BV-BRC SARS-CoV-2 Emerging Variant Report September 6, 2022

Details of the emerging variants analysis can be found in "BV-BRC SARS-CoV-2 Emerging Variant Report – 20220906.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 to date in July and August are **Omicron**, with **BA.2.12.1** displaced by **BA.5** and **BA.4** and their sub-lineages.
 - The CDC Nowcast for the week ending 09/03/22 estimates that BA.5 proportions are now dominating in the United States at 88.6% (95% PI: 87.0-90.0%). Significant regional differences exist: <u>https://covid.cdc.gov/covid-data-tracker/#variantproportions</u>.
 - The CDC Nowcast has split BA.4 and BA.4.6; estimates for BA.4 proportions are now at 2.8% (95% PI: 2.6-3.0%); estimates for BA.4.6 proportions are now at 8.4% (95% PI: 7.1-10.0%)
 - The US CDC Nowcast estimates that **BA.2.12.1** proportions are now at 0.1% (95% PI: 0.1-0.2%)
- Lineages with sequence prevalence >0.5% or growth rate > 2 fold in August are (ranked in order of sequence prevalence):
 - **BA.5.2.1** 30%, 1.2 fold growth
 - **BA.5.2** 13%, 1.5 fold growth
 - **BA.5.1** 13%, 1.2 fold growth
 - **BA.5.5** 7.6%, 0.75 fold growth
 - **BA.5.6** 5.9%, 1.0 fold growth
 - **BA.4.6** 5.4%, 1.9 fold growth
 - **BA.5** 4.9%, 1.3 fold growth
 - **BA.4.1** 3.6%, 0.58 fold growth
 - \circ **BA.4** 2.0%, 0.58 fold growth
 - **BA.5.1.1** 1.9%, 0.98 fold growth
 - **BE.1** 1.8%, 1.1 fold growth
 - **BA.2.12.1** 1.6%, 0.17 fold growth
 - **BF.5** 1.5%, 1.4 fold growth
 - **BE.3** 1.5%, 0.86 fold growth
 - **BE.1.1** 1.2%, 1.1 fold growth

- **BA.2** 0.89%, 0.70 fold growth
- **BA.2.75** 0.28%, *3.5 fold growth*
- Many sub-lineage variants appear to carry ancestral reversion in comparison to the original Omicron consensus, including inconsistent occurrence of A67V, H69-, V70-, G142D, V143-, Y144-, Y145-, N211-, L212I, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, Y505H, N764K. However, these changes are likely due to sequencing artifacts caused by inefficient amplification by certain PCR primers affected by Omicron substitutions.
- Notable substitutions present within the top ten BA.5 sub-lineages in August in the US:
 - One **BA.5** sub-lineage carries the T76I substitution (BA.5.5)
 - One **BA.5** sub-lineage carries the R346T substitutions (BA.5.2.1)
 - One **BA.5** sub-lineage lacks the N440K substitution (BA.5.2.1)
- Notable substitutions present within the top five BA.4 sub-lineages in August in the US:
 - One BA.4 sub-lineage carries the R346T and N658S substitutions
 - One **BA.4** sub-lineages carries the V3G substitution only
 - One **BA.4** sub-lineage carries the N658S substitution only
 - One **BA.4** sub-lineage carries the V3G and R346T substitutions
- Several Omicron sub-lineages appear to carry a recurring mutation at position 346 in the S protein (S:R346T in BA.2.74, BA.2.76, BA.4, BA.4.1, BA.4.6, BA.4.7, BA.5, BA.5.1, BA.2.12.1, BA.2, S:R346S in BA.5.2.10r S:R346I in BA.4.1)
- Several Omicron sub-lineages appear to carry a recurring mutation at position 444 in the S protein (K444R in BA.5.2.1 with 2.2 fold growth rate and K444T in BA.5.6 with 1.7 fold growth rate in August)

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

• No Delta sequences in the US in August so far.

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

• None in July or August.

<u>USA – Recombinants</u>

- XE –none in August so far
- XM –none in August so far
- XY 1 sequence in the US in August so far
- XAA –none in August so far
- XAC –none in August so far
- XAF none in August 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 August:
 - **BA.5.2.1** 23%, 1.2 fold growth
 - **BA.5.2** 19%, 1.4 fold growth
 - **BA.5.1** 18%, 0.99 fold growth
 - **BA.5** 3.9%, 1.2 fold growth
 - **BE.1.1** 3.4%, 0.93 fold growth
 - **BA.5.5** 3.3%, 0.80 fold growth
 - **BA.4.6** 3.2%, 2.0 fold growth
 - \circ **BF.5** 2.9%, 0.92 fold growth
 - **BA.5.6** 2.8%, 1.0 fold growth
 - **BA.4.1** 2.4%, 0.54 fold growth
 - **BE.1** 1.9%, 0.95 fold growth
 - **BA.4** 1.7%, 0.51 fold growth
 - **BA.2** 1.4%, 0.58 fold growth
 - **BA.5.1.1** 0.91%, 1.0 fold growth
 - **BA.2.75** 0.86%, 1.5 fold growth
 - **BA.2.12.1** 0.82%, 0.18 fold growth
 - **BA.5.1.3** 0.61%, 1.0 fold growth
 - **BE.3** 0.59%, 0.91 fold growth
 - **BA.5.3.1** 0.57%, 0.88 fold growth
 - **BA.5.2.3** 0.55%, 1.1 fold growth
- BA.2.75: shows a high growth rate in India (97 fold in June, 4.6 fold in July, and 1.6 fold in August) and comprises 35% of sequences in India in August. It is also present in 40 other countries, including the United States (22 states). Signs of very high growth rates for August in Netherlands, Belgium, Israel, Austia, , UK, and Australia
- *BF.3:* shows a high growth rate in the UK (7.5 fold in August and 4 fold in July) but the numbers are small (n=40 in August)
- BA.3 shows a slight increase in August (2 fold growth rate), with the majority of genomes originating in India. However upon closer inspection, these genomes are of poor quality, and are missing large sections of the spike protein coding region, and are therefore likely to be misassigned as BA.3.
- Similar issues with variable ancestral reversion that are likely due to sequencing artifacts, as described above for US sequences
- Notable substitutions present within the top ten **BA.5** sub-lineages globally in August:
 - One **BA.5** sub-lineage carries the T76I substitution
 - One **BA.5** sub-lineage carries the R346T substitution
 - One **BA.5** sub-lineage lacks the T19I substitution
 - One **BA.5** sub-lineage lacks the N440K substitution
- Notable substitutions present within the top five **BA.4** sub-lineages globally in August so far:
 - One BA.4 sub-lineage (most prevalent) carries 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 N658S substitution only
- One **BA.4** sub-lineage carries the V3G and the R346T substitutions
- Substitutions in spike that we are monitoring (>3 fold growth from July to August with counts >10) include the following (but note that the numbers are still relatively small for most of these):
 - **F486S** 0.16%, 16 fold growth
 - **G261D** 0.07%, 7 fold growth
 - **D1199N** 0.12%, 6 fold growth
 - **K356T** 0.11%, 5.5 fold growth
 - Q14H 0.05%, 5 fold growth
 - F490S 0.04%, 4 fold growth
 - T1116N 0.09%, 3 fold growth
 - A264T 0.03%, 3 fold growth
 - **D1118Y** 0.03%, 3 fold growth
 - **G142-** 0.03%, 3 fold growth
 - G252S 0.03%, 3 fold growth
 - **I1216T** 0.03%, 3 fold growth
 - L1224F 0.03%, 3 fold growth
 - L141- 0.03%, 3 fold growth
 - **P9L** 0.0003%, 3 fold growth
 - **Q954Y** 0.03%, 3 fold growth
 - **Y200C** 0.03%, 3 fold growth

DELTA (B.1.617.2 and AY sub-lineages)

- Eleven Delta isolates globally in August; 36 in July.
- Countries where Delta lineages have been detected in July and August 2022: Austria, Belgium, France, India, Indonesia, Italy, Luxembourg, Philippines, Russia, South Africa, Spain, Switzerland, Ukraine, United Kingdom, USA

World (other VOIs)

• 1 Alpha genome (B.1.1.7) detected in July in the USA; none in August.

<u>World – Recombinants</u>

- XAJ 45 in July, 3 in August
- **XAG** 17 in July; none in August
- XAN 14 in July; 6 in August
- XAF 13 in July; one in August
- XE 8 sequences in July; none in August
- XM 2 in July; none in August
- XAC 2 in July; none in August
- XJ 1 in July; none in August
- XAA 1 in July; none in August
- XAD 1 in July; none in August
- XAE 1 in July; none in August
- XY 1 in August

• See a summary of recombinant lineages at the end of this report.

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

- Risk of BA.5 Infection among Persons Exposed to Previous SARS-CoV-2 Variants
- <u>Covid-19 Vaccines Immunity, Variants, Boosters</u>
- <u>An Antibody from Single Human VH-rearranging Mouse Neutralizes All SARS-CoV-2</u> <u>Variants Through BA.5 by Inhibiting Membrane Fusion</u>
- World's First Covid Vaccine You Inhale Is Approved in China
- <u>The prevalence of SARS-CoV-2 infection and long COVID in US adults during the BA.5</u> <u>surge, June-July 2022</u>
- Bharat Biotech's iNCOVACC world's first Intra Nasal vaccine receives approval for emergency use in India
- <u>Resistance of SARS-CoV-2 Omicron Subvariant BA.4.6 to Antibody Neutralization</u>
- <u>White-tailed deer (Odocoileus virginianus) may serve as a wildlife reservoir for nearly extinct</u> <u>SARS-CoV-2 variants of concern</u>

Recombinant lineages:

Several new recombinant lineages have been added this week: XAS > XAZ. 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-XAZ 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 XE 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
XE	2807	<u>#454</u>	BA.1	BA.2	UK
XF	34	<u>#445</u>	Delta	BA.1	UK
XG	477	<u>#447</u>	BA.1	BA.2	Denmark
XH	174	<u>#448</u>	BA.1	BA.2	Denmark
XJ	254	<u>#449</u>	BA.1	BA.2	Finland

XK	18	<u>#460</u>	BA.1	BA.2	Belgium
XL	119	<u>#464</u>	BA.1	BA.2	UK
XM	538	<u>#472</u>	BA.1.1	BA.2	Multiple EU
XN	158	<u>#480</u>	BA.1	BA.2	UK
XP	57	<u>#481</u>	BA.1.1	BA.2	UK
XQ	142	<u>#468</u>	BA.1.1	BA.2	UK
XR	181	<u>#469</u>	BA.1.1	BA.2	UK
<u>XS</u>	60	<u>#471</u>	Delta	BA.1.1	USA
<u>XT</u>	13	<u>#478</u>	BA.2	BA.1*	S. Africa
XU	17	<u>#522</u>	BA.1*	BA.2	India
XV	42	<u>#463</u>	BA.1*	BA.2*	Denmark
XW	101	<u>#591</u>	BA.1*	BA.2*	JP, DE, SI, CA, UK, US
XY	120	<u>#606</u>	BA.1*	BA.2*	FR, IL, UK, US
<u>XZ</u>	108	<u>#636</u>	BA.2*	BA.1*	Multiple
XAA	96	<u>#664</u>	BA.1*	BA.2*	US, IL
XAB	114	# <u>665</u>	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	206	# <u>590</u>	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	56	<u>#607</u>	BA.2*	BA.1*	CZ,DE,UK
XAE	130	<u>#637</u>	BA.2*	BA.1*	CA,US,NL,CH
XAF	287	<u>#676</u>	BA.1*	BA.2*	CR
XAG	359	<u>#709</u>	BA.1.1	BA.2.23	BR
XAH	82	<u>#755</u>	BA.2*	BA.1*	SI
XAJ	79	<u>#826</u>	BA.2.12.1	BA.4	UK
XAK	55	<u>#823</u>	BA.1*	BA.2*	DE
XAL	95	<u>#757</u>	BA.1.1	BA.2*	DE
XAM	341	<u>#759</u>	BA.1.1	BA.2.9	Panama
XAN	30	<u>#771</u>	BA.2*	BA.5.1	Multiple
XAP	69	<u>#789</u>	BA.2*	BA.1*	US
XAQ	74	<u>#798</u>	BA.1*	BA.2*	Canada
XAR	49	#860	BA.1*	BA.2*	Reunion/France
XAS	48	<u>#882</u>	BA.5*	BA.2*	N. America
XAT	74	<u>#885</u>	BA.2.3.13	BA.1*	Japan

XAU	77	<u>#894</u>	BA.1.1*	BA.2.9*	Multiple
XAV	60	<u>#911</u>	BA.2*	BA.5*	France
XAW	5	<u>#895</u>	BA.2*	AY.122	Russia
XAY	8	<u>#844</u>	BA.2	AY.45	S. Africa
XAZ	974	<u>#797</u>	BA.2.5, BA.5	BA.2.5	Multiple

Newly designated Pango lineages:

Few new lineages designated this week:

- **BA.5.5.3**: BA.5.5 with ORF1a:V3166F and ORF1b:L314R
- BA.2.3.20: BA.2.3 Sublineage with 10 highly convergent S1 mutations
- BP.1: Sublineage of BA.2.3 with S:69-70del, S:R346T, S:R403K, S:L452M, S:A570V, S:Q672E, S:A852V, M:S4F, ORF8:A65V, ORF1a:E2089D, ORF1a:E3310Q, and ORF1a:T4311I
- BA.5.1.20: BA.5.1+C29614T sublineage with Orf1a:K1407M and S:346T
- **BA.5.1.19**: BA.5.1 with ORF1b:G662C
- **BN.1**: BA.2.75.5 (S:K356T) sublineage with S:R346T, S:490S
- **BQ.1**: BE.1.1.1 sublineage with Orf1b:Y264H and S:N460K (45 sequences) emerged in Nigeria
- **BA.5.2.13**: New BA.5.2 + Orf1b:1050N sublineage with Orf1a:I4291V and S:346T
- BM.4 & BM.4.1: BA.2.75.3 sublineage with S:F486S, ORF1a:Q1198K

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: <u>https://docs.google.com/spreadsheets/d/1mAgO2wRJyEyGtL-</u> <u>SBe3NgOjUk7a5nZTeKmSorVkaHSU/edit#gid=0</u>