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Director Walensky:

Viruses mutate as a part of their lifecycle, and frequent mutation is not unexpected from RNA viruses like SARS-CoV-2, the virus that causes COVID-19. While many mutations are of a trivial nature, several genetic mutations in SARS-CoV-2 and viral variants carrying them—in particular, the E484K mutation and the B.1.1.7, P.1, and B.1.351 variants[1]— have emerged that seem to confer functional advantage on the virus and thus raise concerns they will complicate our global fight against the pandemic. At this point, the question seems not to be "if" the variants are present, but "how" present they are in the general population and as a proportion of COVID-19 cases. These variants are circulating globally and have been detected in the majority of states as well as the United Kingdom, Brazil, South Africa, Germany, and other countries. Given this, we write to request detailed information about the status of national efforts regarding genomic surveillance and to ask what next steps the Centers for Disease Control and Prevention (CDC) is taking to ensure we have processes in place to learn from real-time data and track variants and their prevalence across the country.

The variants have raised scientific and public concern because they may pose two connected problems. First, they may make SARS-CoV-2 more transmissible. Although the estimates vary widely, a preliminary study suggested that the B.1.1.7 variant might be 40 to 70 percent more transmissible.[2] As these variants become more widespread, this means that COVID-19 incidence is likely to increase even faster. Second, while we lack sufficient information to say definitively, it is also possible that these mutations may make SARS-CoV-2 more deadly in some way. Even if the mutations do not increase the mortality of SARS-CoV-2, increased transmissibility could result in more deaths.

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[1] Andrew Joseph, "What we now know—and don't know—about the coronavirus variants," *STAT* (19 January 2021), https://www.statnews.com/2021/01/19/coronavirus-variants-transmissibility-disease-reinfection/ (accessed 26 January 2021)

[2] Erik Volz, Swapnil Mishra, Meera Chand, *et al*., "Transmission of SARS-CoV-2 LineageB.1.1.7 in England: Insights from linking epidemiological and genetic data" Imperial College (London) preprint (31 Dec 2020), https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2020-12-31-COVID19-Report-42-Preprint-VOC.pdf (accessed 26 January 2021)

Monitoring virus genomic change is critical for successfully tracing symptomatic and asymptomatic transmission, informing targets for countermeasure and diagnostic development, and evaluating vaccine and therapeutic performance. Countries like the United Kingdom (U.K.) have led in detection of new variants in part because they do substantially more viral genetic sequencing than the United States. The U.K. supported a robust viral genomic sequencing infrastructure long before the pandemic, and this combined with certain domestic characteristics allowed them to rapidly develop and scale up sequencing through their COVID-19 Genomics U.K. Consortium. The United States, unfortunately, does not have the same capacity at present.

Experts have long raised concerns that CDC was not keeping up with technological advances in sequencing and bioinformatics, threatening our ability to stem infectious disease outbreaks. Pathogen genomics has been used in public health for decades and is integrated into numerous CDC activities; the agency responded to these criticisms by establishing its Office of Advanced Molecular Diagnostics in 2014. CDC states that the office has "invested in federal and state public health laboratories to expand the use of pathogen genomics and other advanced laboratory technologies for infectious disease surveillance and outbreak response." In addition, CDC launched the SARS-CoV-2 Public Health Emergency Response, Epidemiology and Surveillance (SPHERES) consortium in May 2020 to further expand the use of whole genome sequencing of SARS-CoV-2. According to CDC, SPHERES is "an ambitious effort to coordinate SARS-CoV-2 sequencing nationally, organizing dozens of smaller, individual networks into a single, distributed network." In November 2020, CDC also established the National SARS-CoV-2 Strain Surveillance System (NS3) to improve the representativeness of domestic SARS-CoV-2 sequences and provide "baseline strain information, [increase] publicly available genomic viral sequence data, and [establish] a representative repository of virus isolates for further characterization."

Despite these efforts, White House coronavirus coordinator Jeffrey Zients noted at a press conference on January 27 that the United States is 43rd in the world in terms of the percentage of COVID-19 cases that it genetically sequences. While the CDC has acknowledged this is an area for improvement, the concrete steps that CDC is taking are not clear. A recent CDC document indicated only that CDC "is monitoring the situation closely. CDC is working to detect and characterize emerging viral variants and expand its ability to look for COVID-19 and new variants."[3] During the January 27 White House press briefing, you said, "CDC is committed to working with international, state, and local partners." We wish to know more of the details.

We are aware that federal laws do not mandate the sharing or protection of viral genomic sequence data. The lack of a clear regulatory pathway and infrastructure to share

[3] Centers for Disease Control and Prevention, "New COVID-19 Variants" (15 January 2021), https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant.html (accessed 26 January 2021).

and protect this information may compound inherent structural challenges that CDC already faces given the sheer number of diverse, independent entities involved in our public health and biosurveillance systems. However, the federal government plays a critical role to coordinate efforts to share this crucial information between levels of government and with private sector partners, particularly during a public health emergency. We seek to obtain more specific information about CDC's efforts in this regard as well.

Please provide answers to the following questions by March 11, 2021.

1. What specific steps is CDC taking to institute, support, coordinate, or improve local, regional, or national programs to regularly check virus genomes for new mutations?
    - What role does the SPHERES consortium play in these efforts? How many SPHERES participants have submitted sequencing data, and is the overall data collected representative in terms of geography?
    - What role does the National SARS-CoV-2 Strain Surveillance System (NS3) play?
    - To what extent does CDC coordinate efforts with the National Institutes for Health's National Center for Biotechnology Information? Would federal and/or interagency efforts benefit from increased standardization for sequencing and submission?
    - What guidance would CDC provide to state, local, tribal, territorial, or other partners to provide for standardized and interoperable data?
2. In order to draw upon best practices and not "reinvent the wheel," how will CDC build upon the sequencing work that is already occurring in the United States, which has been supported through annual and supplemental appropriations over the past year? What can be learned from the U.K.'s sequencing program (or those of other countries)? What are CDC's specific plans for international coordination?
3. What should be the national goal in terms of percent of total positive samples sequenced?
4. Upon finding new mutations, how is CDC assessing the effects of those mutations on virulence and morbidity or mortality?
5. What accounts within the CDC budget or other funding sources will CDC draw upon to conduct this work or support others conducting this work? How many CDC personnel will be dedicated to this work?
    - Does CDC intend to request any new legislative authority to conduct this work or address any barriers?
6. Should viral genome sequences be shared openly on publicly available databases? If so, what are appropriate privacy protections and how should they be communicated to the public?
7. Should viral genome sequences be linked to clinical and epidemiological data and/or integrated with other CDC surveillance programs related to COVID-19? If so, what are the best practices for linking this data in a privacy-protective manner?

8. What guidance, if any, is CDC providing to these entities about safe data sharing practices that protect personal health information?

Thank you for your swift consideration of these questions. We look forward to your reply.

Sincerely,

ANGUS S. KING, JR.
United States Senator

BILL CASSIDY, M.D.
United States Senator