BV-BRC SARS-CoV-2 Emerging Variant Report November 08, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20221108.xlsx" based on sequence data from GISAID.

Keep in mind that the information provided reflects sequence counts and sequence proportions and, as such, is impacted by sampling bias in the sequence databases and should not be interpreted as the prevalence of disease caused by these variants.

In addition, due to sequence anomalies (e.g., ambiguous nucleotides in many sequence records) and other issues, the absolute counts of Variants of Concern sequences are likely to be underestimates of the true sequence prevalence.

The key findings are summarized below.

USA - VOC

OMICRON

- In the US, virtually all sequences reported since July are **Omicron**.
 - O The CDC Nowcast for the week ending 11/05/22 estimates that **BA.5** proportions are still dominating in the United States at 39.2% (95% PI: 36.2-42.3%), but this is a significant decrease from last week. Significant regional differences exist: https://covid.cdc.gov/covid-data-tracker/#variant-proportions.
 - o The CDC Nowcast estimates for **BA.4.6** proportions are slowly decreasing, now at 9.5% (95% PI: 8.6-10.5%)
 - o BQ.1.1 and BQ.1 have been added to the Nowcast tracker. BQ.1 is currently estimated at 16.5% (95% PI: 13.6-20.0%), an increase since last week. BQ.1.1 has overtaken BQ.1 this week and is currently estimated at 18.8% (95% PI: 15.7-22.4%), an increase since last week.
 - o BF.7 has been added to the Nowcast tracker and is currently estimated at 9.0% (95% PI: 7.9-10.1%)
 - o BA.5.2.6 has been added to the Nowcast tracker and is currently estimated at 3.1% (95% PI: 2.5-3.7%)
 - BA.2.75 has been split into BA.2.75 and BA.2.75.2. BA.2.75 is currently estimated at 2.6% (95% PI: 1.9-2.8%). BA.2.75.2 is currently estimated at 1.3% (95% PI: 0.9-1.7%).
- Listed below are lineages with sequence prevalence >1.0% or a growth rate >3 fold and count >10 in October (ranked in order of sequence prevalence). Lineages with fold growth >3 from September to October are highlighted in *bold italic*:
 - o BA.5.2.1 16%, 0.78 fold growth
 - o BA.5.2 11%, 0.97 fold growth
 - \circ BA.4.6 8.7%, 0.90 fold growth
 - \circ BA.5.1 6.7%, 0.80 fold growth
 - \circ BQ.1 4.6%, 6.4 fold growth
 - \circ BF.7 4.1%, 2.6 fold growth

- \circ BQ.1.1 3.6%, 11 fold growth
- \circ BF.10 2.5%, 0.80 fold growth
- BA.2.75 2.2%, 5.1 fold growth
- \circ BA.5.2.9 2.0%, 0.83 fold growth
- \circ BA.5 1.9%, 0.78 fold growth
- BA.5.2.6 1.9%, 3.5 fold growth
- \circ BA.5.6 1.8%, 0.49 fold growth
- \circ BF.5 1.7%, 0.96 fold growth
- \circ BA.5.5 1.7%, 0.53 fold growth
- \circ BF.26 1.5%, 1.1 fold growth
- BA.5.2.21 1.1%, 0.91 fold growth
- \circ BE.1.1 1.0%, 0.93 fold growth
- \circ BE.1 1.0%, 0.66 fold growth
- o BQ.1.2 0.63%, 11 fold growth
- o BA.2.3.20 0.52%, 3.5 fold growth
- o BQ.1.3 0.51%, 13 fold growth
- o XBB 0.34%, 11 fold growth
- o BF.14 0.24%, 3.4 fold growth
- o BA.5.2.13 0.13%, 3.3 fold growth
- o BA.5.2.14 0.12%, 6 fold growth
- o BE.1.2.1 0.11%, 5.5 fold growth
- o BE.4.1.1 0.09%, 9 fold growth
- o XBB.1 0.09%, 9 fold growth
- Several Omicron sub-lineages carry a recurring mutation at position 346 in the S protein (S:R346T in BA.4.6, BF.7, BF.11, BA.5.1.18, BA.5.2.6, BQ.1.1, BA.4.1.8, BA.5.2.1; S:R346S in BF.13, BA.5.2, BF.26, BA.5.2.1; or S:R346I in BA.5.9, BE.1.1, BA.5.2, BA.4.1)
- Several Omicron sub-lineages carry a recurring mutation at position 444 in the S protein (S:K444T in BQ.1, BQ.1.1, BA.5.6.2, BE.1.1.1, BE.1.1 and S:K444R in BA.5.2.1, BF.16, BA.2.3.20)
- Several Omicron sub-lineages carry a recurring mutation at position 445 (S:V445A in BF.25, BA.5.2.23, BA.4.6, BA.5.1.12, BA.5.2)
- Several Omicron sub-lineages carry a recurring mutation at position *446* (S:*G446S* in BA.2.75.2, BA.2.75.5, CA.1, BM.1.1, BY.1, BL.1). (S:*G446D* also occurs in BA.5.2, BA.5.2.1, CD.1).
- Several Omicron sub-lineages carry a recurring mutation at position *460* (S:*N460K* in BQ.1, BQ.1.1, BA.2.75.2, BA.2.3.20, BA.2.75.5, CA.1, BM.1.1, BE.1)

DELTA (B.1.617.2 and AY sub-lineages) (no significant change since previous report)

• Three Delta sequences in the US in September; two in October so far

<u>USA – (other VOCs and VOIs)</u> (no significant change since previous report)

• One Alpha sequence in the US in September. This genome appears to be have accumulated several other mutations in addition to those normally associated with B.1.1.7 genomes (P9L,D80G,G232V,S247N,Y248-,D253Y,Y449H,E484K,F490S,T547K,T572I,K1191N). None in October.

USA – Recombinants

- XBB 24 sequences in September; 109 in October so far
- XBB.1 8 sequences in September; 30 in October so far
- XAZ 54 sequences in September; 22 in October so far
- XAS 4 sequences in September; 2 in October so far
- XAV 1 sequences in September; 1 in October so far
- **XBC** 1 sequences in September; 1 in October so far
- See a summary of recombinant lineages at the end of this report.

World - VOC

OMICRON

- Omicron remains dominant globally. Listed below are lineages showing the highest sequence prevalence (> 1.0%) or a fold growth > 3 fold in October so far. Lineages with fold growth > 3 from September to October are highlighted in **bold italic**:
 - o BA.5.2 13%, 0.74 fold growth
 - o BA.5.2.1 11%, 0.70 fold growth
 - \circ BF.7 7.5%, 2.1 fold growth
 - \circ BA.5.1 6.9%, 0.69 fold growth
 - \circ BQ.1.1 4.3%, 7.4 fold growth
 - \circ BA.4.6 3.8%, 0.74 fold growth
 - \circ BQ.1 3.4%, 5.6 fold growth
 - \circ BA.2.75 2.9%, 3.2 fold growth
 - \circ BF.5 2.8%, 0.74 fold growth
 - \circ BA.5.2.6 2.0%, 2.3 fold growth
 - \circ BE.1.1 1.5%, 0.71 fold growth
 - \circ BA.5 1.4%, 0.83 fold growth
 - \circ BA.2 1.2%, 5.1 fold growth
 - \circ BA.5.2.20 1.2%, 0.83 fold growth
 - \circ XBB 0.8%, 7.3 fold growth
 - o BQ.1.2 0.36%, 5.1 fold growth
 - o XBB.1 0.34%, 3.1 fold growth
 - o BQ.1.3 0.2%, 10 fold growth
 - o BA.5.10.1 0.1%, 3.3 fold growth
 - o BE.4.1.1 0.09%, 9 fold growth
 - BA.2.10.1 0.05%, 5 fold growth
 - CC.1 0.04%, 4 fold growth
- Substitutions in spike that we are monitoring (>3 fold growth from September to October with counts >10) include those listed below (but note that the numbers are still relatively small for some of these). Substitutions with sequence prevalence >1.5% are highlighted in *bold italic*:
 - o G252V 0.79%, 6.6 fold growth
 - o K444T 11%, 5.6 fold growth
 - o I666V 0.44%, 5.5 fold growth
 - \circ V445P 1.3%, 5 fold growth

- \circ L368I 1.2%, 5 fold growth
- o R78M 0.05%, 5 fold growth
- o Y248- 0.05%, 5 fold growth
- E619Q 0.28%, 4.7 fold growth
- \circ Q183E 1.3%, 4.6 fold growth
- F490S 2.5%, 4.5 fold growth
- \circ V83A 1.3%, 4.5 fold growth
- \circ H146Q 1.3%, 4.1 fold growth
- o K147- 0.08%, 4 fold growth
- o N148- 0.08%, 4 fold growth
- o I834M 0.04%, 4 fold growth
- o I931V 0.04%, 4 fold growth
- o T470N 0.04%, 4 fold growth
- \circ V213E 1.4%, 3.8 fold growth
- o N460K 16%, 3.5 fold growth
- o K150E 0.1%, 3.3 fold growth

Note on convergent mutations: Over the past two months we have noted an increase in convergent mutations at several antigenically important sites in addition to L452*: R346*(T/I/S/K), K356*(T/R), K444*(M/T/R/N), V445*(A/P), G446*(D/S/V), N450* and N460*(K/S). Most of these mutations, as well as several others previously reported in Omicron and other lineages, are discussed in a recent preprint below.

"Imprinted SARS-CoV-2 humoral immunity induces convergent Omicron RBD evolution (on convergent mutations at sites: R346, R356, K444, L452, N460K and F486)"

DELTA (B.1.617.2 and **AY** sub-lineages)

• 19 Delta isolates globally in September; 4 in October

World (other VOIs)

- One Alpha genome in September (in US); 16 in October
- Two Beta genome in September (in Germany and Kenya); none in October

World - Recombinants

- **XBB** 1228 in October
- **XBB.1** 529 in October
- XAZ 149 in October
- **XBC** 16 in October
- XAY 10 in October
- XAS 3 in October
- XAN − 2 in October
- XAV 1 in October
- XAH 1 in October

Variants that have been mentioned in the media and/or social media:

- Pfizer and BioNTech Announce Updated Clinical Data for Omicron BA.4/BA.5-Adapted Bivalent Booster Demonstrating Substantially Higher Immune Response in Adults Compared to the Original COVID-19 Vaccine
- mRNA bivalent booster enhances neutralization against BA.2.75.2 and BQ.1.1
- Updated vaccine protects against SARS-CoV-2 variants including Omicron (B.1.1.529) and prevents transmission in hamsters
- Low neutralization of SARS-CoV-2 Omicron BA.2.75.2, BQ.1.1, and XBB.1 by 4 doses of parental mRNA vaccine or a BA.5-bivalent booster
- Risk of reinfection, vaccine protection, and severity of infection with the BA.5 omicron subvariant: a nation-wide population-based study in Denmark
- China posts 6-month high Covid count as it sticks with strategy
- Increased Respiratory Virus Activity, Especially Among Children, Early in the 2022-2023 Fall and Winter
- The COVID-19 Booster: Australia experiences surge in cases as new wave begins

Recombinant lineages:

One new recombinant lineages have been added this week: XBF. A summary table of recombinant lineages can be found below with more details. We have added the number of recombinants genomes for each lineage. XA, XB, and XC have not been detected in the past 6 months. XD-XBF are Omicron/Omicron or Omicron/Delta recombinants. With the exception of XBB, the majority of these recombinant lineages do not appear to have taken off and several have not been detected in recent weeks. The XBB lineage appears to have the largest number of genomes.

Name	number	Github#	Lineage 1	Lineage 2	Location first detected
XA	45	NA	B.1.1.7	B.1.177	UK
<u>XB</u>	3435	<u>#189</u>	B.1.634	B.1.631	N. America
<u>XC</u>	25	<u>#263</u>	Delta (AY.29)	B.1.1.7	Japan
XD	34	#444	Delta (AY.4)	BA.1	France
<u>XE</u>	2829	<u>#454</u>	BA.1	BA.2	UK
<u>XF</u>	34	<u>#445</u>	Delta	BA.1	UK
<u>XG</u>	479	<u>#447</u>	BA.1	BA.2	Denmark
XH	174	<u>#448</u>	BA.1	BA.2	Denmark
XJ	253	<u>#449</u>	BA.1	BA.2	Finland
XK	25	<u>#460</u>	BA.1	BA.2	Belgium

XL	120	#464	BA.1	BA.2	UK	
XM	554	#472	BA.1.1	BA.2	Multiple EU	
XN	290	#480	BA.1	BA.2	UK	
XP	57	#481	BA.1.1	BA.2	UK	
XQ	145	#468	BA.1.1	BA.2	UK	
XR	183	#469	BA.1.1	BA.2	UK	
XS	60	#471	Delta	BA.1.1	USA	
XT	14	#478	BA.2	BA.1*	S. Africa	
XU	16	#522	BA.1*	BA.2	India	
XV	42	#463	BA.1*	BA.2*	Denmark	
XW	195	<u>#591</u>	BA.1*	BA.2*	JP, DE, SI, CA, UK, US	
XY	126	<u>#606</u>	BA.1*	BA.2*	FR, IL, UK, US	
XZ	218	<u>#636</u>	BA.2*	BA.1*	Multiple	
XAA	100	<u>#664</u>	BA.1*	BA.2*	US, IL	
XAB	114	# <u>665</u>	BA.1*	BA.2*	IT, FR, DE, CH, DK	
XAC	207	# <u>590</u>	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US	
XAD	104	<u>#607</u>	BA.2*	BA.1*	CZ,DE,UK	
XAE	132	<u>#637</u>	BA.2*	BA.1*	CA,US,NL,CH	
XAF	300	<u>#676</u>	BA.1*	BA.2*	CR	
XAG	404	<u>#709</u>	BA.1.1	BA.2.23	BR	
XAH	168	<u>#755</u>	BA.2*	BA.1*	SI	
XAJ	103	<u>#826</u>	BA.2.12.1	BA.4	UK	
XAK	148	<u>#823</u>	BA.1*	BA.2*	DE	
XAL	124	<u>#757</u>	BA.1.1	BA.2*	DE	
XAM	543	<u>#759</u>	BA.1.1	BA.2.9	Panama	
XAN	206	<u>#771</u>	BA.2*	BA.5.1	Multiple	
XAP	81	<u>#789</u>	BA.2*	BA.1*	US	
XAQ	81	<u>#798</u>	BA.1*	BA.2*	Canada	
XAR	54	#860	BA.1*	BA.2*	Reunion/France	
XAS	195	<u>#882</u>	BA.5*	BA.2*	N. America	
XAT	99	<u>#885</u>	BA.2.3.13	BA.1*	Japan	
XAU	108	<u>#894</u>	BA.1.1*	BA.2.9*	Multiple	

XAV	80	<u>#911</u>	BA.2*	BA.5*	France	
XAW	45	<u>#895</u>	BA.2*	AY.122	2 Russia	
XAY	44	<u>#844</u>	BA.2	AY.45	S. Africa	
XAZ	2250	<u>#797</u>	BA.2.5, BA.5	BA.2.5	Multiple	
XBA	4	<u>#844</u>	AY.45	BA.2	S. Africa	
XBB*	3049	# <u>1058</u>	BJ.1	BM.1.1.1	Singapore/US	
XBC*	49	#1100	Delta	BA.2	Philippines	
XBD	27	<u>#1137</u>	BA.2.75.2	BF.5	Multiple	
XBE*	88	<u>#1246</u>	BA.5.2	BE.4	USA	
XBF	9	<u>#1259</u>	BA.5.2.3	CJ.1	Australia	

Newly designated Pango lineages:

New lineages designated this week:

- BR.2.1: Fast growing BR.2 with ORF8:S67F, at least 130 samples, Australia, USA and Japan
- **DG.1**: Potential CK.2.1.1 sub-lineage with Spike 252S from Australia, Denmark, South Korea and Spain [16 Sequences] with a sub-cluster of S:F490L and ORF7a: F87C
- <u>DD.1</u>: BA.2.3 Saltation lineage with several mutations (inc Spike R346T, Y449N, N460K, N481K and Q493L) from Philippines and Australia
- BE.5: Third BA.5.3.1 (+ T28693C) sublineage with S:346T circulating in South Africa
- <u>BE.7</u>: Second BA.5.3.1 (+ T28693C) sublineage with S:346T circulating in South Africa
- <u>BA.5.2.39</u>: New BA.5.2 + orf1b:1050N sublineage with S:R346T (44seqs) Usa, Canada, Uk, Germany
- BE.8: South African BA.5.3.1 + T28693C sublineage with S:R346T, Orf3a:P240S
- BA.5.11: Large South African BA.5 + C1627T sublineage (without 28330G) with S:R346T and Orf7a:S44P
- DF.1: Fast BA.5.10.1 (S:R346T) sublineage with S:144del and Orf1a:Q1198R
- XBF: BA.5.2.3 x CJ.1 (BM.1.1.1.1) recombinant
- **DB.1**: BA.5.2.25 (S:K444T)sublineage with S:R346T and S:N460K (T22942G)
- **XAY.1.1**: XAY.1 with S:346T
- DA.1: BA.5.2 (with ORF1b:T1050N) with S:T430I, sublineage with S:R346T
- BA.5.2.38: BA.5.2 (with ORF1b:T1050N) with S:T430I, sublineage with S:R346T
- DH.1: BA.5.1 with additional mutations ORF1a:S2731G, ORF1a:A2199T and deletions S:Y145-,S:H146-