

COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

XLV Report

WASHINGTON, DC

Update: 22 December 2023

OPS



Organización
Panamericana
de la Salud



Organización
Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas



In partnership with

Canada

OFFICIAL REPORTS FROM PHARMACOVIGILANCE PROGRAMS	2
<i>World Health Organization (WHO)</i>	2
PUBLICATIONS ON POTENTIAL SAFETY SIGNALS IDENTIFIED WITH THE USE OF COVID-19 VACCINES	5
<i>Safety of BA.4-5 or BA.1 bivalent mRNA booster vaccines: nationwide cohort study</i>	5
<i>Safety and immunogenicity of the BNT162b2 vaccine co-administered with seasonal inactivated influenza vaccine in adults</i>	6
<i>Type 1 diabetes, COVID-19 vaccines and short-term safety: Subgroup analysis from the global COVAD study</i>	7
<i>Miller Fisher syndrome after COVID-19 infection and vaccine: a systematic review</i>	8
<i>Herpesviruses reactivation following COVID-19 vaccination: a systematic review and meta-analysis</i>	9
<i>The occurrence of acute disseminated encephalomyelitis in SARS-CoV-2 infection/vaccination: Our experience and a systematic review of the literature</i>	10
DECISIONS OF REGIONAL AND INTERNATIONAL REGULATORY AUTHORITIES	12
<i>EMA recommends approval of adapted Nuvaxovid COVID-19 vaccine targeting Omicron XBB.1.5</i>	12
<i>WHO SAGE Good Practice Statement on the use of COVID-19 variant-containing vaccines</i>	13
<i>Updated WHO SAGE roadmap for prioritization of the use of COVID-19 vaccines in the context of the Omicron variant and its sub-lineages</i>	14
<i>U.S. FDA publishes important information about the correct dosage and administration of Moderna COVID-19 vaccine (2023-2024 formula) for individuals 6 months through 11 years of age</i>	15
CLARIFICATIONS/CONCLUSIONS OF EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS	16
<i>WHO Statement on the antigen composition of COVID-19 vaccines</i>	16
OTHER RELATED UPDATES	17
<i>Addition of COVID-19 vaccines to the WHO Emergency Use Listing</i>	17
<i>WHO updates guidelines on COVID-19 treatments</i>	18
<i>European Union (EU) medicines agencies reflect on lessons learned from COVID-19</i>	19
<i>WHO informs that COVID-19 vaccination becomes regular immunization and COVAX comes to an end</i>	20
<i>WHO declares COVID19 variant JN.1 as variant of interest</i>	21

World Health Organization (WHO)

Progress in immunization safety surveillance: worldwide, 2020-2022

On 8 December, a WHO report was released describing global, regional, and country progress from 2020 to 2022 in the use of the newly introduced indicator for immunization safety monitoring, and progress in joint reporting of adverse events following immunization (AEFIs) by expanded programs on immunization (EPIs) and national regulatory authorities (NRAs).

Methods

WHO countries meeting the newly recommended global immunization safety surveillance indicator (**at least 1 serious AEFI reported per million population per year**) were identified using VigiBase, WHO's global pharmacovigilance database. AEFI reports in VigiBase were classified as serious based on information with AEFI reporting forms and associated case investigation forms used by WHO countries. Coordination of AEFI reporting among national EPI and NRA programs was measured annually based on response to the following question in the WHO and UNICEF electronic Joint Reporting Form, a questionnaire for the passive joint collection of aggregate AEFI data: "What is the source of data for the total number of serious adverse events reported?" Possible responses included "EPI only," "NRA only," "both EPI and NRA," or "other" (9,10). National reporting to VigiBase and the Joint Reporting Form is voluntary and varies by year. WHO countries not reporting to these systems during the reporting period (2020–2022) were considered as not meeting the requirements for either the newly recommended indicator or coordination of EPI and NRA AEFI reporting; however, these countries were included in the denominator when calculating percentages.

Results

During 2020, 2021, and 2022, a total of 51 (24%) of 214, 111 (52%) of 214, and 92 (43%) of 215 WHO countries, respectively, achieved the new safety monitoring indicator (i.e., number of serious AEFIs reported per 1 million total national or subnational population in a year). During these same years, 79 (37%), 135 (63%), and 118 (55%) WHO countries, respectively, reported any serious AEFI data to VigiBase. In 2022, the region with the highest proportion of WHO countries meeting the new indicator was EUR (76%), followed by AFR (47%), AMR (32%), EMR (27%), and WPR (22%); the region with the lowest proportion was SEAR (9%). The largest increase in the number and percentage of WHO countries meeting the new indicator occurred in AFR, where the number of WHO countries meeting the indicator increased more than eightfold, from three (6%) in 2020, to 28 (60%) in 2021, but subsequently declined 21%, to 22 (47%) in 2022. Whereas all WHO regions except SEAR observed an overall increase in the number and

percentage of WHO countries achieving the new indicator from 2020 to 2022, a decrease was observed in every region from 2021 to 2022.

Indicator report: Serious AEFI per million population in the Region of the Americas, 2022. Reports to VigiBase.



- Reported, 2022
- Green: greater than or equal to 1 serious AEFI in VigiBase per million population.
 - Yellow: less than 1 serious AEFI per million population in VigiBase
 - Red: zero serious AEFI reported to VigiBase
 - Dark gray: no information available
 - Light gray: not applicable

Source: World Health Organization/UNICEF joint reporting form.

WHO countries in the Region: (35): Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and The Grenadines, Suriname, Trinidad and Tobago, United States, Uruguay, and Venezuela. WHO territories in the Region (9): Anguilla, Aruba, Bermuda, British Virgin Islands, Cayman Islands, Curaçao, Montserrat, Sint Maarten, and Turks and Caicos.

Discussion

Compared with 2020, most WHO regions made progress toward achieving the two immunization safety monitoring measures in 2021 and 2022, by attaining the Global Advisory Committee for Vaccine Safety’s indicator of reporting at least one serious AEFI per 1 million total population per year, and by jointly reporting AEFI data from EPIs and NRAs. Progress has been particularly notable in AFR and EMR. Despite this progress, however, all WHO regions continue to report low percentages of countries jointly reporting EPI and NRA AEFI data; although EMR achieved the highest regional percentage of WHO countries jointly reporting EPI and NRA AEFI data, only 50% of countries in the EMR reported both. Fewer than one half, 92 (43%) of 215 WHO countries are currently meeting the target for the new safety monitoring indicator,

and only in EUR are more than one half of countries reporting, demonstrating that additional work is needed to strengthen global vaccine safety monitoring.

Despite these gains, a slight decrease was observed in the proportion of WHO countries meeting the new reporting indicator in many WHO regions during 2022, likely because of a decline in national COVID-19 vaccination campaigns and less intensive AEFI surveillance. The current findings indicate that further measures are needed to strengthen global vaccine safety monitoring through technical support, standardized tools, and guidelines, and that better approaches to promote nationally coordinated AEFI reporting among EPIs and NRAs are needed.

Source: Erin F. Blau; Madhava Ram Balakrishnan; Helena Sköld; Ravi Shankar Santhana Gopala Krishnan; Pinelopi Lundquist; Shanthi Pal; Jane F. Gidudu. Morbidity and Mortality Weekly Report 1321. US Department of Health and Human Services | Centers for Disease Control and Prevention | MMWR | December 8, 2023, | Vol. 72 | No. 49.

Safety of BA.4-5 or BA.1 bivalent mRNA booster vaccines: nationwide cohort study

On 12 September, a cohort study was published in Denmark whose objective was to examine whether administration of a fourth dose of COVID-19 vaccine, using a bivalent messenger RNA vaccine matched to the Omicron variant, was associated with an increased risk of adverse events in adults over 50 years of age.

The study included 2 225 567 adults who had previously received three doses of COVID-19 vaccine between 1 January 2021 and 10 December 2022. The main outcome measure was rates of hospital visits for 27 different adverse events in a 28 day main-risk period after vaccination with a bivalent omicron-adapted mRNA booster vaccine as a fourth dose compared with reference period rates from day 29 after the third or fourth vaccine dose and onward.

A total of 1 740 417 adults (mean age 67.8 years, standard deviation 10.7 years) received a bivalent mRNA vaccine as a fourth dose. Fourth-dose vaccination with a bivalent mRNA vaccine was not associated with a statistically significant increased rate of any of the 27 adverse outcomes within 28 days (at-risk period) compared with the baseline period (e.g., the incidence rate ratio for ischemic cardiac events was 0.95 [95%CI 0.87 to 1.04] during the 28-day risk period compared with the reference period). Nor were statistically significant risk differences found when analyzing risk according to age, sex, or vaccine type, or when using alternative analytical approaches. However, a subsequent analysis detected statistically significant signs of myocarditis in female participants, although this outcome was rare and based on few cases. No risk of cerebrovascular infarction was found (incidence rate ratio 0.95, 95%CI 0.87 to 1.05).

The results of the study showed that bivalent mRNA booster vaccines administered as a fourth dose were not associated with an increased risk of 27 different adverse events evaluated in the first 28 days, including ischemic cardiac events. These results remained consistent regardless of age, sex, or vaccine type, or when using alternative analytical approaches.

The authors conclude that use of bivalent mRNA vaccines as a fourth vaccine dose against COVID-19 in Denmark was not associated with an increased risk of 27 different adverse events in adults aged ≥ 50 years.

Source: Niklas Worm, Safety of BA.4-5 or BA.1 bivalent mRNA booster vaccines: nationwide cohort study. *BMJ* 2023;382: e075015

Safety and immunogenicity of the BNT162b2 vaccine co-administered with seasonal inactivated influenza vaccine in adults

Safety and immunogenicity of the BNT162b2 vaccine co-administered with seasonal inactivated influenza vaccine in adults.

On 12 September, this randomized phase 3 clinical trial was published that explored the possibility of simultaneously administering the BNT162b2 vaccine against COVID-19 together with the seasonal inactivated influenza vaccine (SIIV), in order to simplify the vaccination process and take advantage of its additional benefits.

Healthy adults, aged 18-64 years, who had already received three doses of the BNT162b2 vaccine, were selected for this study. Participants were randomly assigned (1:1) to two groups based on vaccination strategy: one group received co-administered vaccines (month 0, BNT162b2 + SIIV; month 1, placebo), while the other group received the vaccines separately, at different times (month 0, placebo + SIIV; month 1, BNT162b2).

The main objective of the study was to demonstrate that immune responses elicited by BNT162b2 when co-administered with SIIV were noninferior to those elicited by either vaccine administered alone. To determine this, full-length S-binding immunoglobulin G (IgG) levels, as well as strain-specific hemagglutination assay inhibition (HAI) titers for four influenza strains, were evaluated one month after vaccination. In addition, reactogenicity analyses were performed and adverse event (AE) rates were evaluated.

The results of this randomized study, which included 1128 participants, showed that co-administration of the vaccines met the pre-established criterion of noninferiority in all measures of immunogenicity. This means that the immune responses obtained were comparable to those of the vaccines administered separately. In terms of safety, most of the reactogenic events observed in the group receiving both vaccines were mild or moderate. In addition, serious

adverse events were reported in less than 1% of participants within 1 month after vaccination, and none of these events were considered to be vaccine-related.

The authors conclude that the results of this study would support the idea that co-administration of the BNT162b2 vaccine together with the SIIV vaccine is safe and effective in adults. This would not only simplify the vaccination process, but could also contribute to improved immunization coverage against COVID-19 and influenza in the adult population.

Source: Murdoch L, Quan K, Baber JA, Ho AWY, Zhang Y, Xu X, Lu C, Cooper D, Koury K, Lockhart SP, Anderson AS, Türeci Ö, Şahin U, Swanson KA, Gruber WC, Kitchin N; C4591030 Clinical Trial Group. Safety and Immunogenicity of the BNT162b2 Vaccine Coadministered with Seasonal Inactivated Influenza Vaccine in Adults. *Infect Dis Ther.* 2023 Sep;12(9):2241-2258. doi: 10.1007/s40121-023-00863-5. Epub 2023 Sep 12. PMID: 37698774; PMCID: PMC10581992.

[Type 1 diabetes, COVID-19 vaccines and short-term safety: Subgroup analysis from the global COVAD study](#)

Published on 7 December, this retrospective observational study aimed to evaluate the frequency and severity of short-term adverse events (AE) of vaccination (<7 days), and their risk factors in people who have type 1 diabetes with respect to healthy controls.

The study used data from the COVID-19 vaccination in Autoimmune Diseases (COVAD) survey database, which contains self-reported data from May through December 2021. This database involved the collaboration of 94 countries. The comparison focused on adverse events <7-day COVID-19 vaccine AE among type 1 diabetes patients and healthy controls (HCs). Several analysis techniques were applied, including descriptive statistics, propensity score matching (1:4), using the variables age, sex, and ethnicity, as well as multivariate analysis.

This study analyzed 5480 completed survey responses. Of all responses, 5408 were HCs, 72 were type 1 diabetes patients (43 females, 48.0% white European ancestry), and Pfizer was the most administered vaccine (39%). A total of 4052 (73.9%) respondents had received two vaccine doses.

The results indicated that patients with type 1 diabetes had a comparable risk of injection site pain, minor and major vaccine AEs, as well as associated hospitalizations to HCs. However, type 1 diabetes patients had a higher risk of severe rashes (3% vs 0.4%, OR 8.0, 95% confidence interval 1.7–36), $P = 0.007$), although these were rare and were recorded in only two patients with type 1 diabetes.

The authors concluded that COVID-19 vaccination was safe and well tolerated in patients with type 1 diabetes with similar adverse event profiles to those observed in HCs. Severe rashes were slightly more common in patients with type 1 diabetes, though still uncommon.

Source: Chatterjee T, Ravichandran N, Nair N, Gracia-Ramos AE, Barman B, Sen P, Joshi M, Saha S, Nune A, Pande AKR, Velikova T, Parodis I, Tan AL, Shinjo SK, Boro H, Agarwal V, Aggarwal R, Gupta L; COVAD Study Group. Type 1 diabetes, COVID-19 vaccines, and short-term safety: subgroup analysis from the global COVAD study. *J Diabetes Investig.* 2023 Sep 11. doi: 10.1111/jdi.14079. Epub ahead of print. PMID: 37697820.

[Miller Fisher syndrome after COVID-19 infection and vaccine: a systematic review](#)

On 19 July, a study was published whose objective was to conduct a systematic review of Miller Fisher Syndrome (MFS) cases in relation to COVID-19 infection or vaccination. To conduct this research, a review of the scientific literature was performed in the Medline database. A total of 21 articles were included in the review.

Twenty-two MFS cases (77% males) were identified, 14 related to COVID-19 infection and eight to vaccination against COVID-19. The median age of the adult patients was 50 years (interquartile range 36–63 years). Sixteen patients (73%) had the classic triad of MFS (ophthalmoplegia, ataxia, areflexia), four (18%) had acute ophthalmoplegia and one other characteristic symptom and two patients (9%) had only one other characteristic symptom, but they tested positive for GQ1b antibodies. Nine (41%) patients had positive GQ1b antibodies and were classified as “definite” MFS. Albuminocytologic dissociation was found in half of the cases. The outcome was favorable in the majority of cases (86%) whereas one patient, despite initial improvement, died because of a cardiac arrest, after cardiac arrhythmia.

This study provided evidence that Miller Fisher syndrome after COVID-19 infection or COVID-19 vaccination, exhibited the typical epidemiologic features of classic MFS. This syndrome proved to be rare, occurring more often after infection than vaccination. It predominantly affected middle-aged men, usually within three weeks after the triggering event. It is noteworthy that this syndrome had a favorable prognosis after receiving intravenous gamma globulin (IVIG) treatment or even with no treatment at all. No evidence was found to suggest significant differences between MFS after COVID-19 infection and MFS after COVID-19 vaccination, although it was noted that symptoms of the former tended to appear earlier.

Source: Neophytou P, Artemiadis A, Hadjigeorgiou GM, Zis P. Miller Fischer syndrome after COVID-19 infection and vaccine: a systematic review. *Acta Neurol Belg.* 2023 Oct;123(5):1693-1701.

[Herpesviruses reactivation following COVID-19 vaccination: a systematic review and meta-analysis](#)

On 10 August, a systematic review was published whose objective was to determine whether prior administration of COVID-19 vaccines was associated in any way with reactivation of human herpesviruses (HHVs). To conduct this analysis, a systematic search was conducted on 25 September 2022 in PubMed/MEDLINE, Web of Science, and EMBASE. The analysis included all observational studies, case reports, and case series that reported reactivation of human herpesviruses following administration of COVID-19 vaccines.

The search yielded 80 articles that met the eligibility criteria. Among the various COVID-19 vaccines evaluated in these studies, most were mRNA-based.

The results obtained from observational studies indicated a possible association between administration of COVID-19 vaccines and reactivation of two types of human herpes viruses: varicella-zoster virus (VZV) and herpes simplex virus (HSV). Proportion meta-analysis showed that the rate of VZV reactivation among those who received the COVID-19 vaccine was 14 persons per 1000 vaccinations (95% CI 2.97–32.80). Meta-analysis for HSV reactivation showed a rate of 16 persons per 1000 vaccinations (95% CI 1.06–46.4).

In addition to observational studies, case reports/series showed 149 cases of HHV reactivation. There were several vaccines that caused reactivation including BNT162b2 mRNA or Pfizer–BioNTech ($n = 76$), Oxford-AstraZeneca ($n = 22$), mRNA-1273 or Moderna ($n = 17$), Sinovac ($n = 4$), BBIBP-CorV or Sinopharm ($n = 3$), Covaxin ($n = 3$), Covishield ($n = 3$), and Johnson and Johnson ($n = 1$). Reactivated HHVs included varicella-zoster virus (VZV) ($n = 114$), cytomegalovirus (CMV) ($n = 15$), herpes simplex virus (HSV) ($n = 14$), Epstein-Barr virus (EBV) ($n = 6$), and HHV-6 ($n = 2$). Importantly, most cases reported their disease after the first dose of the vaccine. Many patients reported having comorbidities, of which hypertension, diabetes mellitus, dyslipidemia, chicken pox, and atrial fibrillation were common.

The authors concluded that their findings suggest a possible association between COVID-19 vaccination and herpesvirus reactivation. Although the evidence is strongest for VZV and HSV reactivation, further research, especially from observational studies and clinical trials, is needed to gain a more complete understanding of the interaction between COVID-19 vaccination and the reactivation of other herpes viruses, such as EBV and CMV.

Source: Shafiee A, Amini MJ, Arabzadeh Bahri R, Jafarabady K, Salehi SA, Hajishah H, Mozhgani SH. Herpesviruses reactivation following COVID-19 vaccination: a systematic review and meta-analysis. *Eur J Med Res.* 2023 Aug 10;28(1):278. doi: 10.1186/s40001-023-01238-9. PMID: 37559096; PMCID: PMC10413536.

[The occurrence of acute disseminated encephalomyelitis in SARS-CoV-2 infection/vaccination: Our experience and a systematic review of the literature](#)

On 10 July, a systematic review was published whose aim was to evaluate the diagnosis, clinical characteristics, imaging and laboratory features, evolution, and treatment options for acute disseminated encephalomyelitis (ADEM) and acute hemorrhagic leukoencephalitis (AHLE) developing after COVID-19 infection or vaccination.

Regarding the methods used, a comprehensive literature review was performed following PRISMA guidelines for reporting systematic reviews (Preferred Reporting Items for Systematic Review and Meta-Analysis). This review included ADEM cases published between 1 January 2020

and 30 November 2022 following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and vaccination.

The results of the investigation showed a total of 74 patients diagnosed with ADME, 45 following COVID-19 infection and 29 after a SARS-CoV-2 vaccine. A total of 13 patients (17.33%) presented AHLE. The moderate form of COVID-19 presented a positive correlation with AHLE ($r = 0.691$, $p < 0.001$). More aggressive immunomodulatory therapies applied in severe cases were correlated with poor outcomes (major sequelae and death), namely: therapeutic plasma exchange (TPE) treatment ($r = 382$, $p = 0.01$) and combined therapy with corticosteroids and TPE ($r = 0.337$, $p = 0.03$).

The authors stress the importance of closely monitoring potential neurologic adverse events, such as ADEM and AHLE. Despite these risks, the overall benefits and favorable outcomes of vaccination generally outweigh the potential risks. However, prompt diagnosis is crucial to improve the prognosis of affected patients.

Source: Stoian A, Bajko Z, Stoian M, Cioflinc RA, Niculescu R, Arbănași EM, Russu E, Botoncea M, Bălașa R. The Occurrence of Acute Disseminated Encephalomyelitis in SARS-CoV-2 Infection/Vaccination: Our Experience and a Systematic Review of the Literature. *Vaccines* (Basel). 2023 Jul 10;11(7):1225. doi: 10.3390/vaccines11071225. PMID: 37515041; PMCID: PMC10385010.

EMA recommends approval of adapted Nuvaxovid COVID-19 vaccine targeting Omicron XBB.1.5

On 31 October, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended authorizing an adapted Nuvaxovid vaccine targeting the Omicron XBB.1.5 subvariant of the SARS-CoV-2 virus.

The vaccine, known as Nuvaxovid XBB.1.5, will be used to prevent COVID-19 in adults and children from 12 years of age. In line with previous recommendations by EMA and the European Centre for Disease Prevention and Control (ECDC), adults and adolescents from 12 years of age who require vaccination should receive a single dose, regardless of their COVID-19 vaccination history.

In its decision to recommend the authorization, the CHMP assessed laboratory data showing that the adapted vaccine is able to trigger an adequate immune response against XBB.1.5. The Committee also considered data from a study in previously vaccinated adults showing that when Nuvaxovid was adapted to target another related strain, Omicron BA.5, it was able to trigger a strong immune response against this strain. Based on these data, the Committee concluded that Nuvaxovid XBB.1.5 is expected to trigger an adequate immune response against XBB.1.5.

The safety profile of Nuvaxovid XBB.1.5 is expected to be similar to that of the originally authorized Nuvaxovid. This was also supported by clinical data available with the version of the vaccine targeting Omicron BA.5. The most common side effects with Nuvaxovid XBB.1.5 are pain and tenderness at the injection site, tiredness, headache, muscle pain and feeling generally unwell.

For more information, see: <https://www.ema.europa.eu/en/news/ema-recommends-approval-adapted-nuvaxovid-covid-19-vaccine-targeting-omicron-xbb15>
<https://www.ema.europa.eu/en/news/ema-recommends-approval-adapted-nuvaxovid-covid-19-vaccine-targeting-omicron-xbb15>

WHO SAGE Good Practice Statement on the use of COVID-19 variant-containing vaccines

On 2 November, WHO released the updated Good Practice Statement on the use of variant-containing COVID-19 vaccines, based on the advice of the Strategic Advisory Group of Experts on Immunization (SAGE). The statement synthesizes the current evidence on variant-containing COVID-19 vaccines, particularly those containing the XBB strain. This is a summary of the main recommendations:

- **Initial dose (primary series):** for persons who have not yet been vaccinated against COVID-19. Any of the WHO Emergency Use Listing (EUL) vaccines can be used, including monovalent XBB vaccines.
- **Booster dose:** With the greater immune evasion of Omicron and its descendent sublineages, the use of booster doses of vaccines is justified, in particular for persons at highest risk of developing severe COVID-19. WHO recommends that any of the WHO EUL COVID-19 vaccines or authorized variant-containing vaccines can be used for the booster doses.
- **Heterologous schedules:** There is increasing evidence that booster doses using a different COVID-19 vaccine platform from that used for the initial series (heterologous schedules) may provide superior immunogenicity to use of a homologous dose. For countries considering heterologous schedules, WHO recommends the following, depending on product availability:
 - Inactivated vaccines for initial doses: May consider using WHO EUL vectored or mRNA vaccines for subsequent doses.
 - Vectored vaccines for initial doses: May consider using WHO EUL mRNA or protein subunit vaccines for subsequent doses.
 - mRNA vaccines for initial doses: May consider using WHO EUL vectored or protein subunit vaccines for subsequent doses.

More information is available at: <https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Variants-2022.1>

Updated WHO SAGE roadmap for prioritization of the use of COVID-19 vaccines in the context of the Omicron variant and its sub-lineages

On 10 November, WHO SAGE published an updated roadmap for prioritization of the use of COVID-19 vaccines in the context of the Omicron variant, its circulating sub-lineages of concern, and high population immunity. This updated roadmap also replaces the Good Practice Statement on the use of second booster doses of COVID-19 vaccines, published in August 2022.

The WHO SAGE roadmap was first published in October 2020 and had been updated four times, most recently in March 2023.

The current roadmap considers that the availability of COVID-19 vaccines is sufficient, with high current population-level seroprevalence exceeding 90% in most countries due to increasing vaccination coverage rates and infection-induced immunity. In addition, it addresses changing public health needs as the Omicron variant and its sub-lineages continue to circulate, and provides updated information on COVID-19 vaccination in relation to:

- new priority-use groups for vaccination;
- specific recommendations for primary vaccination and booster doses, according to priority-use groups;
- need and frequency of revaccination after the first booster dose;
- vaccines containing variants;
- vaccination during pregnancy
- post COVID-19 conditions

More information is available at: <https://iris.who.int/handle/10665/367330>

U.S. FDA publishes important information about the correct dosage and administration of Moderna COVID-19 vaccine (2023-2024 formula) for individuals 6 months through 11 years of age

On 1 November, the U.S. Food and Drug Administration (FDA) released important information on the correct dosage and administration of the Moderna COVID-19 vaccine (2023-2024 formula) for individuals aged 6 months to 11 years.

FDA reported that some health care providers may not recognize that the single-dose vial of Moderna COVID-19 vaccine (2023-2024 formula) for use in persons 6 months through 11 years of age contains more than 0.25 mL of vaccine and, therefore, may administer a higher dose than the indicated 0.25 mL. After extracting the correct dose of vaccine, the vial and any excess vaccine should be discarded.

The FDA reported that it had not identified any safety risks associated with administration of a higher dose in persons aged 6 months to 11 years, nor any serious adverse events related to a vaccine dosing error.

More information is available at: <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/important-information-about-correct-dosage-and-administration-moderna-covid-19-vaccine-2023-2024>

WHO Statement on the antigen composition of COVID-19 vaccines

On 13 December, WHO released the statement from its Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC). This is a summary of the highlights:

- SARS-CoV-2 continues to circulate and evolve with important genetic and antigenic evolution of the spike protein;
- Monovalent XBB.1.5 COVID-19 vaccines across different platforms elicit broadly cross-reactive neutralizing antibody responses against circulating SARS-CoV-2 variants;
- Given the current SARS-CoV-2 evolution and the breadth of immune responses demonstrated by monovalent XBB.1.5 vaccines against circulating variants, the TAG-CO-VAC advises retaining the current COVID-19 vaccine antigen composition, i.e., monovalent XBB.1.5 antigen.

The twice-yearly evidence review by the TAG-CO-VAC is based on the need for continued monitoring of the evolution of SARS-CoV-2 and the kinetics of vaccine-derived immunity. The WHO TAG-CO-VAC conducts a biannual review of the evidence to assess the implications of the evolution of SARS-CoV-2, and of the kinetics of vaccine-derived immunity, and to advise WHO on whether or not to make changes to the composition of the COVID-19 vaccine.

More information is available at: <https://www.who.int/news/item/13-12-2023-statement-on-the-antigen-composition-of-covid-19-vaccines>

Addition of COVID-19 vaccines to the WHO Emergency Use Listing

On 30 October, WHO added the COMIRNATY Omicron XBB vaccine to the WHO Emergency Use Listing (EUL) of COVID-19 vaccines. This is a summary of its main characteristics:

Summary of the main characteristics of the COMIRNATY Omicron XBB vaccine

Name	COMIRNATY Omicron XBB Vaccine			
EUL holder	BioNTech Manufacturing GmbH, Germany.			
Responsible RNA	European Medicines Agency (EMA)			
Pharmaceutical form	Sterile dispersion for injection			
Strain	Omicron XBB.1.5			
International nonproprietary name (INN)	Raxtozinameran			
Dosage	30 mcg	10 mcg	10 mcg	3 mcg
Age indication	12 years and older	5 to 11 years old	5 to 11 years old	6 months to 4 years
Vial cap color	gray	orange	blue	brown
Number of doses	1 dose and 6 doses of 0.3 mL	10 doses of 0.2 mL	1 dose and 6 doses of 0.3 mL	10 doses of 0.2 mL
Shelf life	18 months	18 months	12 months	18 months
Storage temperature	-90°C to -60°C	-90°C to -60°C	-90°C to -60°C	-90°C to -60°C
Refrigeration storage time (2°C -8°C):	10 weeks within the 18-month shelf life	10 weeks within the 18-month shelf life	10 weeks within the 12-month shelf life	10 weeks within the 18-month shelf life
Diluent	None	None	None	None

Source: <https://extranet.who.int/prequal/vaccines/comirnaty-omicron-xbb>

WHO updates guidelines on COVID-19 treatments

On 10 November, WHO published *Therapeutics and COVID-19: living guideline*, its 13th ^{update} of COVID-19 treatment guidelines, which includes revised recommendations for patients with non-severe COVID-19.

This update includes new baseline risk levels for hospital admission in patients with non-severe COVID-19, as follows:

- **High risk:** immunosuppressed persons, with an estimated hospitalization rate of 6%.
- **Moderate risk:** people over 65 years of age; people with conditions such as obesity, diabetes, or chronic conditions, especially chronic obstructive pulmonary disease or kidney or liver disease, or active cancer; people with disabilities; and people with comorbidities of chronic diseases are at moderate risk, with an estimated hospitalization rate of 3%.
- **Low risk:** people not in the high or moderate risk categories, with 0.5% risk of hospitalization.

The new moderate risk category now includes people who were previously considered high risk, such as older adults and people with chronic conditions, disability, or comorbidities of chronic diseases.

For treatment, WHO continues to recommend the combined use of nirmatrelvir-ritonavir for people at high and moderate risk of hospitalization, considering it the best option for most eligible patients in view of its therapeutic benefits, ease of administration, and fewer concerns about potential risks.

In the event that combined nirmatrelvir-ritonavir is not available, it is suggested to use molnupiravir, except in patients at moderate risk of hospital admission, as the potential harms are considered to outweigh the limited benefits in patients at moderate risk.

For people at low risk of hospitalization, WHO does not recommend any antiviral treatment. Symptoms such as fever and pain can be treated with analgesics such as paracetamol.

WHO also advises against the administration of a new antiviral drug (VV116) to patients, except in the context of clinical trials, and against the use of ivermectin in patients with non-severe COVID-19. WHO only recommends the use of ivermectin in clinical trials for patients with severe or critical COVID-19.

This guide is available at: <https://iris.who.int/bitstream/handle/10665/373975/WHO-2019-nCoV-therapeutics-2023.2-eng.pdf?sequence=1>. <https://www>

European Union (EU) medicines agencies reflect on lessons learned from COVID-19

On 1 December, EMA published a report with lessons learned from COVID-19, highlighting some of the unprecedented COVID-19-related challenges they had to address, the activities and areas that enabled them to effectively respond to the emergency, and some needed improvements.

Among the recommendations, the EU considers that efforts should be increased in terms of the capacity to conduct large clinical studies in a rapid manner. In order to have real-world information, it is necessary to collect multiple data sources that can generate useful evidence for regulatory assessments. The EU also recognizes the need for a larger pool of experts who can participate in scientific assessments, such as accelerated reviews of promising medicines, when crisis situations arise.

This report has been adopted by EMA's Management Board and several recommendations have already been implemented as part of EMA's expanded mandate, with the Agency assuming an enhanced role on preparedness to be more proactive on public health threats. Work continues on areas such as resourcing, process improvements, and communication. In addition, it is expected that the ongoing review of EU pharmaceutical legislation will also provide a vehicle to bring about further changes to the EU regulatory toolbox.

More information at: <https://www.ema.europa.eu/en/news/eu-medicines-agencies-reflect-lessons-learned-covid-19> <https://www>

WHO reports that COVID-19 vaccination has become regular immunization and COVAX is ending

On 19 December, WHO reported that the COVAX facility will close on 31 December 2023, after delivering nearly two billion doses of vaccines to 146 economies and averting approximately 2.7 million deaths in participating low-income economies.

COVAX's comprehensive efforts helped low-income economies achieve 57% two-dose coverage, compared to the global average of 67%.

Low- and lower-middle-income economies will continue to receive COVID-19 vaccines and delivery support in 2024 and 2025 through the Vaccine Alliance (Gavi).

More information at: <https://www.ema.europa.eu/en/news/eu-medicines-agencies-reflect-lessons-learned-covid-19>

WHO declares the JN.1 variant of COVID19 to be a variant of interest

On 19 December, WHO reported that due to the rapid spread of the JN.1 variant, it will be classified as a variant of interest (VOI) separately from the original BA.2.86 lineage.

The available evidence suggests that the additional global public health risk posed by JN.1 is currently low, but with the onset of winter in the northern hemisphere, the JN.1 variant could increase the burden of respiratory infections in many countries.

WHO is continuously monitoring the evidence and will update the JN.1 risk assessment as needed.

More information is available at: <https://www.who.int/activities/tracking-SARS-CoV-2-variants>

Note: This document includes material published by third parties and compiled by PAHO. PAHO has taken reasonable precautions to verify the information contained in the document. However, this material is being distributed without warranty of any kind. The reader is responsible for the interpretation and use of this information and in no event shall PAHO be held liable for any damages arising from its use.