



COVID-19

SARS-CoV-2 Variant Classifications and Definitions

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Key Points:

- Genetic variants of SARS-CoV-2 have been emerging and circulating around the world throughout the COVID-19 pandemic.
- Viral mutations and variants in the United States are routinely monitored through sequence-based surveillance, laboratory studies, and epidemiological investigations.
- A US government interagency group developed a Variant Classification scheme that defines three classes of SARS-CoV-2 variants:
 - [Variant of Interest](#)
 - [Variant of Concern](#)
 - [Variant of High Consequence](#)
- The B.1.526, B.1.526.1, B.1.525, and P.2 variants circulating in the United States are classified as variants of interest.
- The B.1.1.7, B.1.351, P.1, B.1.427, and B.1.429 variants circulating in the United States are classified as variants of concern.
- To date, no variants of high consequence have been identified in the United States.
- In laboratory studies, specific monoclonal antibody treatments may be less effective for treating cases of COVID-19 caused by variants with the [L452R or E484K substitution](#) in the spike protein.
 - L452R is present in B.1.526.1, B.1.427, and B.1.429.
 - E484K is present in B.1.525, P.2, P.1, and B.1.351, but only some strains of B.1.526 and B.1.1.7.

Viruses constantly change through mutation. A variant has one or more mutations that differentiate it from other variants in circulation. As expected, multiple variants of SARS-CoV-2 have been documented in the [United States](#) and [globally](#) throughout this pandemic. To inform local outbreak investigations and understand national trends, scientists compare genetic differences between viruses to identify variants and how they are related to each other.

Variant classifications

The US Department of Health and Human Services (HHS) established a SARS-CoV-2 Interagency Group (SIG) to improve coordination among 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.

In collaboration with the SIG, CDC established a classification scheme that defines three classes of variants of SARS-CoV-2. These classes include definitions and attributes of the variants. Resulting public health actions are also described in the sections below.

- [Variants of Interest \(VOI\)](#)
- [Variants of Concern \(VOC\)](#)

Notes: Each classification of variant includes the possible attributes of lower classes (e.g., VOC includes the possible attributes of VOI); variant status might escalate or deescalate based on scientific evidence. This page

- [Variants of High Consequence \(VOHC\)](#)

will be updated as needed to show the variants that belong to each class. The [World Health Organization](#) (WHO) also classifies variant viruses as Variants of Concern and Variants of Interest; US classifications may differ from those of WHO since the importance of variants may differ by

location.

See [Variant Proportions in the U.S.](#)

Variant of Interest

A variant with specific genetic markers that have been associated with changes to receptor binding, reduced neutralization by antibodies generated against previous infection or vaccination, reduced efficacy of treatments, potential diagnostic impact, or predicted increase in transmissibility or disease severity.

Possible attributes of a variant of interest:

- Specific genetic markers that are predicted to affect transmission, diagnostics, therapeutics, or immune escape
- Evidence that it is the cause of an increased proportion of cases or unique outbreak clusters
- Limited prevalence or expansion in the US or in other countries

A variant of interest might require one or more appropriate public health actions, including enhanced sequence surveillance, enhanced laboratory characterization, or epidemiological investigations to assess how easily the virus spreads to others, the severity of disease, the efficacy of therapeutics and whether currently authorized vaccines offer protection.

Current variants of interest in the United States that are being monitored and characterized are listed in the table below. The table will be updated when a new variant of interest is identified.

Selected Characteristics of SARS-CoV-2 Variants of Interest⁺

Name (Pango lineage) ^a	Spike Protein Substitutions	Name (Nextstrain) ^b	First Detected	BEI Reference Isolate ^c	Attributes
B.1.526	Spike: (L5F*), T95I, D253G, (S477N*), (E484K*), D614G, (A701V*)	20C/S:484K	United States (New York) – November 2020		<ul style="list-style-type: none"> • Reduced susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment; however, the clinical implications of this are not known.⁷ Alternative monoclonal antibody treatments are available.¹⁴ • Reduced neutralization by convalescent and post-vaccination sera^{22, 24}
B.1.526.1	Spike: D80G, Δ144, F157S, L452R, D614G, (T791I*), (T859N*), D950H	20C	United States (New York) – October 2020		<ul style="list-style-type: none"> • Potential reduction in neutralization by some EUA monoclonal antibody treatments^{7, 14} • Potential reduction in neutralization by convalescent and post-vaccination sera²²

Name (Pango lineage ↗) ^a	Spike Protein Substitutions	Name (Nextstrain ↗) ^b	First Detected	BEI ↗ Reference Isolate ^c	Attributes
B.1.525	Spike: A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L	20A/S:484K	United Kingdom/Nigeria – December 2020		<ul style="list-style-type: none"> • Potential reduction in neutralization by some EUA monoclonal antibody treatments ^{7, 14} • Potential reduction in neutralization by convalescent and post-vaccination sera ²²
P.2	Spike: E484K, (F565L*), D614G, V1176F	20J	Brazil – April 2020		<ul style="list-style-type: none"> • Potential reduction in neutralization by some EUA monoclonal antibody treatments ^{7, 14} • Reduced neutralization by post-vaccination sera ^{22, 23}

(*) = detected in some sequences but not all

⁺ These variants share one specific mutation called D614G. This mutation was one of the first documented in the US in the initial stages of the pandemic, after having initially circulated in Europe^[13]. There is evidence that variants with this mutation spread more quickly than viruses without this mutation^[12].

a – Phylogenetic Assignment of Named Global Outbreak (PANGO) Lineages is software tool developed by members of the Rambaut Lab. The associated web application was developed by the Centre for Genomic Pathogen Surveillance in South Cambridgeshire and is intended to implement the dynamic nomenclature of SARS-CoV-2 lineages, known as the PANGO nomenclature.

b – Nextstrain, a collaboration between researchers in Seattle, USA and Basel, Switzerland, provides open-source tools for visualizing the genetics of outbreaks. The goal is to support public health surveillance by facilitating understanding of the spread and evolution of pathogens.

c – The Biodefense and Emerging Infections Research Resources (BEI Resources) is a NIAID-funded repository to provide reagents, tools, and information to the research community. The reference viruses proposed here facilitate the harmonization of information among all stakeholders in the COVID-19 pandemic research community. Please note that the reference viruses provided in the tables below are based on what is currently available through the BEI Resources.

Variant of Concern

A variant for which there is evidence of an increase in transmissibility, more severe disease (e.g., increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures.

Possible attributes of a variant of concern:

In addition to the possible attributes of a variant of interest

- Evidence of impact on diagnostics, treatments, or vaccines
 - Widespread interference with diagnostic test targets
 - Evidence of substantially decreased susceptibility to one or more class of therapies

- Evidence of significant decreased neutralization by antibodies generated during previous infection or vaccination
- Evidence of reduced vaccine-induced protection from severe disease
- Evidence of increased transmissibility
- Evidence of increased disease severity

Variants of concern might require one or more appropriate public health actions, such as notification to WHO under the International Health Regulations, reporting to CDC, local or regional efforts to control spread, increased testing, or research to determine the effectiveness of vaccines and treatments against the variant. Based on the characteristics of the variant, additional considerations may include the development of new diagnostics or the modification of vaccines or treatments.

Current variants of concern in the United States that are being closely monitored and characterized by federal agencies are included in the table below. The table will be updated when a new variant of concern is identified.

Selected Characteristics of SARS-CoV-2 Variants of Concern⁺

Name (Pango lineage ↗) ^a	Spike Protein Substitutions	Name (Nextstrain ↗) ^b	First Detected	BEI ↗ Reference Isolate ^c	Attributes ^d
B.1.1.7	Δ69/70, Δ144, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)	20I/501Y.V1	United Kingdom	NR-54000 ↗	<ul style="list-style-type: none"> • ~50% increased transmission ⁵ • Potential increased severity based on hospitalizations and case fatality rates ⁶ • No impact on susceptibility to EUA monoclonal antibody treatments ^{7,14} • Minimal impact on neutralization by convalescent and post-vaccination sera ^{8,9,10,11,12,13,19}
P.1	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I	20J/501Y.V3	Japan/ Brazil	NR-54982 ↗	<ul style="list-style-type: none"> • Significant decrease in susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment,⁷ but other EUA monoclonal antibody treatments are available ¹⁴ • Reduced neutralization by convalescent and post-vaccination sera ¹⁵

Name (Pango lineage ↗) ^a	Spike Protein Substitutions	Name (Nextstrain ↗) ^b	First Detected	BEI ↗ Reference Isolate ^c	Attributes ^d
B.1.351	D80A, D215G, Δ241/242/243, K417N, E484K, N501Y, D614G, A701V	20H/501.V2	South Africa	NR-54009 ↗	<ul style="list-style-type: none"> • ~50% increased transmission¹⁶ • Significant decrease in susceptibility to the combination of bamlanivimab and etesevimab monoclonal antibody treatment,⁷ but other EUA monoclonal antibody treatments are available¹⁴ • Reduced neutralization by convalescent and post-vaccination sera^{8,12,18,19,20}
B.1.427	L452R, D614G	20C/S:452R	United States- (California)		<ul style="list-style-type: none"> • ~20% increased transmissibility²¹ • Modest decrease in susceptibility to the combination of bamlanivimab and etesevimab; however, the clinical implications of this decrease are not known.⁷ Alternative monoclonal antibody treatments are available.¹⁴ • Reduced neutralization by convalescent and post-vaccination sera²¹
B.1.429	S13I, W152C, L452R, D614G	20C/S:452R	United States- (California)		<ul style="list-style-type: none"> • ~20% increased transmissibility²¹ • Modest decrease in susceptibility to the combination of bamlanivimab and etesevimab; however, the clinical implications of this decrease are not known.⁷ Alternative monoclonal antibody treatments are available.¹⁴ • Reduced neutralization by convalescent and post-vaccination sera²¹

(*) = detected in some sequences but not all

^a These variants share one specific mutation called D614G. This mutation was one of the first documented in the US in the initial stages of the pandemic, after having initially circulated in Europe^[13]. There is evidence that variants with this mutation spread more quickly than viruses without this mutation^[12].

a – Phylogenetic Assignment of Named Global Outbreak (PANGO) Lineages is software tool developed by members of the Rambaut Lab. The associated web application was developed by the Centre for Genomic Pathogen Surveillance in South Cambridgeshire and is intended to implement the dynamic nomenclature of SARS-CoV-2 lineages, known as the PANGO nomenclature.

b – Nextstrain, a collaboration between researchers in Seattle, USA and Basel, Switzerland, provides open-source tools for visualizing the genetics of outbreaks. The goal is to support public health surveillance by facilitating understanding of the spread and evolution of pathogens.

c – The Biodefense and Emerging Infections Research Resources (BEI Resources) is a NIAID-funded repository to provide reagents, tools, and information to the research community. The reference viruses proposed here facilitate the harmonization of information among all stakeholders in the COVID-19 pandemic research community. Please note that the reference viruses provided in the tables below are based on what is currently available through the BEI resources.

d – Attributes listed are based on data available from pseudoviruses or recombinant viruses containing combinations of substitutions characteristic of specific lineages or from reference virus isolates.

Variant of High Consequence

A variant of high consequence has clear evidence that prevention measures or medical countermeasures (MCMs) have significantly reduced effectiveness relative to previously circulating variants.

Possible attributes of a variant of high consequence:

In addition to the possible attributes of a variant of concern

- Impact on Medical Countermeasures (MCM)
 - Demonstrated failure of diagnostics
 - Evidence to suggest a significantly reduction in vaccine effectiveness, a disproportionately high number of vaccine breakthrough cases, or very low vaccine-induced protection against severe disease
 - Significantly reduced susceptibility to multiple Emergency Use Authorization (EUA) or approved therapeutics
 - More severe clinical disease and increased hospitalizations

A variant of high consequence would require notification to WHO under the International Health Regulations, reporting to CDC, an announcement of strategies to prevent or contain transmission, and recommendations to update treatments and vaccines.

Currently there are no SARS-CoV-2 variants that rise to the level of high consequence.

Treatment considerations for healthcare providers

Substitutions of Concern for SARS-CoV-2 Monoclonal Antibody Therapies

In the United States, there are two anti-SARS-CoV-2 monoclonal antibody treatments with FDA Emergency Use Authorization (EUA) for the treatment of COVID-19: [bamlanivimab plus etesevimab](#) [↗](#) and [casirivimab plus imdevimab](#). [↗](#)

CDC's national genomic surveillance program identifies new and emerging SARS-CoV-2 variants to determine implications for COVID-19 diagnostics, treatments, or vaccines authorized for use in the United States. Sequences with similar genetic changes are grouped into lineages, and multiple lineages can have the same substitutions. For example, the E484K substitution is found in lineages B.1.351, P.1, B.1.526, and many others. Genomic surveillance efforts provide the capability to detect viruses that have reduced susceptibility to treatments more quickly.

In laboratory studies, SARS-CoV-2 variants that contain the L452R or E484K substitution in the spike protein cause a marked reduction in susceptibility to bamlanivimab and may have lower sensitivity to etesevimab and casirivimab.

The table below shows the national and regional unweighted proportions of SARS-CoV-2 that contain the L452R or E484K substitution. As new data become available, additional substitutions may be added to the table below. The national and regional proportions provided in the table below will be updated weekly.

Resources

[Monoclonal Antibody COVID-19 Infusion](#) 

[Statement on Anti-SARS-CoV-2 Monoclonal Antibodies EUA | COVID-19 Treatment Guidelines \(nih.gov\)](#) 

Unweighted Proportions of SARS-CoV-2 Substitutions of Therapeutic Concern



Spike Protein Substitution	National Proportion ^a	Regional Proportions ^b		Common Pango Lineages with Spike Protein Substitutions ^c
L452R	11.5%	Region 1	6.3%	B.1.429 B.1.526.1 B.1.427 B.1
		Region 2	9.6%	
		Region 3	7.4%	
		Region 4	6.1%	
		Region 5	10.0%	
		Region 6	6.8%	
		Region 7	10.3%	
		Region 8	20.5%	
		Region 9	31.0%	
		Region 10	24.6%	
E484K	13.7%	Region 1	19.6%	B.1.526 P.1 B.1.351 B.1.1.318 R.1 B.1.525 B.1.1 B.1 P.2
		Region 2	26.4%	
		Region 3	17.8%	
		Region 4	13.7%	
		Region 5	8.2%	
		Region 6	7.6%	
		Region 7	8.6%	
		Region 8	4.8%	
		Region 9	13.9%	
		Region 10	11.0%	























a – The unweighted proportion of SARS-CoV-2 circulating in the United States that contain the designated substitution, based on >20,000 sequences collected through CDC’s national genomic surveillance during the two-week period ending April 10, 2021.

b – The unweighted regional proportion of SARS-CoV-2 circulating in each HHS region that contain the designated substitution, based on >20,000 sequences collected through CDC’s national genomic surveillance during the two-week period ending April 10, 2021.

c – The lineages listed are the most common lineages within CDC’s national genomic surveillance with these substitutions, but this list is not intended to be a complete list of the lineages that contain the spike protein substitutions.

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*Non-peer-reviewed

Related Resources

[Emerging SARS-CoV-2 Variants](#)

[New Variants of the Virus that Causes COVID-19](#)

[Cases, Data, and Surveillance](#)

[COVID-19 Genomic Epidemiology Toolkit](#)

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