

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

Fortieth report

WASHINGTON, DC

Updated: 29 March 2023









OFFICIAL REPORTS ON PHARMACOVIGILANCE PROGRAMS3
CHILE (First report on bivalent vaccines)5
6
PUBLICATIONS ON POTENTIAL SAFETY SIGNALS IDENTIFIED WITH THE USE OF COVID-19 VACCINES
Maternal mRNA COVID-19 vaccination during pregnancy and Delta or Omicron infection or hospital admission in infants: test-negative design study6
Sex-disaggregated outcomes of adverse events after COVID-19 vaccination: A Dutch cohort study and review of the literature7
Evaluation of the BNT162b2 COVID-19 vaccine in children younger than 5 years of age. Phase 2–3 trial in five countries
DECISIONS OF REGIONAL AND INTERNATIONAL REGULATORY AUTHORITIES12
Brazil's National Health Surveillance Agency (ANVISA) extends the shelf life of the Pfizer-BioNTech COVID-19 vaccine Comirnaty12
The European Medicines Agency (EMA) authorizes extension of the shelf life of the Valneva COVID- 19 vaccine12
EMA recommends approval of Valneva COVID 19 vaccine as booster
U.S. Food and Drug Administration (FDA) updates fact sheet for the Janssen COVID-19 Vaccine13
FDA Authorizes Bivalent Pfizer-BioNTech COVID-19 Vaccine as Booster Dose for Certain Children 6 Months through 4 Years of Age13
EMA updates list of adverse reactions for Pfizer-BioNTech COVID-19 vaccine
SAGE revises roadmap for prioritizing the use of COVID-19 vaccines
15
CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS 15
WHO Strategic Advisory Group of Experts on Immunization (SAGE) update to good practice statement on the use of variant-containing COVID-19 vaccines
OTHER RELATED UPDATES



Organización Panamericana de la Salud



WHO updates working definitions and tracking system for SARS-CoV-2 variants of interest and	
variants of concern	,







Number and reporting rate of adverse events following immunization (AEFI), by country, for all COVID-19 vaccines administered to the general population

Data drawn from public reports available as of 27 March 2023. The dates on which the bulletins were analyzed vary according to the country.

Country	Doses administered	Non-serious		Serious	
		N*	Rate**	N*	Rate**
Argentina 1	109 916 975	60 084	54.7	3006	2.7
Barbados ₂	381 662	527	138.1	87	22.8
Canada ₃	97 597 702	43 884	45.0	10 685	10.9
Chile ₄	52 932 484	15 513	29.3	861	1.6
Colombia ₅	89 120 782	55 697	62.5	1590	1.8
Haiti 2	515 718	1	0.2	0	0.0
Jamaica 2	1 518 792	761	50.1	212	14.0
Paraguay 6	9 505 712	2282	24.0	470	4.9
Peru 7	84 468 527	52 435	861.0	246	0.3
Mexico ₈	133 972 266	37 600	28.1	1157	0.9
Saint Vincent and the Grenadines 2	73 418	17	23.2	6	8.2
Total	580 004 038	268 801	46.3	18 320	3.2

* N= number of reports

** Rate per 100 000 doses administered

Sources:

1. Ministry of Health of Argentina Nineteenth Vaccine Safety Surveillance Report. National COVID-19 Vaccination Campaign, November 2022 (reporting period 29/12/2022 to 21/10/2022). Available from: <u>https://www.argentina.gob.ar/coronavirus/vacuna/equipos-salud/informes-seguridad</u>.

2. The Caribbean Public Health Agency (CARPHA). Caribbean Regulatory System. VigiCarib News Volume 6 Issue 3: 17 March 2023. Data from 1 January 2022 to 15 March 2023. For additional information, see: https://carpha.org/What-We-Do/CRS/VigiCarib.







1

3. Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada. Updated on 17 March 2023, with data up to and including 3 March 2023. https://health-infobase.canada.ca/covid-19/vaccine-safety/.

4. Public Health Institute of Chile (ISP). Department of the National Agency of Medicines. Eleventh Statistical Report, "AEFI associated with the administration of SARS-CoV-2 vaccines in Chile in people 18 years old and older." Period: 24 December 2020 to 1 October 2022. January 2023 Available from: https://www.ispch.cl/isp-covid-19/informes-estadisticos-de-esavi-de-vacunas-sars-cov-2/.

5. Ministry of Health of Colombia, National Institute of Health. Bulletin #18: October 2022. Surveillance of Adverse Events Following Immunization (AEFI) with COVID-19 vaccines in Colombia. Report period: 17 February 2021 to 11 October 2022. Available from: <u>https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/PSP/boletin12-</u> farmacovigilancia-vacunas-abr2022.pdf.

6. Paraguay Ministry of Public Health and Social Welfare. AEFI Surveillance Information Bulletin No. 95 Regarding COVID-19 Vaccination. National Program for Immunopreventable Diseases and Expanded Program on Immunization of 30 December 2022 (reporting period 22/2/2021 to 30/12/2022). Available from: <u>https://pai.mspbs.gov.py/esavis-2022/</u>.

 Ministry of Health. General Directorate of Medicines, Supplies, and Drugs. Pharmacovigilance report. Reported adverse events following immunization (AEFI) with COVID-19 vaccines. Period: 9 February 2021 to 30 September 2022. Available from: <u>https://repositorio.digemid.minsa.gob.pe/handle/DIGEMID/307</u>.
 Undersecretariat of Prevention and Health Promotion General Directorate of Epidemiology. Directorate of Epidemiological Surveillance of Communicable Diseases. COVID-19 AEFI Report, December 2022. Published on 13 January 2023 (reporting period 24/12/2020 to 30/12/2022). Available from: <u>https://www.gob.mx/salud/documentos/reporte-mensual-esavi-por-vacuna-contra-covid19</u>.





Organización Mundial de la Salud GRANL PRA LUS Américas



CHILE (First report on bivalent vaccines)

In January 2023, the Institute of Public Health of Chile (ISP), through its National Center for Pharmacovigilance, published the first statistical report, "AEFI associated with the administration of bivalent COVID-19 vaccines in Chile in people 12 years old and older," with analysis of the report covering the period 11 October 2022 to 3 December 2022.

Number and reporting rate of AEFI wit to 3 December 2022.	h bivalent vaccine	in people 12	years old and ol	der, from 11	October 2022	
		Non-serious		Serious		
Bivalent vaccine	Doses administered	N**	Rate per 100 000 doses administered ***	N*	Rate per 100 000 doses administered ***	
Pfizer-BioNTech*	849 507	146	17.2	3	0.4	
Moderna (original/Omicron)	120 946	3	2.5	0	-	
Total	970 453	149	15.4	3	0.3	

* Includes reports of the original bivalent/Omicron BA.1 vaccine and the original bivalent/Omicron vaccine (BA.4 and BA.5).

** N= number of reports.

Reports initially classified as serious, and later reported to the Bivalent Pfizer-BioNTech COVID-19 vaccine administration, report the following events: stroke, quadriparesis, myositis, meningitis, and paresis.

At the time of the report, the target group for vaccination was small, and included only health professionals, adults over 60 years of age, and immunocompromised patients 12 years old and older.

Source: Public Health Institute of Chile. Ministry of Health. First Statistical Report, "AEFI associated with the administration of SARS-CoV-2 vaccines in Chile in people 18 years old and older." Period: 11 October 2022 to 3 December 2022. Available from: <u>https://www.ispch.cl/isp-covid-19/informes-estadisticos-de-esavi-de-vacunas-sars-cov-2/</u>. Data reproduced by PAHO/WHO.







Maternal mRNA COVID-19 vaccination during pregnancy and Delta or Omicron infection or hospital admission in infants: test-negative design study

On 8 February, a case-control test-negative design study was published, to estimate the test-negative effectiveness of maternal mRNA COVID-19 vaccination during pregnancy, against Delta and Omicron infection, and hospital admission of infants under 6 months of age.

The study, which was conducted in community and hospital SARS-CoV-2 testing facilities in Ontario, Canada, involved infants younger than 6 months of age, born between 7 May 2021 and 31 March 2022, who were screened between 7 May 2021 and 5 September 2022. Information on maternal COVID-19 vaccination was obtained from COVaxON, a centralized COVID-19 vaccine registry in Ontario. BNT162b2 and mRNA-1273 vaccines became available to high-risk Ontario residents 18 years old and older as of December 2020.

The main outcome measures were: Laboratory confirmed Delta or Omicron infection or hospital admission of infants.

Multivariable logistic regression estimated vaccine effectiveness, with adjustments for clinical and sociodemographic characteristics associated with vaccination and infection.

A total of 8809 infants met eligibility criteria; of these, 1600 were Delta or Omicron cases, and 7209 were controls.

The results of the analysis were as follows: The effectiveness of the mRNA vaccine in the child population with two doses of maternal vaccination was:

lundial de la Salud

In partnership

- 95% (CI 95% 88% to 98%) against Delta infection;
- 97% (CI 95% 73% to 100%) against infant hospital admission due to Delta;
- 45% (CI 95% 37% to 53%) against Omicron infection; and
- 53% (CI 95% 39% to 64%) against hospital admission due to Omicron.

Vaccine effectiveness for three maternal doses of mRNA vaccine was:

• 73% (CI 95% 61% to 80%) against Omicron infection; and

• 80% (CI 95% 64% to 89%) against hospital admission due to Omicron.

Vaccine effectiveness for two doses against infant Omicron infection was highest with the second dose in the third trimester (53% [42% to 62%]) compared with the first (47% [31% to 59%]) or second (37% [24% to 47%]) trimesters.

Vaccine effectiveness for two doses against infant Omicron infection decreased from 57% (44% to 66%) between birth and eight weeks to 40% (21% to 54%) after 16 weeks of age.

The authors conclude that maternal COVID-19 vaccination with a second dose during pregnancy was highly effective against Delta infection and moderately effective against Omicron infection and hospital admission in infants during the first six months of life. A third vaccine dose bolstered protection against Omicron. Effectiveness for two doses was highest with maternal vaccination in the third trimester, and effectiveness decreased in infants beyond eight weeks of age.

The clinical implications of this finding on maternal vaccination need to be weighed against the risks to the pregnant woman and the fetus of delaying vaccination. Additionally, receipt of only the first vaccine dose during pregnancy offered less protection than completion of the two- or three-dose series.

Source: Sarah C J Jorgensen. Maternal mRNA COVID-19 vaccination during pregnancy and Delta or Omicron infection or hospital admission in infants: test-negative design study. BMJ 2023; 380 DOI: https://www.bmj.com/content/380/bmj-2022-074035.

Sex-disaggregated outcomes of adverse events after COVID-19 vaccination: A Dutch cohort study and review of the literature

On 30 January, a prospective cohort study was published to assess differences, between men and women in the Netherlands, in the incidence and course of adverse events following immunization (AEFI) with COVID-19 vaccines, and to provide a summary of sex-disaggregated outcomes.

In a cohort event monitoring study, AEFI reports were collected from Dutch patients aged above 16 years who received the COVID-19 vaccine between February and August 2021. Follow-up was conducted over







a period of six months after the first vaccination with Pfizer-BioNTech, AstraZeneca, Moderna, or the Johnson & Johnson vaccine.

Logistic regression was used to assess differences in the incidence of "any AEFI," local reactions, and the 10 most reported AEFIs between the sexes. First, effects of age, vaccine brand, comorbidities, prior COVID-19 infection, and the use of antipyretic drugs were analyzed. Second, time-to-onset, time-to-recovery, and perceived burden of AEFIs were compared between the sexes. Third, a literature review was conducted to retrieve sex-disaggregated outcomes of COVID-19 vaccination.

The cohort included 27 540 vaccinees (38.5% men). The median age for men was 74 years (53–79), and for women 50 years (37–62).

The 10 most frequent reported AEFIs (regardless of sex) consisted of two local reactions (inflammation and injection-site pain) and eight systemic reactions (fatigue, myalgia, headache, malaise, chills, pyrexia, arthralgia, and nausea); all were solicited adverse effects. These events were actively solicited from the patients through specific questions in standardized questionnaires.

Women were about twice as likely as men to have "any AEFI," with the most pronounced differences seen after the first dose, with the adjusted odds ratio of having any AEFI after the first dose: 2.28 (2.13-2.43), and for nausea and injection-site inflammation, 1.91 (1.79–2.02).

The higher proportion of women compared to men who reported an AEFI was consistent for both first and second doses for all four vaccine brands. Men reported three sex-restricted AEFIs, including erectile failure, pain in the testes, and swelling of the scrotum, while in women a variety of sex-restricted AEFIs were reported, mostly associated with the menstrual cycle or menstruation.

Age was inversely associated with AEFI incidence, with AOR values in the 40–54 age group: 0.39 (0.35–0.44); 55–74 age group: 0.19 (0.17–0.22); and \geq 75 age group: 0.10 (0.09–0.11). Having a previous COVID-19 infection; use of antipyretic drugs; history of allergy, cardiovascular disorders, psychological disorders, immunosuppression, and other comorbidities were positively associated with AOR values of: 2.11 (1.78–2.51); 1.35 (1.20–1.50); 1.75 (1.56–1.96); 1,26 (1,14-1,39); 1.59 (1.29–1.97); 1.38 (1.09–1.74) and 1.42 (1.28–1.56), respectively.







By contrast, for several AEFIs, time-to-recovery was significantly longer in women than in men.

Women suffered significantly longer from "any AEFI," local reactions, injection-site pain and inflammation, fatigue, headache, and malaise compared to men when using data from all vaccine brands combined. For most AEFIs the TTR lasted 1-3 days; the longest TTR was reported for injection- site inflammation, with medians of 72 and 96 hours in men and women, respectively. For most AEFIs the median TTRs were equal or lower after the second compared the first dose.

Overall, there was little difference between the time to onset of AEFI symptoms reported by men and women. For both sexes, shorter TTOs were observed for local reactions (medians of 3 and 2 hours for men and women, respectively) compared to systemic reactions such as pyrexia, nausea, and chills, for which the median latency times frequently exceeded eight hours.

The study discusses the possible reasons for this difference in incidence, including biological differences between the sexes, such as the role of sex hormones and differences in gene expression. An inverse association between age and the probability of experiencing AEFIs was also observed, owing to the process of immunosenescence.

The multivariable logistic regression showed that for "any AEFI," vaccinees who reported a burden level of 2 (slightly burdensome), 3 (somewhat burdensome), 4 (moderately burdensome), and 5 (extremely burdensome) were, respectively, 1.40, 2.13, 2.92, and 4.39 times more likely to be women compared to vaccinees who reported the lowest burden (level 1, not at all burdensome). The literature search yielded a total of 84 studies eligible for inclusion in the review. The majority of the studies were performed in Europe (n=26, 31.0%), Asia (n=24, 28.6%), and the Middle East (n=21, 25.0%). With regard to the vaccine brands investigated, the highest percentage of the articles under review assessed the occurrence of AEFIs after vaccination with the Pfizer-BioNTech (n=71, 84.5%), followed by the AstraZeneca (n=34, 40.5%), Moderna (n=24, 28.6%), and Johnson & Johnson (n=9, 10.7%) vaccines.

Nearly all articles reported a higher incidence of AEFIs in women compared to men, with the exception of four articles that found an opposite outcome, for most of which no clear reason could be identified other







than a possible skewed distribution of the sexes and age groups in the studies. Women had a median 1.96 times higher odds of reporting a local reaction compared to men (range: 1.02-2.90, IQR 1.85-2.54).

TTR was assessed in four articles, all of which reported higher TTR in women than in men, ranging from 1.2-1.9 days in men to 1.4-2.2 days in women, though the difference was only statistically significant in one article. The results in the articles regarding health care-seeking behavior, hospital admissions, and absenteeism due to adverse effects were unambiguous across studies. Women showed a higher rate of health care-seeking behavior and absenteeism in two studies, whereas two studies reported higher hospital admission rates for men.

The authors conclude that, in the Netherlands, the outcomes of this cohort study confirm those of previous studies, and aid in gaining knowledge needed to clarify the magnitude of the effect of sex on response to vaccination. While women have a significantly higher probability of experiencing an AEFI than men, the authors observed that the course and burden is only to a minor extent different between the sexes.

Source: Duijster JW, et al. Sex-disaggregated outcomes of adverse events after COVID-19 vaccination: A Dutch cohort study and review of the literature. Front Immunol, 30 January 2023Sec. Vaccines and Molecular Therapeutics. Volume 14 – 2023. doi.org/10.3389/fimmu.2023.1078736.

Evaluation of the BNT162b2 COVID-19 vaccine in children younger than 5 years of age. Phase 2–3 trial in five countries

On 16 February, an ongoing trial was published, presenting the results of a randomized, placebocontrolled, phase 2–3 immunogenicity, safety, and efficacy trial of BNT162b2 for children 6 months to less than 2 years of age, and those 2 to 4 years of age through the data-cutoff dates (29 April 2022, for safety and immunogenicity and 17 June 2022 for efficacy). The phase 2–3 trial was conducted at 65 sites in Brazil, Finland, Poland, Spain, and the United States.

Participants were randomly assigned (in a 2:1 ratio) to receive two 3-µg doses of BNT162b2 or placebo. On the basis of preliminary immunogenicity results, a third 3-µg dose (\geq 8 weeks after dose 2) was administered starting in January 2022, which coincided with the emergence of the B.1.1.529 (Omicron) variant.





Organización Mundial de la Salud comu marus Américas



The 3-µg dose was selected for the phase 2–3 trial, which involved a total of 1178 children aged 6 months to less than 2 years, and 1835 children aged 2 to 4 years, who received BNT162b2 vaccine, while 598 and 915, respectively, received placebo.

The immunobridge success criteria were met in both age groups, both in geometric mean ratio (GMT) and serologic response one month after the third dose (GMT of 1407 for the 6-month to less than 2-year-old group, and 1535 for the 2–4-year-old group, compared with GMT of 1180 for people aged 16 to 25 years who received two doses of 30-µg vaccine). This indicates that the immune response produced by the vaccine in the pediatric population is sufficiently similar to the response produced in the population aged 16 to 25 years, according to the immunobridging success criteria. This approach is commonly used in drug and vaccine development in pediatric populations to extrapolate safety and efficacy data from the adult population to the pediatric population.

BNT162b2 reactogenicity events were mostly mild to moderate, with no grade 4 events. Low, similar incidences of fever were reported after receipt of BNT162b2 (7% among children 6 months to <2 years of age and 5% among those 2 to 4 years of age) and placebo (6 to 7% among children 6 months to <2 years of age and 4 to 5% among those 2 to 4 years of age). The observed overall vaccine efficacy against symptomatic COVID-19 in children 6 months to 4 years of age was 73.2% (CI 95% 43.8-87.6) starting at 7 days after dose 3 (on the basis of 34 cases).

The authors conclude that a three-dose primary series of $3-\mu g$ BNT162b2 was safe, immunogenic, and efficacious in children six months to four years of age.

Source: Flor M. Muñoz. Evaluation of BNT162b2 Covid-19 Vaccine in Children Younger than 5 Years of Age. N Engl J Med 2023; 388:621–634 DOI: 10.1056/NEJMoa2211031.





Organización Mundial de la Salud GRANE RARA LAS Américas



Brazil's National Health Surveillance Agency (ANVISA) extends the shelf life of the Pfizer-BioNTech COVID-19 vaccine Comirnaty

On 11 January, ANVISA authorized extension of the shelf life of the monovalent Pfizer-BioNTech Comirnaty COVID-19 vaccine, from 12 months to 18 months when stored at temperatures between -90°C and -60°C. This shelf life extension applies to vaccine presentations made on or after 9 January 2023.

Additional information available from: <u>https://www.gov.br/anvisa/pt-br/assuntos/noticias-</u> anvisa/2023/autorizada-ampliacao-do-prazo-de-validade-da-vacina-comirnaty-para-covid-19.

The European Medicines Agency (EMA) authorizes extension of the shelf life of the Valneva COVID-19 vaccine.

On 17 February, the EMA updated the product information for Valneva's COVID-19 vaccine, and included extension of the authorized shelf life from 15 months to 21 months when stored at between 2°C and 8°C.

Additional information available from: <u>https://www.ema.europa.eu/en/documents/product-</u> information/covid-19-vaccine-inactivated-adjuvanted-valneva-epar-product-information_en.pdf.

EMA recommends approval of Valneva COVID 19 vaccine as booster

The EMA's Committee for Medicinal Products for Human Use, at its meeting on 20-23 February, recommended that Valneva's COVID-19 vaccine be used as a booster in adults aged 18–50 who had received either this vaccine or an adenovirus vector-based COVID-19 vaccine as a primary vaccination.

Additional information available from: <u>https://www.ema.europa.eu/en/news/meeting-highlights-</u> committee-medicinal-products-human-use-chmp-20-23-february-2023.

https://www.ema.europa.eu/en/documents/product-information/covid-19-vaccine-inactivatedadjuvanted-valneva-epar-product-information_en.pdf. ·







3

U.S. Food and Drug Administration (FDA) updates fact sheet for the Janssen COVID-19

Vaccine

On 14 March, the FDA reported that they had updated the fact sheet for Janssen's COVID-19 vaccine to include:

- Information on adverse events reported following the emergency use authorization: Included
 was a warning about an increased risk of myocarditis and pericarditis, particularly within the
 period zero to seven days after vaccination. Information on reports of facial paralysis (including
 Bell's palsy) was also included.
- Heterologous booster: Janssen's COVID-19 vaccine can be administered as a first booster dose at least two months after completion of primary vaccination with a U.S.-authorized COVID-19 vaccine.

Additional information available from: <u>https://www.fda.gov/news-events/press-announcements/fda-</u> roundup-march-14-2023.

FDA Authorizes Bivalent Pfizer-BioNTech COVID-19 Vaccine as Booster Dose for Certain Children 6 Months through 4 Years of Age

On 14 March, the FDA reported that it had amended emergency use authorization of the bivalent Pfizer-BioNTech COVID-19 vaccine (Original/Omicron BA.4–5) to include a single booster dose for children 6 months through 4 years of age at least two months after completing primary vaccination with three doses of the monovalent Pfizer-BioNTech COVID-19 vaccine.

Additional information available from: <u>https://www.fda.gov/news-events/press-</u> <u>announcements/coronavirus-covid-19-update-fda-authorizes-bivalent-pfizer-biontech-covid-19-vaccine-</u> <u>booster-dose?utm_medium=email&utm_source=govdelivery</u>.

EMA updates list of adverse reactions for Pfizer-BioNTech COVID-19 vaccine

On 15 March, the EMA updated the product information for the Pfizer-BioNTech COVID-19 vaccine to include dizziness, with a frequency of "uncommon," in the list of adverse reactions.

Additional information available from: <u>https://www.ema.europa.eu/en/documents/product-information_en.pdf</u>.







SAGE revises roadmap for prioritizing the use of COVID-19 vaccines

On 28 March, WHO published a summary of updates to the roadmap for prioritizing the use of COVID-19 vaccines, based on the SAGE meeting of 20–23 March. This update establishes three priority groups for COVID-19 vaccination, based primarily on the risk of severe illness and death, as follows:

- High priority: Older adults; young adults with significant comorbidities, such as diabetes and heart disease; people with immunocompromising conditions, such as people living with HIV and transplant recipients, including children 6 months old and older; pregnant women; and frontline health workers. For these groups, an additional booster dose either six or 12 months after the last dose is recommended, depending on factors such as age and immunocompromising conditions.
- Medium priority: Healthy adults without comorbidities, usually under the age of 50-60; and children and adolescents with comorbidities. For this group, SAGE recommends a primary series and first booster dose.
- Low priority: Healthy children and adolescents aged 6 months to 17 years. However, considering the low morbidity in this age group, SAGE recommends considering contextual factors, such as morbidity, cost effectiveness, and other health priorities, in establishing vaccination guidelines.

Additional information available from: <u>https://www.who.int/news/item/28-03-2023-sage-updates-</u> <u>covid-19-vaccination-guidance</u>.







WHO Strategic Advisory Group of Experts on Immunization (SAGE) update to good practice statement on the use of variant-containing COVID-19 vaccines

On 20 February, an update to the SAGE/WHO statement on good practice for the use of variant-containing vaccines, which was initially published on 17 October 2022, was published in the 39th edition of this report. The updated information included the following:

- Authorization by the European Medicines Agency of Sanofi-GSK's monovalent COVID-19 vaccine VidPrevtyn Beta: This is authorized as a vaccine for primary immunization in people aged 18 years and older, and as a booster in individuals who have already received an mRNA or adenovirus vectorbased vaccine.
- Benefit of bivalent mRNA COVID-19 vaccine versus monovalent vaccine as booster dose:
 - Emerging evidence using neutralization models indicates that the greatest benefit is obtained from the application of either of the two types of booster. Results from variant-modified vaccines produced, on average, 1.51 times higher titers (CI 95% 1.4–1.6) than the equivalent ancestral vaccine (p<0.0001). Immune responses induced by variant-containing vaccines cover other subvariants of Omicron beyond specific vaccine strains (1).
 - The available population-based observational studies, while not making a direct comparison with the monovalent ancestral virus vaccine, indicate that bivalent booster doses provided additional protection against the symptoms of SARS-CoV-2 infection during a period when the BA.5 lineages of the Omicron variant and its sublineages predominated (2).
- **Heterologous schedule:** Updated recommendations on heterologous schedules that incorporate protein subunit vaccines in some cases, as follows:
 - WHO/EUL inactivated vaccines as initial doses: Use vectored or WHO/EUL mRNA vaccines for subsequent doses.
 - WHO EUL vectored vaccines as initial doses: Use WHO/EUL mRNA vaccines or protein subunit vaccines for subsequent doses.
 - WHO/EUL mRNA vaccines for initial doses: Use WHO/EUL vectored vaccines or protein subunit vaccines for subsequent doses.









Additional information available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Variants-2022.1.

- (1) Zou J, Kurhade C, Patel S, Kitchin N, Tompkins K, Cutler M et al. Neutralization of BA.4-BA.5, BA.4.6, BA.2.75.2, BQ.1.1, and XBB.1 with Bivalent Vaccine. New England Journal of Medicine. 2023. DOI: 10.1056/NEJMc2103916.
- (2) Tenforde MW, Weber ZA, Natarajan K, et al. Early Estimates of Bivalent mRNA Vaccine Effectiveness in Preventing COVID-19–Associated Emergency Department or Urgent Care Encounters and Hospitalizations Among Immunocompetent Adults - VISION Network, Nine States, September-MMWR November 2022. Morb Mortal Wkly Rep 2022;71:1616-1624. DOI: https://pubmed.ncbi.nlm.nih.gov/36580430/.





Mundial de la Salud Américas



WHO updates working definitions and tracking system for SARS-CoV-2 variants of interest and variants of concern

On 15 March, WHO updated its tracking system and working definitions for variants of SARS-CoV-2, the virus that causes COVID-19, to better correspond to the current global variant landscape; to independently evaluate Omicron sublineages in circulation; and to classify new variants more clearly. Highlights of the update are as follows:

- The previous system classified all Omicron sublineages as part of the Omicron VOC. As of 15 March 2023, the WHO variant tracking system will consider the classification of Omicron sublineages independently as variants under monitoring (VUMs), VOIs, or VOCs.
- Working definitions of VOCs and VOIs were updated.
- WHO will assign Greek labels for VOCs, and will no longer do so for VOIs.

Additional information available from: <u>https://www.who.int/news/item/16-03-2023-statement-on-the-update-of-who-s-working-definitions-and-tracking-system-for-sars-cov-2-variants-of-concern-and-variants-of-interest</u>.

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.





