Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

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.1.1.7, 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.
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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.

- Variants of Interest (VOI)
- Variants of Concern (VOC)
- Variants of High Consequence (VOHC)

Notes: Each classification of variant includes the possible attributes of lower classes (i.e., VOC includes the possible attributes of VOI); variant status might escalate or deescalate based on scientific evidence. This page 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]
B.1.526	**Spike:** (L5F*), T95I, D253G, (S477N*), (E484K*), D614G, (A701V*)	20C/S:484K	United States (New York) – November 2020	
B.1.526.1	**Spike:** D80G, Δ144, F157S, L452R, D614G, (T791I*), (T859N*), D950H	20C	United States (New York) – October 2020	

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B.1.525	**Spike**: A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L	20A/S:484K	United Kingdom/Nigeria – December 2020		• •
P.2	**Spike**: E484K, (F565L*), D614G, V1176F	20J	Brazil – April 2020		• •
B.1.617	**Spike:** L452R, E484Q, D614G	20A	India – February 2021		•

					•
B.1.617.1	**Spike:** (T95I), G142D, E154K, L452R, E484Q, D614G, P681R, Q1071H	20A/S:154K	India – December 2020		• •
B.1.617.2	**Spike:** T19R, (G142D), Δ156, Δ157, R158G, L452R, T478K, D614G, P681R, D950N	20A/S:478K	India – December 2020		• •
B.1.617.3	**Spike:** T19R, G142D, L452R, E484Q,	20A	India – October 2020		•

	D614G, P681R, D950N			

(*) = 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]	
B.1.1.7	Δ69/70, Δ144, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)	20I/501Y.V1	United Kingdom	NR-54000	• • •

					•
P.1	L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I	20J/501Y.V3	Japan/ Brazil	NR-54982	• •
B.1.351	D80A, D215G, Δ241/242/243, K417N, E484K, N501Y, D614G, A701V	20H/501.V2	South Africa	NR-54009	• •

					•
B.1.427	L452R, D614G	20C/S:452R	United States-(California)		• • •
B.1.429	S13I, W152C, L452R, D614G	20C/S:452R	United States-(California)		• •

(*) = 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.

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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.

Monoclonal antibody 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]
		Region 1	6.0%	
		Region 2	8.0%	

L452R	7.6%	Region 3	7.6%	B.1.526.1 B.1.429 B.1.427 B.1.617.2 B.1.617.1 B.1 C.36 A.2.5
		Region 4	4.4%	
		Region 5	6.7%	
		Region 6	4.1%	
		Region 7	6.5%	
		Region 8	14.5%	
		Region 9	16.6%	
		Region 10	18.0%	
E484K	15.8%	Region 1	19.5%	P.1 B.1.526 B.1.1.318 B.1.351 B.1.525 R.1 B.1.1 B.1.621 B.1 B.1.1.7
		Region 2	22.8%	
		Region 3	15.5%	
		Region 4	15.1%	
		Region 5	13.1%	
		Region 6	11.4%	
		Region 7	11.8%	
		Region 8	12.0%	
		Region 9	15.7%	
		Region 10	10.4%	

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 24, 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 24, 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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