COVID-19

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

Forty-second report

WASHINGTON, DC

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OPS Organización Panamericana de la Salud
Organización Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas
In partnership with Canada

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CANADA

As of 17 March, 54 569 individual cases had been reported, of which 10 685 were considered serious. The majority of reports were for wo

men (72.7%). The reporting rate for women was 76.3 reports per 100 000 doses administered, compared with 30.8 per 100 000 doses for men. In the younger age groups (<18 years) the reporting rate was similar for males and females, or slightly higher for males.

Number of reports and reporting rate (per 100 000 doses administered) of main adverse events of special interest (AESI), by vaccine, in the general population, as of 17 March 2023						
AESI	***Vaccine***					
	Pfizer-BioNTech		***Moderna***		***AstraZeneca/Covishield***	
	N*	***Rate*****	***N****	***Rate*****	***N****	***Rate*****
Guillain-Barré syndrome	7	0.01	9	0.04	10	0.36
Thrombocytopenia	105	0.17	34	0.13	52	1.85
Myocarditis/pericarditis	684	1.13	439	1.72	16	0.57
Thrombosis with thrombocytopenia syndrome (TTS)	22	0.04	8	0.03	57	2.03
Bell's palsy/facial paralysis	126	0.21	41	0.16	13	0.46
Anaphylaxis	562	0.92	175	0.68	25	0.89

*N = number of reports

**Rate per 100 000 doses administered

Note: The Janssen, Novavax, and Bivalent (Pfizer Original and Omicron BA.4/BA.5, Moderna Original/Omicron BA.1 and Moderna Original/Omicron BA.4/5) vaccines were not included due to the small number of reported cases.

Source: Public Health Agency of Canada. Canadian COVID-19 vaccine safety report. Ottawa: Public Health Agency of Canada. 17 March 2023. https://health-infobase.canada.ca/covid-19/vaccine-safety/.

Data reproduced by PAHO/WHO.

PERU

As of 9 May, there were 59 809 reports with one or more AEFI. The largest number of reports of AEFI (56.1%) were for adults between the ages of 30 and 59, and in women (64.1%). Of total reports recorded, 0.5% (280 cases) were considered serious. The Ministry of Health's National Center for Epidemiology, Prevention, and Disease Control (CDC) classified 153 of the 280 cases as serious AEFI, with 112 considered coincident events, 14 inconclusive, 14 vaccine-related, and 13 related to vaccination anxiety, while the remaining 126 continue to be investigated and have yet to be classified.

Number of reports and reporting rate (per 100 000 doses administered) of adverse events, by vaccine, as of 28 February 2023			
Vaccine	***Total doses administered***	***Total number of reports of AEFI***	
		****N***	*****Rate***
Sinopharm	21 275 052	19 690	92.55
Comirnaty/Pfizer	51 623 623	23 425	45.38
Vaxzevria/AstraZeneca	8 187 459	3815	46.60
Spikevax/Moderna	66 332 595	11 859	17.88
Pfizer Bivalent Original/Omicron BA.4–5	521 709	1020	195.51
Total	***147 940 438***	***59 809***	***40.43***

*Total number of reports of AEFI

**Rate per 100 000 doses administered

Source: General Directorate of Medicines, Supplies, and Drugs (DIGEMID). National Drug Information and International Coordination Center (CENADIM) Fact Sheet, Period from 9 February 2021 to 28 February 2023. Version 9, May 2023. Available from:

https://bvcenadim.digemid.minsa.gob.pe/index.php/covid-19/ficha-informativa-eventos-adversos-supuestamente-atribuidos-a-la-vacunacion-o-inmunizacion-esavi-reportados-a-la-vacuna-contra-la-covid-19.

Reports of Guillain-Barré syndrome after COVID-19 vaccination in the United States

This study was published in February 2023 to evaluate reports of Guillain-Barré syndrome (GBS) to the Vaccine Adverse Event Reporting System (VAERS) in the United States following COVID-19 vaccination with the Ad26.COV2.S (Janssen), BNT162b2 (Pfizer-BioNTech), or mRNA-1273 (Moderna) COVID-19 vaccine, and to compare reporting patterns within 21 and 42 days after vaccination.

This retrospective cohort study was conducted based on reports made from December 2020 to January 2022. It included validated GBS case reports that met the Brighton Collaboration GBS case definition, in adults who had received a COVID-19 vaccination in the United States.

Descriptive analyses of cases were performed, and GBS reporting rates were calculated, within 21 and 42 days after vaccination with Ad26.COV2.S, BNT162b2, or mRNA-1273, based on the doses administered. Reporting rate ratios (RRRs) after receiving Ad26.COV2.S vs. BNT162b2 or mRNA-1273, within 21 and 42 days of vaccination were calculated. Observed/expected ratios were estimated using published baseline GBS incidence rates.

The results showed that out of a total of 487 651 785 doses of COVID-19 vaccines, 17 944 515 doses (3.7%) were of the Ad26.COV2.S type, 266 859 784 doses (54.7%) were of the BNT162b2 type, and 202 847 486 doses (41.6%) were of the mRNA-1273 type. The 295 validated reports of people identified as having GBS after COVID-19 vaccination were in the following groups: 12 Asian (4.1%), 18 African American (6.1%), 193 White (65.4%), and 17 Hispanic (5.8%). Of the total, 169 were men (57.3%). The median age was 59.0 years (interquartile range [IQR]: 46.0–68.0). In 275 reports (93.2%), hospitalization of the patient was documented.

Within 21 days of vaccination, GBS reporting rates per 1 000 000 doses administered were:

- 3.29 for Ad26.COV2
- 0.29 for BNT162b2 and
- 0.35 for mRNA-1273.

Within 42 days of vaccination, the rates were:

- 4.07 for Ad26.COV2
- 0.34 for BNT162b2 and
- 0.44 for mRNA-1273.

GBS was reported more frequently within 21 days after vaccination with Ad26.COV2.S than after BNT162b2 (RRR = 11.40; CI 95%, 8.11–15.99) or mRNA-1273 (RRR = 9.26; CI 95%, 6.57–13.07); similar findings were observed within 42 days of vaccination (BNT162b2: RRR = 12.06; CI 95%, 8.86-16.43); mRNA-1273: RRR = 9.27; CI 95%, 6.80-12.63).

The observed/expected ratios after vaccination with Ad26.COV2.S were:

- 3.79 (CI 95%, 2.88–4.88) for the 21-day interval and
- 2.34 (CI 95%, 1.83–2.94) for the 42-day interval.

After vaccination with BNT162b2 and mRNA-1273:

- less than one (not significantly increased) within both assessed post-vaccination periods.

According to the authors, the study indicates disproportionate reporting of GBS after vaccination with Ad26.COV2.S, suggesting the possibility that this vaccine is associated with an increased risk of GBS. However, no associations were found between COVID-19 mRNA vaccines and an increased risk of GBS.

Source: Abara WE, Gee J, Marquez P, et al. Reports of Guillain-Barré Syndrome After COVID-19 Vaccination in the United States. JAMA Netw Open 2020. 2023;6(2):E2253845. doi:10.1001/jamanetworkopen.2022.53845.

Bell's palsy and COVID-19 vaccines: A systematic review and meta-analysis

On 20 January 2023, a systematic review was published that aimed to analyze the occurrence of Bell's palsy after COVID-19 vaccination. To carry out this review, the authors conducted comprehensive searches of the PubMed, SCOPUS, EBSCO, and Web of Science databases, covering the date from which information relevant to this topic was first compiled until October 2022. The quality of the selected studies was assessed using the criteria of the Joanna Briggs Institute, the National Institute of Health, and Newcastle-Ottawa. Analysis of the collected data was performed using SPSS statistical software.

This systematic review included cohort (n = 13), case-control (n = 3), cross-sectional (n = 3), and self-controlled case series (n = 2) studies that described the rate ratio of Bell's palsy after administration of COVID-19 vaccines. In addition, the review included case reports (n = 23) and case series (n = 8), which described patients who developed Bell's palsy events after COVID-19 vaccination (n = 105).

Most patients (62.8%) experienced unilateral facial paralysis, according to the results obtained. In addition, it was noted that most cases were reported after the first dose, mostly after administration of the Pfizer, AstraZeneca, and Sputnik V vaccines. Patients treated with corticosteroids, intravenous immunoglobulin, and antiviral drugs subsequently showed marked recovery.

The result of the meta-analysis revealed that the rate ratio of Bell's palsy after COVID-19 vaccination was 25.3 per 1 000 000 people vaccinated. The ratio was higher after the first dose than after the second dose, and higher among those who received the Oxford/AstraZeneca vaccine compared with the other vaccines. The average time to symptom onset after vaccination was 11.6 days. The most frequent comorbidity among the included patients was hypertension (24.8%), followed by diabetes (16.2%) and heart failure (4.8%). The medication most commonly used to manage this condition was prednisone. Among these cases, 36 patients (69.2%) recovered (26 completely and 13 partially).

The authors point out, however, that this condition was reported in a small number of cases among a large number of vaccinated people worldwide. It is fundamental to keep in mind that the benefits of vaccination strongly outweigh the potential risks.

Source: Albakri K, Khaity A, Atwan H, Saleh O, Al-Hajali M, Cadri S, Diab RA, Albazee E, Negida A. Bell's Palsy and COVID-19 Vaccines: A Systematic Review and Meta-Analysis. Vaccines (Basel). 2023 Jan 20;11(2):236. doi: 10.3390/Vaccines11020236. PMID: 36851114; PMCID: PMC 9961047.

Adverse events after the first, second, and third doses of a COVID-19 vaccine in hemodialysis patients

This prospective observational study, published in January 2023, aimed to identify adverse events reported within 7 days of the first, second, and third doses of COVID-19 vaccination in hemodialysis (HD) patients. Risk factors associated with adverse events following vaccination were explored.

The study was conducted in the HD unit of Far Eastern Memorial Hospital, a tertiary medical center located in New Taipei City. Post-vaccination adverse events were prospectively assessed in 438 HD patients who received three doses of COVID-19 vaccines.

The study compared adverse events after all three doses using generalized linear mixed models. The authors assessed factors associated with adverse events using multivariate analysis.

The vast majority of participants received Oxford/AstraZeneca ChAdOx1 as their first two doses and Moderna mRNA-1273 as their third dose. Overall, 79%, 50%, and 84% of the participants experienced at least one adverse event after their first, second, and third doses, respectively. These adverse events were mostly minor, short-lived, and less than 5% reported an effect on daily activities.

Compared with the first dose, the third dose caused a higher rate of injection-site reactions and a lower rate of systemic reactions.

Multivariate analysis revealed that, for every 10-year increase in age, a significant association was observed with a lower risk of adverse events (OR: 0.67, CI 95%, 0.57–0.79), while female sex (OR 2.82, CI 95%, 1.90–4.18) and arteriovenous fistula (OR 1.73, CI 95%, 1.05–2.84) were associated with an increased risk of adverse events. Compared with the Oxford/AstraZeneca ChAdOx1 vaccine, Moderna's mRNA-1273 vaccine was associated with an increased risk of injection-site reactions.

The authors conclude that COVID-19 vaccination was well tolerated in HD patients. Age, sex, dialysis vascular access and vaccine types were associated with the risk of postvaccination adverse events. The study findings support the favorable safety profile of COVID-19 vaccination in HD patients.

Source: Mei-Fen Paia, et al. Adverse events following the first, second, and third doses of a COVID-19 vaccine in hemodialysis patients. RENAL FAILURE 2023, VOL. 45, NO. 1, 2172432 https://doi.org/10.1080/0886022X.2023.2172432.

POTENTIAL SAFETY SIGNS IDENTIFIED WITH THE USE OF COVID-19 VACCINES ASSOCIATED WITH SEX DIFFERENCES

Vulvar aphthous ulcers in adolescents following COVID-19 vaccination: Analysis of an international case series

In December 2021, during a workshop on signal detection using VigiBase, the global database of the World Health Organization (WHO), a preliminary safety signal was detected indicating the occurrence of vulvovaginal ulcers in female adolescents (ages 12–17) after receiving a COVID-19 vaccine.

On 17 March 2023, this analysis was published for the purpose of reviewing and characterizing the reports in VigiBase of vulvar aphthous ulcers (VAUs) after COVID-19 vaccination. The aim was to demonstrate the importance and power of case reports in detecting rare adverse reactions, and to analyze whether these reports suggest a possible link between COVID-19 vaccination and the occurrence of vulvovaginal ulceration.

The authors extracted Cases were selected from VigiBase that informed on the based on the Medical Dictionary for Regulatory Activities (MedDRA), preferred term "vulvovaginal ulceration," and related terms, in adolescent patients ages 12–17 in association with any COVID-19 vaccine. The cases were clinically reviewed, and causality was assessed by applying the Bradford Hill criteria to the obtained case series.

The authors identified a total of 444 reports up to 30 June 2022 for MedDRA's preferred terms "vaginal ulceration," "vulval ulceration," “genital ulceration” and "vulvovaginal ulceration" after COVID-19 vaccination in all age groups. Statistically disproportionate reporting was observed for all terms cited, except "genital ulceration." This indicates that the number of reported cases exceeded the expected number for the combined COVID-19 vaccine plus the terms cited, compared with the vaccine reports in VigiBase.

Although vaccination for the 12–17 age group began in the fourth quarter of 2021, this group already accounted for 23% of the 444 reports. The analysis therefore focuses on this age group.

After removing duplicates and correcting one misdiagnosis, 94 reports remained for analysis. Of these cases, 37 were diagnosed as vulvar aphthous ulcer, or "Lipschütz ulcer" (LU). These 37 reports came from four countries, with most coming from the United States (n = 31; 84%). Most reports were classified as non-serious (n = 34; 92%). Information on the number of administered doses was available in 19 cases,

with most cases occurring after administration of the second dose (n = 16; 84%). Information about the time to onset was available in 34 cases. The median time to onset was 2 days, with an interquartile range between 2 and 3 days.

It was difficult to determine whether the exclusion criteria for infectious and non-infectious causes were fully met, as it was not always clear whether all the necessary exclusion tests had been performed. However, possible alternative causes of acute genital ulceration other than LU were listed in all 94 reports.

By applying the Bradford Hill criteria in the study's case series, a strength of association was found through the statistically significant prominence of vulvovaginal ulceration in combination with COVID-19 vaccine, this is evidenced, by the statistically significant prominence of this association in the WHO global pharmacovigilance database, VigiBase.

Although the number of case reports is limited, an expected time to onset is not known, but the time to onset, within one week, is consistent across the VAU VigiBase reports as well as the published reports. The published case reports of VAUs/LUs occurring in females ages 12-17 were also examined and compared with the VigiBase reports identified as likely VAUs/LUs, with similar descriptions of cases in several countries, lending credence to the findings.

The reports show specificity for causal agent and reported adverse effect: COVID-19 vaccine is the only suspect agent in most reports.

There is the possibility of a dose response, as most reports indicate the onset of symptoms after the second dose of the vaccine, and even some after the third dose. However, it is important to note that, at this time, biologic plausibility is based on hypotheses, as there is no experimental evidence or analogy to support a causal association.

Notably, genital ulcers have not been specifically described as adverse reactions to the vaccine in European Union product summaries, nor on the FDA drug label for the Moderna and Pfizer/BioNTech COVID-19 mRNA vaccines or the Janssen viral vector vaccine.

In the causality assessment, the case series analyzed met six of the nine Bradford Hill criteria, which provides weight to a possible causal association between vulvovaginal ulcers and COVID-19 vaccination. Although the possibility that the vaccine is the trigger for ulcers is mentioned in some reports, this adverse reaction has not been specifically described in official vaccine documents. It is important to consider other possible causes and to make a proper differential diagnosis.

The authors conclude that they have identified a signal of a possible association between COVID-19 vaccination and vulvovaginal ulcers in female adolescents and suggest that well-documented case reports are important for the recognition and assessment of rare adverse events and for expediting their submission to national pharmacovigilance databases. In addition, they emphasize that the experience of VAU can be traumatic, particularly for adolescent patients, and that a risk of misdiagnosis resulting in a load of avoidable investigation and treatment.

Source: Rudolph Annette, Savage Ruth. Vulval Aphthous Ulcers in Adolescents Following COVID-19 Vaccination – Analysis of an international case series. J Pediatr Adolesc Gynecol. 2023 Mar 17: S1083–3188(23)00311-X. doi: 10.1016/j.jpag.2023.03.006. Epub ahead of print. PMID: 36934803; PMCID: PMC9150735.

Association between SARS-CoV-2 vaccination and healthcare contacts for menstrual disturbance and bleeding in women before and after menopause: nationwide, register-based cohort study in Sweden

This study, published on 3 May 2023, aimed to evaluate the risks of any menstrual disturbance and bleeding following SARS-CoV-2 vaccination in women who are premenopausal or postmenopausal. This was a nationwide, register-based cohort study in Sweden, covering both inpatient and outpatient care from 27 December 2020 to 28 February 2022. It included 2 946 448 Swedish women ages 12 to 74. It excluded pregnant women, those living in nursing homes, and those with a history of menstrual or bleeding disorders, breast cancer, cancer of the female genital organs, or those who had undergone a hysterectomy between 1 January 2015 and 26 December 2020.

The main outcome measures were based on contact with health services for menstrual disturbance or bleeding before or after menopause. Different SARS-CoV-2 vaccines, divided by product and dose, were evaluated in two-time windows (one to seven days and eight to 90 days).

In the study, 87.6% of women received at least one dose of SARS-CoV-2 vaccine, and 64.0% of vaccinated women received three doses before the end of the follow-up. Increased risk of bleeding was found in postmenopausal women after the third dose, both in the one-to-seven-day risk window (hazard ratio 1.28, CI 95%, 1.01 to 1.62) and in the 8 to 90 day risk window (1.25, CI 95%, 1.04 to 1.50). However, the impact of adjustment for covariates was modest.

Risk of postmenopausal bleeding suggested a 23%-33% increased risk after 8-90 days following the third dose of the BNT162b2 and mRNA-1273 vaccines. However, the association with ChAdOx1 nCoV-19 was less clear.

For menstrual disturbance or bleeding in women who were premenopausal, adjustment for covariates almost completely removed the weak associations noted in the crude analyses.

The authors conclude that there were weak and inconsistent associations between SARS-CoV-2 vaccination and healthcare contacts for bleeding in women who are postmenopausal, and even less evidence was recorded of an association for menstrual disturbance or bleeding in women who were premenopausal.

Source: Rickard Ljung et al. Association between SARS-CoV-2 vaccination and healthcare contacts for menstrual disturbance and bleeding in women before and after menopause: nationwide, register-based cohort study. BMJ2023;381:e074778.

Global regulators agree on way forward to adapt COVID-19 vaccines to emerging variants

On 30 May, the European Medicines Agency (EMA) published a summary of the report of the last meeting of the International Coalition of Medicines Regulatory Authorities (ICMRA), held on 8 May 2023, in which representatives of international regulators, as well as experts from the World Health Organization (WHO), participated.

This meeting discussed COVID-19 vaccines and the strategy to update their composition, based on the emerging evidence on coronavirus SARS-CoV-2 variants and lessons learned from previous vaccine updates.

The main conclusions were as follows:

- There is a broad agreement that vaccine formulations for the upcoming winter season in the northern hemisphere should include only one virus strain and be based on the XBB family of Omicron subvariants, such as XBB.1.5. These monovalent vaccines could be used for both booster and primary vaccinations, the latter, in children below the 4-5-year age range.

- Only data on manufacturing and quality of the vaccine and laboratory data would be required for the authorization or approval of strain changes for the already authorized COVID-19 vaccines, provided that post-authorization data regarding vaccine quality, effectiveness, immunogenicity, and safety are collected.

Additional information available from: https://www.ema.europa.eu/en/news/global-regulators-agree-way-forward-adapt-covid-19-vaccines-emerging-variants.

U.S. Food and Drug Administration (FDA) authorizes marketing of the oral antiviral nirmatrelvir–ritonavir (Paxlovid)

On 25 May 2023, the FDA approved marketing authorization for the antiviral drug, nirmatrelvir and ritonavir tablets (Paxlovid), for the treatment of mild to moderate COVID-19 in adults at high risk for progression to severe COVID-19, including hospitalization or death. Paxlovid is the fourth drug—and first oral antiviral pill—approved by the U.S. FDA to treat COVID-19 in adults.

This drug was manufactured and packaged under Emergency Use Authorization (EUA) in the U.S. and was distributed by the U.S. Department of Health and Human Services.

In granting approval, the FDA considered the final results of the EPIC-HR clinical trial. EPIC-HR was a randomized, double-blind, placebo-controlled clinical trial studying Paxlovid for the treatment of non-hospitalized symptomatic adults 18 years and older with a laboratory confirmed diagnosis of SARS-CoV-2 infection with risk of progression to severe disease. The EPIC-SR clinical study was conducted in vaccinated patients. The following is a summary of the results reported by the FDA.

In the EPIC-HR study, in the group of patients who had not received a COVID-19 vaccine and had not previously been infected with SARS-CoV-2, 977 patients received Paxlovid and 989 patients received placebo; 0.9% of those who received Paxlovid were hospitalized due to COVID-19 or died from any cause during the 28 days of follow-up, compared with 6.5% of the patients who received the placebo. Paxlovid reduced by 86% the proportion of people with COVID-19-related hospitalization or death from any cause through the 28 days of follow-up, compared to placebo, among patients treated within five days of symptom onset and who did not receive COVID-19 therapeutic monoclonal antibody treatment.

For patients with pre-COVID-19 immunity, this study found that the risk of hospitalization or death from any COVID-19-related cause during the 28-day follow-up was 0.2% among the 490 patients treated with Paxlovid, compared with 1.7% of the 479 patients receiving placebo.

EPIC-SR was another clinical trial that enrolled vaccinated patients with at least one risk factor for progression to severe COVID-19, and although the results were not statistically significant, in vaccinated patients there was a reduction in the risk of COVID-19-related hospitalization or death from any cause.

The FDA noted that, in these two trials, in a subgroup of patients there was a rebound in SARS-CoV-2 (RNA or virus) shedding or COVID-19 symptoms in both the patients receiving Paxlovid and the placebo group; based on the data currently available to the FDA, there is not a clear association between Paxlovid treatment and COVID-19 rebound.

To reduce the risk of significant drug-drug interactions with Paxlovid, the FDA incorporated in the product label and in the Fact Sheet for Health Care Providers a boxed warning with instructions for prescribers, indicating that they should review all medications taken by the patient to assess potential drug-drug interactions and determine whether other medicines that a patient may be taking require a dose adjustment, interruption, and/or additional monitoring.

Additional information available from: https://www.fda.gov/news-events/press-announcements/fda-approves-first-oral-antiviral-treatment-covid-19-adults.

WHO statement on the antigen composition of COVID-19 vaccines

On 18 May of this year, the WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) issued a statement on the antigen composition of COVID-19 vaccines. The key recommendations are as follows:

- There is ongoing and considerable genetic and antigenic evolution of SARS-CoV-2, high seroprevalence, and heterogeneous population immunity to SARS-CoV-2. Vaccination programs should continue to complete the primary series and booster dose(s) for high priority and medium priority groups, as specified in the current WHO SAGE policy for prioritizing the use of COVID-19 vaccines.
- Updates to vaccine antigen composition may enhance vaccine-induced immune responses to circulating SARS-CoV-2 variants, consistent with the previous statement by TAG-CO-VAC published in June 2022.
- As of May 2023, XBB.1 descendent lineages predominate SARS-CoV-2 circulation globally. TAG-CO-VAC recommends the use of a monovalent XBB.1 descendent lineage, such as XBB.1.5 (e.g., hCoV-19/USA/RI-CDC-2-6647173/2022, GenBank: OQ054680.1, GISAID: EPI_ISL_16134259 or WHO Biohub: 2023-WHO-LS-01, GenBank: OQ983940, GISAID EPI_ISL_16760602) as the vaccine antigen.

- The spike antigens of both the XBB.1.5 and XBB.1.16 lineages are genetically and antigenically very closely related, with only two amino acid differences between them (E180V and K478R). Given the small differences, XBB.1.16 may be an alternative (e.g., hCoV-19/USA/MI-CDC-LC1038976/2023, GenBank: OQ931660 GISAID: EPI_ISL_17619088). Other formulations and/or platforms that achieve robust neutralizing antibody responses against XBB descendent lineages can be considered.

- While currently approved COVID-19 vaccines, including those based on the index virus, continue to provide protection against severe disease, TAG-CO-VAC advises moving away from the inclusion of the index virus in future formulations of COVID-19 vaccines. This is based on the fact that the index virus and closely related variants, from the antigenic point of view, no longer circulate in humans; the index virus antigen elicits undetectable or very low levels of neutralizing antibodies against currently circulating SARS-CoV-2 variants, including XBB descendent lineages; inclusion of the index virus in bi- or multivalent vaccines reduces the concentration of the new target antigen(s) as compared to monovalent vaccines, which may decrease the magnitude of the humoral immune response. This is in addition to the immune imprinting, also called immunological fingerprinting, due to repeated exposure to the index virus, which causes the production of memory B cells to this virus, limiting the development of memory B cells and neutralizing antibodies specific for variant strains of COVID-19.[1]

- Given the limitations of the evidence upon which the above recommendations are derived, and the expected continued evolution of the virus, TAG-CO-VAC strongly encourages the generation of data on immune responses and clinical endpoints in humans who receive a COVID-19 vaccine with an updated composition, across different vaccine platforms, as well as further data on the performance of current COVID-19 vaccines against circulating SARS-CoV-2 variants.

- TAG-CO-VAC continues to encourage the further development of vaccines that enhance mucosal immunity because they may improve protection against infection and reduce transmission of SARS-CoV-2, in alignment with the WHO Global COVID-19 Vaccination Strategy, published in July 2022.

- It is imperative for multilateral organizations, governments, and manufacturers to continue collaborating toward achieving access to currently approved COVID-19 vaccines and to ensure

equitable global access to vaccine(s) with an updated antigen composition as they become available.

Additional information available from: https://www.who.int/news/item/18-05-2023-statement-on-the-antigen-composition-of-covid-19-vaccines.

(1) Koutsakos Marios, Ellebedy Ali H. Understanding COVID-19. Immunity 2023. doi: https://doi.org/10.1016/j.immuni.2023.04.012; https://www.cell.com/immunity/fulltext/S1074–7613(23)00181–4.

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

There are no clarifications/conclusions to report at present.

Extension of the shelf life of AstraZeneca AB's EUL COVID-19 vaccine (ChAdOx1-S [recombinant])

WHO updated the shelf-life information for AstraZeneca AB's COVID-19 vaccine (ChAdOx1-S [recombinant]), included in the Emergency Use Listing (EUL), authorized by the European Medicines Agency (EMA). The shelf life of unused vials of this vaccine, stored at 2°C to 8°C (36°F to 46°F), was extended from six to nine months.

The shelf life of AstraZeneca AB's EUL COVID-19 vaccine (ChAdOx1-S [recombinant]), authorized by Australia's Therapeutic Goods Administration (TGA) and Argentina's National Administration of Drugs, Food, and Medical Devices (ANMAT), remains six months for unused vials, stored at 2°C to 8°C (36°F to 46°F).

Additional information available from:

- https://extranet.who.int/pqweb/vaccines/covid-19-vaccine-chadox1-s-recombinant-0
- https://extranet.who.int/pqweb/vaccines/who-recommendation-astrazeneca-eu-approved-Vaxzevria
- https://extranet.who.int/pqweb/vaccines/who-recommendation-astrazenecatga-approved-sites-covid-19-vaccine-chadox1-s-recombinant.