CLADE X
A PANDEMIC EXERCISE

IMPLICATIONS OF CLADE X FOR NATIONAL POLICY

To prevent or reduce the catastrophic outcomes possible in future pandemics like Clade X, the Johns Hopkins Center for Health Security recommends that the United States commit to these 6 strategic policy goals:

1. **Capability to produce new vaccines and drugs for novel pathogens within months not years**.

To prevent a serious epidemic of a novel pathogen from becoming a pandemic or a catastrophic biological event, we need the ability to have a national population-level supply of effective and safe medical countermeasures within a few months of event recognition. The US government has dedicated substantial resources and attention to developing and stockpiling medical countermeasures for a range of biological threats. But we don't have the capacity to rapidly develop large quantities of vaccines and medicines for new pandemic threats that have not already been addressed. The WHO has said the world needs to be ready for a new and unknown Disease X, but neither the United States nor any other country has a system in place now with the capacity to rapidly develop vaccines or medicines for such a disease.

Even for pandemic diseases we know well, like influenza, we are not likely to have enough vaccine to make a difference before the pandemic naturally begins to wane; and for novel diseases or diseases with no previously developed vaccines, the average timeline for vaccine development has been a decade or more. Fortunately, advances in biological science and biotechnology should enable rapid countermeasure development and administration in the future if that goal is pursued. Recent developments in synthetic biology, and investment in syn-bio foundries, are yielding new possibilities for rapid discovery of effective drugs and vaccines. Similarly, novel countermeasure approaches, like self-amplifying mRNA vaccines and baculovirus recombinant vaccine technology, have promise as platforms to enable quick development in an emergency. Manufacturing technologies are also improving with scientific advancement in this space. For example, synthetic biology can harness bacterial chassis organisms to rapidly produce chemical and biologic components of drugs and vaccines, and 3D printing can similarly produce chemical compounds on demand. This could all be done in a distributed way, allowing more people in more places to produce and scale production of countermeasures. And novel technologies like microarray patches and new oral vaccines could make mass dispensing and administration of countermeasures easier.

These relatively nascent technologies and methods already exist and have the potential to dramatically improve or accelerate our ability to develop, manufacture, and distribute medical countermeasures in response to outbreaks of novel pathogens. But the US government needs a greater level of investment in its medical countermeasures enterprise if the goal of safe, effective countermeasures within months is to be realized. We echo calls from the 2016 President's Council

of Advisors on Science and Technology,[1] and by National Institute of Allergy and Infectious Diseases Director Dr. Tony Fauci and colleagues,[2] for increased attention to and uptake of new countermeasure development technologies and methods.

2. A strong and sustainable global health security system.

To stop epidemics from becoming pandemics, countries everywhere must have the ability to rapidly detect and effectively respond to infectious disease outbreaks. These capabilities are at the heart of the 2005 International Health Regulations (IHR). While most countries have signed onto the IHR, few have achieved full compliance. The United States, in collaboration with WHO and other nations, should strengthen efforts to promote full achievement of the IHR goals by all countries through programs like the Global Health Security Agenda and participation in the WHO's Joint External Evaluation process and through efforts to develop, fund, and implement priorities in a follow-on National Action Plan. The greatest threats come from the least prepared and most poorly resourced countries; therefore, it is in the national self-interest of all countries to invest in the public health capabilities of other less well-prepared countries.

Beyond improving response capabilities in each country, international coordination of response must be improved. This includes the coordinated response to outbreaks of international concern by international teams of clinicians and public health professionals. The United States has and should continue to provide substantial international assistance when necessary in the form of public health (eg, epidemiology, risk assessment, emergency operations center response) and movement and provision of assets, as happened in the West Africa Ebola response. Other countries have provided that critical assistance as well.

What is much less developed is the provision by the United States of international assistance in the form of clinical care during infectious disease epidemics. WHO has an initiative on emergency medical teams, which are groups of health professionals who come from governments, NGOs, and militaries and who have the skills to treat people affected by an emergency or disaster. The US government should develop a deployable clinical capability to support the response to an international infectious disease emergency, a capability it does not currently have. Today, the world relies on a limited number of NGOs (eg, Médecins Sans Frontières and the International Medical Corps) and some national medical teams from countries other than the United States to supplement

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[1] Executive Office of the President. President's Council of Advisors on Science and Technology: Letter to the President. November 2016. https://obamawhitehouse.archives.gov/sites/default/files/microsites/ostp/PCAST/pcast_biodefense_letter_report_final.pdf

[2] Graham BS, Mascola JR, Fauci AS. Novel vaccine technologies: essential components of an adequate response to emerging viral diseases. *JAMA* 2018;319(14):1431-1432. https://jamanetwork.com/journals/jama/fullarticle/2676502.

direct patient care during infectious disease outbreaks. In the future, it could be decided that it is in the national interest of the United States to help control an infectious disease epidemic before it crosses international boundaries by providing a substantial clinical response. To do this, the US government would need to develop the capacity to send its own clinical teams in that kind of response. Such teams could function either independently or in support of WHO's emergency medical team initiative.

3. **A robust, highly capable national public health system that can manage the challenges of pandemic response.**

Local, state, and federal public health are a major part of the foundation of a national response to a pandemic. Public health at the local, state, and federal levels has been diminished by years of budgets that are too small for the mission. To respond effectively to a pandemic, there needs to be a well-trained, agile, and strong public health workforce. There must be annual preparedness funding to power the public health infrastructure, and there should be a substantial emergency response fund to allow immediate response to crises. This investment will foster the kinds of fundamental public health capabilities needed to control an infectious disease outbreak: strong surveillance and disease detection, rapid modeling, effective risk communication, and robust laboratories.

A specific priority for pandemic preparedness is the need for the federal government—together with state and local governments, public stakeholder groups, and scientific experts—to develop clear, effective plans regarding whether and how quarantine would be used. Political leaders have called for quarantines in the past, but their value and possible consequences have not been sufficiently studied or understood. A national plan for quarantine in the setting of a pandemic should incorporate best scientific evidence, the lessons of effectiveness of quarantine in the past, and substantial public input. More work needs to be done to provide legal clarity to questions of preemption and transfer of authority during quarantine, and to ensure necessary checks and balances. A national plan for quarantine should anticipate potential adverse consequences of this kind of quarantine, including potential public resistance to its implementation and extraordinary logistical challenges. It should have as its goal the encouragement of voluntary cooperation and coordination with state and local authorities. Plans for managing potential points of conflict between policymakers and different levels of government should be worked through in advance. Appropriate expert legal advice should be available for both policymakers and those potentially affected by such measures. And fast due process for affected members of the public should be assured, or policymakers run the risk of harming public trust, a vital component in a successful response to a pandemic.

With a more resourced and dynamic public health system across the country, broadly capable of effective management of infectious disease crisis, these events are more likely to be quickly controlled so they don't result in epidemic or pandemic spread.

4. **National plan to effectively harness all US healthcare assets in a catastrophic pandemic.**

During a catastrophic pandemic, no single entity will be solely responsible for or capable of mounting the response. Collaboration will be required, both prior to and during the event, between relevant health sector entities—including public health, healthcare facilities, emergency medical services, nongovernment and community organizations, elected officials, law enforcement, and the public. In the complex conditions of a pandemic, strict top-down command and control is unlikely to be effective; therefore, to ensure our national capacity to effectively respond to a pandemic, relevant entities—both within and outside the health sector—need to fully understand their roles and expected actions well before the onset of such an event. This is especially true of the vast majority of the healthcare system that resides in the private sector.

A proactive and dedicated effort is required to identify individual, facility, and agency roles and responsibilities; form necessary interagency and cross-sectoral relationships; facilitate multisectoral collaboration; and establish metrics for assessing the nation's resilience to this type of disaster. Leadership from the highest levels of the federal government, active participation from senior leaders across all federal departments, and input from the many sectors involved with healthcare response will be needed to fully map the complex requirements that will arise in a pandemic, including the plan for maintaining operational and financial systems in healthcare facilities despite enormous pressures and fear.

5. **An international strategy for addressing research that increases pandemic risks.**

The engineered virus in this exercise is fictional. But what is real is that it's now possible to create new pandemic risks through research or the use of new technologies. New pandemic risks include the engineering of new strains of pathogens that have the potential to spread widely and cause illness or death. They also include creating new, simpler pathways for longstanding pandemic risks to emerge, such as publishing the sequence of the horsepox virus and thereby making it easier to synthesize de novo smallpox virus. Few countries in the world have explicitly acknowledged the possibility that new pandemic risks could emerge from scientific research or the application of new biotechnological tools, and there is little policy in place to manage the risks. Deliberate misuse or an accident involving this work could have dire global consequences. A strategic effort is needed to address these risks. Ideally, there should be a consistent international approach: Science is often international, and the risks of accident or deliberate misuse could be global if the biological research or project at hand increases pandemic risks. Having one-off national approaches is a necessary beginning, but it will not be sufficient.

These efforts should include a process for surveying science for new pandemic risk–related developments, and identifying them early, so they are not surprises that must be addressed without

preparation or consideration of what has been learned from earlier challenges. Awareness should be raised in the global science community: If scientists are thinking about these issues, they can help create new norms of scientific practice, discourage irresponsible risks, and have paths for alerting and for responsible action should they become concerned about what they are seeing or hearing in their institutions or in their broader extensive networks. Scientific journals should be engaged in the discussions; they should not be the main point of oversight of management of these problems, but they will on occasion be the last barrier to disclosing pandemic risk information publicly and globally. They have had to deal with these issues intermittently over the years and have had little or no guidance from governments on how to manage them.

An international approach could be built on national oversight systems for any countries where this work is being funded or approved. This process would identify these risks early in new scientific proposals, consider whether the benefits of the work warrant the new pandemic risk being created, and, if the work is to be approved, would establish the highest possible safety systems and practices. Finally, it would be of very high value for the WHO or UN to become engaged in deliberations about the kinds of risks that could emerge from research or biotechnology work that led to new pandemic risks; at a minimum they could issue normative statements about their concerns and the need for special review. It would be even better if there were a special review process for experiments in this realm, along the lines of the Advisory Committee on Variola Virus Research.

6. A national security community well prepared to prevent, detect, and respond to infectious disease emergencies.

The introduction of an infectious disease that transmits readily and has moderate-to-high lethality would simultaneously be a threat to public health and US national security. As events like the 2001 anthrax attacks and the 2014-2016 West African Ebola epidemic demonstrate, biological threats are a source of strategic risk and surprise for the US national security community.[3] At the White House level, national and global health security should continue to be a high priority for both the National Security Council and the Office of Science and Technology Policy. In addition, the Departments of Defense, State, Health and Human Services, Homeland Security, and Justice and the agencies that comprise the US intelligence community have distinct and critical biosecurity assets and responsibilities that should continue to be recognized in national-level plans and strategies and be resourced appropriately by Congress. These departments and agencies should also continue to forge stronger partnerships between the security and health sectors. In addition, there is a need for professionals with health, medical, and life science expertise to enter government service and bolster the health security nexus. A concerted effort to attract such talent should be undertaken. Finally, a

[3] Charlet K. The new killer pathogens. *Foreign Affairs* May/June 2018. https://www.foreignaffairs.com/articles/2018-04-16/new-killer-pathogens.

severe pandemic like the one depicted in this exercise would significantly degrade the ability of national security agencies to function as intended, and additional planning should be dedicated to mitigating and minimizing the worst first, second, and third order effects of a potentially catastrophic pandemic.