## BV-BRC SARS-CoV-2 Emerging Variant Report October 18, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20221018.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**.
  - O The CDC Nowcast for the week ending 10/15/22 estimates that **BA.5** proportions are still dominating in the United States at 67.9% (95% PI: 64.1-71.4%). Significant regional differences exist: <a href="https://covid.cdc.gov/covid-data-tracker/#variant-proportions">https://covid.cdc.gov/covid-data-tracker/#variant-proportions</a>.
  - The CDC Nowcast has split BA.4 and BA.4.6; estimates for **BA.4** proportions continue to fall and are now at 0.6% (95% PI: 0.5-0.6%); estimates for **BA.4.6** proportions are remaining steady, now at 12.2% (95% PI: 11.1-13.4%)
  - o BQ.1.1 and BQ.1 have been added to the Nowcast tracker. BQ.1.1 is currently estimated at 5.7% (95% PI: 3.5-9.1%). BQ.1 is currently estimated at 5.7% (95% PI: 3.5-8.9%).
  - o BF.7 has been added to the Nowcast tracker and is currently estimated at 5.3% (95% PI: 4.6-6.1%)
  - BA.2.75 has been split into BA.2.75 and BA.2.75.2. BA.2.75.2 is currently estimated at 1.4% (95% PI: 0.9-2.2%). BA.2.75 is currently estimated at 1.3% (95% PI: 1.0-1.9%).
- Lineages with sequence prevalence >0.5% 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** 22%, 1.1 fold growth
  - o **BA.5.2** 11%, 0.95 fold growth
  - o **BA.4.6** 10%, 0.99 fold growth
  - $\circ$  **BA.5.1** 6.5%, 0.75 fold growth
  - **BF.7** 4.9%, *3.5 fold growth*
  - $\circ$  BQ.1 4.5%, 7.2 fold growth

- $\circ$  **BQ.1.1** 2.4%, **8.4** fold growth
- $\circ$  **BF.5** 2.4%, 1.3 fold growth
- $\circ$  **BA.5.5** 2.2%, 0.64 fold growth
- **BF.13** 2.0%, 6.5 fold growth
- $\circ$  **BA.5.2.9** 2.0%, 0.85 fold growth
- The **BA.2.3.20** lineage appears to have a significant growth in California. This lineage originated in Asia and may have a similar growth rate to BQ.1 and BQ.1.1.
- Notable substitutions present within the top five BA.5.x sub-lineages in the US in October so far:
  - o One **BA.5** sub-lineage carries the T76I substitution (BA.5.5)
- Notable substitutions present within the top five BA.4.x sub-lineages in the US in September (not enough data from October yet):
  - One **BA.4** sub-lineage carries the R346T and N658S substitutions (most prevalent)
  - o One **BA.4** sub-lineage carries the V3G substitution only
  - o One **BA.4** sub-lineage carries the V3G and R346T substitutions
  - o One **BA.4** sub-lineage carries the R346T and N658S and lacks the N440K substitution
  - o One **BA.4** sub-lineage carries the N658S substitution only
- 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 (K444T in BQ.1, BQ.1.1, BA.5.6.2, BE.1.1.1, BE.1.1 and 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).

#### **USA – Recombinants**

- XAZ 40 sequences in the US in September; none in October so far
- XBB 13 sequences in the US in September; none in October so far
- XBB.1 –7 in August; none in September; 1 in October so far
- XAS 3 in August; none in September; none 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 (> 0.5%) in October so far; lineages with fold growth >3 from September to October are highlighted in **bold italic**:
  - o **BA.5.2** 16%, 0.98 fold growth
  - o **BA.5.2.1** 13%, 0.78 fold growth
  - o **BF.7** 11%, *3.0 fold growth*
  - $\circ$  **BA.5.1** 9.1%, 0.87 fold growth
  - $\circ$  **BE.1.1** 3.8%, 1.7 fold growth
  - $\circ$  **BA.4.6** 3.0%, 0.55 fold growth
  - $\circ$  **BF.5** 2.7%, 0.81 fold growth
  - $\circ$  BQ.1.1 2.2%, 5.4 fold growth
  - $\circ$  **BA.5.2.6** 2.0%, 2.6 fold growth
  - o **BA.2.75** 1.9%, *5.1 fold growth*
  - $\circ$  **BQ.1** 1.9%, 3.3 fold growth
  - **BA.5.2.20** 1.3%, 0.99 fold growth
  - o **BA.5** 1.3%, 0.78 fold growth
  - $\circ$  XBB.1 1.2%, 9.1 fold growth
  - **BA.5.1.10** 1.0%, 1.2 fold growth
  - o **BE.1** 0.84%, 0.61 fold growth
  - o **BF.11** 0.82%, 1.8 fold growth
  - o **BF.10** 0.82%, 0.55 fold growth
  - o **BA.2.3** 0.78%, 39 fold growth
  - o **BA.5.1.5** 0.74%, 1.3 fold growth
  - o **BA.5.9** 0.68%, 1.2 fold growth
  - DA # 1 22 0 670/ 0.02 6.11
  - o **BA.5.1.22** 0.65%, 0.83 fold growth
  - o **BF.14** 0.61%, 2.1 fold growth
  - o **BA.5.2.3** 0.59%, 1.1 fold growth
  - o **BA.5.6** 0.59%, 0.32 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.
- Notable substitutions present within the top five **BA.5** sub-lineages globally in October so far:

- o One **BA.5** sub-lineage carries the R346T substitution only
- One BA.5 sub-lineage carries the Y144- deletion (new)
- Notable substitutions present within the top five **BA.4** sub-lineages globally in October so far:
  - o Two **BA.4** sub-lineages (including the most prevalent) carry the R346T and N658S substitutions (**BA.4.6**)
  - One **BA.4** sub-lineage carries the V3G substitution only
  - One BA.4 sub-lineage carries the W152L substitution (new)
  - One BA.4 sub-lineage carries the R346T and N658S substitutions and lacks the N440K substitution
- 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 most of these):
  - o A1078T 0.14%, 14 fold growth
  - $\circ$  G252V 1.2%, 10 fold growth
  - $\circ$  V445P 1.7%, 8.4 fold growth
  - $\circ$  Q183E 1.7%, 8.3 fold growth
  - $\circ$  V83A 1.6%, 8.2 fold growth
  - $\circ$  L368I 1.6%, 8.0 fold growth
  - $\circ$  H146Q 1.7%, 7 fold growth
  - o I434V 0.14%, 7 fold growth
  - $\circ$  E484R 1.3%, 6.4 fold growth
  - o N164K 1.3%, 6.0 fold growth
  - o H245N 1.3%, 6 fold growth
  - $\circ$  V213E 1.7%, 6 fold growth
  - L452M 1.3%, 5.8 fold growth
  - $\circ$  M153T 1.2%, 5.6 fold growth
  - o G257D 1.3%, 5.6 fold growth
  - $\sim$  **F490S 2.3%**, 5.2 fold growth
  - o K147- 0.15%, 5 fold growth
  - o N148- 0.15%, 5 fold growth
  - o F486I 0.31%, 4.4 fold growth
  - $\circ$  **K444T** 7.2%, 4.4 fold growth
  - S1252P 0.16%, 4 fold growth
  - o H1101Y 0.39%, 3.9 fold growth
  - o A1020V 0.23%, 3.8 fold growth
  - o **N460K 13%**, 3.3 fold growth
  - o K147N 0.44%, 3.1 fold growth
  - A684V 0.15%, 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 new 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)

• 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 92 in October so far
- XBB 24 in October so far
- XAZ 6 in October so far
- XAY 1 in October so far

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

- SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 46
- More than 1,000 students absent, suspected respiratory outbreak under investigation at 2 San Diego County schools
  - World Faces New Threats From Fast-Mutating Omicron Variants
- There's a spike in respiratory illness among children and it's not just COVID
- Experts warn new Covid variant could be widespread within weeks
- German health minister urges stepped-up COVID-19 measures
- COVID-19 hospitalizations on the rise in Canada
- Europe likely entering another COVID wave, says WHO and ECDC
- Singapore's XBB Covid-19 wave to peak in mid-Nov with 15,000 average daily cases, mask rules not ruled out
- Other COVID-19 Proteins Crucial in Disease Severity, Not Just Spike; New Key Genes Identified
  - Estimation of R0 for the spread of SARS-CoV-2 in Germany from excess mortality
- WHO chief urges immediate action to tackle 'devastating' long Covid. https://www.theguardian.com/society/2022/oct/12/long-covid-who-tedros-adhanom-ghebreyesus

#### **Recombinant lineages:**

One new recombinant lineages have been added this week: XBD. 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	#263	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
<u>XH</u>	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
XN	290	<u>#480</u>	BA.1	BA.2	UK
XP	57	<u>#481</u>	BA.1.1	BA.2	UK
XQ	145	<u>#468</u>	BA.1.1	BA.2	UK
XR	183	<u>#469</u>	BA.1.1	BA.2	UK
XS	60	<u>#471</u>	Delta	BA.1.1	USA
XT	14	<u>#478</u>	BA.2	BA.1*	S. Africa
<u>XU</u>	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
XZ	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	144	<u>#823</u>	BA.1*	BA.2*	DE
XAL	124	<u>#757</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	<u>#1137</u>	BA.2.75.2	BF.5	Multiple

# **Newly designated Pango lineages:**

New lineages designated this week:

- <u>BF.7.2</u>: BF.7 with S:H1101Y, S:F486I and ORF3a:T176I in Denmark
- XAY.1: XAY sublineage with S:D253G
- <u>BQ.1.18</u>: BQ.1 with S:144- and C1779T, C8251T
- <u>BA.4.6.2</u>: BA.4.6 sublineage with S:V445A, ORF1a:D1323G
- BA.4.6.3: BA.4.6 + Orf1a: G963C + S:K444N +S:N460K

- BT.2: BA.5.1.21 (Orf1b:G662S) sublineage defined by Orf9b:D2G
- BA.5.6.4: Sublineage of BA.5.6 with S:R346E
- BQ.1.10.1: BQ.1 sublineage with S:H146L and Orf1a:E352A spreading in Italy
- CL.1: BA.5.1.29 sublineage with S:K150E, S:460K, Orf8:F41C
- <u>BR.4</u>: Sublineage of BA.2.75.4 with S:K444T, S:S446G (Rev), ORF3a:T32I
- BN.1.1: BN.1 with S:494P
- CJ.1: BM.1.1.1 sublineage with S:F486P
- BF.29: BA.5.2.1 with ORF3a:M260K via nuc:U26171A [132 good+ seq as of 2022-10-04]
- <u>BG.7</u>: Proposal of new sub-lineage of BA.2.12.1 with additional mutations Orf1ab:E726K, V1020A, F1632L, F2321L
- XBD: Potential BA.2.75.2/BF.5 recombinants
- CA.3: BA.2.75.2 Sub-lineage with N:M101I mutation
- CM.1: Sublineage of BA.2.3.20 with S:N17S
- CG.1: New BA.5.2 + Orf1b:T1050N sublineage with S:K444M and Orf1a:S1520F

### Variants being monitored by various public health agencies:

No new variants added to lists monitored by public health agencies. The latest summary table for all agencies can be found here:

https://docs.google.com/spreadsheets/d/1mAgO2wRJyEyGtL-SPa2NgOilll/7a5n7Ta/ymSarVlgHSIJ/adit#gid=0

SBe3NgOjUk7a5nZTeKmSorVkaHSU/edit#gid=0