Centers for Disease Control and Prevention

COVID-19

Science Brief: Omicron (B.1.1.529) Variant

Updated Dec. 2, 2021

On November 24, 2021, South Africa reported the identification of a new SARS-CoV-2 variant, B.1.1.529, to the World Health Organization (WHO). B.1.1.529 was first detected in specimens collected on November 11, 2021 in Botswana and on November 14, 2021 in South Africa. South Africa has since detected B.1.1.529 in specimens collected on November 8, 2021. On December 1, 2021, the first case attributed to B.1.1.529 was reported in the United States in a person who returned from travel to South Africa. A second case was reported on December 2, 2021 in a person with no international travel history who also attended a convention in the days preceding symptom onset. The Omicron variant has also been detected in travel-related cases in several European countries, as well as Australia, Brazil, Canada, Hong Kong, Israel, Japan, Nigeria, Norway, Sweden, and the United Kingdom. A few countries, including the United States, have reported cases in individuals without travel history to southern Africa.

On November 25, 2021, the United Kingdom Health Security Agency designated B.1.1.529 as a Variant Under Monitoring (VUI-21-NOV-01) [1]. On November 26, 2021, the Technical Advisory Group on SARS-CoV-2 Virus Evolution (TAG-VE)[2] convened to assess B.1.1.529. The TAG-VE advised WHO that this variant should be designated as a Variant of Concern (VOC), and WHO designated B.1.1.529 as a VOC named Omicron.[3]

The WHO classification as a VOC was based on epidemiological data indicating an increase in infections in South Africa in recent weeks that coincided with detection of Omicron. Omicron has many concerning spike protein substitutions, some of which are known from other variants to be associated with reduced susceptibility to available monoclonal antibody therapeutics or reduced neutralization by convalescent and vaccinee sera. The European Center for Disease Prevention and Control also classified this variant as a VOC due to concerns “regarding immune escape and potentially increased transmissibility compared to the Delta variant.”[4]

The SARS-CoV-2 Interagency Group (SIG), established by the U.S. Department of Health and Human Services, is responsible for variant classifications in the United States.[i] The SIG meets regularly to evaluate the risk posed by SARS-CoV-2 variants circulating in the United States and globally and to make recommendations about the classification of variants. On November 30, 2021, the SIG made the decision to classify the Omicron variant as a Variant of Concern (VOC). This decision is based on a number of factors, including, detection of cases attributed to Omicron in multiple countries, including among those without travel history, transmission and replacement of Delta as the predominant variant in South Africa, the number and locations of substitutions in the spike protein, and available data for other variants with fewer substitutions in the spike protein indicating a reduction in neutralization by vaccinee and convalescent sera and certain monoclonal antibody treatments.

There are two variants classified as a VOC by the United States: Omicron and Delta. As of December 2, 2021, two confirmed cases attributed to the Omicron variant have been detected in the United States and additional possible Omicron cases are being investigated. **Delta continues to be the predominant circulating variant. On August 26, 2021, CDC published information on What We Know About the Delta Variant. Importantly, nearly all lineages designated as Delta remain susceptible to available monoclonal antibody therapeutics, and vaccines continue to be highly effective against severe illness, hospitalization, and death among people infected with the Delta variant.**

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[i]The SIG includes representatives from the Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), Biomedical Advanced Research and Development Authority (BARDA), and Department of Defense (DoD). This interagency group is focused on the rapid characterization of emerging variants and actively monitors their potential impact on critical SARS-CoV-2 countermeasures, including vaccines, therapeutics, and diagnostics.

Omicron (B.1.1.529) Characteristics

WHO Label: Omicron

Pango Lineage: B.1.1.529

Nextstrain clade: 21K

The spike protein of the Omicron variant is characterized by at least 30 amino acid substitutions, three small deletions, and one small insertion. Notably, 15 of the 30 amino acid substitutions are in the receptor binding domain (RBD). There are also a number of changes and deletions in other genomic regions.

- **Key Amino Acid Substitutions in Spike Protein (RBD substitutions in bold type):** A67V, del69-70, T95I, del142-144, Y145D, del211, L212I, ins214EPE, **G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H**, T547K, D614G, H655Y, N679K, P681H, N764K, D796Y, N856K, Q954H, N969K, L981F

Transmissibility: Currently, it is unknown how efficiently the Omicron variant can spread from person to person. The replacement of Delta by Omicron as the predominant variant in South Africa raises concerns that the Omicron variant may be more transmissible than Delta, but due to the low number of cases in South Africa when Omicron emerged, it is unclear if this variant is more transmissible than the Delta variant. Further, the relatively small number of cases documented to date makes it difficult to estimate transmissibility. Analysis of the changes in the spike protein indicate that the Omicron variant is likely to have increased transmission compared to the original SARS-CoV-2 virus, but it is difficult to infer if it is more transmissible than Delta.

- N501Y increases binding to the ACE2 receptor, which could increase transmission, and the combination of N501Y and Q498R may increase binding affinity even more; however, other substitutions in the Omicron spike protein are expected to decrease binding to ACE2. As such, receptor binding affinity needs to be assessed using the full spectrum of spike protein substitutions found in the Omicron variant.
- H655Y is proximal to the furin cleavage site and may increase spike cleavage, which could aid transmission.
- N679K is proximal to and adds to the polybasic nature of the furin cleavage site, which may also increase spike cleavage and could aid transmission.
- P681H has been shown to enhance spike cleavage, which could aid transmission. This mutation is found in Alpha and an alternate mutation at this position (P681R) is found in Delta.

Disease Severity: Currently, it is unclear if infection with the Omicron variant is associated with more severe disease. Due to the small number of cases attributed to the Omicron variant, assessment of disease severity is difficult. Preliminary information from South Africa indicates that there are no unusual symptoms associated with Omicron variant infection, and as with other variants, some patients are asymptomatic.[5]

Impact on Vaccine-Induced Immunity or Immunity from Previous Infection: Currently, there are no data available to assess the ability of sera from vaccinated persons or those with previous SARS-CoV-2 infection to neutralize the Omicron variant. However, the U.S. Government SIG and global public health partners are working to generate these data in laboratory settings and will also continue to monitor epidemiological and clinical indicators.

The spike protein is the primary target of vaccine-induced immunity. The Omicron variant contains more changes in the spike protein than have been observed in other variants, including 15 in the RBD. Based on the number of substitutions, the location of these substitutions, and data from other variants with similar spike protein substitutions, significant reductions in neutralizing activity of sera from vaccinated or previously infected individuals, which may indicate reduced protection from infection, are anticipated.

Laboratory and epidemiological studies are needed to assess the impact of the Omicron variant on vaccine effectiveness and breakthrough infections, including in individuals who have received booster doses. However, vaccination is anticipated to continue to offer protection against hospitalization and death, and vaccines continue to play a critical role in controlling the COVID-19 pandemic.

Impact on Monoclonal Antibody Treatments: Currently, there are no virus-specific data available to assess whether monoclonal antibody treatments will retain efficacy against the Omicron variant. Based on data from other variants with significantly fewer changes in the RBD, the expectation is that the Omicron variant will remain susceptible to some monoclonal antibody treatments, while others may have less potency.

Mutations within the RBD are most relevant for monoclonal antibody therapeutics available under Emergency Use Authorization (EUA). Currently, there are three monoclonal antibody treatments with EUA: Sotrovimab, Bamlanivimab and Etesevimab, and REGEN-COV.

The table below shows data only for single RBD substitutions that are within the binding site of the indicated monoclonal antibody. However, mutations in the monoclonal antibody binding site do not always result in a loss of binding or neutralization. **Importantly, data are needed with the full spectrum of spike protein changes to understand the impact on available monoclonal antibody therapeutics.** As data becomes available, the Department of Health and Human Services will rapidly communicate changes in treatment guidance to public health departments and health care providers, as appropriate.

In vitro Therapeutic Activity of Single RBD Substitutions found in Omicron¥

Data in the table shows data available on the NCATS OpenData Portal[6] that has been tested against a viral variant containing only a single amino acid substitution from a wild-type SARS-CoV-2 in an in vitro neutralization assay.

RBD Substitution	Eli Lilly – Bamlanivimab	Eli Lilly – Etesevimab	Regeneron-Imdevimab	Regeneron – Casirivimab	GSK/VIR-Sotrovimab
G339D					1.18*
S371L					
S373P	No data available				
S375F					
K417N	0.12* 0.367*	>1,000* 381.6*	0.0789* 0.25* 1.2* 1.35*	4.3* 5.67* 7* (7) 13.1* 48.74*	
N440K	No data available		95.63* (28)	1*	0.48*
G446S			No data available		
S477N		0.5*	2.28*	0.91* 2.85*	
T478K	1.25 *	0.231*	0.571*	0.5*	
E484A	No data available			No data available	
Q493R	(100)	No data available		(70)	
G496S	No data available				
Q498R			No data available	No data available	
N501Y	1* 1.13* (5)	1.65* 2.6* 2.9* (5)	0.1* 0.2* 0.5* 0.62* 0.75* 0.77* 0.95* (2)		
Y505H		No data available			

¥ data as of December 1, 2021

* denotes data from a publication; references below[7, 8, 9, 10, 11, 12, 13, 14, 15]

( ) denotes data from FDA EUA Fact Sheets

Black shaded cells indicate that the substitution is not located in the monoclonal antibody epitope binding region

Impact on Diagnostics: For the most up to date information and guidance on diagnostic assays, which will be updated to reflect the impact of the Omicron variant, please refer to the U.S. Food and Drug Administration web page on SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests .

- The CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel and the Multiplex Assay for Flu and SARS-CoV-2 are expected to detect the Omicron variant.
- The Thermo Fisher TaqPath COVID-19 Combo Kit (3 total targets) has significantly reduced S-gene target sensitivity due to the deletion at H69 and V70 in the B.1.1.529 (Omicron) spike protein. Specimens being tested using the TaqPath COVID-19 Combo Kit that yield an S gene target failure (SGTF) *could* be Omicron. Importantly, any possible Omicron specimen must be confirmed by sequencing. Since the TaqPath COVID-19 Combo Kit is designed to detect multiple genetic targets, the overall test sensitivity should not be impacted.[16]

Scientists are working to learn more about the Omicron variant to better understand how easily it might be transmitted and the effectiveness of currently authorized or approved medical countermeasures, such as vaccines, therapeutics, and diagnostic tests, against this variant. New information about the virologic, epidemiologic, and clinical characteristics of the Omicron variant is rapidly emerging. CDC and other federal agencies are working closely with international public health agencies to monitor the situation closely. CDC will provide updates as more information and data become available.

Public Health Response to the Omicron Variant

On December 1, 2021, the first case attributed to the Omicron variant was identified in the United States in a person who recently return from travel to South Africa. A second case was reported on December 2, 2021 in a person with no international travel history who also attended a convention in the days preceding symptom onset. Additional possible Omicron cases are under investigation. CDC's national genomic surveillance efforts are statistically powered to detect a variant that is circulating at 0.1% with 99% confidence and can monitor changes over time. CDC and the SIG are implementing several activities in response to the Omicron variant that are summarized below.

- **Implementation of Enhanced Surveillance under the National SARS-CoV-2 Strain Surveillance (NS3) Program –** In partnership with U.S. public health laboratories and the Association of Public Health Laboratories, CDC is implementing enhanced surveillance for specimens with S-gene target failures (SGTFs) by requesting public health laboratories to send SGTF specimens to CDC as quickly as possible to speed the confirmation of possible Omicron cases and subsequent virological characterization.[ii] If public health laboratories detect Omicron through state-level surveillance activities, CDC is also requesting public health laboratories send sequence-confirmed Omicron specimens to CDC for virological characterization.
  - CDC and other federal agencies continue to work with international partners to learn more about variants circulating globally and will continue to monitor all data sources closely to identify cases of Omicron in the United States.

- **Airport Surveillance Post-Arrival Testing and Sequencing –** CDC is collaborating with two commercial partners on a SARS-CoV-2 surveillance program that involves voluntary testing of arriving international travelers at select U.S. airports. Arriving air travelers are offered[ii] pooled testing conducted in the airport and offered at-home kits for saliva sampling that are taken 3-5 days after arrival and returned to the laboratory for RT-PCR testing. All positive samples are sequenced, enabling detection of novel SARS-CoV-2 variant among travelers entering the United States. On Sunday November 28, 2021, the program began expanding to test air travelers entering the United States from southern Africa, including passengers making connections through Europe.

- **Prioritization of laboratory studies –** The SIG has prioritized laboratory studies to evaluate the impact on available medical countermeasures, such as vaccines, therapeutics, and diagnostics. These studies include assessing the ability of vaccinee and convalescent sera to neutralize the Omicron variant, the susceptibility of the variant to treatments, and the ability of vaccine-induced immunity to protect against illness and death.
- **Support for state, local, tribal, and territorial health departments –** CDC is working closely with jurisdictions to facilitate rapid, bidirectional sharing of information. CDC staff are available to provide in-person or remote technical support for the public health response to the Omicron variant, including investigations of the epidemiologic and clinical characteristics of Omicron or other SARS-CoV-2 variant infections.

- **Travel:** On Friday, November 26, 2021, the White House issued a Presidential Proclamation suspending entry from eight countries in southern Africa for foreign nationals who were physically present in those countries during the 14 days prior to travel. CDC is working to modify the current Testing Order for travel as we learn more about the Omicron variant; a revised order would shorten the timeline for required testing for all international air passengers to one day before departure to the United States. This strengthens already robust protocols in place for international travel, including requirements for foreign nationals to be fully vaccinated. CDC continues to monitor the global epidemiology of the Omicron variant. This is a rapidly evolving situation and CDC will adjust travel recommendations and requirements, as necessary. For the most current information about travel recommendation and requirements, see International Travel.
  - CDC continues to recommend:
    - All travelers should get a COVID-19 viral test 3-5 days after arrival.
    - Travelers who are not fully vaccinated should self-quarantine for 7 days, even if their test is negative.
    - Travelers should self-isolate if they test positive or develop COVID-19 symptoms.
  - These measures are required for foreign national who are not fully vaccinated.

- **Vaccination:** The COVID-19 vaccines approved or authorized in the United States are highly effective at preventing severe disease and death, but they are not 100% effective, and some fully vaccinated people will become infected (breakthrough infection) and experience illness. For all eligible persons, the vaccine provides the best protection against serious illness and death from COVID-19.
  - Vaccines are playing a crucial role in limiting spread of SARS-CoV-2 and minimizing severe disease. As of December 1, 2021, more than 197 million Americans are fully vaccinated and more than 233 million Americans have received at least one dose, and these numbers are increasing. Low vaccination coverage may drive increases in cases, which also increases the chances that variants could emerge.
  - Everyone 5 years and older is eligible for COVID-19 vaccination.
  - If you have received the first dose of a two dose primary vaccine series, you should get your second dose as close to the recommended 3-week or 4-week interval as possible.
  - Everyone ages 18 years and older should get a booster shot when they are eligible.
  - Data from clinical trials showed that a booster shot increased the immune response in trial participants who finished a Pfizer-BioNTech or Moderna primary series 6 months earlier or who received a J&J/Janssen single-dose vaccine 2 months earlier. With an increased immune response, people should have improved protection against COVID-19, including variants such as the Delta variant, which currently represents greater than 99% of circulating viruses in the United States. For Pfizer-BioNTech and J&J/Janssen, clinical trials also showed that a booster shot helped prevent COVID-19 with symptoms.
- **Mitigation:** Given what we know, layered prevention strategies are needed to reduce the transmission of Delta, Omicron, and all other SARS-CoV-2 variants. As we continue to build the level of vaccination nationwide and globally, we must also use all the prevention strategies available, including masking, improving ventilation, distancing, handwashing, and testing to slow SARS-COV-2 transmission and stop the COVID-19 pandemic. CDC recommends that everyone ages 2 years or older, including those who are fully vaccinated, wear masks in public indoor places in areas of substantial or high transmission.

[ii]Delta variant specimens do not yield an SGTF result using the TaqPath COVID-19 Combo Kit. Given that nearly 100% of SARS-CoV-2 circulating in the United States are the Delta variant, specimens with an SGTF using this diagnostic test may be presumptive Omicron variants and should be prioritized for sequencing confirmation.

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