

BV-BRC SARS-CoV-2 Emerging Variant Report September 27, 2022

Details of the emerging variants analysis can be found in “BV-BRC SARS-CoV-2 Emerging Variant Report – 20220927.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 September 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**, with **BA.2.12.1** displaced by **BA.5** and **BA.4** and their sub-lineages.
 - The CDC Nowcast for the week ending 09/24/22 estimates that **BA.5** proportions are now dominating in the United States at 83.1% (95% PI: 81.3-84.7%). Significant regional differences exist: <https://covid.cdc.gov/covid-data-tracker/#variant-proportions>.
 - The CDC Nowcast has split BA.4 and BA.4.6; estimates for **BA.4** proportions are now at 1.4% (95% PI: 1.3-1.5%); estimates for **BA.4.6** proportions are now at 11.9% (95% PI: 10.6-13.4%)
 - ***BF.7 has been added to the Nowcast tracker and is currently estimated at 2.3% (95% PI: 1.7-3.0%)***
 - ***BA.2.75 has been added to the Nowcast tracker and is currently estimated at 1.4% (95% PI: 0.9-2.0%)***

- Lineages with sequence prevalence >0.5% in September so far are (ranked in order of sequence prevalence):
 - **BA.5.2.1** - 29%, 0.95 fold growth
 - **BA.5.2** - 18%, 1.2 fold growth
 - **BA.5.1** - 13%, 1.0 fold growth
 - **BA.4.6** – 9.6%, ***1.6 fold growth***
 - **BA.5.5** – 4.5%, 0.65 fold growth
 - **BA.5.6** – 4.4%, 0.79 fold growth
 - **BA.5** – 4.3%, 1.0 fold growth
 - **BA.4.1** – 1.7%, 0.55 fold growth
 - **BF.5** – 1.7%, 1.1 fold growth
 - **BE.1.1** – 1.5%, 1.3 fold growth

- **BA.5.1.1** – 1.5%, 0.85 fold growth
 - **BE.1** – 1.4%, 0.82 fold growth
 - **BA.4** – 1.0%, 0.58 fold growth
 - **BE.3** – 1.0%, 0.73 fold growth
 - **BA.2.75** - 0.76%, **1.9 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.x sub-lineages in the US in September so far:
 - One **BA.5** sub-lineage carries the T76I substitution (BA.5.5)
 - Two **BA.5** sub-lineages carry the R346T substitution (BA.5.2.1 and BA.5.1)
 - Notable substitutions present within the top five BA.4.x sub-lineages in the US in September so far:
 - 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.5.2.1**; or S:R346I in **BA.4.1**)
 - Two 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)
 - At least 4 Omicron sublineages carry a recurring mutation at position 445, V445A (BA.4.1 - 2 fold growth rate, BA.4.6 – 3 fold growth rate, BA.5.1 – 3.5 fold growth rate, BA.5.2 – 8 fold growth rate in September)

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

- Two Delta sequences in the US in September so far

USA – (other VOCs and VOIs) *(no significant change since previous report)*

- One Alpha sequence in the US in September so far. This genome appears to have accumulated several other mutations in addition to those normally associated with B.1.1.7 genomes.

USA – Recombinants

- **XE** –none in August; none in September so far
- **XM** –none in August; none in September so far
- **XY** – 1 sequence in the US in August; none in September so far
- **XAA** –none in August; none in September so far
- **XAC** –none in August; none in September so far
- **XAF** - none in August; none in September 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%) or growth rate > 2 fold in September so far:
 - **BA.5.2.1** - 25%, 1.0 fold growth
 - **BA.5.2** - 22%, 1.0 fold growth
 - **BA.5.1** - 15%, 0.91 fold growth
 - **BA.4.6** – 5.8%, **1.6 fold growth**
 - **BA.5** – 3.6%, 0.98 fold growth
 - **BE.1.1** – 2.6%, 0.86 fold growth
 - **BF.5** – 2.5%, 0.80 fold growth
 - **BA.5.6** – 2.4%, 0.82 fold growth
 - **BA.5.5** – 2.3%, 0.71 fold growth
 - **BA.2.75** – 1.6%, **1.5 fold growth**
 - **BE.1** – 1.3%, 0.75 fold growth
 - **BA.4.1** – 1.2%, 0.54 fold growth
 - **BA.4** - 0.79%, 0.54 fold growth
 - **BA.5.1.1** - 0.77%, 0.86 fold growth
 - **BA.5.2.3** - 0.62%, 1.2 fold growth
 - **BA.2.3** - 0.13%, **2.6 fold growth**
- **BA.2.75 and BA.4.6 continue to show growth rates greater than 1.0 both globally and in the US**
- Similar issues with variable ancestral reversion that are likely due to sequencing artifacts, as described above for US sequences
- **A BA.2.3 sublineage (designated BA.2.3.20 but 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 ten **BA.5** sub-lineages globally in September so far:
 - Two **BA.5** sub-lineages carry the R346T substitution only
 - One **BA.5** sub-lineage carries the T76I substitution
 - One **BA.5** sub-lineage lacks the N440K substitution
- Notable substitutions present within the top five **BA.4** sub-lineages globally in September so far:
 - One **BA.4** sub-lineage (the 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 R346T substitutions
- Substitutions in spike that we are monitoring (>3 fold growth from August to September with counts >10) include the following (but note that the numbers are still relatively small for most of these):
 - **E484R** - 0.13%, 13 fold growth
 - **H245N** - 0.16%, 8 fold growth
 - **M153T** - 0.15%, 7.5 fold growth
 - **D1163H** - 0.06%, 6 fold growth
 - **G257D** - 0.17%, 5.7 fold growth
 - **A260V** - 0.05%, 5 fold growth
 - **L368I** - 0.05%, 5 fold growth
 - **V445P** - 0.05%, 5 fold growth
 - **F490S** - 0.2%, 4 fold growth
 - **A1174V** - 0.04%, 4 fold growth
 - **D1127G** - 0.04%, 4 fold growth
 - **K444T** - **0.95%**, 3.5 fold growth
 - **L1224F** - 0.07%, 3.5 fold growth
 - **P272L** - 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: R346*, K356*, K444*, V445*, and N460*. 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)

- 14 Delta isolates globally in August; 8 in September so far

World (other VOIs)

- One Alpha genome in September so far

World – Recombinants

- **XAJ** – 45 in July; 3 in August; none in September so far
- **XAG** – 17 in July; none in August; none in September so far
- **XAN** – 14 in July; 6 in August; none in September so far
- **XAF** – 13 in July; 2 in August; none in September so far
- **XE** – 8 sequences in July; none in August; none in September so far
- **XM** – 2 in July; none in August; none in September so far
- **XAC** – 2 in July; none in August; none in September so far
- **XJ** – 1 in July; none in August; none in September so far
- **XAA** – 1 in July; none in August; none in September so far
- **XAD** – 1 in July; 1 in August; none in September so far
- **XAE** – 1 in July; none in August; none in September so far
- **XY** – 1 in August; none in September so far
- See a summary of recombinant lineages at the end of this report.

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

- Updated data from Yunlong Cao on multiple variants' immune and antiviral escape: BA.2.3.20, BN.1, BA.2.10.4, BN.2.1, BA.4.6.1, BQ.1, BQ.1.1
https://twitter.com/yunlong_cao/status/1573391234118610944
<https://www.biorxiv.org/content/10.1101/2022.09.15.507787v1>
- [SARS-CoV-2 Omicron boosting induces de novo B cell response in humans](#)
- [Exposure to BA.4/BA.5 Spike glycoprotein drives pan-Omicron neutralization in vaccine-experienced humans and mice](#)
- [WHO warns ability to identify new Covid variants is diminishing as testing declines](#)
- [What to know about the BA.4.6, BF.7 and BA.2.75 variants now growing nationwide](#)
- [Big COVID-19 waves may be coming, new Omicron strains suggest](#)
- [These scientists traced a new coronavirus lineage to one office — through sewage](#)
- [Covid hospitalisations rise by nearly 20% in a week in England](#)

Recombinant lineages:

Two new recombinant lineages have been added this week: XBA and XBB. 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-XBB 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	#189	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
XE	2818	#454	BA.1	BA.2	UK
XF	34	#445	Delta	BA.1	UK
XG	479	#447	BA.1	BA.2	Denmark
XH	174	#448	BA.1	BA.2	Denmark
XJ	254	#449	BA.1	BA.2	Finland
XK	18	#460	BA.1	BA.2	Belgium
XL	119	#464	BA.1	BA.2	UK

XM	540	#472	BA.1.1	BA.2	Multiple EU
XN	158	#480	BA.1	BA.2	UK
XP	57	#481	BA.1.1	BA.2	UK
XQ	143	#468	BA.1.1	BA.2	UK
XR	181	#469	BA.1.1	BA.2	UK
XS	60	#471	Delta	BA.1.1	USA
XT	13	#478	BA.2	BA.1*	S. Africa
XU	17	#522	BA.1*	BA.2	India
XV	42	#463	BA.1*	BA.2*	Denmark
XW	105	#591	BA.1*	BA.2*	JP, DE, SI, CA, UK, US
XY	121	#606	BA.1*	BA.2*	FR, IL, UK, US
XZ	114	#636	BA.2*	BA.1*	Multiple
XAA	96	#664	BA.1*	BA.2*	US, IL
XAB	114	#665	BA.1*	BA.2*	IT, FR, DE, CH, DK
XAC	206	#590	BA.1*	BA.2*	IL, DE, CA, IR, NL, JP, UK, US
XAD	57	#607	BA.2*	BA.1*	CZ,DE,UK
XAE	130	#637	BA.2*	BA.1*	CA,US,NL,CH
XAF	288	#676	BA.1*	BA.2*	CR
XAG	368	#709	BA.1.1	BA.2.23	BR
XAH	82	#755	BA.2*	BA.1*	SI
XAJ	79	#826	BA.2.12.1	BA.4	UK
XAK	55	#823	BA.1*	BA.2*	DE
XAL	95	#757	BA.1.1	BA.2*	DE
XAM	341	#759	BA.1.1	BA.2.9	Panama
XAN	30	#771	BA.2*	BA.5.1	Multiple
XAP	69	#789	BA.2*	BA.1*	US
XAQ	74	#798	BA.1*	BA.2*	Canada
XAR	49	#860	BA.1*	BA.2*	Reunion/France
XAS	48	#882	BA.5*	BA.2*	N. America
XAT	74	#885	BA.2.3.13	BA.1*	Japan
XAU	77	#894	BA.1.1*	BA.2.9*	Multiple
XAV	60	#911	BA.2*	BA.5*	France

XAW	5	#895	BA.2*	AY.122	Russia
XAY	8	#844	BA.2	AY.45	S. Africa
XAZ	974	#797	BA.2.5, BA.5	BA.2.5	Multiple
XBA	4	#844	AY.45	BA.2	S. Africa
XBB	8	#1058	BJ.1	BM.1.1.1	Singapore/US
XBC	7	#1100	Delta	BA.2	Philippines

Newly designated Pango lineages:

New lineages designated this week:

- BA.5.2.23: Sublineage of BA.5.2 with S:Y145H, S:S255F, & S:V445A
- BA.5.2.25: BA.5.2 Orf1b:1050N with S:K444T (71 sequences) with high prevalence in Guinea.
- BL.1.1: Sublineage of BL.1 with S:G614S
- BL.1.2: BL.1 sublineage with S:G261D, S:V308L
- XBC: Delta (21I) / BA.2 recombinant (5 seq. Philippines, Austria)

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-SBe3NgOjUk7a5nZTeKmSorVkaHSU/edit#gid=0>