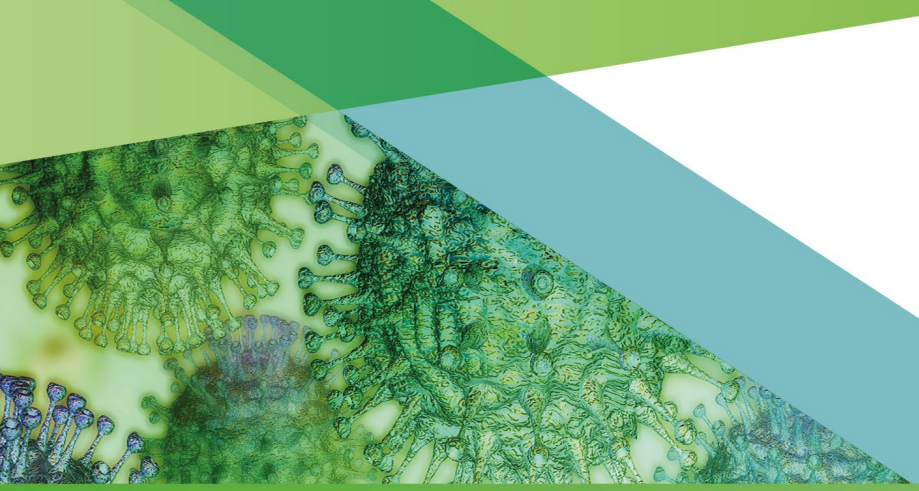


EPIDEMIOLOGICAL UPDATE

Spread of the SARS-CoV-2 Omicron variant sub-lineage BQ.1 in the EU/EEA

21 October 2022

Key messages

- European Union/European Economic Area (EU/EEA) countries have detected the circulation of SARS-CoV-2 variant sub-lineages BQ.1 in levels ranging from 0–19% during week 40. This variant originates from the BA.5 Omicron Variant of Concern (VOC).
- BQ.1, including its sub-lineages, has been designated as Variant of Interest (VOI) by ECDC as of 20 October 2022. Based on modelling estimates, it is expected that by mid-November to beginning of December 2022, more than 50% of SARS-CoV-2 infections will be due to BQ.1/BQ.1.1. By the beginning of 2023, more than 80% of SARS-CoV-2 cases are expected to be due to BQ.1/BQ.1.1.
- The observed increase in the growth rate of BQ.1 is probably driven mainly by immune escape. This variant and its sub-lineages will probably contribute to a further increase in cases of COVID-19 in the EU/EEA in the coming weeks and months. The extent of the increase in COVID-19 cases will depend on various factors, including immune protection against infection influenced by the timing and coverage of COVID-19 vaccination regimes, and the extent, timing and variant landscape of previous SARS-CoV-2 pandemic waves. Based on limited available data, there is no evidence of BQ.1 being associated with a greater infection severity than the circulating variants BA.4/BA.5.
- Countries should remain vigilant for signals of BQ.1 emergence and spread; maintain sensitive and representative testing and genomic surveillance with timely sequence reporting and strengthen sentinel surveillance systems (primary care ILI/ARI and SARI).
- Countries should continue to monitor COVID-19 case rates - especially in people aged 65 years and older - and severity indicators such as hospitalisations, ICU admissions, ICU occupancy and death.
- Improving COVID-19 vaccine uptake of the primary course and first booster dose remains a priority for all eligible individuals that are not up-to-date with the recommended schedule. For the time being, for current autumn/winter vaccination campaigns, an additional booster dose should also be offered, prioritising individuals who are at risk of progression to severe disease, such as older adults (e.g. above 60 years of age), immunocompromised individuals and those with underlying medical conditions, and pregnant women. Residents and staff in long-term care facilities, as well as healthcare workers should also be considered among priority groups.

Suggested citation: European Centre for Disease Prevention and Control. Spread of the SARS-CoV-2 Omicron variant sub-lineage BQ.1 in the EU/EEA – 21 October 2022. ECDC: Stockholm; 2022.

Event background

As of 20 October 2022, ECDC has categorised SARS-CoV-2 variant BQ.1, including its sub-lineages, as a variant of interest [1]. This variant is also part of the broader variant Omicron+K444X+N460X which is currently being monitored.

BQ.1 is a sub-lineage of BE.1.1.1, which in turn is a sub-lineage of BA.5, carrying additional changes K444T and N460K in the spike receptor-binding domain (RBD) compared to BA.5. There is also a sub-lineage of BQ.1 designated BQ.1.1 circulating, carrying the additional RBD change R346T. BQ.1, along with its sub-lineages, is designated as clade 22E (Omicron) by Nextstrain. There are indications that the variant may have emerged in central or western Africa and subsequently spread to Europe and other parts of the world.

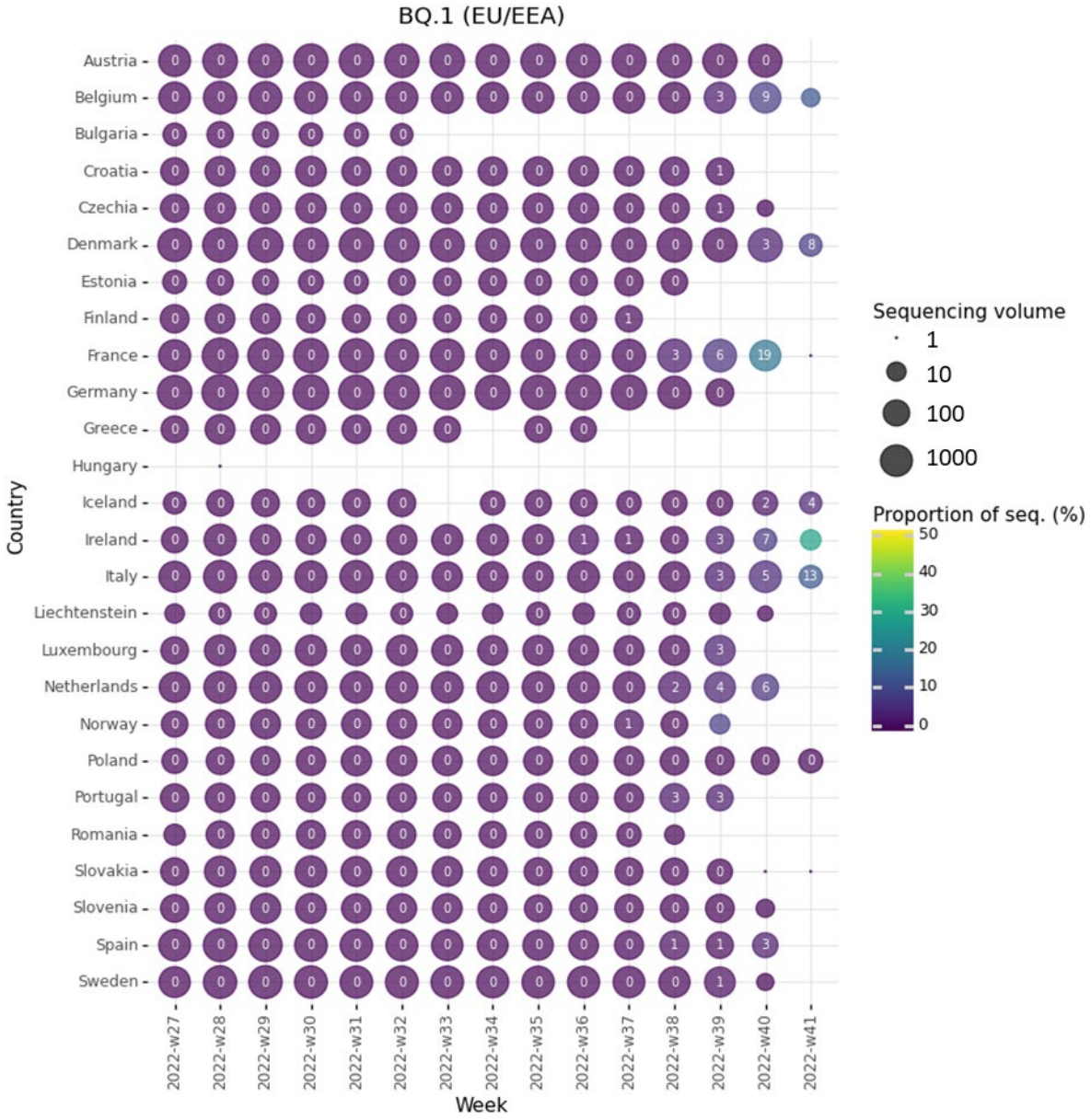
A recent pre-print study examined neutralisation of variant pseudo-viruses by sera from individuals vaccinated three times using CoronaVac, combined with previous infection with either BA.1, BA.2 or BA.5. In this assay, using BA.5 convalescent sera, BQ.1 was associated with a 3.8-fold reduction in neutralising activity and BQ.1.1 with a 6.7-fold reduction of neutralising activity compared to BA.5. [2] The same preprint also shows that BQ.1 is resistant to additional therapeutic monoclonal antibodies (Evusheld™ (tixagevimab and cilgavimab); bebtelovimab), in contrast to BA.5. No sources reporting reduced activity of Paxlovid™ (nirmatrelvir/ritonavir) against BQ.1 and BQ.1.1 have been identified.

BQ.1 in the EU/EEA as of 17 October 2022

According to data from GISAID EpiCoV, BQ.1 and BQ.1.1 are present at significant levels in the EU/EEA. The EU/EEA countries with the highest proportions reported for samples collected in week 40 are France (19%), Belgium (9%), Ireland (7%), The Netherlands (6%), and Italy (5%). (Figure. 1) According to data reported to GISAID EpiCoV, the non-EU/EEA countries with the highest reported proportions for samples collected in week 40 are Switzerland (9%) and the United Kingdom (8%). The US estimates that the variant corresponded to around 11% of their national COVID-19 cases in week 42, 2022. There are gaps in sequencing coverage world-wide, and the variant could therefore also be circulating undetected at high levels in other parts of the world.

These proportions are not high enough for the variant to already have had a large impact on the epidemiological situation in the affected countries, this generally happens when the variant approaches 50% proportion. Any major effect on the number of cases by BQ.1 will come in the coming weeks to months depending on the current proportion of BQ.1 in each country (Fig. 1).

Figure 1. Proportion of BQ.1 among sequences reported by EU/EEA countries to GISAID EpiCoV, as of 17 October 2022 (size of the bubbles indicates sequence reporting volume)

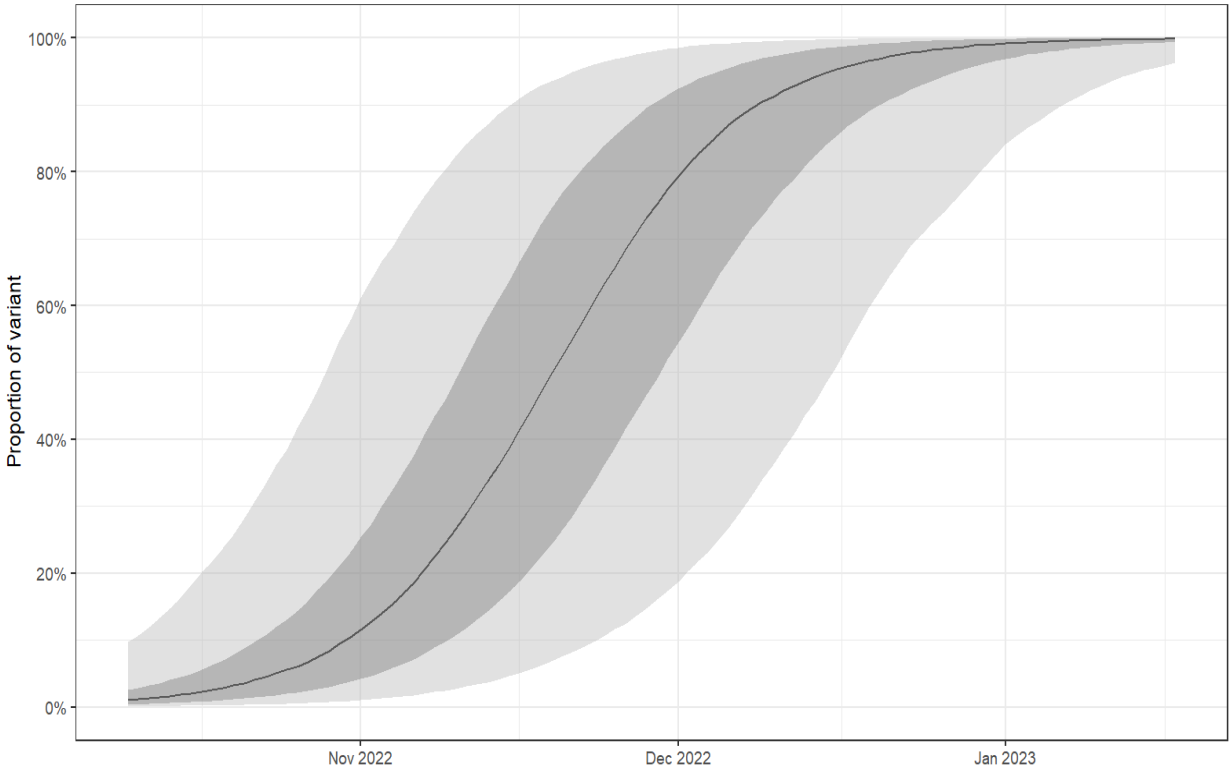


Estimates of BQ.1 growth advantage indicate that the doubling time for the proportion of COVID-19 cases caused by this variant is around or just under one week, although this may vary between settings. It is likely that the observed growth rate is mainly driven by immune escape, caused by the presence of mutations in the RBD. It is possible, but unlikely that the variant is also associated with an increase in intrinsic transmissibility compared to BA.5. There is currently no indication that BQ.1 is associated with any greater infection severity than BA.5, and it is unlikely that this will be the case due to its high genetic similarity to BA.5.

Due to the observed increase in growth rate, probably driven mainly by immune escape, it is likely that the presence of BQ.1 will contribute to a further increase in cases of COVID-19 in the EU/EEA in the coming weeks and months.

Modelling results

Figure 2. The estimated proportion of BQ.1/BQ.1.1 cases among all SARS-CoV-2 cases in the EU/EEA



The results are based on drawing 1 000 values from a random distribution of the growth rate advantage and initial proportion of BQ.1/BQ.1.1 cases.[1] The solid black line represents the median, the dark grey area corresponds to the 50% credible interval (CrI), and the light grey area corresponds to the 90% CrI.

Figure 2 shows the expected proportion of SARS-CoV-2 infections due to the BQ.1/BQ.1.1 sub-lineages in the EU/EEA. By mid-November to the beginning of December 2022, we expect that the majority (over 50%) of SARS-CoV-2 infections will be due to BQ.1/BQ.1.1. By the beginning of 2023, it is expected that the vast majority (over 80%) of SARS-CoV-2 cases will be due to BQ.1/BQ.1.1. Countries that currently have larger proportion of BQ.1/BQ.1.1 are expected to see its dominance sooner. Figure 2 shows that the BQ.1/BQ.1.1 sub-lineages will become dominant towards the end of 2022, which coincides with the winter holiday period. The expected increase in social contacts during this period, together with the potential increase in cases due to the dominance of the BQ.1/BQ.1.1 sub-lineages, might result in increased viral transmission and a corresponding public health burden.

[1] The curves in Figure 2 were generated by assuming that cases $x_a(t)$ due to the current variants, other than BQ.1/BQ.1.1, grow at some exponential growth rate r_a, and that the cases $x_b(t)$ due to the BQ.1/BQ.1.1 subvariants grow at some exponential growth rate $r_b > r_a$. Hence, it holds that $\dot{x}_a(t) = r_a x_a(t)$ and $\dot{x}_b(t) = r_b x_b(t)$. The growth rate advantage is defined as $\Delta r = r_b - r_a$. We capture the uncertainty of the BQ.1/BQ.1.1 subvariants by describing their daily growth rate advantage Δr, relative to other currently circulating variants, as a Gaussian random variable $\Delta r \sim \mathcal{N}(\mu, \sigma^2)$ with mean $\mu = 0.11$ and standard deviation $\sigma = 0.02$. The values for the mean μ and the standard deviation σ were obtained using GISAID EpiCoV data as of 17 October 2022 from the reporting countries in the EU/EEA. We aim to predict the proportion $x_b(t)/(x_a(t) + x_b(t))$ of all cases that are due to the BQ.1 and BQ.1.1 subvariants, which follows from the growth rate advantage Δr and the initial number of cases $x_a(t_0), x_b(t_0)$ that are currently due to BQ.1/BQ.1.1 and due to other variants, respectively. We modelled the uncertainty of the initial proportion of the BQ.1/BQ.1.1 sub-lineages through random draws from a normal distribution on the logit scale of the initial proportion. We chose the values of this distribution such that the median proportion is 1%, and 95% of draws yield initial proportions below 10%: $\text{logit}(x_b(t_0)/(x_a(t_0) + x_b(t_0))) \sim \mathcal{N}(-4.6, 1.5)$, which is in agreement with GISAID EpiCoV data as of 17 October 2022. The random distribution of the initial proportion accounts, among other uncertainties, for introduction delays for countries that are not reporting sequencing data in sufficiently large numbers.

There are several limitations for interpreting the results shown in Figure 2:

- Sub-lineages other than BQ.1/BQ.1.1 were not considered. If another sub-lineage emerges with a substantial growth rate advantage relative to BQ.1/BQ.1.1, then this sub-lineage will take over instead of BQ.1/BQ.1.1. Apart from potentially shifting the curve in time (i.e. to the right in Figure X), the slope of the curve could also change with any changes in the growth rate advantage (meaning that 50% could be reached more quickly or slowly than estimated here).
- Due to limited data, we described the takeover of BQ.1/BQ.1.1 as an average across the whole of the EU/EEA. There will be national and subnational variations of the takeover speed of BQ.1/BQ.1.1, due to regional differences in vaccination uptake, prior infections, social mixing, non-pharmaceutical interventions (such as mask wearing), demographics, human mobility between regions, surveillance system coverage and sequencing volumes (that may change over time), and the true (but unknown) initial number of BQ.1/BQ.1.1 cases. Nevertheless, the results in Figure 2 serve to give an order-of-magnitude evolution, and the modelled randomness of the growth rate advantage does account for (some) regional differences. While Figure 2 shows the proportion of BQ.1/BQ.1.1 cases, the impact of BQ.1/BQ.1.1 on the future absolute number of cases is currently unclear due to substantial uncertainties associated with seasonality, human behaviour and the waning of natural /vaccine-induced immunity.

Monitoring and reporting

ECDC encourages countries to remain vigilant for signals of increases in the proportion of BQ.1. Sensitive and representative testing policies and genomic surveillance are required to accurately determine the extent to which these variants may contribute to any observed increases in severe outcomes in the population (e.g. increases in hospital or ICU admissions).

Countries should therefore:

- Strengthen sentinel systems (primary care ILI/ARI and SARI) and continue to collect data on laboratory-confirmed cases (from non-sentinel sites) and on hospitalisations/ICU admissions and hospital bed occupancy [3].
- Remain vigilant and scale up testing and sequencing, if required.
- Continue to sequence positive specimens and share sequence data in a timely manner [4-6]. SARS-CoV-2 consensus sequences should be deposited in the GISAID database and, if available, raw data of SARS-CoV-2 sequences should be deposited in the COVID-19 data portal through the European Nucleotide Archive (ENA) [7].
- If possible, undertake antigenic characterisation this will contribute to an understanding of the properties of these variants and specimens/isolates could also be shared for characterisation with the ECDC Laboratory Support Consortium and/or the WHO reference laboratories [8].

Data on cases with known variants, irrespective of disease severity, should be reported to TESSy case-based record type RESPISURV (including epidemiological and virological information) or in aggregated form to NCOVVARIANT. BQ.1 will be added to the coded value list as a virus variant. Until then please use the free text variable in 'VirusVariantOther' (NCOVVARIANT) and 'VirusVariantCOVIDOther' (RESPISURV) for reporting. If possible, GISAID accession numbers of sequenced cases should also be reported in variable SequenceId in RESPISURV.

ECDC has invited nominated users of countries to use the EpiPulse event on BQ.1, including sub-lineages, to discuss and share information as it becomes available. Of particular interest is any information on virus characterisation, evidence of changes in disease severity, virus transmissibility, immune evasion and effects on diagnostics and therapeutics.

Vaccination

Improving COVID-19 vaccine uptake of the primary course and first booster dose remains a priority for all eligible individuals that are not up-to-date with the recommended schedule, especially among population groups at higher risk of severe disease and in countries with lower vaccine uptake. For the current autumn/winter vaccination campaigns, an additional booster dose (e.g. second or third booster dose following the primary course) should also be offered, prioritising individuals that are at risk of progression to severe disease, such as older adults (e.g. over 60 years of age), immunocompromised individuals, those with underlying medical conditions, and pregnant women. Residents and staff in long-term care facilities, as well as healthcare workers should also be considered among priority groups [9].

Since September 2022, new Omicron adapted bivalent COVID-19 vaccines have been approved for use in the EU/EEA to be used as booster doses for individuals aged 12 years of age and above that have completed at least a primary series [10]. The use of these adapted vaccines should remain limited to boosters for the time being. Current monovalent vaccines incorporating the original strain are still to be used for effective priming and for inducing sufficient initial protection in naïve individuals. In addition, timely vaccination is more important than which booster vaccine is administered. Current monovalent vaccines based on the original strain are still providing protection from severe disease and should be considered if adapted vaccines are not yet available [9].

Synchronising booster vaccination just before or at the beginning of high viral circulation, as is normally expected with respiratory viruses at the start or during the cold season, would be highly desirable. Consideration should also be given to combining campaigns for vaccination against COVID-19 and influenza.

Depending on how the epidemiology evolves, including further dominance of the Omicron variant sub-lineage BQ.1, as well as forthcoming variant-specific data on vaccine effectiveness (including for the new Omicron-adapted bivalent vaccines), it will be important to re-assess these considerations over time.

Detailed information on COVID-19 vaccine doses administered and vaccine uptake rates are available on the ECDC Vaccine Tracker [11].

Consulted experts

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References

1. European Centre for Disease Prevention and Control (ECDC). SARS-CoV-2 variants of concern as of 14 October 2022. 2022 October 2022 Available at: https://www.ecdc.europa.eu/en/covid-19/variants-concern
2. Cao Y, Jian F, Wang J, Yu Y, Song W, Yisimayi A, et al. Imprinted SARS-CoV-2 humoral immunity induces convergent Omicron RBD evolution. bioRxiv. 2022:2022.09.15.507787. Available at: https://www.biorxiv.org/content/biorxiv/early/2022/10/04/2022.09.15.507787.full.pdf
3. European Centre for Disease Prevention and Control/World Health Organization Regional Office for Europe. Operational considerations for influenza surveillance in the WHO European Region during COVID-19: interim guidance 2020. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Joint-influenza-interim-guidance.pdf
4. European Centre for Disease Prevention and Control/World Health Organization Regional Office for Europe. Operational considerations for respiratory virus surveillance in Europe 2022. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/Operational-considerations-respiratory-virus-surveillance-euro-2022.pdf
5. European Centre for Disease Prevention and Control (ECDC). Sequencing of SARS-CoV-2: first update. 2021 January 2021 Available at: https://www.ecdc.europa.eu/en/publications-data/sequencing-sars-cov-2
6. European Centre for Disease Prevention and Control (ECDC). Guidance for representative and targeted genomic SARS-CoV-2 monitoring. May 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/guidance-representative-and-targeted-genomic-sars-cov-2-monitoring
7. COVID-19 Data Portal. Available at: https://www.covid19dataportal.org/
8. European Centre for Disease Prevention and Control (ECDC). Technical guidance for antigenic SARS-CoV-2 monitoring. June 2022. Available at: https://www.ecdc.europa.eu/en/publications-data/technical-guidance-antigenic-sars-cov-2-monitoring
9. European Centre for Disease Prevention and Control/European Medicines Agency. ECDC-EMA statement on booster vaccination with Omicron adapted bivalent COVID-19 vaccines 2022 Available at: https://www.ema.europa.eu/en/documents/public-statement/ecdc-ema-statement-booster-vaccination-omicron-adapted-bivalent-covid-19-vaccines_-0.pdf
10. European Medicines Agency (EMA). COVID-19 vaccines: authorised. Available at: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#adapted-covid-19-vaccines-section
11. European Centre for Disease Prevention and Control (ECDC). COVID-19 Vaccines Tracker 2022. Available at: https://vaccinetracker.ecdc.europa.eu/public/extensions/COVID-19/vaccine-tracker.html#uptake-tab