BV-BRC SARS-CoV-2 Emerging Variant Report October 25, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20221025.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.

This report includes preliminary/incomplete stats for the month of October in order to identify early signs of novel variants emerging.

The key findings are summarized below.

USA – VOC

OMICRON

- In the US, virtually all sequences reported since July are **Omicron**.
 - The CDC Nowcast for the week ending 10/15/22 estimates that BA.5 proportions are still dominating in the United States at 62.2% (95% PI: 57.8-66.3%). Significant regional differences exist: <u>https://covid.cdc.gov/covid-data-tracker/#variantproportions</u>.
 - The CDC Nowcast estimates for **BA.4.6** proportions are slowly decreasing, now at 11.3% (95% PI: 10.2-12.6%)
 - BQ.1.1 and BQ.1 have been added to the Nowcast tracker. BQ.1 is currently estimated at 9.4% (95% PI: 6.7-12.9%); this had nearly doubled since last week! BQ.1.1 is currently estimated at 7.2% (95% PI: 4.8-10.4%).
 - *BF.7 has been added to the Nowcast tracker and is currently estimated at 6.7% (95% PI: 5.8-7.6%)*
 - BA.2.75 has been split into BA.2.75 and BA.2.75.2. BA.2.75 is currently estimated at 1.6% (95% PI: 1.3-1.9%). BA.2.75.2 is currently estimated at 1.3% (95% PI: 0.9-1.9%).
- Lineages with sequence prevalence >1.0% or a growth rate >3 fold and count >10 in October are (ranked in order of sequence prevalence; numbers are still relatively small in October so far):
 - o BA.5.2.1 18%, 0.85 fold growth
 - BA.5.2 11%, 0.96 fold growth
 - \circ BA.4.6 9.5%, 0.96 fold growth
 - \circ BA.5.1 6.5%, 0.77 fold growth
 - *BF*.7 4.2%, 2.7 fold growth
 - BQ.1 3.5%, 4.8 fold growth
 - \circ BF.10 2.6%, 0.86 fold growth

- $\circ \quad BA.5.5-2.2\%, 0.65 \ fold \ growth$
- \circ BQ.1.1 2.2%, 6.4 fold growth
- \circ BF.5 2.0%, 1.1 fold growth
- \circ BA.5.6 2.0%, 0.54 fold growth
- BA.2.75 1.8%, 4.9 fold growth
- \circ BF.26 1.7%, 1.2 fold growth
- $\circ \quad BA.5-1.6\%, 0.66 \ fold \ growth$
- $\circ \quad BA.5.2.6-1.5\%,\, 2.9 \text{ fold growth} \\$
- \circ BA.5.2.9 1.5%, 0.65 fold growth
- \circ BE.1 1.2%, 0.78 fold growth
- \circ BA.5.2.21 1.0%, 0.88 fold growth
- \circ BA.5.2.20 1.0%, 1.2 fold growth
- BQ.1.2 0.48%, 9.6 fold growth
- BA.5.2.24 0.35%, 3.2 fold growth
- BQ.1.3 0.3%, 10 fold growth
- BF.14 0.26%, 3.7 fold growth
- XBB 0.13%, 6.5 fold growth
- BF.7 & BQ.1 predominant spike substitutions (substitutions that differ from BA.4/BA.5 are highlighted in *bold italic*):

T19I,L24-,P25-,P26-,A27S,H69-,V70-

,G142D,V213G,G339D,R346T,S371F,S373P,**S375F**,T376A,D405N,R408S,K417N,N4 40K,L452R,S477N,T478K,E484A,F486V,Q498R,N501Y,Y505H,D614G,H655Y,N679 K,P681H,N764K,D796Y,Q954H,N969K

• BQ.1.1 predominant spike substitutions (substitutions that differ from BA.4/BA.5 are highlighted in *bold italic*):

T19I,L24-,P25-,P26-,A27S,H69-,V70-

,G142D,V213G,G339D,R346T,S371F,S373P,**S375F**,T376A,D405N,R408S,K417N,N4 40K,**K444T**,L452R,**N460K**,S477N,T478K,E484A,F486V,Q498R,N501Y,Y505H,D614 G,H655Y,N679K,P681H,N764K,D796Y,Q954H,N969K

- Several Omicron sub-lineages appear to 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 appear to 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; none 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).

<u>USA – Recombinants</u>

- XAZ 49 sequences in the US in September; 3 in October so far
- XBB 19 sequences in the US in September; 11 in October so far
- XBB.1 –8 in August; none in September; 9 in October so far
- XAS 3 in August; none in September; 1 in October so far
- XAJ 2 in August; none in September; none in October so far
- XAV 1 in August; none in September; none in October so far
- XBC 1 in August; none in September; none in October so far
- See a summary of recombinant lineages at the end of this report.

World – VOC

OMICRON

- Omicron remains dominant globally, with the following 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*:
 - BA.5.2 13%, 0.78 fold growth
 - BA.5.2.1 11%, 0.70 fold growth
 - \circ BF.7 8.0%, 2.2 fold growth
 - BA.5.1 7.4%, 0.73 fold growth
 - BA.4.6 3.6%, 0.683 fold growth
 - \circ BQ.1.1 2.7%, 5.7 fold growth
 - BF.5 2.5%, 0.71 fold growth
 - BA.2.75 2.5%, 3.5 fold growth
 - \circ BQ.1 2.4%, 4.1 fold growth
 - BE.1.1 1.8%, 0.83 fold growth
 - BA.5.2.6 1.7%, 2.2 fold growth
 - \circ BA.5 1.4%, 0.82 fold growth
 - \circ BA.5.2.20 1.4%, 1.0 fold growth
 - o BA.2 0.86%, 3.9 fold growth
 - XBB.1 0.79%, 6.6 fold growth
 - XBB 0.43%, 4.8 fold growth
 - BQ.1.2 0.19%, 3.2 fold growth
 - BA.2.3 0.14%, 7 fold growth
 - BO.1.3 0.1%, 5 fold growth
 - BE.4.1.1 0.08%, 8 fold growth
- A **BA.2.3** sublineage (designated **BA.2.3.20**, not yet updated in GISAID) has several additional spike mutations (BA.2.3 + M153T, N164K, H245N, G257D, K444R, N450D, L452M, N460K, E484R, and a R493Q reversion) and has increased in September (n=80) compared to August (n=12) in several countries. Singapore: an increase from n=3/1566

(0.2%) to 24/617 (4%) ~19 fold. Denmark: from 0/13550 to 19/8583 genomes in September. USA: from n=6/123781 (0.005%) to n=8/26214 (0.03%) 6-fold increase. Austria: from n=0/13861 (0%) to n=10/4920 (0.2%). Canada: 0/14793 (0%) to 9/3274 (0.27%). Australia 3/7439 (0.04%) to 6/1161 (0.5%) 13-fold increase.

- Substitutions in spike that we are monitoring (>3 fold growth from September to October with counts >10) include the following (but note that the numbers are still relatively small for some of these) (substitutions with sequence prevalence >1.0% are highlighted in *bold italic*:
 - o G252V 0.94%, 7.8 fold growth
 - o L368J 0.06%, 6 fold growth
 - L368I 1.3%, 6.0 fold growth
 - V445P 1.4%, 5.9 fold growth
 - Q183E 1.4%, 5.8 fold growth
 - V83A 1.4%, 5.6 fold growth
 - H146Q 1.4%, 5.0 fold growth
 - D614S 0.05%, 5 fold growth
 - G75D 0.05%, 5 fold growth
 - I834M 0.05%, 5 fold growth
 - R78M 0.05%, 5 fold growth
 - V213E 1.4%, %, 4.5 fold growth
 - K147- 0.09%, 4.5 fold growth
 - N148- 0.09%, 4.5 fold growth
 - F490S 2.2%, 4.3 fold growth
 - E619Q 0.21%, 4.2 fold growth
 - \circ K444T 7.4%, 4.2 fold growth
 - A1078T 0.04%, 4 fold growth
 - R346E 0.04%, 4 fold growth
 - I666V 0.25%, 3.6 fold growth
 - S691P 0.07%, 3.5 fold growth
 - E484R 0.68%, 3.4 fold growth
 - S929I 0.1%, 3.3 fold growth
 - o L452M 0.69%, 3.1 fold growth
 - N164K 0.68%, 3.1 fold growth
 - H245N 0.71%, 3.1 fold growth
 - M153T 0.7%, 3.0 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 new preprint below.

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

DELTA (B.1.617.2 and AY sub-lineages)

• 23 Delta isolates globally in September; none in October so far

World (other VOIs)

- One Alpha genome in September (in US); none in October so far
- One Beta genome in September (in Germany); none in October so far

World – Recombinants

- XBB.1 402 in October so far
- **XBB** 217 in October so far
- XAZ 60 in October so far
- XBC 8 in October so far
- XAY 1 in October so far
- XAS 1 in October so far

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

- Newer coronavirus subvariants ticking up in California amid concerns of winter wave
- <u>A 'Tripledemic'? Flu and Other Infections Return as Covid Cases Rise</u>
- New immune-evasive Omicron strains are coming. Is Canada ready?
- Cases of BQ.1, BQ.1.1 COVID variants double in U.S. as Europe warns of rise
- Why Omicron subvariants BQ.1 and BQ.1.1 are poised to take over in the U.S.
- Antibody responses to Omicron BA.4/BA.5 bivalent mRNA vaccine booster shot
- Distinct Neutralizing Antibody Escape of SARS-CoV-2 Omicron Subvariants BQ.1, BQ.1.1, BA.4.6, BF.7 and BA.2.75.2
- <u>Scientists explain what we should expect as COVID variants XBB, BQ.1 spread in Europe and Asia</u>
- Omicron keeps finding new evolutionary tricks to outsmart our immunity
- <u>Global COVID-19 cases down, but rising in Western Pacific</u>

Recombinant lineages:

One new recombinant lineages have been added this week: XBE. 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-XBD are Omicron/Omicron or Omicron/Delta recombinants. The majority of these recombinant lineages do not appear to have taken off and several have not been detected in recent weeks. The XB 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
XB	3435	<u>#189</u>	B.1.634	B.1.631	N. America

XC	25	<u>#263</u>	Delta (AY.29)	B.1.1.7	Japan
XD	34	<u>#444</u>	Delta (AY.4)	BA.1	France
<u>XE</u>	2829	<u>#454</u>	BA.1	BA.2	UK
XF	34	<u>#445</u>	Delta	BA.1	UK
XG	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	<u>#464</u>	BA.1	BA.2	UK
XM	553	<u>#472</u>	BA.1.1	BA.2	Multiple EU
<u>XN</u>	290	<u>#480</u>	BA.1	BA.2	UK
<u>XP</u>	57	<u>#481</u>	BA.1.1	BA.2	UK
<u>XQ</u>	145	<u>#468</u>	BA.1.1	BA.2	UK
XR	183	<u>#469</u>	BA.1.1	BA.2	UK
<u>XS</u>	60	<u>#471</u>	Delta	BA.1.1	USA
<u>XT</u>	14	<u>#478</u>	BA.2	BA.1*	S. Africa
XU	16	<u>#522</u>	BA.1*	BA.2	India
XV	42	<u>#463</u>	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
<u>XZ</u>	217	<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	378	<u>#709</u>	BA.1.1	BA.2.23	BR
XAH	167	<u>#755</u>	BA.2*	BA.1*	SI
XAJ	103	<u>#826</u>	BA.2.12.1	BA.4	UK

XAK XAL	144 124	<u>#823</u>	BA.1*	BA.2*	DE
XAL	124	uaca	1		
		<u>#/5/</u>	BA.1.1	BA.2*	DE
XAM	541	<u>#759</u>	BA.1.1	BA.2.9	Panama
XAN	97	<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	186	<u>#882</u>	BA.5*	BA.2*	N. America
XAT	98	<u>#885</u>	BA.2.3.13	BA.1*	Japan
XAU	87	<u>#894</u>	BA.1.1*	BA.2.9*	Multiple
XAV	79	<u>#911</u>	BA.2*	BA.5*	France
XAW	40	<u>#895</u>	BA.2*	AY.122	Russia
XAY	23	<u>#844</u>	BA.2	AY.45	S. Africa
XAZ	1979	<u>#797</u>	BA.2.5, BA.5	BA.2.5	Multiple
XBA	4	<u>#844</u>	AY.45	BA.2	S. Africa
XBB	235	# <u>1058</u>	BJ.1	BM.1.1.1	Singapore/US
XBC	14	#1100	Delta	BA.2	Philippines
XBD	27	#1137	BA.2.75.2	BF.5	Multiple
XBE	122	<u>#1246</u>	BA.5.2	BE.4	USA

Newly designated Pango lineages:

New lineages designated this week:

- <u>XBE</u>: recombinant between BA.5.2+Orf1b:1050N+S:346T and BE.4+29868A
- <u>BN.1.2.1</u>: BN.1.2 sublineage with S:T470N, Orf1b:K1471I
- <u>CQ.2</u>: Potential new BE.4.1.1 (= S:346T+S:444R) sublineage with S:V445A and Orf1a:H1141Y
- <u>BQ.1.1.2</u>: BQ.1.1 with S:D253G <u>BA.5.2.36 & CT.1</u>: Sublineage of BA.5.2 (ORF1b:T1050N) with S:K444T, S:K356T + S:K444T lineage