Senate Homeland Security and Governmental Affairs Committee
Subcommittee on Emerging Threats and Spending Oversight

Credible pandemic virus identification will trigger the immediate proliferation of agents as lethal as nuclear devices

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Introduction

Senator Hassan, Senator Paul, and members of the subcommittee, thank you for inviting me to testify on the subject of emerging threats from pandemic virus identification and enhancement research.

A million Americans have lost their lives to COVID-19, more than have perished in combat in all of our nation's foreign wars. **A pandemic virus can demonstrably kill more people than any single operational nuclear weapon.**[1]

For 75 years, the United States has successfully kept nuclear capabilities out of the hands of terrorists. Due to recent technological advances that have made it easy to assemble viruses from synthetic DNA, pandemics now represent a considerably greater challenge for nonproliferation, not least because they are wrongly viewed as a problem for health agencies that largely lack security expertise.

The threat of pandemic proliferation is still nascent: we do not yet know of any credible examples of novel viruses likely to cause a new pandemic if released.

If numerous pandemic-capable viruses are credibly identified and their genome sequences are shared with the world – as is the goal of well-meaning programs operated by the U.S. National Institutes of Health and the U.S. Agency for International Development – individual terrorists will gain the ability to unleash more pandemics at once than would naturally occur in a century.[2]

We know of at least one historical individual who both sought to acquire weapons of mass destruction for use against civilians and possessed an educational background, technical skills, and resources that would have allowed him to assemble and release viruses had he lived today.[3] Other highly capable mass murderers, including the Unabomber and certain technically skilled gunmen, would plausibly have sought out the ability to cause pandemics had they been given the opportunity. Still others may have remained unknown to us because they lacked the capability to cause sufficient damage and consequently declined to act. These examples suggest that at least one such would-be terrorist may be active today.

As a practicing biotechnologist who specializes in harnessing evolution using viruses as tools and inventing methods of editing laboratory organisms that will controllably spread in the wild,[4] **I am reasonably confident that pandemic virus identification represents a greater near-term threat to national security than anything else in the life sciences – and a more severe proliferation threat than nuclear has ever posed.**

To help understand the framework for this conclusion, my assessment considers questions of threat magnitude, proliferation, credibility, and utility. I conclude by outlining congressional actions that can delay the identification of pandemic-capable viruses long enough for us to build adequate defenses using new technologies.

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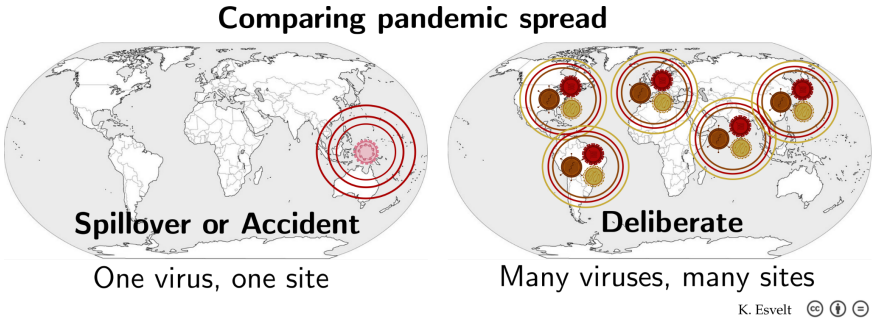
[1] Adam, "15 Million People Have Died in the Pandemic, WHO Says"; "NUKEMAP by Alex Wellerstein."
[2] Willman and Muller, "A Science in the Shadows"; Rogin, "The U.S. Government Is Rushing to Resume Risky Virus Research. Not so Fast"; Grange et al., "Ranking the Risk of Animal-to-Human Spillover for Newly Discovered Viruses."
[3] Danzig et al., "Aum Shinrikyo: Insights into How Terrorists Develop Biological and Chemical Weapons."
[4] Esvelt, Carlson, and Liu, "A System for the Continuous Directed Evolution of Biomolecules"; DeBenedictis et al., "Systematic Molecular Evolution Enables Robust Biomolecule Discovery"; Esvelt et al., "Concerning RNA-guided Gene Drives for the Alteration of Wild Populations"; Noble et al., "Daisy-Chain Gene Drives for the Alteration of Local Populations."

Deliberate pandemics can inflict more harm than any nuclear device or natural pandemic

SARS-CoV-2 has demonstrated that a pandemic virus spreading from a single point of origin can cause more deaths than any operational nuclear warhead, inflicting trillions in economic damages and disrupting lives worldwide. A single point of origin is the expected outcome of both natural spillovers and of lab-associated accidents, one of which was the cause of the Covid-19 pandemic in 2019.[5] At this time, the available evidence appears insufficient to determine which was responsible.

However, we can safely conclude that a deliberate pandemic involving the same virus would have been worse. A malevolent actor could have released SARS-CoV-2 in multiple travel hubs, resulting in considerably faster spread across the world and many more infections and deaths before the advent of vaccines. Indeed, unless a proven vaccine is already stockpiled in large numbers near major cities, distribution cannot plausibly inoculate people as quickly as a deliberately released virus will spread: the omicron variant spread from a single point of origin to infect 26% of Americans on the other side of the world within 100 days of detection.[6]

If many pandemic-capable viruses become known – even if each has only a moderate chance of causing a pandemic – a terrorist could assemble and release them all, potentially unleashing more and faster-spreading pandemics at the same time than would naturally occur in a century.



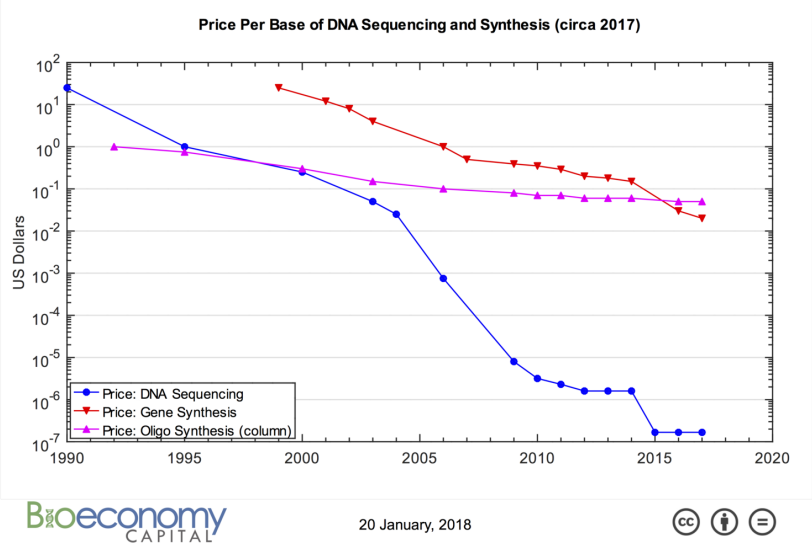
Successful pandemic virus identification will immediately cause widespread proliferation

Acquiring a pandemic-class agent requires 1) knowing of one or more viruses likely to cause a new pandemic, and 2) obtaining an infectious sample. Twenty years ago, the only way to obtain physical virus samples was from clinical specimens or laboratory stocks. **Today, thousands of individuals can assemble many types of viruses from commercially available synthetic DNA and virus assembly instructions**, often called "reverse genetics" protocols.

[5] Sewell, "Laboratory-Associated Infections and Biosafety"; Merler et al., "Containing the Accidental Laboratory Escape of Potential Pandemic Influenza Viruses"; Klotz and Sylvester, "The Consequences of a Lab Escape of a Potential Pandemic Pathogen"; Lipsitch and Inglesby, "Moratorium on Research Intended to Create Novel Potential Pandemic Pathogens"; Gryphon Scientific, "Risk and Benefit Analysis of Gain of Function Research"; Manheim and Lewis, "High-Risk Human-Caused Pathogen Exposure Events from 1975-2016"; Bloom et al., "Investigate the Origins of COVID-19."

[6] Clarke et al., "Seroprevalence of Infection-Induced SARS-CoV-2 Antibodies - United States, September 2021-February 2022."

Ingredient 1: Inexpensive Synthetic DNA



In 2002, poliovirus was successfully assembled from chemically synthesized DNA.[7] Since then, the cost of synthetic genes has fallen by a factor of a thousand.

The members of the International Gene Synthesis Consortium, an industry group, have taken the lead in voluntarily screening customer orders for dangerous agents at their own expense, going well beyond the weak regulatory requirements imposed by the Department of Health and Human Services.[8] However, members comprise only an estimated 80% of the market and the membership list is publicly available.[9]

Despite the best efforts of the International Gene Synthesis Consortium, it is currently easy to obtain unscreened synthetic DNA.

Ingredient 2: Virus assembly protocols that can be performed by individuals with little tacit knowledge

Meanwhile, **virus assembly instructions have been developed for nearly all families of viruses to facilitate research on treatments**[10]. For well-studied viral subfamilies, these step-by-step protocols are so detailed that they can be successfully performed by non-specialists with basic molecular or cellular biology skills, as long as their skillset includes mammalian cell culture: the protocols are designed to remove any need for "tacit knowledge". A recently published protocol to engineer coronaviruses such as SARS-1 and SARS-2 explicitly stated that it aimed to "enable researchers from different research backgrounds to master the use of the reverse genetic system".[11]

Ingredient 3: Many individuals with the technical skills and resources needed to succeed at virus assembly

A large number of scientists, engineers, and lab technicians have the skills required to obtain many types of infectious viruses from publicly available genome sequences. Most presumably have access to laboratory facilities due to their professional work, but even if not, **a laboratory stocked with the relevant used equipment is affordable on an upper-middle-class salary in most developed nations**.

[7] Cello, Paul, and Wimmer, "Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template."
[8] Diggans and Leproust, "Next Steps for Access to Safe, Secure DNA Synthesis"; International Gene Synthesis Consortium, "Harmonized Screening Protocol V2."
[9] "International Gene Synthesis Consortium"; Johns Hopkins Center for Health Security, "Gene Synthesis Companies."
[10] Maroun et al., "Designing and Building Oncolytic Viruses."
[11] Xie et al., "Engineering SARS-CoV-2 Using a Reverse Genetic System."

How many people can build viruses? In the U.S. alone, twenty-five new individuals receive their doctorate in the life sciences or bioengineering each day[12]; in the last 30 years, over two million people have received an equivalent degree worldwide per OECD records[13]. Even assuming that only one in ten received any training in mammalian cell culture – which is especially common among biomedical researchers – and that just one in twenty of the remainder are skilled and well-practiced enough to successfully follow a virus assembly protocol, over 10,000 people with doctorates can generate many known viruses from families for which a relevant assembly protocol is available. The number of research technicians and students may be comparable.

Another way to estimate the number is to consider how many PhDs are granted in virology, as the vast majority of such individuals must be presumed capable of following a reverse genetics protocol. The U.S. grants 125 doctoral degrees in virology each year, accounting for one-third of the total worldwide. At least four times as many individuals with degrees in related fields – such as my own PhD in biochemistry – possess similar skills. If we assume a 20-year active career, **approximately 30,000 individuals are capable of assembling any influenza virus for which a genome sequence is publicly available**.

These skills are vital to the bioeconomy, which in turn is becoming essential to human health, industrial production, environmental protection, and the continued development of a flourishing and sustainable society. The number of individuals capable of single-handedly assembling viruses from synthetic DNA will continue to grow.

Ingredient 4 (missing): Credible knowledge of novel viruses that could likely cause a new pandemic

Readily available synthetic DNA, step-by-step virus assembly protocols, and thousands of technically skilled individuals add up to many individuals who can assemble viruses, but that doesn't mean we know of any likely to cause a new pandemic. Pandemic proliferation is a nascent threat that will not be realized until someone credibly identifies a novel virus that would likely spread on its own and shares the complete genome sequence.

Consider an analogy: **we live in the biological version of a world in which weapons-grade plutonium can be mail-ordered and thousands of engineers have the skills to assemble a nuclear device, but no one knows exactly which design would work**. In that alternate reality, it's hard to imagine anyone openly seeking to identify such designs and share them online. But if cities were randomly destroyed by naturally occurring nuclear explosions, no one had ever died from a deliberate detonation, and scientists suspected that understanding how it happens might help prevent some of those natural casualties, perhaps they would. Key questions include whether doing so would be worth the cost, and how it can be done.

[12] National Center for Science and Engineering Statistics, "Doctorate Recipients from U.S. Universities, 2019."
[13] OECD, "OECD: Graduates by Field."

How can we learn whether a virus would likely cause a pandemic if exposed to humans?

Malevolent actors interested in pandemic-capable viruses as a "poor man's nuke" will not bother trying to assemble one unless they are at least moderately confident that it would cause a pandemic. An estimated 10,000 to 320,000 mammalian viruses are thought capable of infecting humans.[14] But infection alone isn't enough: **only a tiny fraction of human-infecting animal viruses – certainly no more than a few thousand – might be transmissible enough to cause a pandemic**. By default, we can safely assume that most viruses are not pandemic-capable, even if they have been flagged by computational tools or mutated by researchers in the lab to increase transmissibility. For now, the only way to substantially increase our confidence that a given virus would cause a new pandemic is to perform a certain set of laboratory experiments.

Here is the logic: viruses currently circulating in humans are very good at infecting us and making our bodies churn out more viruses. But because most of us have already been infected and acquired some immunity, they mostly spread to children who have not been exposed or to people with weak immune systems. Pandemics happen when a new virus that can be readily transmitted jumps from animals to people: no one has much immunity, so each person infects more than one other on average, causing it to spread like wildfire. Once most people have encountered the new virus and developed resistance, it behaves like its human-adapted relatives: the average infected person passes on the virus exactly once.

This means that **any virus that is immunologically new to human populations and can efficiently infect our cells, replicate in our cells, and/or be transmitted between animals chosen for their similarity to humans nearly as well as a long-circulating human virus from the same family is reasonably likely to cause a pandemic**. Even if it is subpar at one or two of these, it only needs to be good enough to keep going long enough for a variant to arise with a mutation that makes it better – just as the original SARS-CoV-2 was outcompeted by subsequent more infectious and/or immune-evasive variants. In a deliberate large-scale release, such evolution would become more likely.

Scientists attempting to identify pandemic-capable respiratory viruses typically perform experiments measuring their ability to infect and replicate in primary human airway epithelial cells and to be transmitted between human-relevant animal models, such as engineered mice, ferrets, or primates. With NIH and USAID support, scientists from EcoHealth Alliance and the Wuhan Institute of Virology with performed these types of experiments on bat coronaviruses newly collected by virus hunters to learn whether they might cause new pandemics, and also on synthetic viruses created by mixing and matching those that seemed risky in order to learn whether such recombination might produce a pandemic-capable virus.[15] Researchers working to enhance the transmissibility of especially lethal animal viruses, like the bird flu strains engineered to be transmitted more efficiently between ferrets with NIH funding, also conduct these experiments to see whether mutated versions of these viruses may have acquired the ability to cause a pandemic.[16] **These pandemic virus identification experiments are the virological equivalent of nuclear testing**. As yet, none of them have succeeded in producing any credible threats.

[14] Carlson et al., "Global Estimates of Mammalian Viral Diversity Accounting for Host Sharing"; Anthony et al., "A Strategy to Estimate Unknown Viral Diversity in Mammals."
[15] Hu et al., "Discovery of a Rich Gene Pool of Bat SARS-Related Coronaviruses Provides New Insights into the Origin of SARS Coronavirus."
[16] Herfst et al., "Airborne Transmission of Influenza A/H5N1 Virus between Ferrets"; Imai et al., "Experimental Adaptation of an Influenza H5 HA Confers Respiratory Droplet Transmission to a Reassortant H5 HA/H1N1 Virus in Ferrets."

Key experiments that can increase our confidence that a novel animal virus is pandemic-capable
1. Quantify the growth of the novel virus in relevant human primary cells (e.g. respiratory epithelial) 2. Quantify transmissibility in a human-relevant animal model (e.g. transgenic mice or ferrets)

Will pandemic virus identification save or cost lives?

Natural pandemics killed over a million people in 1889-91, 1918-20, 1957-59, 1968-70, and 2019-21. Might the alleged benefits of pandemic virus identification outweigh the expected harms of accident risks? What of the risks of deliberate misuse?

The issue of whether we should identify pandemic-capable viruses is entirely distinct from the controversy over the origin of SARS-CoV-2. Groups promoting and performing pandemic identification virus identification research – such as EcoHealth Alliance, the Wuhan Institute of Virology, and the Global Virome Project – believe that identifying a risky virus before the first cases appear will help prevent spillover by limiting human-animal contact and blocking transmission, and hope that it might also accelerate vaccine development. But many of the most vocal proponents of a natural origin for SARS-CoV-2 have vociferously argued that it will do neither.[17] These scientists fully support the other aspects of the One Health program for spillover prevention that are backed by USAID, but they view pandemic virus identification as a wasteful diversion of resources that would be better spent monitoring high-risk populations at the animal-human interface and helping those communities contain outbreaks.

To understand whether pandemic virus identification is worth the risk, we need low and high estimates of the benefits from early therapeutic development and improved spillover prevention, the likelihood of accidents that lead to outbreaks and then pandemics, and the probability of deliberate pandemics caused by terrorists who release one or many candidate viruses across multiple sites.

Pandemic virus identification will not significantly accelerate vaccine development. Moderna's SARS-CoV-2 vaccine was designed in less than two days. With suitable manufacturing facilities, we can produce enough doses in a week to run combined Phase I and II trials using ring vaccination to simultaneously maximize the chance of containment and learn whether our vaccine is effective. Early identification will not accelerate this timeline because we cannot run Phase II challenge trials of candidate vaccines in advance: doing so would require us to deliberately infect people with presumed pandemic-capable viruses of unknown lethality that have never infected a human and may never do so. Moreover, there are so many viruses in nature that the odds are strongly against identifying the one that will actually cause the next natural pandemic. With such a low expected rate of return, we are extremely unlikely to fund the development of such vaccines in the first place.[18] Broad-spectrum vaccines are different: they could be stockpiled in advance, but do not require us to know anything about which viruses could cause pandemics – after all, the entire point is to develop vaccines that work against an entire family of viruses – so their development will not benefit from pandemic virus identification.

[17] Holmes, Rambaut, and Andersen, "Pandemics: Spend on Surveillance, Not Prediction"; Wille, Geoghegan, and Holmes, "How Accurately Can We Assess Zoonotic Risk?".
[18] Holmes, Rambaut, and Andersen, "Pandemics: Spend on Surveillance, Not Prediction"; Wille, Geoghegan, and Holmes, "How Accurately Can We Assess Zoonotic Risk?"

Pandemic virus identification may help prevent spillover – *if* the virus would have spilled over. Since there are many more pandemic-capable viruses in animals than there are severe pandemics in a century – likely at least 100-fold more – even perfect prevention of a successfully identified virus would on average prevent only 1/100 of a pandemic. Still, for a virus equivalent to SARS-CoV-2, that would save an expected 10,000 American lives. There is a reason that many scientists think it worth trying.

The risk of an accidental pandemic may or may not outweigh the benefits of identification. Lab accidents happen routinely, but estimates of the frequency and the likelihood that they would prove infectious enough to seed a pandemic (1-30%) vary enough that the expected number of lives to accidental pandemics could be lower or higher than the lives saved through spillover prevention.[19] Perhaps surprisingly, learning the true origin of SARS-CoV-2 would barely budge these numbers.

Deliberate pandemics are expected to kill many more people than identification could save. While the possibility of deliberate pandemics has seldom been raised, simple risk calculations are straightforward.[20] Given the known existence of capable mass-murderers such as Seiichi Endo of the apocalyptic cult Aum Shinrikyo, the Aurora shooter, and the Unabomber, all of whom had or plausibly could have obtained the skills to assemble and release a virus if they lived today[21], it would be surprising if the chance that any given identified virus will be released by a terrorist was less than 1% per year… meaning each identified virus would be released within a century. Because a virus deliberately introduced at multiple sites would spread more rapidly than if the same virus were to cause a natural pandemic, successfully identifying a new equivalent of SARS-CoV-2 and sharing its genome with the world is expected to cost well over a million American lives.

Even if identifying a pandemic-capable virus in nature allowed us to perfectly prevent that virus from causing a natural pandemic, and we could do so with zero risk of accidents, we should expect terrorists to use the same virus to kill a hundred times as many Americans as would be saved.

Will malicious actors identify viruses capable of causing new pandemics if we do not?

Judging by the history of nuclear weapons, many will argue that malevolent actors will eventually identify pandemics on their own, so it's better if the good guys do it first. That may have been true of the atom bomb, but the strategic calculus for pandemics could not be more different. **Malicious actors are exceedingly unlikely to identify pandemic-capable viruses if health agencies decline to do so**.

First, it's true that rogue nations and extremist groups could gain tremendous coercive power by possessing viruses understood to be capable of causing new pandemics. These could serve as "dead-hand" switches for autocratic regimes or as convenient sources of leverage for extremist groups making demands. But neither type of actor wants to actually release such an agent, let alone give access to ideological zealots who would use it to kill them.

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[19] Klotz and Sylvester, "The Consequences of a Lab Escape of a Potential Pandemic Pathogen"; Gryphon Scientific, "Risk and Benefit Analysis of Gain of Function Research"; Dobson et al., "Ecology and Economics for Pandemic Prevention."
[20] Inglesby and Relman, "How Likely Is It That Biological Agents Will Be Used Deliberately to Cause Widespread Harm? Policymakers and Scientists Need to Take Seriously the Possibility That Potential Pandemic Pathogens Will Be Misused"; Katz et al., "Mapping Stakeholders and Policies in Response to Deliberate Biological Events"; "A Spreading Plague: Lessons and Recommendations for Responding to a Deliberate Biological Event"; Sandberg and Nelson, "Who Should We Fear More: Biohackers, Disgruntled Postdocs, or Bad Governments? A Simple Risk Chain Model of Biorisk."
[21] Levy and Smithson, "Ataxia: The Chemical and Biological Terrorism Threat and the US Response"; Wikipedia contributors, "James Holmes (mass Murderer)"; Kaczynski, "The Unabomber Manifesto: Industrial Society and Its Future."

Second, whereas nuclear tests yield unmistakable seismological signatures of success or failure, experimental data indicating pandemic capability is easily fabricated. Even if a rogue state or extremist group were to threaten to release a pandemic, there is no reason to believe they have a capable virus, nor to accept the validity of any alleged experimental results they might provide. Threats from rogue actors will only be taken seriously if more trustworthy actors have independently identified the virus as likely to cause a pandemic. **Since credible pandemic virus identification would give access to every ideological terrorist intent on mass murder, it is against the strategic interests of every non-suicidal malicious actor** – but if well-meaning scientists unaware or dismissive of security identify it first, many non-state actors will presumably make threats with their newly credible nuclear-equivalent capabilities.

Third, pandemic virus identification experiments are far more difficult to perform than virus assembly. While the modern equivalent of a trained mass murderer such as Seiichi Endo could unquestionably assemble many viruses, they lack the technical capability to perform basic science research at the scale needed to find the pandemic needle in the animal virus haystack. Despite recent technological advances that have made success more likely, professional scientists funded by NIAID and USAID's PREDICT program have already spent hundreds of millions of taxpayer dollars searching for pandemic viruses without finding any truly credible threats. Therefore, **while bioterrorist zealots could assemble pandemic-capable viruses that health researchers helpfully identify for them, they could not find such viruses on their own**.

Most importantly, the security agencies of established nations can be persuaded that pandemic virus identification is not in their strategic interest. Pandemic-class agents kill indiscriminately and cannot currently be engineered to spare one's own population. Large nations that attempt to vaccinate their own populations in advance would likely be discovered by foreign intelligence agencies, and even if population-specific targeting became possible, its use by a nation-state would be so obvious as to invite mass retaliation. Therefore, **pandemic-capable viruses offer little if any strategic utility to powerful nation-states; indeed, quite the opposite**. The United States, China, and even Russia have a shared interest in joining forces to prevent rogue actors and terrorist zealots from gaining access to pandemic-capable viruses.

If the United States, which historically has been the largest backer of pandemic virus identification, halts such research and explains why, even our strategic rivals are likely to follow suit.

Regulatory reforms that could prevent proliferation

COVID-19 demonstrated that we remain profoundly vulnerable to pandemic viruses spreading outwards from a single point of introduction. There is no question that would fail to contain multiple pandemic agents simultaneously released in travel hubs. But multiple new technologies need not remain helpless.

Recommendation I – announce findings, redirect funds away from pandemic virus ID, and fix oversight

Our best current defense against pandemic weapons of mass destruction is to keep them from being developed in the first place.

- First, **Congress can publicly assess the threat and release a clear finding**. A Congressional finding that experiments capable of increasing public confidence that a particular virus could cause a pandemic threatens national and international security would prove instructive for security and health agencies as well as the State Department.

- Second, **Congress can stop funding pandemic virus identification experiments**. Existing programs, whether focused on naturally collected viruses or those generated by so-called "gain-of-function" research aiming to increase transmissibility, are primarily funded by governments, including our own. I deeply respect the researchers working on these programs, who have dedicated their lives to preventing natural pandemics. I do not expect them to have carefully considered the possibility of misuse.[22] Scientists are not incentivized to become security experts; even those with an interest are unlikely to be aware of many details relevant to proliferation, such as falling gene synthesis costs, the current efficacy of DNA synthesis screening, the obviating of tacit knowledge requirements by modern virus assembly protocols, the history of nuclear weaponry, and strategic game theory.

  USAID has already pledged to cease funding transmissibility enhancement ("gain-of-function") experiments, and may not have become aware of the security implications of identifying natural pandemic-capable viruses until late 2021. Even so, they remain the largest funder of such efforts, including a new program, "DEEP VZN", that is the direct successor of the PREDICT program that funded the pandemic virus identification research in Wuhan. Because these are offshoots of larger One Health programs focused on useful virus discovery and monitoring work at the animal-human interface,[23] there would be no need to revoke any funding or break contracts: the DEEP VZN program could simply direct funds towards early warning systems rather than laboratory pandemic virus characterization. They should also refrain from publicly sharing the entire genome sequences of newly discovered viruses, as much of the genome is not relevant to vaccine or antiviral therapeutic development. USAID's "STOP SPILLOVER" program need only announce that it will no longer maintain a list of viruses rank-ordered by perceived threat level[24] due to national security and proliferation risks. Behavioral studies and public health interventions, which are important for reducing the spillover of animal pathogens into human populations and containing them when possible, can and should continue.[25] Pandemic virus identification experiments represent considerably less than 1% of all virology; banning them would be much less of an imposition on the field than are the security measures governing nuclear physics.

  NIH has a long history of funding projects aiming to enhance the transmissibility of viruses, including but not limited to lethal pathogens such as H5N1 and MERS. Many of these projects, which have been compiled and summarized by reporters from the *Washington Post*, were not covered by the moratorium on "gain-of-function" research due to disputes over what exactly is meant by that term.[26] **Congress can resolve the confusion over definitions by blocking federal funding of pandemic virus identification experiments, defined as those that could substantially increase our confidence that a virus would cause a pandemic if repeatedly introduced.**

[22] "Opportunities Exist for the National Institutes of Health To Strengthen Controls in Place To Permit and Monitor Access to Its Sensitive Data."
[23] "WSU to Lead USAID's Global Sampling Project for Discovery of Emerging Viral Zoonoses - Global Biodefense"; "STOP Spillover."
[24] "SpillOver — Global Virome Project"; Grange et al., "Ranking the Risk of Animal-to-Human Spillover for Newly Discovered Viruses"; "STOP Spillover."
[25] Saylors et al., "Socializing One Health: An Innovative Strategy to Investigate Social and Behavioral Risks of Emerging Viral Threats.".
[26] Willman and Muller, "A Science in the Shadows."

Experiments that may increase our confidence that a virus is pandemic-capable
1. The comparative growth of an animal virus or chimera in relevant human primary cells 2. The comparative transmission of an animal virus in a human-relevant animal model 3. The capacity of an engineered human virus* to evade innate immunity 4. The capacity of an engineered human virus* to evade pre-existing humoral immunity 5. The capacity of an engineered human virus* to evade pre-existing cellular immunity
* This category would not include viral mutants and variants thought to already be present in nature.

- **Third, Congress can require external security oversight of life sciences research**. At present, health agencies and funding recipients are instructed to regulate themselves with respect to security issues:

  > "The Department of Health and Human Services (HHS) Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens is intended to guide HHS funding decisions…"
  >
  > "Funders of life sciences research and the institutions and scientists who receive those funds have a shared responsibility for oversight of DURC (dual use research of concern) and for promoting the responsible conduct and communication of such research."

  No funding agency or recipient can be expected to oversee itself; that is the definition of a conflict of interest. The National Science Advisory Board on Biosecurity (NSABB) consists of ostensibly independent researchers, but most are primarily funded by NIH, they are appointed by HHS, and they can be dismissed at any time. Indeed, 11 of the inaugural members who had participated in discussions over research enhancing the transmissibility of highly lethal H5N1 influenza were summarily dismissed in 2014 amidst a controversy over laboratory safety mishaps involving smallpox, influenza, and anthrax. During the vote on whether to discontinue the moratorium on "gain-of-function" research involving potential pandemic pathogens, the directors of the NIH and the NIAID, whose opinions on the matter are well-known, were allegedly present in the room.

  Congress can establish a panel of experts from security agencies to provide oversight for life sciences research funded by the U.S. government, including reviewing and approving all requests for proposals before they are released. Members should be required to recuse themselves from oversight of proposals from their own agencies.

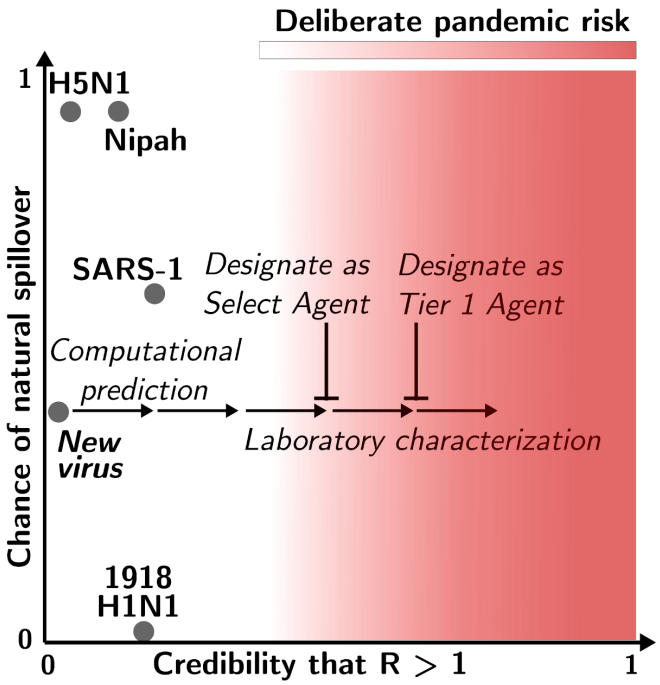
Recommendation II – Amend the 2002 Bioterrorism Response Act to update the Select Agent program

The Federal Select Agent & Toxin Program (FSAP) is unique in regulating all research in the United States, not just federally-funded entities, and additionally impacts the export control list. However, it is updated slowly, doesn't include most viruses that might be pandemic-capable, and the Act was last amended before we developed techniques such as virus chimerism, directed evolution, ancestral protein reconstruction, and machine learning approaches, all of which can plausibly generate new threats from existing ones.

Congress can update the Federal Select Agent & Toxin Program to:

1. Automatically list a virus as soon as a single result from a pandemic virus identification experiment suggests that it may be pandemic-capable[27]
2. Regulate any DNA construct that was generated from pieces of regulated Select Agents
3. Give the program the power to immediately lift all restrictions on any Select Agent confirmed to be actively spreading in order to accelerate research on countermeasures

In addition to reducing accident risks and requiring background checks of anyone working with viruses that might cause new pandemics – clearly the most hazardous of biological agents – these rules would disincentivize researchers from performing experiments to determine whether a virus they study is pandemic-capable, as doing so would automatically render it a Select Agent and increase their laboratory's cost of research several fold. As a gesture of good faith to the scientific community, FSAP might also be instructed to consider removing many listed agents that are incapable of autonomous spread and pose comparatively little risk of deliberate misuse.



Assessing pandemic risks. Pandemics may result from natural spillover, laboratory accidents, or deliberate misuse of viruses identified as credibly pandemic-capable (basic reproductive number R>1: the typical infected person infects more than one other person). Designating viruses as Select Agents upon obtaining the first experimental evidence indicative of pandemic potential could preserve the hypothesized benefits of virus discovery for "universal" virus family vaccine and broad-spectrum antiviral development while reducing accident risks and deterring characterization experiments that would otherwise result in the proliferation of viruses with presumed nuclear-equivalent lethality.

[27] **Defining pandemic-capable:** Any virus that normally circulates in a population (R~1) will cause a pandemic when introduced into a more susceptible population that lacks pre-existing immunity (R>1). This is why pandemics typically arise from viruses that spill over from other species, which spread rapidly before becoming endemic. Therefore, a virus is a credible pandemic threat if it:

- Can grow in relevant human tissues or be transmitted between relevant animal models nearly as well an endemic human virus of the same family
- Is poorly recognized by the immune systems of most humans relative to endemic human viruses of the same family

Recommendation III – leverage shared strategic interests to prevent pandemic proliferation globally

The nature of many emerging technologies places the U.S. and China at loggerheads, but our strategic interests are nearly perfectly aligned when it comes to the proliferation of access to pandemic viruses: both nations have little to gain and much to lose. This is an opportunity for the United States to gain leverage by offering information exchange and inviting co-leadership in global health security, and may help build diplomatic channels to address more challenging issues around other key technologies.

One way to marshal global action against pandemic virus prediction would utilize the Biological Weapons Convention (BWC), which prohibits the "development, stockpiling, acquisition, retention and production of biological agents" while "permitting the fullest possible exchange of equipment, materials, and information for peaceful purposes." Today, it's impossible to identify a credible pandemic-capable virus from most families, including corona-, influenza- and paramyxoviruses, without immediately giving thousands of individuals the ability to assemble infectious samples. There is a strong argument that Article III compels BWC signatories to block pandemic virus identification despite the good-intentions provisions of Article X.[28] However, the BWC is normatively important, but too general and without enforcement provisions to address pandemic proliferation. Instead, **Congress can instruct the State Department to begin negotiating a Pandemic Test-Ban Treaty that would narrowly forbid pandemic virus identification experiments, defined as those that could substantially increase our confidence that an animal virus or an engineered virus could cause a new pandemic**.

Recommendation IV – require DNA synthesis screening matching or exceeding the industry standard

Most researchers who can follow a virus assembly protocol cannot synthesize and assemble the requisite DNA or RNA, so the fact that we can order synthetic viral DNA and have it come in the mail substantially increases the number of actors capable of assembling a pandemic weapon. California's legislature passed a bill that would require all providers of synthetic DNA and manufacturers of synthesis machines to screen orders at least as well as the International Gene Synthesis Consortium, but it was vetoed on the grounds that federal legislation is needed to avoid a regulatory patchwork.[29]

A federal law requiring DNA synthesis screening would pressure domestic and international providers to screen, nudging firms to engage with the NTI/WEF stakeholder discussions on a cooperative framework and the SecureDNA project to implement new advances, including in "desktop" synthesizers, that will allow automated screening for the latest threats without having to disclose customer orders or jeopardize trade secrets.[30] Similar regulations could be encouraged internationally using the BWC or other diplomatic means.

[28] Butler, "Bioweapons Treaty in Disarray as US Blocks Plans for Verification."
[29] "California Legislature - AB-70 Gene Synthesis Providers."
[30] "Biosecurity Innovation and Risk Reduction: A Global Framework for Accessible, Safe and Secure DNA Synthesis"; The SecureDNA team, "Secure DNA Project - DNA Synthesis Screening."

Recommendation V – implement catastrophe liability and require insurance coverage

Despite the recently demonstrated catastrophic potential of pandemics and the controversy over accident risks, there have been surprisingly few professional risk assessments. Indeed, the United States imposed a moratorium on poorly-defined "gain-of-function" research, removed it, and replaced it with an equally poorly defined and readily evaded framework governing research on "enhanced potential pandemic pathogens" without any publication of a quantitative risk model.

Pandemic virus identification may offer great rewards – preventing 10,000 American deaths would be a major accomplishment – but there is currently no way to assess the negative externalities, let alone any market-based way to incorporate those costs into the decision-making process. With the narrow exception of nuclear policy, other actions with potentially catastrophic consequences are similarly unregulated.

Congress can encourage market-based professional risk assessment of potential catastrophes by:

1. **Passing legislation to ensure that institutions causally linked to catastrophic outcomes involving the death or disablement of a million or more Americans can be held legally liable, even for providing information permitting deliberate misuse by others, and**
2. **Requiring that general liability insurance cover such claims, up to a very large market cap chosen to prevent insurers and re-insurers from going bankrupt while providing a very strong incentive to evaluate potential sources of catastrophic risks**

The Covid-19 pandemic is the only historical event to have caused a million American deaths. World War I, World War II, HIV, the 1918 influenza pandemic, and even the Civil War did not claim so many.[31] This inherently limits the number of actions that would require review. Not only is it entirely reasonable to hold responsible anyone whose actions are subsequently shown – through the due process of law – to be instrumental in the genesis of such catastrophes, but requiring general liability insurance to cover that liability would effectively require professional risk analysts to evaluate the likelihood and set rates accordingly. That is, such a law would induce the market to impose costs upon institutions proportional to the available information concerning the likelihood that their current and planned actions will, at even very low probabilities, lead to extreme catastrophe. Requiring any findings above a minimal expected consequence (for example, probability x magnitude > 10,000 American deaths) to be made public following review and potential classification by a panel of security experts would add to society's understanding of which actions might trigger catastrophe, including by improving future assessments of the same type by insurers and prediction markets.

If a catastrophe liability and insurance act already existed, there might not be a need for Congress to determine whether to ban pandemic virus identification experiments: simply informing the insurance companies covering the institutions involved would trigger professional assessment and a corresponding increase in premiums, forcing the involved institutions to internally evaluate whether to continue with the risky behavior. If deemed worth the cost, then such actions would proceed. If not, the problem would solve itself. Either way, the negative externalities of actions with sufficiently low-probability and high-consequence outcomes would be incorporated into decision-making.

[31] Roos, "The Deadliest Events in US History."

Congressional regulation can buy time sufficient to render the U.S. able to withstand pandemics

There is a saying in cybersecurity: any system vulnerable to accidents is helpless against deliberate attack. Covid-19 may have arisen from nature or the accidental infection of a virus hunter or laboratory researcher, but it was unquestionably an accident. It follows that we are currently helpless against deliberate attacks involving pandemic-class agents. **Our current vulnerability to pandemics underscores the vital importance of ensuring that blueprints do not become publicly available.**

But if our vulnerability is extreme enough to make the situation seem hopeless, it might impede productive efforts to take action: there is a natural human inclination to freeze when confronted with a seemingly intractable problem. The deliberate release of pandemic viruses may well threaten the United States in ways that cannot be solved by medical countermeasures due to logistical constraints, no matter how quickly developed. This does not mean pandemics represent an insoluble problem. **We can immunize our country against pandemic events within a decade without any advances in biomedicine.**[32]

New algorithms are making it possible to automatically screen all DNA synthesis without revealing which sequences are considered hazardous, reducing unauthorized access to pandemic-class threats by a hundredfold and nudging scientists away from publicly disclosing them in the first place.[33] Advances in DNA sequencing will provide the United States with reliable early warning of all exponentially spreading biological threats, even those such as HIV that would not immediately show up in the clinic, for under a billion dollars a year.[34] Early warning will allow us to provide essential workers with protective equipment sufficient to enable them to do their jobs without risking their lives – an N95 mask is unlikely to suffice for a SARS-CoV-2-equivalent virus with 30% lethality, let alone something as contagious as measles, but slightly improved powered air-purifying respirators would – and enabling us to contain and eliminate threats even if groups of pandemic viruses are released in multiple airports. Personalized risk assessments provided by improved versions of contact tracing apps could tell people what fraction of their first-, second-, third-, fourth, and fifth-degree contacts have been infected, allowing only those at-risk to take precautions and dramatically reducing the cost of extinguishing small outbreaks brought in from outside our borders.[35] Perhaps most importantly, we're learning that certain wavelengths of light can kill viruses and pathogenic bacteria without even penetrating our skin or eyes; if we determine that they are as safe as preliminary studies indicate and install them in fixtures throughout the country, we could plausibly suppress a future Covid-19 or possibly even a measles-class pandemic without anyone having to wear a mask or change their routine at all… and virtually eliminate the common cold and flu while we're at it.[36]

[32] Esvelt, "Delay, Detect, Defend: Preparing for a future in which tens of thousands can unleash new pandemics." Unpublished; draft available upon request.
[33] The SecureDNA team, "Secure DNA Project - DNA Synthesis Screening"; Gretton D, Wang B, Foner L, DeBenedictis EA, Liu AB, Chory E, Cui H, Li X, Dong J, Fabrega A, Dennison C, Don O, Tong Y, Uberoy K, Rivest R, Gao M, Yu Y, Baum C, Damgard I, Yao AC, Esvelt KM, "Random Adversarial Threshold Search Enables Specific, Secure, and Automated DNA Synthesis Screening"; The SecureDNA cryptography team, "Hiding Dangerous DNA in Plain Sight."
[34] The Nucleic Acid Observatory Consortium, "A Global Nucleic Acid Observatory for Biodefense and Planetary Health."
[35] Loh, "NOVID - a New Approach to Pandemics"; Loh, "Flipping the Perspective in Contact Tracing."
[36] Blatchley et al., "Far UV-C Radiation: An Emerging Tool for Pandemic Control."

Developing and implementing these defenses will take time. Without action by Congress, the first highly credible pandemic viruses might be publicly identified and their complete genomes irreversibly shared by well-meaning scientists funded by USAID, NIH, or other agencies as soon as this coming year. We need to keep the risk window closed for as long as possible. Disagreements over public health policy, accidents, and the origin of SARS-CoV-2 appear trivial next to this emerging technological threat to national security.

For 75 years, the United States has successfully kept nuclear capabilities out of the hands of terrorists. Today, we're on the verge of irreversibly handing them blueprints for viruses as lethal as nuclear weapons – all in the name of public health. Let's not.

This testimony reflects the personal opinions and technical expertise of Dr. Kevin M. Esvelt.
Dr. Esvelt is currently a professor at MIT, but does not speak on behalf of the Institute on this occasion.

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