Centers for Disease Control and Prevention

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 (Alpha), B.1.351 (Beta), B.1.617.2 (Delta), and P.1 (Gamma), 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.
- Laboratory studies suggest specific monoclonal antibody treatments may be less effective for treating cases of COVID-19 caused by variants with certain substitutions or combinations of substitutions in the spike protein.
  - L452R is present in B.1.526 (Iota), B.1.427 (Epsilon), and B.1.429 (Epsilon) lineages, as well as the B.1.617 (Kappa, Delta) lineages and sub-lineages.
  - E484K is present in B.1.525 (Eta), P.2 (Zeta), P.1 (Gamma), and B.1.351 (Beta), but only some strains of B.1.526 (Iota) and B.1.1.7 (Alpha).
  - The combination of K417N, E484K, and N501Y substitutions is present in B.1.351 (Beta).
  - The combination of K417T, E484K, and N501Y substitutions is present in P.1 (Gamma).

Get Variant Classification and Definition Updates

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What's this? Submit

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) – View current VOI in the United States that are being monitored and characterized
- Variants of Concern (VOC) – View current VOC in the United States that are being closely monitored and characterized by federal agencies
- Variants of High Consequence (VOHC) – Currently there are no SARS-CoV-2 variants that rise to the level of high consequence

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. To assist with public discussions of variants, WHO proposed using labels consisting of the Greek Alphabet, i.e., Alpha, Beta, Gamma, as a practical way to discuss variants by non-scientific audiences. The labels assigned to each variant are provided in the tables below.

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

B.1.427 (Pango lineage)[a]

Spike Protein Substitutions: L452R, D614G

Name (Nextstrain)[b]: 20C/S:452R

WHO Label: Epsilon

First Identified: United States-(California)

Attributes:

- ~20% increased transmission [21]
- 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 sera [21]
- Deescalated from a VOC on June 29, 2021 due to the significant decrease in the proportion of B.1.427 lineage viruses circulating nationally and available data indicating that vaccines and treatments are effective against this variant.

B.1.429 (Pango lineage)[a]

Spike Protein Substitutions: S13I, W152C, L452R, D614G

Name (Nextstrain)[b]: 20C/S:452R

WHO Label: Epsilon

First Identified: United States-(California)

Attributes:

- ~20% increased transmission [21]
- Reduced 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 sera [21].
- Deescalated from a VOC on June 29, 2021 due to the significant decrease in the proportion of B.1.429 lineage viruses circulating nationally and available data indicating that vaccines and treatments are effective against this variant.

B.1.525 (Pango lineage)[a]

Spike Protein Substitutions: A67V, 69del, 70del, 144del, E484K, D614G, Q677H, F888L

Name (Nextstrain)[b]: 20A/S:484K

WHO Label: Eta

First Identified: United Kingdom/Nigeria – December 2020

Attributes:

- Potential reduction in neutralization by some EUA monoclonal antibody treatments [7, 14]
- Potential reduction in neutralization by convalescent and post-vaccination sera [22]

B.1.526 (Pango lineage)[a]

Spike Protein Substitutions: L5F, (D80G*), T95I, (Y144-*), (F157S*), D253G, (L452R*), (S477N*), E484K, D614G, A701V, (T859N*), (D950H*), (Q957R*)

Name (Nextstrain)[b]: 20C/S:484K

WHO Label: Iota

First Identified: United States (New York) – November 2020

BEI Reference Isolate[c]: NR-55359

Attributes:

- 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 sublineage has been consolidated with this parent lineage

B.1.617.1 (Pango lineage)[a]

Spike Protein Substitutions: (T95I), G142D, E154K, L452R, E484Q, D614G, P681R, Q1071H

Name (Nextstrain)[b]: 20A/S:154K

WHO Label: Kappa

First Identified: India – December 2020

Attributes:

- Potential reduction in neutralization by some EUA monoclonal antibody treatments [7, 14]
- Potential reduction in neutralization by post-vaccination sera [26]

B.1.617.3 (Pango lineage)[a]

Spike Protein Substitutions: T19R, G142D, L452R, E484Q, D614G, P681R, D950N

Name (Nextstrain)[b]: 20A

First Identified: India – October 2020

Attributes:

- Potential reduction in neutralization by some EUA monoclonal antibody treatments [7, 14]
- Potential reduction in neutralization by post-vaccination sera [26]

P.2 (Pango lineage)[a]

Spike Protein Substitutions: E484K, (F565L*), D614G, V1176F

Name (Nextstrain)[b]: 20J

WHO Label: Zeta

First Identified: Brazil – April 2020

Attributes:

- Potential reduction in neutralization by some EUA monoclonal antibody treatments [7, 14]
- Reduced neutralization by post-vaccination sera [22, 23]

Footnotes for Variants of Interest

(*) = detected in some sequences but not all

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

B.1.1.7 (Pango lineage)[a]

Spike Protein Substitutions: 69del, 70del, 144del, (E484K*), (S494P*), N501Y, A570D, D614G, P681H, T716I, S982A, D1118H (K1191N*)

Name (Nextstrain)[b]: 20I/501Y.V1

WHO Label: Alpha

First Identified: United Kingdom

BEI Reference Isolate[c]: NR-54000

Attributes:

- ~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]

B.1.351 (Pango lineage)[a]

Spike Protein Substitutions: D80A, D215G, 241del, 242del, 243del, K417N, E484K, N501Y, D614G, A701V

Name (Nextstrain)[b]: 20H/501.V2

WHO Label: Beta

First Identified: South Africa

BEI Reference Isolate[c]: NR-55282

Attributes:

- ~50% increased transmission [16]
- Significantly reduced 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 [8,12,18,19,20]

B.1.617.2 (Pango lineage)[a]

Spike Protein Substitutions: T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, D950N

Name (Nextstrain)[b]: 20A/S:478K

WHO Label: Delta

First Identified: India

Attributes:

- Increased transmissibility [29]
- Potential reduction in neutralization by some EUA monoclonal antibody treatments [7, 14]
- Potential reduction in neutralization by post-vaccination sera [21]

P.1 (Pango lineage)[a]

Spike Protein Substitutions: L18F. T20N. P26S. D138Y. R190S. K417T. E484K. N501Y. D614G. H655Y. T1027I

Name (Nextstrain)[b]: 20J/501Y.V3

WHO Label: Gamma

First Identified: Japan/Brazil

BEI Reference Isolate[c]: NR-54982

Attributes:

- Significantly reduced 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]

Footnotes for Variants of Concern

(*) = detected in some sequences but not all

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 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 three anti-SARS-CoV-2 monoclonal antibody treatments with FDA Emergency Use Authorization (EUA) for the treatment of COVID-19: bamlanivimab plus etesevimab, casirivimab plus imdevimab,, and sotrovimab.

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 certain substitutions in the spike protein cause a marked reduction in susceptibility to bamlanivimab and may have reduced sensitivity to etesevimab and casirivimab. The L452R substitution found in the B.1.427 and B.1.429 lineages has been shown to cause a significant reduction in susceptibility to bamlanivimab and a modest decrease in susceptibility to the combination of bamlanivimab and etesevimab, although the clinical implications of this modest decrease are not known. [7] The E484K substitution found in the B.1.351, P.1, and B.1.526 lineages also results in a marked reduction in susceptibility to bamlanivimab, as well as the combination of bamlanivimab and etesevimab.[7] Laboratory studies also suggest that the K417N and K417T substitutions, which are present in the B.1.351 and P.1 variants, respectively, along with the E484K mutation, reduces virus susceptibility to casirivimab, although the combination of casirivimab and imdevimab appears to retain activity.[14] There is no reported reduction in susceptibility of variants to sotrovimab.[28]

The table below shows the national and regional unweighted proportions of SARS-CoV-2 that contain the L452R or E484K substitution, individually, as well as the unweighted proportions of SARS-CoV-2 that contain the combination of K417N, E484K, and N501Y substitutions or the combination of K417T, E484K, and N501Y substitutions. 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

L452R Spike Protein Substitution
National Proportion[a]: 15.3%

Regional Proportions[b]		Common Pango Lineages with Spike Protein Substitutions[c]
		B.1.617.2
Region 1	14.3%	B.1.526
Region 2	19.7%	B.1.429
Region 3	12.1%	B.1.427
Region 4	7.7%	AY.2
Region 5	6.4%	B.1
Region 6	13.9%	A.2.5
Region 7	41.0%	C.36.3
Region 8	27.1%	B.1.623
Region 9	22.8%	
Region 10	14.6%	

Region 10	14.6%

E484K Spike Protein Substitution
National Proportion[a] : 19.6%

Regional Proportions[b]		**Common Pango Lineages with Spike Protein Substitutions[c]**
		P.1
Region 1	29.0%	B.1.526
Region 2	20.7%	B.1.621
Region 3	13.5%	B.1.1.318
Region 4	24.0%	B.1.351
Region 5	17.1%	B.1.623
Region 6	15.4%	P.1.1
Region 7	11.5%	B.1.1.7
Region 8	8.1%	B.1.525
Region 9	21.0%	
Region 10	27.1%	

K417N, E484K, N501Y Spike Protein Substitution
National Proportion[a] : 0.3%

Regional Proportions[b]		**Common Pango Lineages with Spike Protein Substitutions[c]**
		B.1.351
Region 1	0.0%	B.1.351.3
Region 2	0.2%	
Region 3	0.4%	
Region 4	0.4%	
Region 5	0.3%	
Region 6	0.2%	
Region 7	0.9%	
Region 8	0.0%	
Region 9	0.2%	
Region 10	0.7%	

K417T, E484K, N501Y Spike Protein Substitution
National Proportion[a] : 11.3%

Regional Proportions[b]		**Common Pango Lineages with Spike Protein Substitutions[c]**
		P.1
Region 1	12.4%	P.1.1
Region 2	7.9%	
Region 3	4.6%	
Region 4	13.7%	
Region 5	10.3%	
Region 6	7.5%	
Region 7	8.8%	
Region 8	3.5%	
Region 9	14.7%	
Region 10	21.5%	

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

a – The unweighted proportion of SARS-CoV-2 circulating in the United States that contain the designated substitution, based on >6,500 sequences collected through CDC's national genomic surveillance during the two-week period ending June 5, 2021.

b – The unweighted regional proportion of SARS-CoV-2 circulating in each HHS region that contain the designated substitution, based on >6,500, sequences collected through CDC's national genomic surveillance during the two-week period ending June 5, 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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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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