DEPARTMENT OF HEALTH AND HUMAN SERVICES

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"Preparing for the Next Pandemic: Lessons Learned and The Path Forward"

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INTRODUCTION

Thank you, Chairman Wenstrup, Ranking Member Ruiz, and distinguished Members of the Subcommittee. I appreciate the opportunity to be here today to discuss the critical role of research at the National Institutes of Health (NIH) to prepare for—and respond to—emerging and re-emerging infectious diseases. NIH has mounted major research responses and developed effective medical countermeasures (MCMs) to emerging infectious diseases, including those caused by SARS-CoV-2 and Ebola virus, and continues to play a central role in addressing avian influenza, Marburg virus disease (MVD), and other infectious disease threats by capitalizing on decades of basic, clinical, and applied research to facilitate the rapid development of vaccines, therapeutics, and diagnostics. As the Principal Deputy Director of NIH, I am pleased to discuss the ongoing and future NIH research to help prepare for and respond to critical public health threats.

PANDEMIC PREPAREDNESS PLAN

NIH, largely through work supported by the National Institute of Allergy and Infectious Diseases (NIAID), is working to prepare the nation for public health emergencies caused by infectious diseases through the implementation of a bold Pandemic Preparedness Plan.[1] This plan leverages NIH's broad research portfolio in basic and translational research, long-standing expertise in conducting clinical trials and product development, capacity to engage both domestic and international partners, and flexible infrastructure to:

- systematically characterize pathogens of concern and increase research and surveillance to identify threats before they emerge or re-emerge;

[1] www.niaid.nih.gov/sites/default/files/pandemic-preparedness-plan.pdf

- help speed development of candidate diagnostics and MCMs, such as therapeutics and vaccines, thereby shortening timelines between pathogen emergence or outbreak onset and the Food and Drug Administration's (FDA) authorization/approval; and
- bridge or eliminate existing gaps in research, infrastructure, and technology and expand pre-clinical and clinical testing capacity.

Importantly, it is not feasible to fully characterize all the viruses known to cause human disease and preemptively develop MCMs for each. Thus, in its plan, NIAID has outlined an approach that prioritizes selection of representative viruses from each virus family to offer a viable pathway to gain knowledge that may be applicable to part—or all of—a particular virus family. These representative viruses are considered *prototype pathogens*. For example, within the *Filoviridae* family, Ebola virus is the prototypic pathogen as it can cause public health outbreaks and it shares functional and structural properties with viruses across the *Filoviridae* family, such as Marburg virus. Increasing fundamental knowledge and developing MCMs for a prototype virus not only provides ready potential prevention and treatment strategies for these viruses, but also the framework for a rapid research and product development response to other viruses within that family in the event of an outbreak.

Complementing this approach, NIAID also characterizes, develops reagents for, and conducts pre-clinical and clinical testing of pathogens considered a high public health priority that are in urgent need of research. NIAID refers to these as *priority pathogens*. This pathogen-specific research prioritizes viruses most likely to cause significant human morbidity and

mortality. NIAID supports priority pathogen research to enhance our understanding of—and preparedness for—known public health threats.

BUILDING PANDEMIC PREPAREDNESS INFRASTRUCTURE

The COVID-19 pandemic revealed the need for sustained, coordinated, and integrated research infrastructure that effectively leverages long-term partnerships with scientists, scientific organizations, and governments worldwide. To achieve these aims, NIH works in close partnership with the White House Office of Pandemic Preparedness and Response Policy (OPPR), and the Centers for Disease Control and Prevention (CDC); the FDA; and the Administration for Strategic Preparedness and Response (ASPR) and its Biomedical Advanced Research and Development Authority (BARDA).

NIH is also relying on new and innovative approaches to solve challenges of the future. At the start of the COVID-19 pandemic, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) established the Rapid Acceleration of Diagnostics (RADx®) Tech program, a part of the broader NIH RADx initiative. The RADx Tech program, with supplemental appropriations from Congress, helped rapidly increase COVID-19 testing capacity in the United States through the development and manufacturing of lab-based, point-of-care and, for the first time, over-the-counter COVID-19 diagnostic tests. During the peak of the COVID-19 pandemic, the program engaged hundreds of government, academic, and private industry partners through an "innovation funnel" approach, popularly known as a "shark tank." This process involved milestone-based funding to assess, validate, and de-risk technologies. Between 2020 and 2023, RADx Tech investments increased national COVID-19 testing capacity by more

than 8 billion tests and test products. These included 56 COVID-19 and 15 COVID-19 + flu combination tests that received emergency use authorization (EUA) from the FDA. As result, RADx Tech helped drive a paradigm shift from predominantly lab testing early in the COVID-19 pandemic to the current home and point of care testing widely used throughout the country.

Working with interagency partners, RADx Tech continues to develop the appropriate testing platforms to respond to national needs and maintain pandemic preparedness. This includes responding to urgent and potential emerging threats, e.g., COVID-19, H5N1, mpox, and seasonal flu; as well as growing public health challenges, e.g., sexually transmitted infections (including syphilis and HIV) and hepatitis (Hep) C and Hep B. Through partnerships, RADx Tech supports technology development at a level that helps to ensure sufficient operational readiness activities to be able to deliver tests that meet the constantly growing personal and public health demand for rapid diagnostics, particularly in home and point of care settings.

Many of these partnerships are structured around the RADx Tech Independent Test Assessment Program (ITAP). ITAP was created during the COVID-19 pandemic to focus on accelerating regulatory review and authorization of high-priority diagnostic tests. This unique NIH-FDA partnership remains a cornerstone of pandemic preparedness by supporting promising technologies that can quickly scale production. ITAP allows RADx Tech teams to work with both FDA and manufacturers to independently validate test performance using protocols agreed upon by the FDA. In addition to performing validation data activities to support FDA's review of EUA requests during the COVID-19 pandemic, RADx Tech ITAP has worked with FDA to gather and review validation data that supported traditional regulatory authorization for the first

at-home COVID-19/flu combination test and the first point of care Hep C test. These successes have helped pave the way for more streamlined review of marketing submissions to support clearances of similar tests in the future. Other key RADx Tech programs include optimizing test designs for improved accessibility (e.g., users with low or no vision, reduced dexterity, etc) and performance, as well as digital health platforms for distributing tests, reporting test results, and enabling "test-to-treat" programs which provide testing, consultation with a health care provider, and treatment in one location.

NIH is poised to leverage its existing research investments to develop and test candidate vaccines and therapeutics. Longstanding NIAID clinical research networks, which conduct clinical trials on candidate interventions, are critical to these efforts. Additionally, the Centers of Excellence for Influenza Research and Response and Centers for Research in Emerging Infectious Diseases advance our understanding of the emergence and spread of viruses and support early identification and characterization of emerging viruses with pandemic potential. NIAID also recently established the Research and Development of Vaccines and Monoclonal Antibodies for Pandemic Preparedness network, which will focus research efforts on prototype pathogens and high-priority pathogens in the families of viruses that cause dengue, chikungunya, Nipah, Crimean Congo hemorrhagic fever, Oropouche virus disease, Lassa fever, and other emerging and re-emerging infectious diseases. NIAID continues to support research on the preclinical discovery, evaluation, and development of oral direct-acting therapeutics targeting select viruses of pandemic potential in order to build a more robust pipeline of candidate antiviral drugs suitable for widespread use in the community in future outbreaks and/or pandemics.

RESPONSE TO SELECTED EMERGING DISEASES

Avian influenza. In March 2024, highly pathogenic avian influenza A (H5N1) was detected in dairy cattle. NIH-supported researchers and public health officials continue to closely monitor the outbreak as part of overarching pandemic preparedness efforts. As outlined in the U.S. Highly Pathogenic Avian Influenza A (H5N1) Research Priorities: October 2024,[2] NIH, along with ASPR, CDC, and FDA, is part of the U.S. Department of Health and Human Services (HHS) response team. The team is working closely with the U.S. Department of Agriculture to address the ongoing H5N1 outbreak in dairy and poultry farms. The NIAID research agenda for H5N1 influenza[3] is aligned with this collaborative, whole-of-government, one-health response to H5N1 influenza and focuses on four key objectives:

1. increasing understanding of the biology of H5N1 viruses and the factors that influence their ability to transmit and cause disease, particularly in novel animal species and humans;
2. developing and evaluating human infection prevention strategies, such as vaccines;
3. advancing existing and novel human treatments, including antivirals and monoclonal antibodies; and
4. supporting strategies for detecting H5N1 virus in humans.

NIAID-supported researchers have found that preexisting immunity from prior H1N1 influenza infections protected animal models from lethal H5N1 virus infection and provides evidence for the relatively mild human disease observed thus far in the current outbreak. NIAID-

[2] www.hhs.gov/programs/public-health-safety/us-highly-pathogenic-avian-influenza-a-h5n1-research-priorities-october-2024/index.html
[3] www.niaid.nih.gov/sites/default/files/niaid-h5n1-research-agenda.pdf

supported scientists and their collaborators have also conducted studies on milk from affected dairy cattle and findings from these studies supported the recommendation that individuals should avoid consuming raw milk. Moreover, NIAID-supported investigators are studying how the virus is changing over time as it spreads in cows and working to understand how the virus began infecting cows, which could enhance preparedness for future zoonotic events. NIAID will continue to support research on candidate mRNA and nanoparticle vaccines against H5N1.

The global outbreak of H5N1 virus, its seasonal spread of strain reassortments through migrating waterfowl, and resulting detections in novel animal species and humans in contact with those animals reaffirms the need to develop broadly protective "universal" influenza vaccines. Ideally, a safe and effective universal flu vaccine would protect against a wide variety of flu strains and provide durable, long-lasting immunity, reducing the need for annual vaccinations. NIAID-developed universal influenza vaccine candidates utilizing various vaccine platform technologies (e.g., mRNA, nanoparticle, and inactivated whole virus) are now being tested in clinical trials, including through the NIAID Collaborative Influenza Vaccine Innovation Centers.

Marburg virus disease (MVD). On September 27, 2024, the Republic of Rwanda's Ministry of Health reported cases of MVD in seven districts around the country and declared an outbreak. MVD is a severe, often fatal illness in humans and there are no FDA-approved therapeutics or vaccines available for the disease. NIAID is working with HHS counterparts and international partners to support the research response to the ongoing MVD outbreak. NIAID intramural and extramural investigators participate in the Marburg virus vaccine consortium

(MARVAC), a WHO-coordinated consortium to promote international collaboration for the development of MVD vaccines. MARVAC prioritizes sharing assays and reagents; promoting access to laboratory networks in MVD-endemic countries; and promoting structural support for preclinical development of upcoming MVD vaccine and therapeutic candidates. MARVAC has been rapidly convened in response to the current outbreak in Rwanda.

NIAID has supported research on candidate MVD therapeutics and vaccines. ASPR, in partnership with the Rwanda Ministry of Health and international colleagues, has helped make therapeutic and vaccine candidates available in Rwanda to enable patient treatment and vaccination of contacts and healthcare workers. NIAID will continue to support critical research on candidate therapeutics and vaccines for MVD.

CONCLUSION

NIH remains committed to supporting biomedical research to advance pandemic preparedness and enhance international research capacity to respond to emerging and re-emerging infectious diseases. Continued success in NIH's pandemic preparedness and biodefense efforts is contingent upon sustained congressional support. The President's FY25 budget request includes $20 billion in mandatory funding for the Public Health and Social Services Emergency Fund, of which $2.69 billion is earmarked for NIH. This funding is crucial for NIH's role in supporting the National Biodefense Strategy and Implementation Plan, which spans biosurveillance, biosecurity, the development of medical countermeasures, and emergency response activities. Ongoing congressional commitment will be vital to achieving these comprehensive health security goals. Together with academia, industry, and national and

international partners, NIH will continue to meet public health emergency needs by advancing high-priority research for infectious disease threats. These efforts include pathogen-specific research, the application of a prototype-pathogen approach, and the development of platform technologies, to enhance pandemic preparedness and response efforts.