Hearing of the House Select Subcommittee on the Coronavirus Pandemic

"Strengthening Biosafety and Biosecurity Standards: Protecting Against Future Pandemics"

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Statement for the Record

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Introduction.

I come before you today as an individual who has spent an entire career in biodefense, public health preparedness, and health security from research in a high containment laboratory to strategic, operational, and policy levels; and now mentoring our next generation of public health and biodefense professionals.

I will offer insights from my role as a public servant that spanned 26 years of active-duty military service and another ten years in the career senior executive service. During my military career, I had the opportunity to serve in leadership roles, primarily in military medical research & development at the United States Army Medical Research and Materiel Command. I served as Deputy Commander and Commander of the United States Army Medical Research Institute of Infectious Diseases (USAMRIID) as well as in senior executive leadership roles at the Department of Homeland Security (DHS), Department of Health and Human Services (HHS), and the Department of Defense (DOD).

But today, the views and opinions I offer are my own, and not representative of past or current organizational affiliations, employers, or advisory boards.

Background:

Naturally emerging and reemerging infectious disease outbreaks are occurring with alarmingly increased frequency. Globalization of travel and trade, urbanization, wildlife, and food-animal close contacts, failing states, and other anthropogenic factors have created environmental conditions that favor the emergence and reemergence of infectious diseases.

In addition to natural biological threats, ready access to advanced dual-use technologies, the expansion of high-containment laboratories worldwide, and the availability of dangerous pathogens are simultaneously increasing the potential for unnatural accidental or deliberate outbreaks with potentially grave consequences.

Preparedness authorities, intelligence agencies, and scholars were aware before COVID-19 of the growing risks biological threats whether, natural, accidental, or deliberate in origin and the significant economic, humanitarian, and global security implications. Yet, we were not prepared.

Just weeks before SARS-CoV-2 emerged in Wuhan, the World Bank and World Health Organization forewarned in their 2019 World at Risk Report about the growing risk of a viral pandemic that could occur through accidental laboratory escape or intentional release after being engineered in a laboratory (WorldBank, 2019).

The definitive pathway of when, where, and how SARS-CoV-2 arose to trigger the COVID-19 pandemic remains elusive. The two prevailing hypotheses include, 1) Natural zoonotic spillover, or 2) inadvertent research associated accident. Both are plausible.

It is unfortunate that last Congress and the Administration did not authorize a COVID-19 bi-partisan commission to take stock of lessons learned, like the 9/11 Commission. Our nation deserves an objective, transparent after-action analysis to better understand, “what went right, what did not work, and what is needed to fix preparedness and response gaps.”

I am grateful the House of Representatives Select Subcommittee on the Coronavirus Pandemic has taken up the challenge of an after-action review.

After action lessons learned are an essential element of the preparedness cycle, especially at the congressional and executive branch levels. This is necessary to put in place new evidence-based policies, authorities, appropriations, and national strategies needed to prevent, prepare for, and respond to the next inevitable major epidemic or a pandemic.

Had such an after action been completed, I am confident the report would have concluded we were much better prepared for the emergence of SARS-CoV-2 than we would have been without the long-term support of infectious disease research and our high containment laboratory ecosystem.

Basic science and applied research with hazardous pathogens are essential for understanding, monitoring, and providing insights for the development of vaccines, therapeutics, and diagnostics. High containment laboratories are also the foundation of the response to emerging and remerging infectious diseases, regardless of source. These unique laboratories are needed to rapidly characterize new or reemerging pathogens which in-turn enables an evidence-base surge response.

The accelerated development of safe and effective COVID vaccines through Operation Warp Speed will go down in history as a tremendous success. But Operation Warp Speed would not have been possible without investments fundamental infectious disease research, advanced medical countermeasures research, development, and manufacturing technologies, as well as a commitment to improving regulatory science.

Operation Warp Speed provides lessons learned and is an exceptional bright spot in a sea of many COVID-19 response failures. Response failures demand further, objective investigation to enable new evidence-based preparedness and response policies for the future.

A bi-partisan COVID-19 commission is also necessary to enable an objective assessment free of conflicts of interests to attribute the most likely source of SARS-CoV-2. This is essential given the fact that definitive evidence has dissipated due to the Chinese Communist Party's (CCP) denial, deception, destruction, and obfuscation campaign.

If the CCP would have allowed a transparent, international, and collaborative outbreak investigation free of conflicts of interest starting in January 2020, the origin of SARS-CoV-2 could have been determined rapidly, whether from animals or a laboratory. It only required a few months to determine an intermediate animal source during the 2002-2003 SARS outbreak (Wang LF, 2007).

Since that is no longer possible, an objective bi-partisan assessment of COVID-19 origins through analysis of all available source information will provide insights for new policies needed to prevent community outbreaks, epidemics, or a pandemic.

Regardless, we already have enough information to know we must act to strengthen biosecurity at the animal, human, and environmental interface. Whether in the nature, but especially in laboratories worldwide.

My testimony will focus on the need to strengthen and harmonize biorisk management laboratory standards, norms, reporting, and transparency to reduce risks for laboratory workers and public safety worldwide. This will include a summary of the laboratory biorisk management framework in the United States and a discussion of recommendations to strengthen oversight of especially dangerous dual use enhanced pathogen research. Finally, I will provide my recommendations for consideration by the Committee.

Evolving Biorisk Management Framework in the United States:

The United States has multiple, overlapping policies and regulations that provide biosafety and biosecurity oversight for life science research with hazardous pathogens and toxins.

The following is summary of the biosafety and biosecurity policies and regulations in the United States, or events that led to the promulgation of a new policy or regulation. This review spans

from the 1975 Asilomar Conference on Recombinant DNA to the 2023 Report from the National Science Advisory Board for Biosecurity (NSABB).

This summary is provided to convey an historical context and show today's controversies surrounding especially dangerous dual use research is a long-standing, unresolved policy debate.

Asilomar Conference on Recombinant DNA, 1975

. In the 1970s, scientists were learning how to manipulate DNA through newly discovered recombinant technologies to unleash the power of genetic engineering. Although the benefits, risks, and ethical dilemmas of genetic engineering are understood today, that was not the case in 1975. At the time, scientists envisioned the potential benefits that genetic engineering would bring to society, but scientists themselves sounded the alarm about unknown risks to laboratory workers, the environment, and public safety.

Scientists called for a worldwide moratorium on this line of research until there was an agreement on how to proceed in a way that minimized risks. An International Congress on Recombinant DNA Molecules was held at the Asilomar Conference Center, California, in February 1975.

Conference attendees that consisted primarily of scientists and physicians, with limited public input, recommended that research involving recombinant DNA molecules could continue, but under stringent guidelines.

The NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)

 (NIH, NIH Guidelines for Research Involving Recombinant of Synthetic Nucleic Acid Molecules (NIH Guidelines), 2019). The foundational biosafety guidance documents are the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules (NIH Guidelines)* and the *NIH and CDC Biosafety in Microbiological and Biomedical Laboratories (BMDL*).

The NIH Guidelines were initially released in 1976 following the Asilomar conference. The guidelines specify the practices for safely constructing and handling recombinant nucleic acid molecules and synthetic nucleic acid molecules.

The NIH Guidelines focus on risk assessment, risk group classification of pathogens based on their ability to cause disease in humans and the availability of medical countermeasures, physical biological containment levels, laboratory practices, personal protective equipment, and occupational health.

All gain of function and genetic engineering research involves recombinant nucleic acid activities, and this research, if funded by the NIH, is subject to the *NIH Guidelines,* requiring review by local Institutional Biosafety Committees (NIH, 2019).

Biosafety in Microbiological and Biomedical Laboratories, 6th Edition (BMDL). The BMBL, initially released in 1984*,* describes the process of biological risk assessment, which enables the appropriate selection of microbiological practices, safety equipment, and facility safeguards that can prevent laboratory-associated infections.

Biosafety levels are described in Appendix 1 and the BMBL (CDC, 2020). There are 4 Biosafety Levels (BSL), 1) BSL-1; 2) BSL-2; 3) BSL 3; and 4) BSL-4 with BSL-4 being the highest. High containment laboratories described in this testimony consist of BSL-3 and BS-4.

Compliance with both the NIH Guidelines and the BMDL are voluntary. These guidelines are not regulations. However, both are considered the authoritative biosafety reference guidelines in the United States and are considered international gold standards. Federal funding may be contingent upon compliance with the guidelines. Guidance is updated regularly to account for scientific advances. Guidelines are easier to update compared to regulations and law.

The Federal Select Agent Program (FSAP) (CDC/USDA, 2021). The Antiterrorism and Effective Death Penalty Act of 1996 was passed following an incident where an individual inappropriately ordered plague strains from a supplier of biological agents and toxins after it was realized there was no legal mechanism to charge the person with a crime other than mail fraud. This led to the "Select Agent Rule" that regulated the transfer of a specified list of 38 biological agents and toxins at that time.

Congress legislated the *Federal Select Agent Regulation* as part of the Public Health Security and Bioterrorism Act of 2002 in response to the 2001 Anthrax letter attacks. The Department of Health and Human Services (DHHS) and Agriculture (USDA) manage and regulate the federal select agent program consisting of a prescribed list of sixty-eight biological agents and toxins that have the potential to pose a severe threat to public health and safety, animal or plant health, or animal or plant products. Individuals and institutions that possess, use, or transfer any select agent on the list must be registered with the select agent program, follow appropriate biosafety/biosecurity procedures, and undergo periodic inspections. Individuals must undergo periodic FBI (Federal Bureau of Investigation) background security risk assessment.

While the Select Agent Program addresses security and biosafety aspects of possession and use of the agents listed in the select agent program, federal select agent regulations do not apply to research information, including that obtained from dual use enhanced pathogen research, which the information itself could be used for malevolent purposes or potentially catastrophic if a laboratory acquired infection goes unnoticed.

Dual use research of concern, gain of function research of concern, and enhanced potential pandemic pathogen research will be discussed below.

2004 Biotechnology in the Age of Terrorism**.** The latest and ongoing reactionary phase began twenty years ago when the National Research Council released a report in 2004, "Biotechnology in the Age of Terrorism" (Fink G. R., 2004). This report is commonly recognized as the Fink Report and its findings and recommendations initiated an intense policy debate about how to govern dual use research in the life sciences.

This policy debate remains unresolved and intensified after COVID-19.

The Fink Report provided recommendations to the United States government that catalyzed the concept of Dual Use Research of Concern (DURC), and initiated deliberations about biosecurity implications for what is commonly referred today as dangerous enhanced pathogen research, gain of function research of concern (GOFROC), or enhanced potential pandemic pathogen (ePPP) research.

The Fink Report provided recommendations to mitigate biosecurity risks associated with the rapid advances in biotechnology, and how those same technologies and information essential for public health preparedness and biodefense could also be intentionally misused to cause harm - *The dual use research threat.*

The Fink report identified seven categories of experiments that constitute significant security risk and should not be performed without additional review and stringent oversight. The experiments of concern identified in 2004 are like the experimental categories of concern involving dual use enhanced pathogen research today. The seven categories of high-risk experiments include,

1. Research that demonstrates how to render a vaccine ineffective (human and animal vaccines)
2. Research that confers resistance to therapeutically useful antibiotics or antiviral agents (humans, animals, and plants)
3. Research that enhances the virulence of a pathogen or renders a non-pathogen virulent (human, animal, and plant)
4. Research that increases transmissibility of a pathogen within or between species.
5. Research that alters the host range of a pathogen (i.e., animal to human or vice versa).
6. Research that enables the evasion of diagnostic/detection modalities.
7. Research that enables the weaponization of a biological agent or toxin.

The National Science Advisory Board for Biosecurity (NSABB) (NSABB, 2023)**.** Shortly after the Fink Report, the White House established the National Science Advisory Board for Biosecurity (NSABB) in 2005. Congress subsequently authorized the NSABB as federal advisory

board that could be charged to assist the United States government (USG), upon request, to consider policy options needed to strengthen oversight of Dual Use Research of Concern (DURC) while minimizing impacts to scientific innovation. The NSABB published a seminal report in 2007, *"Proposed Framework for the Oversight of Dual Use Life Sciences Research: Strategies for Minimizing the Potential Misuse of Research Information"* (NSABB, 2007).

The NSABB provided twelve comprehensive reports since 2006 to the NIH on Dual Use Research of Concern, Synthetic Biology, and Gain of Function Research of Concern (NSABB, 2006-2017). NSABB reports for oversight of dual use of concern and gain of function research include,

1. *Proposed Framework for the Oversight of Dual Use Life Science Research (2007)*
2. *Plan for Strategic Outreach and Education on Dual Use Research Issues (2008)*
3. *Enhancing Responsible Science: Development of Codes of Conduct for Dual Use Research (2010)*
4. *Framework for Conducting Risk Benefit Analysis for Gain of Function Research (2015)*
5. *Recommendations for Evaluation of Proposed Gain of Function Research (2016)*
6. *Proposed Biosecurity Framework for the Future of Science (March 2023)*

2012 and 2014 Dual Use Research of Concern Policies

. The United States government did not act on the 2007 NSABB report, *"Proposed Framework for the Oversight of Dual Use Life Science Research"* until 2012, and then only in response to two controversial studies that generated novel, enhanced highly pathogenic avian influenza strains in the laboratory capable of airborne transmission in a mammalian animal model (Ron Fouchier, 2012) (Yoshihiro Kawaoka, 2012).

Public health, national security, and arms control professionals were concerned that explicit methodological details in the manuscripts could be misused by malevolent actors – nation state or terrorists – and constituted a dual use security risk.

Scientists engaged with these risky studies argued these studies were essential for public health and existing oversight provided by the NIH Guidelines and the BMBL were sufficient.

During NSABB deliberations, the NIH and NIAID Directors declared dangerous gain of function research were essential and outweighed the risks of an accidental or intentional pandemic (Anthony Fauci, 2011) (Fauci A. , 2012). The NIAID Director also acknowledged especially dangerous dual use enhanced pathogen research could be intentionally replicated and haphazardly performed in laboratories that lacked a culture of responsible science and rigorous bio-risks management controls (Fauci, 2012).

Dual Use Research of Concern (DURC) oversight policies were implemented in 2012 and 2014 as corrective actions to close security gaps (OSTP, 2012) (OSTP, 2014).

These two DURC policies have a limited scope and only involve fifteen specific pathogens or toxins, and seven categories of experiments like those described by the "Biotechnology in the Age of Terrorism" report. The DURC policies are security focused to reduce the likelihood that knowledge, information, products, or technologies emanating from research can be intentionally misused by malevolent actors to pose a risk to public health or national security.

2014 Moratorium on funding new gain of function research with potential pandemic pathogens. But just one month later, OSTP imposed a moratorium on gain of function research with Avian Influenza, SARS, and MERS in 2014 after a rash of significant laboratory biosafety incidents occurred in premier research laboratories in the United States (ObamaWhiteHouse, 2014).

During the moratorium, OSTP and NIH charged the NSABB to develop policy options for consideration by the OSTP and NSC to govern and oversee risky gain of function research. There were intense debates during the Board's deliberations.

Once again, scientists active in this line of research argued dangerous dual use enhanced pathogen research was essential for vaccine development and pandemic preparedness. They asserted the knowledge gained was essential for vaccine development and public health preparedness and outweighed the risks, even if a laboratory accident, albeit a low probability, might trigger a pandemic.

However, other scientists questioned the benefits for public health preparedness and together with biosecurity and arms control professionals argued the risks of laboratory accidents that could trigger a pandemic were too great (Cambridge_Working_Group, 2014).

The NSABB recommended that a small subset of risky research with potential pandemic pathogens could continue with restrictions. The federal advisory board proposed that the NIH and OSTP establish an additional independent multidisciplinary interagency review above the funding agency level.

The Board recommended additional oversight reviews must include rigorous benefit / risk analysis and ongoing oversight to mitigate risks. The Board felt it was essential that risks and benefits be quantified and rigorously resolved before federal agencies render a decision to proceed, or not, with proposed gain of function research of concern. The use of safer, alternative experimental approaches not requiring the generation of novel, dangerous viruses in the laboratory was encouraged by the board.

Public transparency into the review process was viewed by board members as an essential element needed to maintain public confidence and trust in this especially dangerous and controversial research.

The NSABB report, *Recommendations for the Evaluation and Oversight of Proposed Gain of Function Researc*h was provided to the NIH on May 24th, 2016 (NSABB, 2016).

Unfortunately, the term "*gain of function,"* a common experimental procedure that is safe when conducted in compliance with the NIH Guidelines and the BMBL, was used to describe "*dangerous enhanced pathogen research"* in the 2014 moratorium. The use of the term gain of function caused confusion then, and it continues to cause confusion today amongst scientists, policy makers, and the public.

The 2016 NSABB report adopted the term, "gain of function research of concern" to differentiate relatively safe gain of function from especially dangerous enhanced pathogen research.

In summary, the 2016 NSABB report concluded that only an exceedingly small subset of life science research should warrant additional review and oversight as involving "gain of function research of concern," or especially dangerous enhanced pathogen research.

2017 Pandemic Pathogen Care and Oversight Framework (P3C0). The OSTP "*Recommended Policy Guidance for Potential Pandemic Pathogen Care*" and the Department of Health and Human Services (HHS) "*Potential Pandemic Pathogen Care and Oversight Framework (P3C0)*", informed by the 2016 NSABB report, were adopted in January and December 2017, respectively (ObamaWhiteHouse, 2017) (DHHS, 2017). The gain of function moratorium imposed in 2014 was lifted (Collins, 2017).

Importantly, the P3CO framework moved away from the term "*gain of function*" to research that could generate "*enhanced potential pandemic pathogens (ePPP)*". An enhanced potential pandemic pathogen is defined as a *potential pandemic pathogen resulting from the enhancement of the transmissibility and/or virulence of a pathogen.*

A potential pandemic pathogen (PPP) is a pathogen that satisfies both of the following criteria:

1. *Likely highly transmissible and likely capable of wide and uncontrolled spread in human populations; and*
2. *Likely highly virulent and likely to cause significant morbidity or mortality in humans.*

An enhanced PPP is defined as a PPP resulting from the enhancement of the transmissibility and/or virulence of a pathogen.

To summarize, an ePPP or PPP is a novel, especially dangerous enhanced pathogen generated in the laboratory that has potential to spark a pandemic.

The P3CO Framework requires funding agencies to identify and refer high-risk research proposals that could be *"reasonably anticipated to create, transfer, or use enhanced*

potential pandemic pathogens" to a higher federal department level for an additional interagency, multisectoral review of associated risks and benefits, and other identified criteria.

This additional review and oversight were intended to capture research proposals that could potentially cause a pandemic if the information is misapplied or if laboratory generated pathogens with epidemic or pandemic potential accidentally – knowingly or unknowingly – escape from high containment laboratories.

It is critical to note that laboratory acquired infections are often not recognized until days or weeks later after the incident or exposure occurs, knowingly or unknowingly.

The 2017 P3CO Framework gained the most attention regarding governance of dangerous enhanced pathogen research after COVID-19 with potential implications for the origin of SARS-CoV-2.

2023 NSABB Recommendations. The NIH and OSTP again charged the NSABB in February 2022 to review DURC and P3CO policies while controversies swirling around COVID-19 origins supercharged the debate about dangerous dual use enhanced pathogen research.

The NSABB received input from federal department and agency representatives; research investigators and institutional compliance officials familiar with DURC and ePPP research; national security experts; professional and scientific societies; the publishing community; and public comments.

The NSABB through the NIH released a report in March 2023, "*Proposed Biosecurity Framework for the Future of Science*", that includes 12 findings and recommendations (NSABB, 2023).

Recommendations include,

1) Develop an integrated approach for oversight of research that raises significant biosafety and biosecurity concerns, including ePPP research and DURC
2) Expand the scope of ePPP research
3) Remove unnecessary blanket exclusions
4) Enhance institutional responsibility to include articulating specific roles, responsibilities, and expectations across the research review continuum, as well as strengthen, harmonize, and provide financial and technical resources for institutional compliance at all levels
5) Dedicate resources and personnel needed to provide comprehensive implementing directives, guidance, and a standard for risk benefit analysis for the entire research review continuum with provisions for ongoing oversight
6) Take steps to increase transparency in the review process, including sharing a summary of key determinants that informs ePPP research funding decisions
7) Adopt functional criteria for DURC and P3CO (not pathogen list based)

8) Require adoption and compliance by all federal departments and non-federally funded ePPP research in the U.S.
9) Require federal funding agencies supporting international research to comply with U.S. guidelines and standards and recommit to provide leadership to harmonize and strengthen international norms, standards, education, and training related to biosafety and biosecurity oversight of DURC and ePPP research

The expanded scope, or recommendation 2, is intended to clarify that additional federal department-level review is required for research that is reasonably anticipated to enhance the transmissibility and/or virulence of *any pathogen (i.e., PPPs and non-PPPs)* if the resulting pathogen is reasonably anticipated to exhibit the following characteristics that meet the definition of a PPP:

1. Likely moderately or highly transmissible and likely capable of wide and uncontrollable spread in human populations; and/or
2. Likely moderately or highly virulent and likely to cause significant morbidity and/or mortality in humans; And, in addition
3. Likely to pose a severe threat to public health, the capacity of public health systems to function, or national security.

To summarize, the expanded criteria describe the characteristics of viruses and diseases like SARS-CoV-2 and COVID-19.

Discussion:

Naturally occurring biological threats pose a risk to our health and national security. Globalization, population growth, urbanization, conflict, and other factors are creating conditions that favor the emergence and reemergence of infectious diseases.

The threat of unnatural (accidental and deliberate) outbreaks is growing, too.

Research with hazardous pathogens in high-containment laboratories using advanced technologies is enabling unprecedented scientific achievements around the world to benefit society. Infectious disease research and high containment laboratories are essential to our health security, biodefense, and pandemic preparedness.

But advanced technologies and information useful for biodefense and pandemic preparedness could intentionally be misapplied by malevolent actors or lead to accidental biocontainment breaches through inexperienced staff, inadequately maintained laboratories, failure to follow protocols, or failure to report and contain laboratory breaches – *the dual use research threat.*

It is important to note that almost all life science research with hazardous pathogens performed in high-containment laboratories can be accomplished safely and securely if all staff strictly adhere to biosafety and biosecurity guidelines, controls, best practices, and reporting of

accidents and near misses. But this requires leadership and strong institutional support grounded in responsible research and ethical norms.

Laboratory and institutional-level leadership are essential to instill a culture throughout the lab of accountability, responsibility, and ethical values that enables and promotes responsible science with a biosafety-first culture and transparency to report even the smallest of human errors, near misses, or potential biocontainment breaches.

Regrettably, ethical norms and value systems vary among countries and even across agencies and laboratories within countries. Not all nations and laboratories share strong institutional values and norms for biosafety and biosecurity, to include a biosafety-first culture that permits and encourages reporting of even the slightest of laboratory incidents, safety protocol deviations, and near misses by all laboratory staff. This is a significant challenge in autocratic regimes, countries, and laboratories that lack strong intuitional norms. Concerns about the lack of strong institutional norms in autocratic regimes were forewarned in 2017 prior to opening of the BSL-4 laboratory at the Wuhan Institute of Virology (Cyranoski, 2017).

Before COVID-19, construction of high-containment laboratories was steadily increasing. In the wake of COVID-19, new research agendas are accelerating high-containment laboratory expansion worldwide. Many are now realizing the scope, breadth, and risks of the global expansion of high-containment laboratories. Concerns about high-containment laboratory expansion are coupled to advancing, readily available dual-use technologies with uneven international laboratory biosafety and biosecurity standards and controls.

International guidelines and codes of conduct, effective international oversight institutions, and international governance standards and controls for especially dangerous dual-use research that could generate novel pathogens with potential for widespread human-to-human transmission have been absent until recently.

The World Health Organization released guidance in 2022, in response to COVID-19, "*The Global guidance framework for the responsible use of the life Sciences: mitigating biorisks and governing dual-use research".* The WHO guidelines aim to provide values and principles, tools, and mechanisms to support Member States establish their own guidelines and regulatory regimes (WHO, 2022).

The United States Biorisk Management Framework.

The United States has a comprehensive bio-risk management system that has evolved over several decades. Some assert we have the most comprehensive bio-risk management system in the world.

However, the United Kingdom and Canada are two countries that I believe have more effective systems largely because those two countries have mitigated the potential for organizational conflicts of interest by incorporating independent biosafety and biosecurity oversight from the funding agencies and institutions conducting the research (GAO, 2017).

Even though the U.S. biorisk management framework is comprehensive, it is fragmented simply because it has responsively evolved over four decades in reaction to new technologies, advancing science, new threats, new challenges, and lessons learned. The patchwork of governance policies and regulations depends on the source of funding, pathogens studied, specific oversight authority, and laboratory location.

This overlapping and fragmented oversight system is confusing for principal investigators and research institutions. This is a growing compliance and biosafety challenge that is increasing biosecurity risks.

For example, CDC and USDA regulate laboratories that handle a defined list of sixty-eight select agents (viruses, bacteria, and toxins), codified in law, and strictly regulated by the Federal Select Agent Program (FSAP). There are human pathogens, animal pathogens, and crossover pathogens that fall under regulations issued by either CDC, USDA, or both.

But regulations and law governing other, and often more transmissible, hazardous pathogens are absent.

Dual use ePPP research is governed by a 6-page policy, The P3CO Framework, that was adopted to aid federal funding decisions. Especially dangerous enhanced pathogen research is not highly regulated.

Although the P3CO Framework document was adequate at a strategic policy level as understood in 2017, the framework had significant implementation limitations, most were reported before COVID-19. Limitations include:

1. The policy was not accompanied by implementing directives that should have provided the following
    - Guidance documents with ePPP examples
    - Accompanying educational and training materials
    - Expectations for ongoing review at all levels
    - Standards for risk/benefit analysis
    - Expectations for transparency
    - Resources - funding, technical, and personnel – were not provided to effectively implement the P3CO Framework.

Not surprisingly, the Government Accountability Office and the HHS Office of Inspector General (OIG) reported deficiencies in HHS oversight of dual use enhanced pathogen research (GAO, 2023) (HHSOIG, 2023). Perhaps as a result, only three projects have been referred by the funding agency to the federal department level for additional review since 2017 under the P3CO Framework (Kuiken, 2022). It is unknown how many projects should have been forwarded by the funding agency for additional review in accordance with P3CO guidance. Once NIH recognized gain of function research of concern was encountered at the Wuhan Institute of

Virology, they should have made a reasonable notification to higher authorities highlighting the need for ongoing oversight.

On the other hand, the NIH Guidelines and the BMBL have been largely effective for the vast majority of infectious disease research with naturally occurring pathogens that does not involve dangerous dual use ePPP research despite the fragmented oversight system. But as described later, the frequency of laboratory accidents and incidents is significant indicating the need to harmonize and improve biosafety and biosecurity oversight and enhance transparency.

The NIH Guidelines and BMBL are flexible and can more readily adapt to changes required to keep pace with rapid scientific advances compared to regulations and law. Also, receipt of federal funding is contingent upon compliance. This contingency should be a strong incentive to comply with guidance for federally funded research.

But are compliance incentives tied to federal funding always effective in practice?

It took HHS over 3 years to publicly acknowledge compliance failures at the Wuhan Institute of Virology (WIV). HHS decided to debar the WIV in 2023 for failure to comply with sub-contractual requirements with their prime contractor to the NIH that included non-compliance with biosafety and biosecurity reporting requirements. Permitting unnecessarily dangerous research is not consistent with the NIH Guidelines and the BMBL (Wenstrup, 2023).

U.S. government biosafety guidelines, like the NIH Guidelines, BMBL, DURC, and P3CO only apply to federally funded research. This is also becoming a significant policy gap and risk due to an increasing proportion of biomedical research that is supported by non-federal sources, thus not governed by federal guidance and policies.

The Federal Select Agent Program is the only biosecurity and biosafety policy described in this review with legally binding authority that incorporates enforcement procedures codified by law. It is also the only policy that requires a personnel reliability requirement.

Personnel reliability qualification is not a requirement for especially dangerous dual use enhanced pathogen research unless the pathogen is a select agent.

The GAO has published several reports highlighting deficiencies with the Select Agent program judged against the program's legislative authority. But the Federal Select Agent Program has never been reviewed to determine what works well, and what constitutes unnecessary oversight providing a false sense of security.

Biosafety programs and oversight staff are vulnerable to undue pressure and conflicts of interests due to organizational placement within federal agencies and institutions that are evaluated by their research progress and publications, not core biosafety and biosecurity practices. To compound this problem, biosafety and biosecurity are overhead expenses that must compete against expanding indirect costs at the institutional level.

Finally, responsibility to verify compliance resides primarily at local institutional levels, but that is a strength if principal investigators, Institutional Biosafety Committees, biosafety/biosecurity authorities, Institutional Animal Care and Use Committees, Institutional Review Boards, and institutional leadership remain responsible and accountable for their actions. Responsible institutional compliance officials and institutions in the United States are conscientious about their responsibilities, even though there is considerable variability across institutions regarding oversight capabilities, capacities, and procedures.

Biosafety and biosecurity management practices and oversight are dependent upon "self-policing" by the research enterprise itself that funds and conducts the research. While self-policing with accountability standards has been somewhat effective over the years in the United States, the research enterprise must continually demonstrate that we are worthy of the public's trust.

It is now clear that unnecessarily dangerous research was conducted at the Wuhan Institute of Virology, some funded by U.S. federal agencies. Further, a few western scientists involved with this research were not forthcoming nor transparent about the extraordinary degree of unnecessarily dangerous research they managed in Wuhan laboratories without adequate biosafety oversight (OIG, 2023) (DHHS, 2023).

These facts are impacting public trust in the research enterprise and have raised legitimate questions about especially dangerous dual use ePPP research that cannot be ignored.

Although dual use ePPP research only represents an exceedingly small subset of all pathogen research, misapplication and inadvertent research associated accidents with dangerous enhanced pathogens have the potential to ignite community outbreaks, epidemics, or a pandemic.

Whether or not COVID-19 was caused by a laboratory accident, this policy gap must be closed to mitigate future risk and restore public trust.

The NSABB provided NIH and OSTP common sense recommendations that if implemented and resourced will strengthen oversight of dual use enhanced potential pandemic pathogen research without impacting life science innovation and pandemic preparedness.

The American Society for Microbiology initially urged swift adoption of the NSABB recommendations (ASM, 2023). However, the few scientists and institutions that are engaged in especially dangerous dual use ePPP research and their supporters are concerned about the potential for additional oversight burdens (Salzberg, 2023) (Goodrum, 2023). Institutional oversight concerns should be evaluated for merit and balanced against the United States Government's primary responsibility to protect public safety against an inadvertent or deliberate laboratory generated pandemic.

It is also important for everyone involved in this debate to avoid conflating that vast majority of relatively safe infectious disease research with the exceedingly small subset of especially dangerous dual use enhanced pathogen research.

The NSABB report recognized the essential role of principal investigators and institutions in the review and oversight continuum. Scientists and institutions are most familiar with their research and must have confidence that the review process will be fair, timely, efficient, and effective.

Principal investigators and institutions must also accept enhanced responsibility and accountability, including their responsibility to identify research that could fall under dual use ePPP guidelines. If so, they need to provide objective justification of benefits and verification that risks will be mitigated. This should include verification that alternative, safer experimental approaches are not feasible to address their basic science questions important to public health. They must also permit ongoing, stringent oversight of especially dangerous dual use research with public transparency and active engagement of local public health authorities.

It is essential to link bottom-up responsibility and accountability to top-down guidance, regulation, and oversight.

Laboratory Accidents. An evolving and learning biorisk management framework with harmonized biosafety, biosecurity, and reporting standards are essential for laboratory workers and public safety. Laboratory accidents, equipment failures, and facility breaches occur more frequently than the public realizes.

Laboratory accidents are rarely a threat to public health, until they are.

In 2019 alone, there were 219 reports of potential occupational exposures or release of biological pathogens or toxins outside of the primary barriers of biocontainment reported to the Federal Select Agent Program from laboratories in the United States. Of these 219 reported incidents, 1,076 individuals were referred to occupational health for medical assessments, and if needed diagnostics, prophylaxis, and treatment (USDA, 2019). It is important to note that publicly available data is only made available at an aggregate level.

Fortunately, none of the laboratory incidents resulted in illnesses, deaths, or transmission among workers or outside the laboratory. Most laboratory incidents are minor and rapidly mitigated and contained, but some can be serious threatening public health.

On the one hand, this is a testament that laboratories in the United States have the capability to report in a timely manner to oversight authorities, at least to the Select Agent Program.

But these data also show that laboratory mishaps or safety/security deviations occur frequently. Unfortunately, explicit, and immediate reporting requirements are limited to Select Agent registered laboratories and to the specific 68 select agents (viruses, bacteria, and toxins)

regulated by the Federal Select Agent Program in the United States. There are few other requirements for laboratories to timely report laboratory incidents and to share those incidents with the public.

The most complete publicly available information regarding laboratory accidents, laboratory acquired infections, equipment failures, laboratory breaches, and other mishaps other than Select Agents laboratories can be found from investigative journalists and others who use Freedom of Information Act procedures, often requiring legal action, to inform the public (Young, 2023). Many significant mishaps, lax reporting, and biosafety oversight failures have been revealed that otherwise would not be publicly available.

One especially troubling incident included an equipment malfunction with a confusing picture of oversight and incident reporting that occurred while working with an enhanced lethal pandemic potential Influenza strain approved by the P3CO (Young, 2023).

Most hazardous pathogen research is publicly funded and is not classified. The public has a right to know about research conducted in their community. Federal agencies and research laboratories have a responsibility to engage in meaningful dialogue with the public about these issues. Enhanced transparency is needed to better inform the public about the importance of infectious disease research and biosafety/biosecurity control measures.

Enhanced transparency is also required to enable biosafety research, thereby decreasing biosafety/biosecurity risks through public accountability and lessons learned. Congress should mandate laboratory incident reporting.

Common themes in most laboratory biosafety accidents include non-compliance with biosafety guidelines and best practices, equipment or facility failures, human error and bad judgement, needle sticks and animal bites, unchecked academic egos, and failure of management and leadership to prioritize a culture of safe, secure, and responsible science.

There are no international reporting systems for laboratory accidents or biocontainment breaches.

I am especially concerned that concealment and denial of laboratory accidents and containment breaches are common in autocratic regimens. Staff inside their laboratories along with local authorities may be afraid to report mistakes in fear of extreme admonishment. Once national leaders are appraised of laboratory and other facility failures, they are likely to do everything possible to protect the state and their hold on power.

Similar and related challenges are more likely to occur in any country that does not understand or embrace the need for strong, value-based institutions that are fully staffed by experienced personnel and resourced to carry out their mission safely and securely, including institutions that manage high containment laboratories. This is especially concerning with the global expansion of high containment laboratories.

Unique and highly specialized high containment laboratories are expensive to design and construct, and I submit even more expensive to operate, maintain, and sustain. All too often, resources needed to support operations, maintenance, and sustainment are an afterthought until it is too late.

I do not have direct experience with high containment laboratories in China, but I have colleagues who do. They will attest to the scientific acumen of their colleagues.

But many scientists and science funding agencies, including some in the United States, do not appreciate or take the time to fully understand the full spectrum of needs to achieve fully functional intuitions and the totality of resources needed to maintain and sustain safe and secure operations of specialized high containment laboratories.

Serious challenges, concerns, and deficiencies within China's high containment laboratories were reported by the former director of the BSL-4 laboratory suite at the Wuhan Institute of Virology and Co-Editor of the Journal of Biosafety and Biosecurity managed by the Chinese National Academy of Science (Zhiming, 2019).

Challenges included,

- Uneven biocontainment construction standards
- Inadequate biosafety equipment
- Neglected maintenance
- Insufficient operational funds
- Lack of specialized laboratory biosafety managers
- Lack of building engineers to operate highly specialized biocontainment laboratories
- Lack of biosafety training
- Inadequate harmonized biosafety standards
- Lax enforcement of biosafety regulations that included pathogen and biohazardous waste disposal

The author emphasized laboratory operational challenges are *"putting biosafety at risk"*. More startling, the author noted, *"Maintenance cost is generally neglected and several high-level BSLs have insufficient operational funds for routine yet vital processes. Due to the limited resources, some BSL-3 laboratories run on extremely minimal operational costs or in some cases none at all"* (Zhiming, 2019).

High Containment laboratories are complex facilities. It is common for senior executives at government agencies, universities, the private sector, and other organizations that host high containment laboratories within their larger Institutions to lack sufficient awareness of resources needed to operate, maintain, and sustain these unique, complex laboratories, even in the United States (LeDuc J. , 2020).

I suspect most senior executives have not considered the financial and moral liabilities that will impact their Institutions if an accidental laboratory breach under their management ignites a community outbreak, epidemic, or a pandemic. Even if it is a low probability, it must be considered in a post COVID-19 environment.

The Administration and Congress have several biosafety and biosecurity oversight policies to consider. But you now have an opportunity to work in a bi-partisan manner with the Administration to require implementation of common-sense recommendations to strengthen oversight and responsible governance of especially dangerous dual use enhanced pathogen research. Congress also has the opportunity to mandate a holistic review of the entire biorisk management framework. Modernization of the U.S. oversight system is essential for rapid life science advancements, as well as effective and efficient biosafety and biosecurity.

The goal is harmonized biosafety/biosecurity norms and standards, domestically and worldwide.

Recommendations. For this testimony, I will only try to address a limited number of the biosafety and biosecurity policy recommendations.

Recommendation 1. Strengthen responsible governance and oversight of dual use enhanced potential pathogen (ePPP) research***. Congress should act to ensure the Administration adopts, implements, and resources a revised policy to responsibly govern especially dangerous enhance pathogen research***.

Background for recommendation 1. The Administration and Congress must commission a larger, holistic review of the entire biorisk management framework. In the interim, Congress should require the Administration to responsibly strengthen governance and oversight of especially dangerous dual use enhanced pathogen research.

I want to emphasize my confidence that the United States government has the ability and resources to implement a revised policy to responsibly govern dual ePPP research without impeding life sciences innovation or the speed with which we can develop new pandemic preparedness tools and countermeasures. Implementation details requires further consultation with scientists, biosafety/biosecurity professionals, and meaningful public engagement.

The NSABB report provided 12 common sense recommendations for Administration and Congressional consideration.

But federal advisory boards do not make policy. The NSABB provides recommendations upon request by the NIH. Congress and the Administration make policy.

Any revised policy, to include retaining the status quo with the 2017 P3CO Framework, will require a comprehensive implementation directive, guidance, and resources (financial, personnel, and technical).

The NSABB report reflects input from stakeholders across the life sciences research community, public health, agriculture, scientific publishing community, government funding agencies, national security experts, and the public.

Still, OSTP published a request for information to obtain additional feedback on the NSABB report. OSTP is seeking feedback on the potential implications and burdens on the few scientists and institutions engaged in dual use enhanced pathogen research.

However, OSTP must also consider the greater importance of protecting the well-being of humans, animals, plants, and the environment from especially dangerous dual use research. Reducing the risks of accidental or deliberate creation of novel pathogens with epidemic or pandemic potential and their release is the primary responsibility of the United States government.

The general population of the United States has a fundamental interest in such protection. All Americans have the potential to be harmed if ePPP research increases pandemic risk, and they have neither consented to nor in most cases been informed of the risk, despite public dollars often funding this research. Given the potential for a dangerous pathogen to cross national borders, the global population also has a legitimate interest in such protections.

OSTP must keep this balance in mind and consider public safety concerns relative to the concerns of the few scientists and institutions engaged in this line of especially dangerous research.

Congress should mandate laboratory incident reporting for dual use ePPP research and all research with hazardous pathogens to enable biosafety lessons learned and enhanced public transparency.

Although the Administration can act without additional authorization, expansion of oversight to non-federally funded research will require legislation.

Congress and the Administration should also consider restricting the exceedingly small subset of dangerous dual use ePPP research to a single laboratory, the National Biodefense Analysis and Analysis Center (NBACC). NBACC was originally funded by Congress, designed, and constructed specifically to conduct threat and vulnerability assessment research at this single laboratory. Threat and vulnerability assessment research utilizes equivalent experimental approaches as dual use enhanced pathogen research.

This would significantly reduce biosafety/biosecurity risks and lessen the impact of additional oversight burdens on universities engaged on especially dangerous enhanced pathogen

research. This approach will also reduce liability risks on those few universities engaged in this line of risky research.

The dialogue surrounding hazardous pathogen research must move beyond unproductive arguments that conflate the vast majority of relatively safe infectious disease research with the exceedingly small subset of especially dangerous dual use ePPP research.

Only a few scientists and institutions are engaged with dangerous dual use ePPP research and many of their basic science questions related to public health can be accomplished with safer experimental alternatives. The dialogue around this topic should pivot to a strategy that incentivizes safer experimental strategies that minimizes or eliminates the need to generate novel dangerous pathogens in the laboratory.

Recommendation 2. Commission a comprehensive review and analysis of the United States Biorisk Management Framework

. Congress should direct the administration to commission an analysis and holistic review of the entire biorisk management framework. The goal is to harmonize biosafety and biosecurity oversight with agility to advance scientific advances while minimizing unnecessary or unproductive oversight/regulatory burdens on research institutions. This is long overdue and is needed to address growing and unproductive compliance challenges with the current fragmented system.

Background for recommendation 2. It was an important step when the NIH and OSTP initiated a review of DURC and the P3CO Framework and are now considering a revised policy, but that should not be the only review undertaken.

The United States has a comprehensive biorisk management framework to protect worker and public safety as well as national security interests while also permitting rapid scientific advances, but it is not perfect. Gaps, overlaps, and confusion with the current fragmented system are making compliance increasingly challenging for research institutions and increasing biosafety and biosecurity risks.

Today, scientific advances are accelerating faster than ever before and are outpacing our ability to implement effective and agile laboratory and biosafety guidelines and regulations.

Yet, policies and guidance are revised in a piecemeal fashion rather than taking stock of the entire biorisk framework. A review and analysis will find opportunities for efficiencies, reduce overlaps, close gaps and do so in a manner that better supports research institutions while keeping pace with scientific advances and decreasing risks.

Responsible universities and other research organizations have developed disciplined Institutional Review Boards and compliance offices despite the federal government's fragmented oversight system that spans across the federal interagency.

There is also no single, independent authority at the federal level that has responsibility and accountability for laboratory biosafety and biosecurity.

A comprehensive holistic review and analysis of the entire biorisk management framework is overdue. This is needed as a prerequisite to harmonize biosafety and biosecurity oversight in the United States.

Recommendation 3. Commission an analysis of alternatives to identify options and recommendations to establish an independent biosafety and biosecurity oversight framework. *Congress should direct the Administration to commission an independent analysis of alternatives and propose recommendations to establish an independent biosafety and biosecurity oversight framework independent of funding agency research decisions*

Background for recommendation 3. This recommendation is related to and a component of recommendation 1 and 2, but the importance of this recommendation warrants a separate item.

There are many options that could be considered to establish independent biosafety and biosecurity oversight, to include incorporating lessons learned from the United Kingdom and Canada.

Another option that has been proposed by others is the establishment of an independent Bio-Risk Management Federal Authority (Cosagrande, 2022).

A proposed Bio-Risk Management Authority or Framework could consolidate the patchwork of current biosafety and biosecurity policies and regulations. The new authority could also be responsible for continuously updating policies to keep pace with scientific advances and new threats, and funding biosafety research. The intent of this proposed authority is to improve the efficiency of the scientific enterprise by setting national biosafety and biosecurity standards, providing resources, conducting bio-risk management research, supporting the workforce, and harmonizing oversight of high containment laboratories.

However, caution must be exercised when considering establishing additional government organizations with attendant bureaucracy. But the proposal to establish an independent biosafety and biosecurity oversight authority, however implemented, is overdue. This concept should be fully analyzed to evaluate the feasibility of this recommendation.

An analysis of alternatives should include options on how to elevate Institutional Biosafety Committees (IBC) and biosafety professionals to be on par legally and functionally with the Intuitional Animal Care and Use Committees (IACUC) for laboratory animal care and the Institutional Review Boards (IRB) for clinical research.

The importance of having a single authority even if located within an existing but independent federal regulatory agency with a sole focus on, and responsibility for laboratory biosafety, biosecurity, personnel reliability, training, and bio-risk management with an emphasis on a laboratory accreditation with accountable local institutional capacities versus overly restrictive federal regulations cannot be overemphasized. This would also enhance transparency and enable a more meaningful way to engage with the public.

Recommendation 4. Elevate as a Diplomatic Priority Efforts to Establish an International Biorisk Management Framework*: Congress should direct the State Department to elevate international biosafety and biosecurity harmonization as a diplomatic priority with support of relevant department/agencies. The goal is to establish an International Biorisk Management Framework that harmonizes biosafety and biosecurity norms and standards worldwide.*

Background for recommendation 4. Although there are biorisk management challenges we must address domestically I am much more concerned about the global expansion of high containment laboratories and readily available advancing technology with uneven biosafety and biosecurity institutional norms, standards, and controls worldwide.

Administration and Congressional action may be limited to diplomacy on the international stage. That means we must update biosafety and biosecurity oversight domestically if we hope to be effective leading international diplomacy.

An effective international biorisk management framework is one that optimizes the benefits of pathogen research and mitigates risks, to decrease the possibility of unnatural, accidental, or deliberate biological events.

Harmonized international biosafety and biosecurity standards and norms with codes of conduct required to strengthen responsible pathogen research are lacking. International governance and safety controls for especially dangerous dual use enhanced pathogen research are absent.

The Department of State has established a diplomatic dialogue in collaboration with G-7 nations and ABSA International to promote harmonized international laboratory bio-risk management standards. Their efforts should be elevated at the Secretarial level as a science diplomacy priority, and appropriately resourced.

As a component of this effort, the Department of State is collaborating with USDA and a public private partnership consisting of veterinary high containment research laboratories, the Research Alliance for Veterinary Science and Biodefense BSL-3 Network (RAV3N) (Hunt, 2023).

The RAV3N coalition of laboratory partners are sharing best practices, supporting biosafety research, and preparing surge response plans for transboundary infectious disease crises. Their public private coalition, that includes an international veterinary high containment laboratory, is a best practice that should be encouraged and resourced for extension to other high

containment laboratories, whether supporting human, animal, or plant infectious disease research and diagnostics.

Biosafety and Biosecurity diplomacy will require effective international collaborations, agreements, and the development of harmonized national legislative regimes appropriate to the life sciences.

Leadership is essential and leadership starts at the laboratory level, worldwide.

International agreements must include emphasis on scientific and biosafety leadership at the laboratory and institutional level. It is necessary to build a culture of accountability and responsibility from the bottom-up. Promoting and supporting effective leadership at the laboratory and institutional level, mentoring next-generation scientists, and elevating the profession of biosafety scientists are essential to provide effective biosafety and biosecurity assurances to mitigate risks. Leadership and a culture of safe, secure, and responsible science cannot be legislated. It requires leadership and mentorship at institutional levels worldwide.

Bottom-up responsibility and accountability must be coupled to top-down national guidance and regulation.

Due to the growing scientific curiosity of especially dangerous enhanced pathogen research worldwide, it is imperative that member states enact effective legislation to govern and strictly regulate especially dangerous dual use enhanced pathogen research, including the United States.

The recently released guidance from WHO provides guidance for member states to establish biorisk management systems and governance of dangerous dual use research.

All member states that manage high-containment laboratories and hazardous pathogen research are responsible for establishing bio-risk management legislation and guidelines with resource provision to enable effective institutional norms. Member states must ensure their laboratories operate with a culture of biosafety-first, responsible science, and transparency with independent oversight. Member states also have a responsibility to ensure operations and maintenance of high containment laboratories are adequately resourced and staffed with trained, experienced personnel, with a commitment to sustainment.

Continued international scientific collaboration and international development are also essential, but how we pursue such collaborations is equally important.

Unnecessarily dangerous dual-use research performed in international laboratories without adequate oversight funded by the United States government, directly or indirectly, must be avoided (GAO, 2023) (HHSOIG, 2023). The United States through federally funded research grants and cooperative agreements must avoid naïve, reckless sharing of advanced dual-use technology and expertise (Jacobsen, 2021).

The United States has an opportunity and leadership responsibility to galvanize work through diplomacy toward harmonized international biosafety and biosecurity standards, controls, reporting, and mentorship needed to achieve responsible, safe, secure, and transparent pathogen research worldwide.

Recommendation 5. Establish a National Strategy for High Containment Laboratories in the United States. *Congress should direct the Administration to develop a national strategy that includes implementation, operations, and sustainment plans for all high containment research laboratories in the United States that support human, animal, plant infectious disease research. The plan should include a needs assessment for national laboratory capacity.*

Background for recommendation 5. The GAO has repeatedly highlighted deficiencies with federal oversight of biosafety, biosecurity, and high containment laboratories.

An overarching gap is the lack of a coordinated national strategy for high containment laboratory oversight. This gap was first reported in 2009 (GAO, 2009). Unfortunately, federal agencies have not taken sufficient action to address this and other GAO and Congressional concerns.

Specifically, GAO reported no federal entity responsible for the planning and oversight of high containment laboratories. Biosafety and biosecurity incidents occur at the laboratory level.

Laboratories and Institutions would benefit by having a comprehensive national strategy that includes critical elements of operations, maintenance, sustainment, and uniform timely laboratory incident reporting guidance. The plan needs to provide guidance and incentives for networking opportunities that go beyond the research mission. This recommendation is a component of, or complimentary to recommendations 2, 3, and 4.

Laboratory expansion accelerated after the 2001 Anthrax letter attacks, but the number, capacity, and specific biocontainment laboratory requirements were not based on a needs assessment tied to a coordinated government-wide plan. Without a needs assessment even 20 years later, there is limited ability to determine if we have sufficient capacity to meet the national infectious disease mission.

Alternatively, it is worth considering whether the federal government and non-federal institutions built too much capacity, therefore making it more challenging to sustain laboratories and increasing biosafety and security risks.

GAO also reported there are insufficient standards for design, construction, operations, maintenance, and sustainment other than guidance offered by the Biosafety in Microbiological and Biomedical Laboratories (BMBL). There are also limited standards to assess whether design

and construction achieved desired goals which would be helpful as laboratories constructed 10-15 years earlier need renovation and upgrades.

Universities that constructed high containment labs, either with federal fund or state funds, or self-funded, are challenged by exceedingly high operations, maintenance, and sustainment costs that are not fully covered by research sponsors, including federal research sponsors. Some report significant financial losses that are jeopardizing the integrity of the medical and public health, as well as agricultural biodefense laboratories that have their own unique challenges (LeDuc J. , 2020).

These are critical issues, especially in light growing awareness of the frequency of laboratory accidents, equipment failures, or biocontainment breaches.

One goal of a high containment laboratory strategy is an integrated biocontainment laboratory network, implementation plan, and business model that links and optimally utilizes all federal and non-federal high containment laboratories, scientific expertise, biosafety professionals, and building engineers in a distributed, network system. The plan must address operations, maintenance, and sustainment costs.

The strategy must include plans for uniform reporting and sharing of laboratory incidents to enable biosafety lessons learned and enhanced public transparency. Federal guidance and regulations must incentivize high containment laboratories and federal agencies to move beyond a culture of secrecy to open communication with the public.

Public health and national security authorities need to have assurances that we have the right high containment laboratory capacity and plans to meet mission needs, safely and securely. Laboratory directors must do more to educate the public in their community about the importance of their research and research operations. Finally, the public must have confidence that our high containment laboratories will have the resources needed to operate safely and securely without unnecessary risks for their community, or beyond their community.

Conclusion.

I am concerned that COVID-19'S demoralizing experience may trigger malevolent actors to pursue and intentionally use dangerous pathogens for the foreseeable future to achieve their goals and the increasing probability of laboratory accidents or biocontainment breaches with potentially grave consequences.

I am also concerned about wanning public trust in naturally occurring infectious disease and toxin research and our high containment laboratory ecosystem. Our infectious disease high containment research enterprise is essential for public health preparedness, national security, and global health security.

The vast majority of infectious disease high containment research is relative safe when conducted in compliance with NIH Guidelines and the BMBL. However, the exceedingly small subset of especially dangerous dual use enhanced pathogen research has the potential to trigger a pandemic, accidentally or deliberately.

Congress should require the Administration to urgently revise policies governing especially dangerous dual use research that includes comprehensive implementation plans with resources, and additional appropriations as needed. Congress should monitor implementation progress through its oversight role.

The Administration and Congress should also establish incentives to move beyond the exaggerated need to generate dangerous novel pathogens in the laboratory. Life science funding agencies can move this debate forward on a productive path by funding safer alternatives rather than encouraging ePPP research.

Until then, I want to emphasize, once again, my confidence that the United States has the capability and resources to implement a revised dual use ePPP policy without impeding life sciences innovation or the speed with which we can develop new pandemic preparedness tools and countermeasures.

I must also emphasis that effective implementation of a revised policy, even if it is the status quo, will require resourcing – financial, technical, and personnel.

Further, it is essential that Members of Congress and federal agencies, especially those in life science that lack security awareness and a security culture, obtain an accurate picture of the threat landscape (Haines, 2023).

Life science federal agencies and university scientists can no longer ignore national security implications of advanced dual use research, along with inadvertent or overt technology transfer and deemed export of dual use technologies and expertise.

We face a growing risk from unintentional laboratory accidents due to the global expansion of high containment laboratories and ready access to advanced dual use technologies and expertise worldwide without harmonized international biorisk management norms, standards and controls.

As the former commander of a high containment laboratory, I cannot emphasize enough the need to prioritize and properly fund laboratory biosafety, biosecurity, operations, maintenance, and support for strong institutional norms worldwide. That means funding biosafety and supporting ongoing operations and maintenance, as well as resources to develop, train, and hire skilled biosafety professionals and high containment building engineers.

Responsible universities and research institutions have worked hard to build exemplary local institutional biosafety practices and compliance structures. However, instead of having to

compete against expanding overhead requirements and other indirect costs at institutional levels, biosafety should be funded directly.

Congress can support the sharing of best practices and enhancement of institutional responsibility by treating biosafety as a distinct and valuable operational component that each institution must be able to resource and staff by requiring line-item budget support from federal and other funding sources.

Further, federal guidelines and regulations governing research with potentially hazardous pathogens and select agents must encourage and facilitate maximal transparency with the public about laboratory operations, including laboratory accidents and near misses. This information is also required for biosafety research to better understand how to mitigate risks.

Congress should mandate enhanced public transparency and rigorous biosafety lessons learned.

High containment laboratory directors must collaborate closely with their local communities to maintain public trust about the importance of their research and their commitment to laboratory biosafety and biosecurity.

It is our shared responsibility to reduce the risk of deadly accidents, especially when the United States is viewed around the world as a model for the biosafety and biosecurity practices. This is particularly important after the pandemic because research agendas in the wake of COVID-19 are accelerating high containment laboratory expansion plans worldwide.

Congress must exercise oversight responsibility to ensure the Administration, and future Administrations, take a more active diplomatic approach to promote and galvanize international initiatives needed to harmonize biosafety and biosecurity standards, controls, and norms worldwide. This is long overdue.

Congress must act to implement a holistic review of the entire biorisks management framework in the United States. The biorisks management oversight framework must be modernized. Congressional action on this and the other four recommendations are essential for rapid life science advancements, effective and efficient biosafety and biosecurity.

The goal is harmonized biosafety/biosecurity norms and standards, domestically and worldwide.

Scientists, policy makers, and legislators have a dilemma and should ask themselves and their colleagues the following 2 questions.

“Can government policies, guidance, and regulations governing hazardous pathogen research keep pace with rapid scientific advances, affordable and readily accessible technologies, global

expansion of high containment laboratories, and scientists well-meaning intent to push the boundaries of knowledge through dual use enhanced pathogen research"?

"Can we also keep pace with those who choose to misuse knowledge and advanced dual use biotechnologies"?

Thank you for the opportunity to appear before the Committee today. I look forward to answering your questions.

Appendix 1. Laboratory Biosafety Levels.

Laboratory biosafety describes the application of specific practices, safety equipment, and specialty designed laboratories to create safe environments within and outside of the laboratory to enable research with dangerous pathogens and toxins. There are four biosafety levels that are applied to activities performed in laboratories in ascending order of containment based on the degree of risk (NIH, 2011). Biosafety Level-4 (BSL-4) is the highest. In the United States, the Biosafety in Microbiological and Laboratory Guidelines prescribe requirements for each level of biocontainment for the four biological safety designations, 1) BSL-1, 2) BSL-2, 3) BSL-3, and 4) BSL-4 (CDC, Biosafety in Microbiological and Biomedical Laboratories (BMDL) 6th Edition, 2020). Each biological safety level has specially defined building design, construction, equipment, safety protocols, safety practices, personnel training, and other requirements to work with infectious and virulent pathogens and other biological hazards to protect workers and the

environment. Pathogens and toxins regulated by the Federal Select Agent list require additional security and personnel reliability compliance measures (CDC-USDA, 2020).

There are two additional designations within the four biosafety levels. The first is an additional designation for housing and working with research animals in biocontainment. For example, if the biocontainment facility is designed to accommodate research animals in BSL-3 laboratories, then the designation is called Animal Biosafety Level-3 (ABSL-3). Most high containment animal research laboratories that support public health and medical research accommodate only small animals, such as rodents and non-human primates. The second additional designation is unique to agriculture biosecurity, Biosafety Level-3 Agriculture (BSL-3Ag).

BSL-3Ag high containment facility, equipment, and personnel standards build upon BSL-3 minimum requirements and includes almost all features required for BSL-4 facilities when working with high consequence livestock animal disease pathogens, such as Foot and Mouth Disease, African Swine Fever, and others (Kozlovac, 2007). Research laboratory risk assessment criteria for agriculture are different than those for public health and place more focus on biocontainment and environmental protection in addition to worker safety, since the primary concern is the potential economic impact on agricultural species, and the international trade implications of a disease outbreak that could occur because of a laboratory accident and/or biocontainment breach. Research and diagnostic work involving high consequence agriculture pathogens have the highest economic consequence to the animal health status of the United States, and requires BSL-3Ag, the highest level for agriculture biocontainment. BSL-3 Ag facilities must be designed, constructed, and operated as primary containment barriers and allow work with large animals and wildlife, such as cattle, swine, poultry, horses, buffalo, deer, nil guy, camels, etc.

Bibliography

ABSA. (2022, February 11). *ABSA Interntional Laboratory Accreditation Program*. Retrieved from ABSA International, The Association of Biosafety and Biosecurity: https://absa.org/lab-accred/?gclid=EAIaIQobChMIkcbDvv739QIVEo3ICh2CTAdIEAAYASAAEgLdn_D_BwE

Anthony Fauci, G. N. (2011, December 20). *A flu virus risk worth taking*. Retrieved from Washington Post: https://www.washingtonpost.com/opinions/a-flu-virus-risk-worth-taking/2011/12/30/gIQAM9sNRP_story.html

ASM. (2023, Jan 20). *American Society for Microbiology*. Retrieved from ASM comments NSABB's proposed Biosecurity Oversight Framework: https://asm.org/Press-Releases/2023/January/ASM-Commends-NSABB-Report

ASM. (2023, January 20). *ASM Commends the NSABB Proposed Biosecurty Framework*. Retrieved from The American Society for Microbiology: https://asm.org/Press-Releases/2023/January/ASM-Commends-NSABB-Report

Cambridge_Working_Group. (2014, July 14). *The Cambridge Working Group consensus statement on the creatrion of potential pandemic pathogens*. Retrieved from The Cambridge Working Group: http://www.cambridgeworkinggroup.org/

CDC. (2020, November 17). *Biosafety in Microbial and Biomedical Laboratories (BMDL) 6th Edition*. Retrieved June 1, 2021, from https://www.cdc.gov/labs/BMBL.html

CDC. (2020, November 17). *Biosafety in Microbiological and Biomedical Laboratories (BMDL) 6th Edition*. Retrieved from Centers for Disease Control and Prevention: https://www.cdc.gov/labs/BMBL.html

CDC. (2021, May 14). Retrieved June 1, 2021, from https://www.selectagents.gov/

CDC/USDA. (2021). *CDC USDA Federal Select Agent Program*. Retrieved from Select Agents: https://www.selectagents.gov/index.htm

CDC-USDA. (2020, August 27). *Federal Select Agent Program*. Retrieved from eFSAP Resouce Center: https://www.selectagents.gov/efsap/index.htm

Collins, F. (2017, December 19). *NIH Lifts Funding Pause on Gain of Function Research*. Retrieved from National Institutes of Health: https://www.nih.gov/about-nih/who-we-are/nih-director/statements/nih-lifts-funding-pause-gain-function-research

Cosagrande, R. (2022, February 9). Managing Director, Gryphon Scientific. (G. W. Parker, Interviewer)

Cyranoski, D. (2017, February 23). *Inside the Chinese lab poised to study world's most dangerous pathogens*. Retrieved from Nature: https://www.nature.com/articles/nature.2017.21487

DHHS. (2012, March). Retrieved June 1, 2021, from https://osp.od.nih.gov/biotechnology/dual-use-research-of-concern/

DHHS. (2014, September 24). Retrieved June 1, 2021, from https://www.phe.gov/s3/dualuse/Documents/durc-policy.pdf

DHHS. (2017, December). *Framework for Guiding Funding Decisions about Proposed Research Involving Enhanced Potential Pandemic Pathogens*. Retrieved from Department of Health and Human Services / Assistant Secretary for Preparedness and Response: https://www.phe.gov/s3/dualuse/Documents/P3CO.pdf

DHHS. (2023, July 17). *Action Referral Memorandum for Wuhan Institute of Virology (WIV)*. Retrieved from United States House of Representatives Oversight Committee: https://oversight.house.gov/wp-content/uploads/2023/07/Notice-Memo.pdf

Fauci. (2012, October 9). *Research on Highly Pathogenic H5N1 Influenza Virus: The Way Forward*. Retrieved from American Society for Microbiology: https://journals.asm.org/doi/10.1128/mbio.00359-12

Fauci, A. (2012, Sept-Oct). *Research on highly pathogenic H5N1 Influenza Virus: The way forward*. Retrieved July 21, 2021, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3484390/

Fink. (2004). *Biotechnology Research in the Age of Terrrorism*. Retrieved from National Research Council: https://nap.nationalacademies.org/catalog/10827/biotechnology-research-in-an-age-of-terrorism

Fink, G. R. (2004). *Biotechnology in the Age of Terrorims*. Retrieved from The National Academies in Science, Engineering, and Medicine:

https://nap.nationalacademies.org/catalog/10827/biotechnology-research-in-an-age-of-terrorism
GAO. (2009, September 21). *High containment laboratories: national strateyg for oversigtht is needed*. Retrieved from Government Accountaility Office: https://www.gao.gov/products/gao-09-574
GAO. (2017, October). *High Containment Laboratories: Coordinated Actions Needed to Enhance the Select Agent Program's Oversight of Hazardous Pathogens*. Retrieved from United States Government Accountability Office: https://www.gao.gov/assets/gao-18-145.pdf
GAO. (2023, January). *HHS Could Improve Oversight of Research Involving Enhanced Potential Pandemic Pathogens*. Retrieved from Government Accountability Office: https://www.gao.gov/assets/gao-23-105455.pdf
GAO. (2023, June). *NIH Could Take Additional Actions to Manage Risks Involving Foreign Subrecipients* . Retrieved from Government Accountability Office: https://www.gao.gov/assets/gao-23-106119.pdf
Goodrum, A. L. (2023, January 26). *Virology under the microscope: A call for rational discourse*. Retrieved from Journal of Virology: https://journals.asm.org/doi/10.1128/jvi.00089-23
Haines, A. (2023, February 6). *Annual Threat Assessment of the United States Inteligence Community*. Retrieved from Office of the Director of National Intelligence: https://www.odni.gov/files/ODNI/documents/assessments/ATA-2023-Unclassified-Report.pdf
Herfst S, S. E. (2012, June 22). *Airborne transmission of influenza A/H5N1 virus between ferrets.* Retrieved from Science: https://www.science.org/doi/10.1126/science.1213362
HHSOIG. (2023, January 25). *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*. Retrieved from Department of Heath and Human Services Office of the Inspector General: https://oig.hhs.gov/oas/reports/region5/52100025.asp
Hunt, C. L. (2023, September). *The Research Alliance for Veterinary Science and Biodefense BSL-3 Network: Report on Network origins and phase I activities*. Retrieved from Antiviral Research: https://doi.org/10.1016/j.antiviral.2023.105693
Inglesby, M. L. (2018, February 17). *The U.S. is funding dangerous research it does not want you to know about*. Retrieved from Washington Post: https://www.washingtonpost.com/opinions/the-us-is-funding-dangerous-experiments-it-doesnt-want-you-to-know-about/2019/02/27/5f60e934-38ae-11e9-a2cd-307b06d0257b_story.html
Jacobsen, R. (2021, June 29). *Inside the risky bat-virus engineering that links America to Wuhan*. Retrieved from MIT Technology Review: https://www.technologyreview.com/2021/06/29/1027290/gain-of-function-risky-bat-virus-engineering-links-america-to-wuhan/
Kozlovac, R. H. (2007). Biosafety Levels for Animal Agriculture Pathogens. *Applied Biosafety*, 168-174.
Kuiken, T. (2022, May 26). *Oversight of Gain of Function Research with Pathogens: Issues for Congress*. Retrieved from Congressional Research Service: https://crsreports.congress.gov/product/pdf/R/R47114

LeDuc, J. (2020). Biocontainment Laboratories: A Critical Component of the U.S. Bioeconomy in Need of Attention. *Health Security*, 61-66.

LeDuc, J. (2020, February 17). *Biocontainment laboratories: A critical component of the US bioeconomy in need of attention*. Retrieved from Health Security: https://www.liebertpub.com/doi/10.1089/hs.2020.0002

Masaki Imai, T. W. (2012, May 2). *Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets*. Retrieved from Nature: https://www.nature.com/articles/nature10831

NAS. (2004). *Biotechnology Research in the Age of Terrorism*. Retrieved June 1, 2021, from https://www.nap.edu/catalog/10827/biotechnology-research-in-an-age-of-terrorism

NIH. (2011, May 12). *Biosafety Labs*. Retrieved from National Institutes of Allergy and Infectious Diseases: https://www.niaid.nih.gov/research/biodefense-biosafety-labs

NIH. (2019). Retrieved from NIH GUIDELINES FOR RESEARCH INVOLVING RECOMBINANT OR SYNTHETIC NUCLEIC ACID MOLECULES (NIH GUIDELINES): https://osp.od.nih.gov/wp-content/uploads/2019_NIH_Guidelines.htm

NIH. (2019, 2019). *NIH Guidelines for Research Involving Recombinant of Synthetic Nucleic Acid Molecules (NIH Guidelines)*. Retrieved from National Institutes of Health Office of Science Policy: https://osp.od.nih.gov/wp-content/uploads/NIH_Guidelines.pdf

NSABB. (2006-2017). *Natinal Science Advisory Board for Biosecurity*. Retrieved July 22, 2021, from https://osp.od.nih.gov/biotechnology/national-science-advisory-board-for-biosecurity-nsabb/#reports_recommendations

NSABB. (2007, June). *Proposed Framework for the Oversight of Dual Use Life Sciences Reserach: Strategues to Minimizing the Potential Misuses of Research Information*. Retrieved from National Science Advisory Board for Biosecurity: https://osp.od.nih.gov/wp-content/uploads/Proposed-Oversight-Framework-for-Dual-Use-Research.pdf

NSABB. (2016, May). *Recommendations for the evaluation and oversight of proposed gain of function research*. Retrieved June 1, 2021, from https://osp.od.nih.gov/wp-content/uploads/2016/06/NSABB_Final_Report_Recommendations_Evaluation_Oversight_Proposed_Gain_of_Function_Research.pdf

NSABB. (2016, May). *Recommendations for the Evaluation and Oversight of Proposed Gain of Function Research* . Retrieved from National Science Advisory Board for Biosecurity: https://osp.od.nih.gov/wp-content/uploads/2016/06/NSABB_Final_Report_Recommendations_Evaluation_Oversight_Proposed_Gain_of_Function_Research.pdf

NSABB. (2023). *National Science Advisory Board for Biosecurity (NSABB)*. Retrieved from National Institutes of Health Office of Science Policy: https://osp.od.nih.gov/policies/national-science-advisory-board-for-biosecurity-nsabb/

NSABB. (2023, March). *Proposed Biosecurity Oversight Framework for the Future of Science*. Retrieved from Naitonal Science Advisory Board for Biosecurity: https://osp.od.nih.gov/wp-content/uploads/2023/03/NSABB-Final-Report-Proposed-Biosecurity-Oversight-Framework-for-the-Future-of-Science.pdf

NSABB. (2023, March). *PROPOSED BIOSECURITY OVERSIGHT FRAMEWORK FOR THE FUTURE OF SCIENCE*. Retrieved from National Science Advisory Board for Biosecurity:

https://osp.od.nih.gov/wp-content/uploads/2023/03/NSABB-Final-Report-Proposed-Biosecurity-Oversight-Framework-for-the-Future-of-Science.pdf

ObamaWhiteHouse. (2014, October 17). *Doing Diligence to Assess the Risks and Benefits of Life Sciences Gain-of-Function Research*. Retrieved from Obama White House (Archives): https://obamawhitehouse.archives.gov/blog/2014/10/17/doing-diligence-assess-risks-and-benefits-life-sciences-gain-function-researcH

ObamaWhiteHouse. (2017, January 9). *Recommended Policy Guidance for Potential Pandemic Pathogen Care and Oversight*. Retrieved from Obama White House (Archive): https://obamawhitehouse.archives.gov/blog/2017/01/09/recommended-policy-guidance-potential-pandemic-pathogen-care-and-oversight

OIG. (2023, January 25). *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*. Retrieved from Department of Health and Human Services Office of the Inspector General: https://oig.hhs.gov/oas/reports/region5/52100025.asp

OSTP. (2012). *United States Government Policy for Oversight of Life Science Dual Use Reserch of Concern*. Retrieved from Departmenr of Health and Human Services / Assistant Secretary for Preparedness and Response: https://www.phe.gov/s3/dualuse/documents/us-policy-durc-032812.pdf

OSTP. (2014, September 24). *United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern*. Retrieved from Department of Health and Human Services / Assistant Secretary for Preparedness and Response: https://www.phe.gov/s3/dualuse/documents/durc-policy.pdf

OSTP. (2017, January 9). *Recommended Policy Guidance for Potential Pandemic Pathogens Care and Oversight*. Retrieved June 1, 2021, from https://obamawhitehouse.archives.gov/blog/2017/01/09/recommended-policy-guidance-potential-pandemic-pathogen-care-and-oversight

Ron Fouchier, S. H. (2012). Airborne transmission of influenza A/H5N1 virus between ferrets. *Science*, 1534-41.

Salzberg, S. (2023, February 6). *Virologists object to any new restrictions on dangerous gain of function resarch*. Retrieved from Forbes: https://www.forbes.com/sites/stevensalzberg/2023/02/06/experts-recommend-new-limits-on-dangerous-gain-of-function-research-now-what/?sh=429805cb21bd

USDA, C. &. (2019). *2019 Annual Report of the Federal Select Agent Program*. Retrieved July 23, 2021, from https://www.selectagents.gov/resources/publications/docs/FSAP_Annual_Report_2019_508.pdf

Wang LF, B. T. (2007). *Bats, Civets and the Emergence of SARS*. Retrieved from .Wildlife and Emerging Zoonotic Diseases: The Biology, Circumstances and Consequences of Cross-Species Transmission. Current Topics in Microbiology and Immunology: https://doi.org/10.1007/978-3-540-70962-6_13

Wenstrup, B. (2023, September 20). *Wenstrup Issues Statement After Wuhan Institute of Virology Formal Debarment*. Retrieved from House Select Subcommittee on the

Coronvirus Pandemic: https://oversight.house.gov/release/wenstrup-issues-statement-after-wuhan-institute-of-virology-formal-debarment/

WHO. (2022, September 13). *Global guidance framework for use of the life sciences: mitigating biorisks and governing dual-use research*. Retrieved from The World Health Organization: https://www.who.int/publications/i/item/9789240056107

WorldBank. (2019, September). *World At Risk: Annual Report on Global Pandemic Preparedness for Health Emergencies*. Retrieved from World Health Organization: https://apps.who.int/gpmb/assets/annual_report/GPMB_annualreport_2019.pdf

Yoshihiro Kawaoka, M. I. (2012). Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets. *Nature*, 420-428.

Young, A. (2023, April 12). *Lab-created bird flu virus accident shows lax oversight of risky 'gain of function' research*. Retrieved from USA Today: https://www.usatoday.com/story/opinion/2023/04/11/lab-leak-accident-h-5-n-1-virus-avian-flu-experiment/11354399002/

Young, A. (2023). *Pandoras Gamble: Lab leadks, pandemics, and a world at risk.* New York: Hatchet Book Group.

Zhiming, Y. (2019, September). *Current status and future challenges of high-level biosafety laboratories in China*. Retrieved from Journal of Biosafet and Biosecurity: https://pubmed.ncbi.nlm.nih.gov/32501434/