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COVID-19

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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

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 Department of Health and Human Services (HHS) established a SARS-CoV-2 Interagency Group (SIG) to improve coordination among the US Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), US 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
- Variants of Concern
- Variants of High Consequence

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

Notes: Each class of variant includes the possible attributes of lower classes; 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 demonstrates 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 risk of reinfection, 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.

Name (Pango lineage)	Substitution	Name (Nextstrain[a])	First Detected	BEI Reference Isolate[b]	Pre Att
B.1.526	**Spike:** (L5F*), T95I, D253G, (S477N*), (E484K*), D614G, (A701V*) **ORF1a:** L3201P, T265I, Δ3675/3677 **ORF1b:** P314L, Q1011H **ORF3a:** P42L, Q57H **ORF8:** T11I **5’UTR:** R81C	20C	New York/November 2020		• Pc re ne by m an tre • Pc re ne by co an va se
B.1.525	**Spike**: A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L **ORF1b**: P314F **ORF1a**: T2007I **M**: I82T **N:** A12G, T205I **5’UTR**: R81C	20C	New York/December 2020		• Pc re ne by m an tre • Pc re ne by co an va se
P.2	**Spike**: E484K, D614G, V1176F **ORF1a**: L3468V, L3930F	20J	Brazil/April 2020		• Pc re ne by m an tre

	ORF1b: P314L **N:** A119S, R203K, G204R, M234I **5’UTR**: R81C				• Po re ne by co an va se

(*)=detected in some sequences but not all
a – Nextstrain
b – 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.

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].

Variant of Concern

A variant for which there is evidence of an increase in transmissibility, more severe disease (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, and vaccines
    - Widespread interference with diagnostic test targets
    - Evidence of substantially increased resistance 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.

Name (Pango lineage)	Spike Protein Substitutions	Name (Nextstrain[a])	First Detected	BEI Reference Isolate[b]	Known Att
B.1.1.7	Δ69/70 Δ144Y (E484K*) (S494P*) N501Y A570D D614G P681H	20I/501Y.V1	United Kingdom	NR-54000	- ~50% in transmi - Likely increas severity on hospital and cas fatality - Minima on neutrali by EUA monocl antibod therape [14] - Minima on neutrali by convale and pos vaccina sera [8,9,10,11,12]

P.1	K417N/T E484K N501Y D614G	20J/501Y.V3	Japan/ Brazil	NR-54982	- Modera impact neutrali by EUA monocl antibod therape - Reduce neutrali by convale and pos vaccinat sera [15]
B.1.351	K417N E484K N501Y D614G	20H/501.V2	South Africa	NR-54009	- ~50% in transmi - Modera impact neutrali by EUA monocl antibod therape - Modera reducti neutrali by convale and pos vaccinat sera [8,12
B.1.427	L452R D614G	20C/S:452R	US-California		- ~20% in transmi [21] - Significa impact neutrali by som not all, therape - Modera reducti

					neutrali using convale and pos vaccinat sera [21]
B.1.429	S13I W152C L452R D614G	20C/S:452R	US-California		- ~20% in transmi [21] - Significa impact neutrali by som not all, therape - Modera reductic neutrali using convale and pos vaccinat sera [21]

(*)=detected in some sequences but not all
a – Nextstrain
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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 significant 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.

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*Non-peer-reviewed

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