. While the intelligence community is divided on whether the virus emerged in Wuhan due to a spillover or laboratory accident, most intelligence agencies have determined that the virus was not genetically engineered. [1]

There are strongly held views on both sides of this debate. Unfortunately, until there is an independent, international, and transparent investigation that can fully explore both of these

[1] Office of the Director of National Intelligence, *Updated Assessment on COVID-19 Origins* (August 2021), https://www.dni.gov/files/ODNI/documents/assessments/Declassified-Assessment-on-COVID-19-Origins.pdf.

pathways, it will be difficult to reach a definitive conclusion about the origins of COVID-19 that satisfies both sides of the debate.

It is my judgment that a natural spillover event is the most likely cause of the pandemic. However, a laboratory or research-related origin cannot be ruled out. The inability to rule out a lab-origin of the virus is disturbing and indicative of significant weaknesses in global biorisk management as well as the lack of transparency by China.

It is not my intention to review this debate today. Instead of looking backwards, I prefer to look forward and plan for the future. The reality is that we are not as well prepared as we should be to prevent, detect, and respond to future pandemics, regardless of their origin. The ongoing H5N1 outbreak in the United States is a testament to the challenges we still face and the urgency of addressing them.

Key Questions

During my testimony today, I will attempt to address several broader questions:

First, how do you determine the origin of a biological incident?

Second, what role does determining the origin of a biological incident play in biodefense?

Third, what are the challenges to determining the origin of a biological incident?

Fourth, what are the implications of failing to determine the origin of a biological incident?

Fifth, what should we be doing now to improve our ability to determine the origin of a biological incident?

Key Definitions

At the outset, let me define some key terms. According to the national biodefense strategies published by the Trump and Biden administrations, a biological incident refers to the outbreak of a disease caused by a biothreat agent, such as a bacteria, virus, fungus, or toxin, that harms humans, animals, plants, or the environment.[2] For the purpose of this hearing, I will focus on nationally or internationally significant biological incidents which are biological incidents of a scale, severity, complexity, or unpredictability to cause harm to the United States, overwhelm existing public health resources, and threaten U.S. or global health, national, economic, or food security.[3] Recent examples of nationally or internationally significant biological incidents include the 2009 H1N1 influenza pandemic, the 2014-2016 Ebola outbreak in West Africa, the

[2] *National Biodefense Strategy* (Washington, DC: White House, 2018), 28 [hereafter *National Biodefense Strategy 2018*], https://www.phe.gov/Preparedness/legal/boards/nbsb/meetings/Documents/National-Biodefense-Strategy-508.pdf; and *National Biodefense Strategy and Implementation Plan for Countering Biological Threats, Enhancing Pandemic Preparedness, and Achieving Global Health Security* (Washington, DC: White House, 2022), 14 [hereafter *National Biodefense Strategy 2022*], https://www.whitehouse.gov/wp-content/uploads/2022/10/National-Biodefense-Strategy-and-Implementation-Plan-Final.pdf.

[3] *National Biodefense Strategy 2022*, 15.

2015-2016 Zika outbreak in the Americas, the global COVID-19 pandemic, and the international outbreak of mpox in 2022-2023. The H5N1 outbreak in dairy cows and spillover to humans is poised to become a nationally significant biological incident if it cannot be contained. For the sake of simplicity, I will use the term biological incident to refer to this class of severe public health emergencies.

The 2018 and 2022 national biodefense strategies recognize that the cause of a biological incident can be natural, accidental, or deliberate.[4] The risks posed by each of these threats are rising. The loss of biodiversity, climate change, growing human encroachment on animal habitats, and globalization are increasing the frequency and severity of zoonotic spillover events and the spread of vector-borne diseases.[5] An estimated 75% of disease outbreaks in human populations are caused by zoonotic diseases.[6] Spillover events have caused five viral pandemics in the last 100 years, each of which has tested our response measures in increasingly complex ways.[7]

The risk of research-related accidents is also increasing due to the growing number of maximum containment labs around the world, the growth in high-consequence research enabled by powerful emerging biotechnologies, and weaknesses in national and international biosafety measures.[8] The last known cases of smallpox and SARS (in 1978 and 2004, respectively) were both caused by laboratory exposures, and both viruses were able to spread from infected researchers to a small number of individuals outside of the laboratory.[9] In addition, the 1977-1978 influenza pandemic, which involved a flu strain identical to one last seen in 1951, was likely caused by an improperly attenuated live flu vaccine or vaccine challenge trial.[10]

The deliberate misuse of biology by a government or terrorist group is a constant threat due to renewed geopolitical tensions, the persistence of extremist groups interested in causing mass casualties, and the global diffusion of biotechnologies that make biological weapons more

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[4] *National Biodefense Strategy 2018*, 2; and *National Biodefense Strategy 2022*, 6.

[5] Carlson CJ, et al. Climate change increases cross-species viral transmission risk. *Nature*. 2022;607: 555-62. https://doi.org/10.1038/s41586-022-04788-w; and Mahon, M.B., et al. A meta-analysis on global change drivers and the risk of infectious disease. *Nature* 629, 830–836 (2024). https://doi.org/10.1038/s41586-024-07380-6; and Baker, R.E. et al. Infectious disease in an era of global change. *Nat Rev Microbiol* **20**, 193–205 (2022). https://doi.org/10.1038/s41579-021-00639-z

[6] Taylor LH, Latham SM, Woolhouse ME: Risk factors for human disease emergence. Philos *Trans R Soc Lond B Biol Sci* 2001, 356:983-989; and Jones KE, Patel NG, Levy MA, Storeygard A, Balk D, Gittleman JL, Daszak P: Global trends in emerging infectious diseases. *Nature* 2008, 451:990-993.

[7] Neil M. Vora, et al., "The *Lancet*–PPATS Commission on Prevention of Viral Spillover: Reducing the Risk of Pandemics through Primary Prevention," *The Lancet*, Vol. 403, No. 10427 (February 17, 2024), https://doi.org/10.1016/S0140-6736(23)01064-4

[8] Filippa Lentzos, Gregory D. Koblentz, and Joseph Rodgers, "The Urgent Need for an Overhaul of Global Biorisk Management," *CTC Sentinel*, Vol. 15, No. 4 (April 2022): 23-29, https://ctc.westpoint.edu/the-urgent-need-for-an-overhaul-of-global-biorisk-management/; and Filippa Lentzos and Gregory D. Koblentz, *Global BioLabs 2023* (London: King's College London, March 2023), https://www.kcl.ac.uk/warstudies/assets/global-biolabs-report-2023.pdf

[9] Gregory D. Koblentz, "Quandaries in Contemporary Biodefense Research," in Filippa Lentzos, ed., *Biological Threats in the 21st Century* (London: Imperial College Press, 2016), 303-328.

[10] Michelle Rozo and Gigi Kwik Gronvall, "The Reemergent 1977 H1N1 Strain and the Gain-of-Function Debate," *mBio*, Vol. 6 Issue 4 (July/August 2015): e01013-15, https://doi.org/10.1128/mbio.01013-15; and Martin Furmanski, "The 1977 H1N1 influenza virus reemergence demonstrated gain-of-function hazards," *mBio* Vol. 6, No. 5 (September 29, 2015): e01434-15. doi:10.1128/mBio.01434-15.

accessible.[11] According to the U.S. government, Russia and North Korea maintain offensive biological warfare programs in violation of the Biological Weapons Convention (BWC) while Iran and China are engaged in dual-use research that raises concerns about their compliance with the treaty.[12] The Islamic State explored the development of biological weapons, including anthrax, botulinum toxin, and ricin, before the fall of Mosul in 2017, and several members of its chemical and biological weapons program remain at large.[13]

How do you determine the origin of a biological incident?

Determining the origin of an outbreak or a nationally or internationally significant biological incident can be divided into four stages: detecting an outbreak, identifying the pathogen, characterizing the outbreak, and attribution. Understanding how a specific pathogen entered and spread in a population to cause a biological incident is a multidisciplinary undertaking that requires expertise in epidemiology, human and veterinary medicine, biology, genetics, bioinformatics, ecology, anthropology, and related fields.

The first stage involves establishing the existence of an outbreak, meaning more cases of a disease than expected in a group of people, location, level of severity, or period of time. Outbreak detection goes beyond human diseases and can include the identification of disease in plants or animals at a scale, level of severity, or complexity that is beyond the normal level of infectious disease activity for that region, season, or population. This detection can occur based on clinical diagnoses by a physician or veterinarian, laboratory diagnosis, syndromic surveillance, wastewater surveillance, an epidemiological investigation, biological aerosol detection, or some combination of these methods. This collection of tools and capabilities is collectively known as biosurveillance.

Once an outbreak is detected, the second stage. which often occurs concurrently, is identification of the infectious agent and strain responsible for the cases. For a nationally or internationally significant biological incident, the agent could be a new strain of an endemic disease, an emerging infectious disease that is new to a region, or a novel pathogen that has not

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[11] Gregory D. Koblentz, "Biological Weapons and Bioterrorism," in Simon Rushton and Jeremy Youde, eds., *The Routledge Handbook of Global Health Security* (Oxford: Routledge, 2014), 118-129.

[12] Department of State, *Adherence to and Compliance with Arms Control, Nonproliferation, and Disarmament Agreements and Commitments* (April 2024), https://www.state.gov/wp-content/uploads/2024/04/2024-Arms-Control-Treaty-Compliance-Report.pdf; and Department of Defense, *2023 Biodefense Posture Review* (August 2023), https://media.defense.gov/2023/Aug/17/2003282337/-1/-1/1/2023_BIODEFENSE_POSTURE_REVIEW.PDF

[13] United Nations Investigative Team to Promote Accountability for Crimes Committed by Da'esh/Islamic State in Iraq and the Levant (UNITAD), "Twelfth report of the Acting Special Adviser and Head of the United Nations Investigative Team to Promote Accountability for Crimes Committed by Da'esh/Islamic State in Iraq and the Levant," S/2024/408, May 24, 2004, https://www.unitad.un.org/sites/www.unitad.un.org/files/general/unitad_12th_report_to_the_un_sc_june_2024_en.pdf; and Joby Warrick, "ISIS planned chemical attacks in Europe, new details on weapons program reveal," *Washington Post*, July 11, 2022, https://www.washingtonpost.com/national-security/2022/07/11/isis-chemical-biological-weapons/

been previously identified. Thanks to advances in genome sequencing, it is now possible to identify known and novel pathogens in a matter of hours.

The third stage involves descriptive epidemiology, which characterizes the outbreak through data collection and analysis to ascertain potential sources, trends, and other key information to guide the public health and medical response. The information collected during this stage can also point to whether a biological incident is natural, accidental, or deliberate. Given the frequency of naturally occurring disease outbreaks compared to human-made incidents, it is logical for the starting assumption of any outbreak investigation to focus initially on a natural origin. Traditional epidemiological tools such as case histories and contact tracing are complemented by genomic sequencing and molecular epidemiology to trace the evolution and spread of the pathogen responsible for a biological incident in near-real-time. Serological testing can be used to identify cases who have been previously exposed to a pathogen and retrospective testing of previously collected biomedical samples can provide insights into how long a pathogen has been circulating in a population before its emergence was detected. If the outbreak is suspected of being caused by a zoonotic or an insect-borne pathogen, then the epidemiological investigation will also need to collect and analyze samples from domesticated and wild animals and their environs. If the route of transmission is suspected of being foodborne or waterborne, then environmental samples will also need to be analyzed. Modern outbreak investigations can also take advantage of geospatial analysis, open source information, computer modeling, phylogenetic analysis, and other advanced techniques to understand how a pathogen spread in a population and work backwards to determine its source.

If a public health investigation uncovers evidence that an incident may have been caused by an accident or a deliberate act, then law enforcement and intelligence agencies may become involved in the characterization process. Since September 11 and the Amerithrax attack, there have been additional efforts to coordinate public health and law enforcement agencies, including the establishment of new procedures and new techniques, such as forensic epidemiology, to conduct joint criminal-epidemiological investigations.

The final stage in this process is the identification of the likely source(s) for the outbreak. In public health, this process has traditionally been called origin analysis but is sometimes referred to as source attribution. Attribution is commonly used in the law enforcement and national security context to refer to the identification of the state, group, lab, or individual responsible for the deliberate release of a pathogen. For both natural and human-made outbreaks, the attribution process can be used to both rule-in as well as rule-out potential sources. Such determinations are rarely definitive and need to be carefully qualified to reflect the strength of the available evidence as well as gaps and uncertainties. In both the health and security contexts, the process begins the same: with an epidemiological and scientific analysis to determine transmission patterns and identify a probable source.

For a naturally occurring incident, the gold standard is the identification of the specific source that infected the first human in the outbreak, known as the primary case or Patient Zero. Identification of the primary case provides investigators with the key information for understanding the source of the exposure that led to the infection. As I will discuss shortly, this is a very high bar to clear. Even without identification of the primary case, it may be possible to identify the source of an outbreak based on environmental or biomedical samples that

demonstrate likely routes of infection at the human/animal interface or contamination in the food supply chain.

In the event of a suspected accidental or deliberate incident, microbial forensic techniques can be used to identify genetic, physical, chemical or other signatures of the biothreat agent that could provide more information about the origin of the agent and contribute to identification of the responsible party.[14]

What I have just described is obviously an idealized process for determining the origin of a biological incident. The key point is that seeking the origin of a biological incident requires collecting and analyzing a large amount of data from disparate sources by a range of agencies and organizations with a variety of scientific and technical capabilities and disciplinary specializations. The quality of the data and rigor of the epidemiological and scientific investigation will affect the level of confidence for each determination. Such a determination can range from full attribution (determination to a high level of scientific certainty that an infectious agent came from a particular source) to full exclusion (determination to a high level of scientific certainty that the agent did not come from a particular source) with a large grey area in between representing low and moderate confidence determinations.[15]

What role does determining the origin of a biological incident play in biodefense?

Biodefense encompasses actions to prevent, prepare for, respond to, and recover from biological incidents, regardless of whether the origin is Mother Nature, a laboratory, a criminal or terrorist group, or a state. Determining the origin of a biological incident can improve the effectiveness of the response to an ongoing incident, reduce the likelihood or consequences of future incidents, or even prevent future incidents all together.

The classic example is John Snow's investigation of a cholera outbreak in London in 1854 which demonstrated that contaminated water from a specific pump was the source of the outbreak. Understanding the origin of the cholera outbreak led to a simple and highly effective solution: remove the handle from the water pump. This intervention not only stopped the outbreak, but demonstrated conclusively that cholera was a waterborne disease. This insight provided the basis for a national effort to improve sanitation and the provision of clean water which led to a dramatic reduction in the threat posed by cholera and other waterborne diseases.[16]

In modern times, determining the origin of a biological incident, particularly one caused by a novel pathogen, can be used to guide scientific research on the organism and its ecosystem. Such research will improve our understanding of the conditions under which this type of novel pathogen is more likely to cross over into human populations which is key to designing policies

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[14] Gregory Lewis, et al., "The Biosecurity Benefits of Genetic Engineering Attribution," *Nature Communications*, Vol. 11, No. 1 (2020): 6294-6297, https://doi.org/10.1038/s41467-020-19149-2; Gregory D. Koblentz and Jonathan B. Tucker, "Tracing an Attack: The Promise and Pitfalls of Microbial Forensics," *Survival*, Vol. 52, No. 1 (February/March 2010): 159-186, https://doi.org/10.1080/00396331003612521; and Jonathan B. Tucker and Gregory D. Koblentz, "The Four Faces of Microbial Forensics," *Biosecurity and Bioterrorism*, Vol. 7, No 4 (2009): 389-397, https://doi.org/10.1089/bsp.2009.0043

[15] Koblentz and Tucker, "Tracing an Attack," 173.

[16] Theodore H. Tulchinsky, "John Snow, Cholera, and the Broad Street Pump," *Case Studies in Public Health* (London, UK: Academic Press, 2018): 77-99, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7150208/

to reduce this risk. This information can also be used to bolster biosurveillance systems that increase the likelihood that a biological incident will be detected in a timely manner. This early warning can enable national governments and international organizations to implement public health and medical measures that can mitigate the impact of a biological incident. The current H5N1 outbreak illustrates the importance of this approach. Understanding how the H5N1 virus spread from migratory birds into dairy cows, humans, cats, and mice will help us not only respond to the outbreak, but also provide insights into preventing, forecasting, and containing future spillover events with this virus.

Determining the origin of a biological incident caused by a biosafety or biosecurity breach is necessary to adopt new policies and procedures to prevent future such incidents. In 2014-2015, the National Institutes of Health (NIH), Centers for Disease Control and Prevention (CDC), and the U.S. Army suffered a series of biosafety mishaps. These incidents did not lead to any known infections, but they did reveal important lapses in the handling of high-consequence pathogens.[17] Identifying the causes of these lapses was key to putting in place new policies and capabilities to prevent a recurrence.[18] Following the identification of Bruce Ivins, a researcher at a US Army biodefense lab, as the perpetrator of the 2001 anthrax letter attacks, the United States adopted new biosecurity regulations that placed a stronger emphasis on preventing insider threats.[19] Conducting investigations of such incidents in a transparent manner increases the likelihood that biosafety and biosecurity shortcomings identified at a specific facility will generate corrective actions that are applied across the research enterprise.

Determining the origin of a deliberate incident is necessary for the responsible parties to be held accountable. For biocrimes and bioterrorism, attribution is necessary for the criminal justice system to arrest and prosecute the perpetrator. In the event of a biological attack by a government, then attribution is necessary to inform decisions on how to respond, from diplomacy to sanctions to covert action to the use of military force. For all types of deliberate

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[17] Centers for Disease Control and Prevention (CDC), *Report on the Potential Exposure to Anthrax* (July 2014), http://www.cdc.gov/about/pdf/lab-safety/Final_Anthrax_Report.pdf; CDC, *Report on the inadvertent cross-contamination and shipment of a laboratory specimen with influenza virus H5N1* (August 2014), https://stacks.cdc.gov/view/cdc/24766; National Institute of Health (NIH), *Report of the Blue Ribbon Panel to Review the 2014 Smallpox (Variola) Virus Incident on the NIH Campus* (May 2017), https://osp.od.nih.gov/wp-content/uploads/Final_Report_of_the_Variola_BRP.pdf; and Department of Defense, *Review Committee Report: Inadvertent Shipment of Live Bacillus anthracis Spores by DoD* (July 13, 2005), https://dod.defense.gov/Portals/1/features/2015/0615_lab-stats/Review-Committee-Report-Final.pdf

[18] John Holdren and Lisa Monaco, "Enhancing Biosafety and Biosecurity in the United States," White House Memorandum, August 18, 2014, https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/enhancing_biosafety_and_biosecurity_19aug2014_final.pdf; John Holdren and Lisa Monaco, "Next Steps to Enhance Biosafety and Biosecurity in the United States," White House Memorandum, October 29, 2015, https://obamawhitehouse.archives.gov/sites/default/files/docs/10-2015_biosafety_and_biosecurity_memo.pdf; and *Implementation of Recommendations of the Federal Experts Security Advisory Group (FESAP) and the Fast Track Action Committee on Select Agent Regulations (FTAC-SAR)*, (October 2015), https://www.phe.gov/s3/Documents/fesap-ftac-ip.pdf.

[19] George W. Bush, "Strengthening Laboratory Biosecurity in the United States," Executive Order 13486, January 9, 2009, https://www.federalregister.gov/documents/2009/01/14/E9-818/strengthening-laboratory-biosecurity-in-the-united-states; Department of Health and Human Services (HHS), "Report of the Working Group on Strengthening the Biosecurity of the United States," October 1, 2009, https://apps.dtic.mil/sti/tr/pdf/ADA514745.pdf; Barack H. Obama, "Optimizing the Security of Biological Select Agents and Toxins in the United States," Executive Order 13546, July 2, 2010, https://www.selectagents.gov/compliance/faq/legislature.htm; and HHS, "Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review," *Federal Register*, Vol. 77, No. 194 (October 5, 2012), 61084-61115.

biological incidents, attribution is the first step to accountability, which forms the basis for deterrence.[20]

What are the challenges to determining the origin of a biological incident?

Determining the origin of an outbreak, let alone a nationally or internationally significant biological incident, however, is not always straightforward and is not always successful. The process of investigating the source of an outbreak is like putting together a puzzle when you don't know what the final picture is supposed to look like, the pieces change shape and move around, and other pieces are added and removed apparently at random. There are temporal, biological, political, and economic reasons for this.

The first reason is that the index case, the first patient diagnosed by health authorities, may be distant from the primary case, the first human infected as part of the outbreak. The longer it takes to detect an outbreak and begin an investigation, the harder it will be to trace the chain of transmission from the index case back to the primary case and identify the source exposure such as an infected animal, contaminated food, research-related accident, or deliberate release. Retrospective analysis, a key feature of epidemiology, has inherent limitations that are exacerbated by the passage of time. As with any type of investigation, the passage of time leads to memories fading, evidence being degraded or discarded, and changes to the natural and human landscapes that complicates efforts to reconstruct the sequence of events that caused the biological incident.

A common mistake is to expect that the exact moment of exposure, such as when a human interacts with an infectious animal, will always be identified. Exposures like spillover events happen more frequently than is commonly understood, but not all of them lead to disease. Pinpointing the exact moment where transmission occurred is a luxury we are rarely afforded. Consider a respiratory virus going around your office –your risk of becoming infected will be a function of the frequency of your contact with co-workers and environmental factors, but it's unlikely you would be able to figure out the exact moment when you were exposed. Was it during the early morning staff meeting, when you shook hands with a visitor, during the working lunch in the crowded restaurant, or when you borrowed someone's pen? Simply put, a smoking gun may not always be identified and that's not a result of secrecy or obfuscation, but rather the reality of interactions between infectious diseases and humans.

Second, the biological features of the pathogen may make it harder to identify the primary case or how the pathogen infected the primary case or subsequent index cases. For example, we now know that the SARS-CoV-2 virus is well-suited to spreading quickly and undetected due to its

[20] Koblentz and Tucker, "Tracing an Attack."

transmission by asymptomatic and presymptomatic cases,[21] airborne transmission of the virus,[22] and propensity for superspreader events.[23] These features of the virus allow it to spread via silent or cryptic transmission which complicated efforts to identify how the virus was introduced into new populations.[24] For example, it is now clear that local transmission of SARS-CoV-2 was occurring in the United States for about a month before public health authorities identified the first laboratory-confirmed, non-travel cases of the disease.[25]

In contrast, neither SARS-CoV-1 nor MERS are associated with high levels of asymptomatic or presymptomatic transmission. As a result, both SARS-CoV-1 and MERS could be contained using standard public health practices such as isolating cases and tracing and quarantine contacts.[26] Moreover, this facilitated the likely sources of infection, which was the case with SARS-CoV-1.

Third, determining the origin of a novel pathogen, or a known pathogen that is being transmitted within a new population, is more challenging since the biological and epidemiological features of this pathogen, and how it interacts with its hosts and the environment, will not be well understood. For example, coronaviruses became a major subject of study by virologists only after the 2003 SARS outbreak. By 2019, 200 bat coronaviruses had been identified but the genomes of only 30 bat coronaviruses had been fully sequenced.[27] To further illustrate this point, consider that between 1949 and 2002, 86 scientific articles related to coronaviruses were published each year.[28] This rate jumped to 678 articles per year between

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[21] Pratha Saha, et al., "Asymptomatic SARS-CoV-2 infection: A systematic review and meta-analysis," *Proceedings of the National Academies of Science*, Vol. 118 No. 34 (2021): e2109229118, https://doi.org/10.1073/pnas.2109229118; Qiuyue Ma, et al., "Global Percentage of Asymptomatic SARS-CoV-2 Infections Among the Tested Population and Individuals With Confirmed COVID-19 Diagnosis: A Systematic Review and Meta-analysis," *JAMA Network Open*, Vol. 4, No. 12 (2021): e2137257, doi:10.1001/jamanetworkopen.2021.37257; and Seyed M. Moghadasa, et al, "The Implications of Silent Transmission for the Control of COVID-19 Outbreaks," *Proceedings of the National Academies of Science*, www.pnas.org/cgi/doi/10.1073/pnas.2008373117.

[22] Chia C. Wang, et al., "Airborne transmission of respiratory viruses," *Science* 373 (August 27, 2021): eabd9149, https://doi.org/10.1126/science.abd9149; and Matthew Meselson, "Droplets and Aerosols in the Transmission of SARS-CoV-2," New England Journal of Medicine, April 15, 2020, DOI: 10.1056/NEJMc2009324

[23] Dyani Lewis, "Superspreading Drives the COVID Pandemic —and Could Help to Tame It," *Nature* 590 (February 23, 2021): 544-546, https://www.nature.com/articles/d41586-021-00460-x**;** Dillon C. Adam, et al., "Clustering and Superspreading Potential of SARS-CoV-2 Infections in Hong Kong," *Nature Medicine*, September 17, 2020. https://doi.org/10.1038/s41591-020-1092-0; and B. M. Althouse, et al., "Superspreading Events in the Transmission Dynamics of SARS-CoV-2: Opportunities for Interventions and Control," *PLOS Biology*, *18* (11), (2020): e3000897. https://doi.org/10.1371/journal.pbio.3000897

[24] J.T. Davis, et al., "Cryptic Transmission of SARS-CoV-2 and the First COVID-19 Wave," *Nature* 600, (2001: 127-132, https://doi.org/10.1038/s41586-021-04130-w.

[25] Jorden MA, et al. Evidence for Limited Early Spread of COVID-19 Within the United States, January–February 2020. *MMWR Morbidity and Mortal Weekly Report* 2020;69:680–684. DOI: http://dx.doi.org/10.15585/mmwr.mm6922e1; and Hernandez, M.M., et al. Molecular evidence of SARS-CoV-2 in New York before the first pandemic wave. *Nature Communications* **12**, 3463 (2021). https://doi.org/10.1038/s41467-021-23688-7

[26] Monica Gandhi, et al., "Asymptomatic Transmission, the Achilles' Heel of Current Strategies to Control Covid-19," *New England Journal of Medicine*, April 24, 2020, DOI: 10.1056/NEJMe2009758.

[27] Arinjay Banerjee, et al., "Bats and Coronaviruses," *Viruses* 2019, 11, 41; doi:10.3390/v11010041; and Antonio C. P. Wong, et al., "Global Epidemiology of Bat Coronaviruses," *Viruses* 2019, 11, 174; doi:10.3390/v11020174

[28] These numbers are based on a search of PubMed (https://pubmed.ncbi.nlm.nih.gov/), an online database of life science and biomedical research articles.

2003 and 2019. In contrast, influenza has been a known pandemic threat since 1918. Between 1949 and 2002, an average of 982 articles were published each year on influenza and between 2003-2019, 4,842 articles a year were published on this family of viruses. For comparison, 2,409 scientific articles on HIV were published between 1949 and 2002 and 14,400 articles per year between 2003 and 2019.

Even viruses that we think we understand well are constantly surprising us. H5N1 avian influenza, which first emerged in 1996, has evolved to infect a wider range of mammalian species and there is increasing evidence that the virus is now capable of mammal-to-mammal transmission.[29] Part of the reason for the months-long delay in identifying H5N1 avian influenza as the cause of illnesses in dairy cows in Texas earlier this year was because the virus did not have a history of infecting cows.[30]

Third, biological incidents can also pose political challenges, at the local or national level, which might result in a delayed or lackluster public health investigation, censorship, or other forms of interference. These challenges are particularly acute in authoritarian regimes which are highly sensitive to perceived threats to their stability and legitimacy, suffer from excessive secrecy, and have well-developed apparatuses for controlling information.[31] For example, local and national Chinese government authorities have a long history of covering up disease outbreaks, including HIV/AIDS in the 1990s, SARS in 2002-2003, and SARS-CoV-2 in 2019-2020.[32]

Fourth, economic considerations can also impede the investigation into a biological incident. For outbreaks involving the agricultural sector or in countries heavily dependent on tourism, there can be an economic motivation for not reporting the outbreak in order to avoid restrictions on trade and travel. We are currently facing this challenge in the H5N1 outbreak in dairy cows as farmers resist testing their herds to avoid travel restrictions or culling and migrant farm workers avoid testing for fear of missing work or being deported.[33] In addition, if there are illegal activities associated with the origin and transmission of the pathogen, such as the hunting, trafficking, and consuming of wildlife, public health investigators may find it difficult to collect

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[29] India Bourke, "'Unprecedented': How bird flu became an animal pandemic," *BBC*, April 26, 2024, https://www.bbc.com/future/article/20240425-how-dangerous-is-bird-flu-spread-to-wildlife-and-humans; Pablo I. Plaza, Víctor Gamarra-Toledo, Juan Rodríguez Euguí, Sergio A. Lambertucc, "Recent Changes in Patterns of Mammal Infection with Highly Pathogenic Avian Influenza A(H5N1) Virus Worldwide," *Emerging Infectious Diseases*, Vol. 30, No. 3 (March 2024): 444-452, DOI: https://doi.org/10.3201/eid3003.231098; and Marcela Uhart, et al., "Massive outbreak of Influenza A H5N1 in elephant seals at Peninsula Valdés, Argentina: increased evidence for mammal-to-mammal transmission," *bioRxiv*, June 1, 2024, doi: https://doi.org/10.1101/2024.05.31.596774

[30] Amy Maxmen, "Clues From Bird Flu's Ground Zero on Dairy Farms in the Texas Panhandle," *KFF Health News*, May 23, 2024, https://kffhealthnews.org/news/article/bird-flu-ground-zero-texas-dairy-farms-whodunit-h5n1/

[31] Dali L. Yang, *Wuhan: How the COVID-19 Outbreak in China Spiraled Out of Control* (New York: Oxford University Press, 2024).

[32] Yue Guan, "China's Blood-Borne HIV Catastrophe Revisited," *Modern China* 46, no. 4 (August 28, 2019): 372–99. https://doi.org/10.1177/0097700419871223; Amy Freedman, "SARS And Regime Legitimacy in China," *Asian Affairs* 36, No. 2 (July 2005): 169–80, https://doi.org/10.1080/0306837050013612; and Yang, *Wuhan*.

[33] Amy Maxmen, "Clues From Bird Flu's Ground Zero on Dairy Farms in the Texas Panhandle," *KFF Health News*, May 23, 2024, https://kffhealthnews.org/news/article/bird-flu-ground-zero-texas-dairy-farms-whodunit-h5n1/; and Céline Gounder, "H5N1 doesn't have to be a repeat of Covid-19's 'public health versus the economy'," *KFF Health News*, May 17, 2024, https://www.statnews.com/2024/05/17/h5n1-bird-flu-do-not-repeat-covid-19-public-health-versus-economy-battle/

information from individuals engaged in these activities because they are afraid of the legal repercussions. If these illegal activities are conducted with the knowledge or complicity of government authorities, then the chance of a proper investigation is further reduced. For example, a survey of animals for sale at markets in Wuhan right before the pandemic found several protected species, evidence that wild animals were illegally harvested for sale, a lack of legal paperwork by the vendors, and lax enforcement of the rules against the exploitation of protected species.[34]

Fifth, if a biological incident was caused deliberately, then it is likely that the perpetrator will take steps to hide their responsibility and maybe even try to shift blame to another party. For example, Bruce Ivins, the scientist responsible for mailing the letters containing anthrax spores to media outlets and senators in 2001, took several steps to hide his responsibility such as including a message in each letter that mimicked the language used by foreign jihadist groups, such as Al Qaeda, to misdirect the attention of investigators.[35]

The key point is that the process of determining the origin of a biological incident is scientifically complex, but can also be politically fraught and subject to countervailing pressures by actors that have a self-serving interest in delaying, halting, or obscuring the outcome of an origin investigation.

What are the implications of failing to determine the origin of a biological incident?

The implications of failing to determine the origin of a biological incident depend in part on whether the origin of the incident is natural, accidental, or deliberate.

The inability to identify the origin of a naturally occurring biological incident could impair response efforts and impede future efforts at prevention or risk reduction. In the worst case, the failure to identify the origin of a pathogen would allow the source to continue generating new infections. This type of scenario is why speed is of the essence in investigations of foodborne outbreaks. To prevent further illnesses, such investigations focus on identifying as specifically as possible the type or source of the food responsible for the outbreak. Failure to attribute the outbreak to a specific restaurant, farm, market, ranch, or factory could allow the source to continue generating contaminated food and foil efforts to remove contaminated food from circulation.

In other types of natural outbreaks, where there is a single or small number of infection events, determining the exact origin may not have a significant impact on the public health and medical response to the outbreak. For an outbreak caused by a zoonotic disease, it would be most useful, but most difficult, to identify the specific animal ("Animal X") that infected the primary case. Understanding how a zoonotic disease jumped from animals to humans or why an insect-borne disease is causing an epidemic in a new region, however, does not require that level of specificity. A more realistic goal is to identify the reservoir species of the pathogen, any intermediate hosts involved in the transmission of the pathogen to human population, and what systemic conditions and proximate factors increase the likelihood of that pathogen causing

[34] X Xiao, et al., "Animal Sales From Wuhan Wet Markets Immediately Prior to the COVID-19 Pandemic," *Sci Rep* **11**, 11898 (2021). https://doi.org/10.1038/s41598-021-91470-2

[35] R. Scott Decker, *Recounting the Anthrax Attacks: Terror, the Amerithrax Task Force, and the Evolution of Forensics in the FBI* (New York: Rowman & Littlefield, 2018).

human infections. In this context, the origin of a novel pathogen should be thought of less as a location or single event, but more as "a permanent process of evolution, adaptation and selection shaped by chance and environment which gives rise to novel lineages."[36]Achieving this more comprehensive and holistic understanding of a pathogen's ecosystem may not be as satisfying psychologically, but can be of sufficient resolution to enable the adoption of risk reduction measures such as protecting key species and their habitats or identifying high-risk populations.[37]

The inability to determine the origin of a biological incident caused by an accident makes it harder to prevent future such accidents, both at the lab responsible for the specific incident as well as future accidents that could have similar causes.

In the case of deliberate incidents, failure to identify the perpetrators responsible could have multiple negative consequences. Most seriously, a delay in attributing the biological attack could allow the perpetrator to replenish their supply of a pathogen and continue conducting attacks.[38] For example, Ivins sent two batches of anthrax spore-laced letters several weeks apart.[39] In the event of a biological attack by a government, failure to attribute the attack will undermine deterrence and embolden that government, or other actors, to continue conducting such attacks.[40]

What should be done to improve our ability to determine the origins of a biological incident?

Today, I would like to highlight two areas that would not only enhance our ability to determine the origin of a future biological incident, but also improve our capability to prevent an outbreak from becoming a severe public health emergency. I would like to recommend concrete steps to strengthen biosurveillance and biorisk management in the United States and globally.

Biosurveillance

Biosurveillance entails the full range of programs, technologies, and tools used to detect, identify, and characterize biological agents. Biosurveillance is the foundation of an effective public health system. Biosurveillance systems are based on trust and require collaboration and partnership to operate effectively. Without reliable and credible data, public health officials, policy-makers, and the public can't make good decisions about how to respond to a disease

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[36] Roger Frutos, et al., "There is No "Origin" to Sars-CoV-2," *Environmental Research*, Vol. 207 (May 1, 2022), https://doi.org/10.1016/j.envres.2021.112173

[37] Neil M. Vora, et al., "Interventions to Reduce Risk for Pathogen Spillover and Early Disease Spread to Prevent Outbreaks, Epidemics, and Pandemics," *Emerging Infectious Diseases*, Vol. 29, No. 3, March 2023, DOI: https://doi.org/10.3201/eid2903.221079; Jamie K. Reaser, et al., "Looking Left: Ecologically Based Biosecurity to Prevent Pandemics," *Health Security*, Vol. 22, No. 1, 2024, DOI: 10.1089/hs.2023.0089; Raina K. Plowright, et al., "Ecological Countermeasures to Prevent Pathogen Spillover and Subsequent Pandemics," *Nature Communication*, 15, Article number: 2577 (2024), https://doi.org/10.1038/s41467-024-46151-9; and Holmes EC, et al. Pandemics: spend on surveillance, not prediction. *Nature*. 2018;558(7709):180-182. doi:10.1038/d41586-018-05373-w

[38] Richard Danzig, *Catastrophic Bioterrorism: What is to be Done?* (Washington, DC: National Defense University, August 2003), https://ndupress.ndu.edu/Portals/68/Documents/occasional/CTNSP/Catastrophic-Bioterrorism.pdf?ver=2017-06-16-151712-560

[39] Decker, *Recounting the Anthrax Attacks.*

[40] Koblentz and Tucker, "Tracing an Attack."

outbreak or what actions need to be taken to prevent an outbreak from becoming a pandemic. The COVID-19 pandemic demonstrated serious shortfalls and gaps in national and international biosurveillance capabilities, but also led to innovative new techniques for collecting and analyzing information for biosurveillance purposes. This section provides recommendations for enhancing biosurveillance in the United States and internationally.

Enhancing National Biosurveillance

Biosurveillance in the United States is conducted by the Federal government, state and local health departments, academic research institutions, and the private sector. The establishment of the Center for Forecasting and Outbreak Analytics (CFA) and the Response Ready Enterprise Data Integration (RREDI) platform at the CDC were important steps to strengthen national biosurveillance capabilities. However, biosurveillance in the United States continues to suffer from fragmentation, antiquated technology, a chronic underinvestment in public health capacity at the state, tribal, territorial, and local levels, and the lack of capacity to rapidly develop and widely deploy diagnostic tests.[41] In addition, public health data collection authorities granted to CDC under the COVID-19 pandemic declaration have expired which impedes the agency's effort to track disease outbreaks, including the ongoing multi-state outbreak of H5N1 in dairy cows and humans.

To strengthen biosurveillance, which is a vital prerequisite to determining the origin of a biological incident that occurs in the United States, I recommend the following:

First, the CDC should be provided the resources and authorities it needs to fully implement its Public Health Data Strategy for 2024-2025 which would allow it to accelerate the exchange of data between healthcare organizations and public health authorities and between state, tribal, local, territorial and federal public health authorities.[42]

Second, the Senate should approve the bipartisan Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA). The approval of PAHPRA is necessary to rebuild and reinforce the public health workforce and infrastructure at the state, tribal, local, and territorial levels that national biosurveillance efforts rely on.[43] PAHPRA would, among other things, enhance

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[41] Arielle D'Souza and Janika Schmitt, *Mapping America's Biosurveillance* (Institute for Progress, April 3, 2004), https://ifp.org/mapping-americas-biosurveillance/; Trust for America's Health, *The Impact of Chronic Underfunding on America's Public Health System: Trends, Risks, and Recommendations 2023* (June 2023), https://www.tfah.org/wp-content/uploads/2023/06/TFAH-2023-PublicHealthFundingFINALc.pdf; and Jennifer B. Nuzzo, Aquielle Person, Elizabeth Cameron, Jill Taylor, Ewa King, Mara Aspinall, and Scott Becker, "The United States Needs A Better Testing Playbook For Future Public Health Emergencies," *Health Affairs*, 43:6 (June 2024): 768-775, https://doi.org/10.1377/hlthaff.2024.00038

[42] Centers for Disease Control and Prevention, "CDC Data Modernization Efforts Accelerate Nation's Ability to Detect and Rapidly Respond to Health Threats," April 11, 2024, https://www.cdc.gov/media/releases/2024/p0411-CDC-data-modernization.html

[43] Trust for America's Health, *Ready or Not: Protecting the Public's Health from Diseases, Disasters, and Bioterrorism 2024* (March 2024), https://www.tfah.org/wp-content/uploads/2024/03/2024-ReadyOrNot-FINAL.pdf; Deloitte Center for Government Insights, *What the Pandemic Can Teach Us About Building a Resilient Public Health Workforce* (April 2024), https://www2.deloitte.com/us/en/insights/industry/public-sector/what-the-pandemic-can-teach-us-about-building-resilient-public-health-workforce.html; and Poja Kumar, Emily Lurie, and Ramya Parthasarathy, "Building the US Public-Health Workforce of the Future," *McKinsey and Company Insights*,

domestic wastewater surveillance which has emerged as a powerful tool for detecting, tracking, and forecasting infectious disease outbreaks that is applicable regardless of the source of the outbreak.[44]

Third, Congress should provide the resources for the development and implementation of a national biodetection strategy that would include the development of diagnostics capable of simultaneously testing for multiple pathogens, diagnostics designed for use in low-resource settings, rapid point-of-care diagnostics, the establishment of a permanent public-private coordination forum for diagnostic testing, and a system for widely deploying accessible diagnostics in response to a public health emergency.[45] There are already worrying signs that the United States is unprepared to rapidly develop and widely deploy diagnostics to detect H5N1 if the virus demonstrates a greater pandemic threat.[46]

Enhancing Global Biosurveillance

Due to globalization, the United States is only one or two airplane flights away from every disease outbreak in the world. Our national health security depends on the ability of other nations to detect and report disease outbreaks as quickly as possible and the ability of the World Health Organization (WHO) to coordinate an effective international response.

Global biosurveillance efforts also need to be governed by a recognition that Mother Nature is unpredictable. During the 2000s, the primary concern was that the next pandemic would be a strain of H5N1 that would spillover from birds to humans in Asia. The 2009 influenza pandemic, however, was caused by a new strain of H1N1 that spilled over from pigs to humans in Mexico. When it comes to pandemics, we must expect the unexpected. WHO embraced this approach in 2018 when they designated "Disease X" as a research priority for

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February 2, 2022, https://www.mckinsey.com/industries/public-sector/our-insights/building-the-us-public-health-workforce-of-the-future#/

[44] Zev Goldberg, et al., "Wastewater Collection and Sequencing as a Proactive Approach to Utilizing Threat Agnostic Biological Defense," *Health Security*, Vol. 22, No. 1 (2024), https://doi.org/10.1089/hs.2023.0075

[45] Bipartisan Commission on Biodefense, *The Athena Agenda: Advancing the Apollo Program for Biodefense* (April 2022), https://biodefensecommission.org/reports/the-athena-agenda-advancing-the-apollo-program-for-biodefense/; Gigi Kwik Gronvall, et al., "Proposal for a national diagnostics action plan for the United States," *Health Policy Open*, Volume 5, (December 15, 2023), https://doi.org/10.1016/j.hpopen.2023.100099; Amesh A. Adalja Kelsey Lane Warmbrod, and Mary J. Lancaster, "Introduction to the Special Feature: Threat Agnostic Approaches to Biodefense and Public Health Are Now a Reality," *Health Security*, Vol. 22, No. 1 (2024), https://www.liebertpub.com/doi/10.1089/hs.2024.0010; Mary J. Lancaster Mary.Lancaster@pnnl.gov, Amesh A. Adalja, and Kelsey Lane Warmbrod, "Introduction to the Special Feature, Part 2: Enabling and Implementing Threat Agnostic Approaches to Biodefense and Public Health," *Health Security*, Vol. 22, No. 2 (2024), https://www.liebertpub.com/doi/10.1089/hs.2024.0026; and Brown Pandemic Center, *Testing Playbook for Biological Emergencies* (October 2023), https://www.aphl.org/aboutAPHL/publications/Documents/Testing-Playbook-Biological-Emergencies.pdf

[46] Amy Maxmen and Arthur Allen, "Bird Flu Tests Are Hard To Get. So How Will We Know When To Sound the Pandemic Alarm?" *KFF Health News*, June 11, 2024, https://kffhealthnews.org/news/article/bird-flu-tests-pandemic-possibility-preparedness/

development of medical countermeasures to reflect "the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease."[47]

Unfortunately, multilateral efforts to strengthen global biosurveillance following COVID-19 have not been as successful as hoped. The negotiation of a new pandemic agreement has been delayed by at least a year and the recently agreed to amendments to the International Health Regulations (IHR) don't address the fundamental unwillingness of some countries and the inability of others to fulfill their disease detection capability and outbreak reporting obligations under the IHR.[48]

To strengthen global biosurveillance, I recommend the following:

First, Congress should provide the Biden Administration with the resources necessary to implement the programs and objectives described in the *U.S. Government Global Health Security Strategy 2024*.[49] Through the Global Health Security Agenda (GHSA), the United States is already working with more than 50 countries to strengthen their capabilities to prevent, detect, and control disease outbreaks. Efforts to strengthen surveillance capabilities should focus on countries that, due to ecological factors, are hot spots for disease emergence and countries that serve as hubs in the global transportation system. These efforts should be based on the concept of One Health and integrate human and veterinary disease surveillance, which is especially important for dealing with zoonotic pathogens.

Second, the United States should support efforts by the WHO to enhance international capabilities to investigate the origin of biological incidents. The WHO's Science Advisory Group for the Origin of Novel Pathogens (SAGO) is currently developing a Global Framework for Emerging and Re-emerging Diseases to provide a structured, multidisciplinary One Health-based approach to investigating the origins of a biological incident. The framework will provide guidance on how to structure the initial investigation into the origin of a novel pathogen including the epidemiology of human cases, human/animal interface studies, environmental studies, genomic and phylogenetic analyses, and consideration of the possibility of a biosafety or biosecurity breach.[50] A strength of this framework is that it provides a comprehensive and coordinated approach to investigating the origin of a biological incident and takes a holistic approach that considers both natural, accidental, and deliberate origins. Implementing this

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[47] World Health Organization (WHO), *2018 Annual Review of Diseases Prioritized Under the Research and Development Blueprint* (February 2018), https://www.who.int/docs/default-source/blue-print/2018-annual-review-of-diseases-prioritized-under-the-research-and-development-blueprint.pdf

[48] Chloe Searchinger, "Why Pandemic Agreement Negotiations Failed to Land," *Think Global Health*, May 24, 2024, https://www.thinkglobalhealth.org/article/why-pandemic-agreement-negotiations-failed-land; and David P. Fidler, "The Amendments to the International Health Regulations Are Not a Breakthrough," *Think Global Health*, June 7, 2024, https://www.thinkglobalhealth.org/article/amendments-international-health-regulations-are-not-breakthrough

[49] White House, *U.S. Government Global Health Security Strategy 2024* (April 2024), https://www.whitehouse.gov/wp-content/uploads/2024/04/Global-Health-Security-Strategy-2024-1.pdf

[50] Science Advisory Group for the Origin of Novel Pathogens (SAGO), *Preliminary Report* (June 2022), https://cdn.who.int/media/docs/default-source/scientific-advisory-group-on-the-origins-of-novel-pathogens/sago-report-09062022.pdf?sfvrsn=42b55bbc_1&download=true; and SAGO, "Presentation to Member States COVID-19 Information Sessions," March 30, 2023, https://cdn.who.int/media/docs/default-source/documents/emergencies/sago_member_states_-30march2023.pdf?sfvrsn=ba295d2c_1&download=true

framework will require building a globally distributed cadre of trained experts and advanced analytical capabilities that are able to contribute to such an investigation at a moment's notice.

Biorisk Management

The second area that requires further investment is biorisk management which encompasses field and laboratory biosafety, laboratory biosecurity, and oversight of dual-use research. Even if the origin of the COVID-19 pandemic is presumed or proven to be the result of a natural zoonotic spillover event, the pandemic raised important questions about the efficacy of oversight on research with pathogens engineered to be more virulent or transmissible. The pandemic has also dramatically illustrated the consequences if such a pathogen escaped from a lab and sparked a pandemic. Regardless of one's views on the origin of the COVID-19 pandemic, we should all be able to agree that we want to minimize the risk that a laboratory will become the source of the next pandemic.

Last year, the Global BioLabs Initiative, which I co-direct, published a report documenting the growing number of laboratories around the world that conduct high-consequence research, weaknesses in national biosafety and biosecurity legislation in those countries, and gaps in the global governance of biorisks.[51] The Global BioLabs Initiative, in cooperation with the Bulletin of the Atomic Scientists, created an interactive website GlobalBioLabs.org to document the location and key characteristics of high-consequence biological research facilities (BSL-4 and BSL-3+ labs), improve transparency about these facilities, and educate the public and policy-makers about biosafety, biosecurity, and dual-use research oversight. According to our report, there are more than 100 high and maximum containment labs around the world conducting high-consequence research, with more planned. The United States has more such labs than any other country.

Strengthening Biorisk Management in the United States

Historically, the United States has taken a reactive approach to biosafety and biosecurity which has resulted in a fragmented approach to biorisk management. As a result, labs are subject to a patchwork of regulations, guidance, and policies based on the specific pathogen being researched, the type of research being conducted, and the source of funding. As a result, some research doesn't fall under any agency, leaving an oversight vacuum.[52]

The *United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential* issued in May 2024 is a significant step forward in improving oversight of high-consequence research.[53] The new policy consolidates several previous policies, expands the list of pathogens and types of research subject to

[51] Filippa Lentzos and Gregory D. Koblentz, *Global BioLabs 2023* (London: King's College London, March 2023), www.globalbiolabs.org

[52] Gregory D. Koblentz and Rocco Casagrande, "Biology is Dangerously Outpacing Policy," *New York Times*, February 20, 2023, https://www.nytimes.com/2023/02/20/opinion/biology-is-dangerously-outpacing-policy.html

[53] White House, *United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential*, May 2024, https://www.whitehouse.gov/wp-content/uploads/2024/05/USG-Policy-for-Oversight-of-DURC-and-PEPP.pdf

oversight, and is applicable to all Federally funded research. There are two immediate steps that could be taken to strengthen implementation of this new policy.

First, Congress should provide funding for the Biden Administration's Biosafety and Biosecurity Initiative, led by the Department of Health and Human Services, to provide awareness raising, education, and training to stakeholders affected by this new policy. Given the longer list of biological agents subject to oversight under this new policy (an increase from 14 to approximately 95 pathogens and toxins), a much wider swathe of the microbiology community will now be subject to this policy. Scientists, administrators, graduate students, and biosafety professionals at a wide variety of institutions will need to be educated about the new policy, learn how to identify whether their research falls under its scope, and, if so, how to develop risk mitigation plans that balance the benefits and risks of the research. Research institutions will also need to develop or update processes and mechanisms to ensure their compliance with the new policy. While the 84-page implementation guidance for the new dual-use research oversight policy is helpful, the length of the guidance is a testament to the complexity of this issue.[54] Since the policy is due to enter into effect in May 2025, it is imperative that engagement with these stakeholders start as soon as possible to minimize the disruption caused by this new oversight policy.

Second, Congress should pass legislation that would enable Federal agencies to extend their implementation of this policy to dual-use research that is privately funded. In 2022, Boston University claimed that an experiment to create a chimeric coronavirus was not subject to review under the existing P3CO oversight policy because even though the lab received funding from NIH, the experiment in question was paid for with private funds.[55] Congress could rectify this situation by granting authority to Federal agencies to require that research institutions, as a condition of receiving Federal funding, implement this oversight policy for life science research they conduct that is not Federally funded. While this additional authority would not extend the policy to labs that operate solely on private funding, it would close an important loophole that enables Federally funded labs to avoid oversight of potentially risky experiments by funding this work with private money.

Another area that requires immediate attention is the development of national standards for field biosafety. Field biosafety policies and practices are designed to prevent researchers from becoming exposed to an infectious disease while collecting biomedical and environmental samples in the field and handling wild animals. The safe collection of samples from wild and domesticated animals that may be infected with a zoonotic pathogen is an underdeveloped component of biosafety. Congress should direct the CDC, NIH, and USDA to collectively develop national field biosafety standards for high-consequence zoonotic pathogens and incorporate these standards into the next issue of the

Over the longer term, it is necessary to modernize the U.S. biorisk management system to address the growth in laboratories conducting high-consequence research and the impact of

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[54] White House, *Implementation Guidance for the United States Government Policy for Oversight of Dual Use Research of Concern and Pathogens with Enhanced Pandemic Potential*, May 2024, https://www.whitehouse.gov/wp-content/uploads/2024/05/USG-DURC-PEPP-Implementation-Guidance.pdf

[55] Gregory D. Koblentz and Rocco Casagrande, "Beyond gain of function: strengthening oversight of research with potential pandemic pathogens," *Pathogens and Global Health* (October 4, 2023), 6, https://doi.org/10.1080/20477724.2023.2265627

emerging technologies such as genome editing, synthetic biology, and artificial intelligence on biosecurity. Congress should establish an independent Federal agency responsible for reducing the risks posed by the accidental or deliberate misuse of biology and biotechnology in the United States. This national biorisk management agency, modeled after the Nuclear Regulatory Commission, Federal Aviation Administration, or the National Highway Traffic Safety Administration, would be responsible for overseeing biosafety, biosecurity, and oversight of dual-use research, including publicly and privately funded research.[56] The agency would develop and implement regulations and standards related to biosafety, biosecurity, and dual-use research oversight, conduct and sponsor applied biosafety and biosecurity research, provide training and education to scientists, biosafety officers, and lab managers on biosafety, biosecurity, and dual-use research oversight, administer a no-fault accident notification system, investigate biosafety and biosecurity incidents, and serve as a forum for biorisk management professionals to share biosafety and biosecurity best practices.

The creation of this agency would address two major shortcomings in current biorisk management policy. First, giving the agency the authority to regulate biosafety, biosecurity, and dual-use research conducted in privately funded facilities would close a major loophole in biorisk management. A private company that does not receive federal funding for life sciences research can modify a select agent (with a few minor exceptions), or other pathogens not included in that list, with no obligation to review the research for potential dual-use implications or seek approval from a government agency before conducting the research. This means that almost all dual-use research based on non-government sources of funding—such as from corporations, foundations, wealthy individuals, and crowdfunding sites is not covered by either the current dual-use oversight policies or the new one recently introduced by the Biden Administration.[57] According to a forthcoming study, about 25% of human pathogen research performed in the United States is conducted by the private sector.[58] The synthesis of horsepox virus by Canadian scientists, with funding from a U.S. biotech company, illustrates how privately funded research can stray into the realm of dual-use research.[59] The fortuitous discovery of an illegal biotech company in Reedley, California that was storing human pathogens without proper biosafety is a cautionary tale.[60] Given the growing role of the private sector in conducting

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[56] Ryan Ritterson, et al., "A Call for a National Agency for Biorisk Management," *Health Security,* Vol. 20, No. 2 (2022): 1-5, https://doi.org/10.1089/hs.2021.0163; and Gregory D. Koblentz and Rocco Casagrande, "Biology is Dangerously Outpacing Policy," *New York Times*, February 20, 2023, https://www.nytimes.com/2023/02/20/opinion/biology-is-dangerously-outpacing-policy.html

[57] Filippa Lentzos, Gregory D. Koblentz, and Joseph Rodgers, "The Urgent Need for an Overhaul of Global Biorisk Management," *CTC Sentinel*, Vol. 15, No. 4 (April 2022): 23-29, https://ctc.westpoint.edu/the-urgent-need-for-an-overhaul-of-global-biorisk-management/.

[58] Daniel Greene, et al., "Characterizing the Private Sector in Human Pathogen Research," *Health Security*, forthcoming.

[59] Gregory D. Koblentz, "The *De Novo* Synthesis of Horsepox Virus: Implications for Biosecurity and Recommendations for Preventing the Reemergence of Smallpox," *Health Security*, Vol. 15, No. 5 (2017), pp. 1-9. https://doi.org/10.1089/hs.2017.0061; and Gregory D. Koblentz, "A Critical Analysis of the Scientific and Commercial Rationales for the Synthesis of Horsepox Virus," *mSphere*, Vol. 3, No. 2 (March/April 2018): 1-10. https://doi.org/10.1128/mSphere.00040-18

[60] House Select Committee on the Chinese Communist Party, *Investigation into the Reedley Biolab* (November 15, 2023), https://selectcommitteeonthecp.house.gov/sites/evo-subsites/selectcommitteeonthecp.house.gov/files/evo-media-document/scc-reedley-report-11.15.pdf

biotechnology research and the growth of the bioeconomy, the exclusion of almost all of the work of the private sector from dual-use research oversight is an increasingly large loophole.

Second, the creation of an independent agency responsible for oversight of dual-use research would remove the conflict of interest inherent in having funding agencies play the primary role in overseeing their own research portfolio. NIH's implementation of the P3CO Framework has been problematic, including its mishandling of the EcoHealth Alliance grant that involved the creation of chimeric coronaviruses at the Wuhan Institute of Virology (WIV), its lack of transparency about how it reviewed projects under the "gain of function" pause and the P3CO Framework, and misleading statements on its approval of genetic engineering experiments to enhance the virulence of mpox.[61] Separating decisions to fund research from assessments about the risks posed by such research and necessary risk mitigation measures would remove this inherent conflict of interest and be more effective at ensuring that dual-use research of concern is properly identified and conducted safely, securely and responsibly.

Strengthen Global Biorisk Management

As highlighted by the work of the Global BioLabs Initiative, the global biorisk management system is fragmented, stovepiped, and has significant gaps. There are several valuable initiatives underway to strengthen biosafety and biosecurity, but they are underfunded and uncoordinated. The United States and WHO can each take immediate steps to strengthen global biorisk management.

The U.S. Role in Strengthening Global Biorisk Management

The United States should leverage its leading role in global health to encourage more labs around the world to adopt the international standard for laboratory biorisk management called ISO 35001.[62] This standard provides a template for establishing a management system to identify and mitigate safety and security risks as part of a continual improvement process. Since the standard is more concerned with the risk assessment and mitigation process than specific containment or security measures, it is compatible with existing national biosafety and

[61] David Willman and Madison Muller, "A Science in the Shadows," *Washington Post*, August 26, 2021, https://www.washingtonpost.com/nation/interactive/2021/a-science-in-the-shadows/; Gregory D. Koblentz, "Beyond Gain of Function: Evaluating HHS Oversight of Research with Potential Pandemic Pathogens," prepared statement for the Virtual Meeting and Listening Session on USG Oversight Framework for Research Involving Enhanced Potential Pandemic Pathogens, National Institutes of Health, Bethesda, MD, April 27, 2022; Department of Health and Human Services Office of Inspector General, *The National Institutes of Health and EcoHealth Alliance Did Not Effectively Monitor Awards and Subawards, Resulting in Missed Opportunities to Oversee Research and Other Deficiencies* (January 2023), https://oig.hhs.gov/documents/audit/7905/A-05-21-00025-Complete%20Report.pdf; and House Commerce and Energy Committee, *Interim Staff Report on Investigation into Risky MPXV Experiment at the National Institute of Allergy and Infectious Diseases* (June 11 2024), https://d1dth6e84htgma.cloudfront.net/MPVX_Interim_Staff_Report_and_Appendices_final_844c87e06f.pdf.

[62] International Standards Organization (ISO), "ISO 35001:2019 Biorisk management for laboratories and other related organisations," November 2019, https://www.iso.org/standard/71293.html

biosecurity laws and regulations. For labs operating in countries without comprehensive biosafety and biosecurity laws and regulations, it provides a roadmap to best practices in biorisk management.

The adoption of this biorisk management standard would not only reduce the risk of accidents, but also contribute to efforts to determine the origin of an outbreak if the lab is suspected of being a possible source. Since ISO 35001, like all ISO standards, is designed to be audited by an outside party, it requires documentation of its implementation. These documents could be made available to local, national, or international authorities conducting an outbreak origin investigation.

To incentivize adoption of ISO 35001, the United States should phase-in a requirement that labs located in countries that do not have a comprehensive national biorisk management system adopt this standard as a condition for receiving Federal funding. This requirement would be accompanied by assistance to those labs to meet this standard provided through cooperative bioengagement programs run by the Departments of Defense, Energy, and State and by global health security programs run by the CDC and USAID. These programs will need additional resources to implement this biorisk management capacity building initiative.

The WHO's Role in Strengthening Global Biorisk Management

In May 2024, the World Health Assembly endorsed a resolution on strengthening laboratory biosafety and biosecurity. The resolution calls on Member States to develop or update national plans to include biorisk mitigation management, build human capacity for biorisk management, and promote a culture of biosafety and biosecurity. The resolution also calls on the WHO Secretariat to provide technical assistance to Member States, monitor developments in this area, and convene discussions to develop standards.[63] To support implementation of this new WHO initiative, I recommend three initiatives.

First, the WHO should establish collaborating centers for biorisk management in Africa, Southeast Asia, the Eastern Mediterranean, and the Western Pacific so that every WHO region has at least one such center. The purpose of these centers would be to conduct and sponsor applied research in field and laboratory biosafety and laboratory biosecurity, develop biorisk management policies and practices, provide training on biorisk management, assist with capacity-building programs, and serve as forums for exchanging information and sharing lessons learned among the key stakeholders. Together, these centers could help implement the WHO's Global Guidance Framework for the Responsible Use of the Life Sciences, ISO 35001, the 2019 World Organization for Animal Health (WOAH) Guidelines for Responsible Conduct in Veterinary Research, and the Tianjin Biosecurity Guidelines for Codes of Conduct for Scientists.[64]

Second, WHO should use its convening and standard-setting powers to lead an effort to develop guidance on BSL3+ labs to ensure that the physical and procedural safety measures adopted by these labs are evidence-based and commensurate with the level of risk associated

[63] WHO Executive Board, "Strengthening laboratory biological risk management," EB154(10), January 25, 2024, https://apps.who.int/gb/ebwha/pdf_files/EB154/B154(10)-en.pdf
[64] Letnzos and Koblentz, *Global Bio Labs 2023*.

with the research they conduct. BSL-3+ labs are BSL-3 labs that have adopted additional physical and/or operational biosafety and biosecurity precautions for carrying out particularly risky research. BSL-3+ labs are used to study highly pathogenic avian influenza, conduct research on pandemic pathogens, such as the reconstructed 1918 pandemic influenza virus, and conduct experiments to enhance the virulence or transmissibility of potential pandemic pathogens. According to the Global BioLabs Initiative, there are already 57 BSL-3+ labs operating in 28 countries and 80% of these labs are located in urban areas. However, there is limited national biosafety guidance, and no international guidance, on what constitutes BSL-3+ lab. In addition, there has been little to no research demonstrating that these enhancements provide an adequate level of additional safety commensurate with the higher risk research conducted in these labs. Given the number of BSL3+ labs already in operation, the almost complete lack of national guidance on the type of enhancements that such labs need, and the lack of evidence-based research evaluating whether these enhancements provide increased protection commensurate with the level of risk of the research performed at these labs, an international effort to specify the BSL-3+ category more clearly is sorely needed.[65]

Third, the development of international standards for field biosafety for zoonotic pathogens should be a high priority. Field biosafety policies and practices are designed to prevent researchers from becoming exposed to an infectious disease while collecting biomedical and environmental samples in the field and handling wild animals. The safe collection of samples from wild and domesticated animals that may be infected with a zoonotic pathogen is an underdeveloped component of biosafety. Few countries, including the United States, have national field biosafety standards and there is no international guidance available on this subject.[66] As the Director of National Intelligence testified to Congress last year, "A lack of global field biosafety standards and protective measures continues to raise concerns of viral spillover worldwide. Increased interest in field sampling and advanced biological research since the onset of the COVID-19 pandemic, poor training, and lack of international inspection and standardized regulatory requirements have all been implicated in contributing to the risk of contamination and/or breaches in biocontainment."[67] The WHO should lead an international effort to develop field biosafety standards applicable to Risk Group 4 pathogens and their most common animal reservoirs, hosts, and vectors. This guidance should be incorporated into the next edition of the WHO's Laboratory Biosafety Manual.

Conclusion

Determining the origin of a nationally or internationally significant biological incident is a crucial capability within the U.S. biodefense enterprise. Identifying the source of an outbreak t can improve the public health and medical response and provide insights to how to prevent future outbreaks or at least reduce their likelihood and magnitude. However, our inability to determine the origin of a biological incident with a high degree of confidence should not paralyze our efforts to learn from it and adopt new approaches to prevent future outbreaks and pandemics. As noted above, it can take years to confidently identify the origin of an outbreak or

[65] Letnzos and Koblentz, *Global Bio Labs 2023*.
[66] Letnzos and Koblentz, *Global Bio Labs 2023*.
[67] Office of the Director of National Intelligence, "Annual Threat Assessment of the U.S. Intelligence Community," February 6, 2023, https://www.dni.gov/files/ODNI/documents/assessments/ATA-2023-Unclassified-Report.pdf

pandemic. Even then, the origin may be defined only in general terms, not the exact source and sequence of events that led to the original outbreak.

Resolving the debate on the origin of COVID-19 is not necessary to take steps today to reduce the risk of future pandemics. We know enough about the two primary pathways to future pandemics— the demonstrated route of natural spillover and the potential for a research-related accident—to take concrete steps now to reduce both types of risks. Waiting to take decisive action until we have definitive proof about which pathway led to COVID-19 means holding ourselves hostage.