VIGICARIB NEWS

15TH DECEMBER, 2022

OVERVIEW

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Image by: Polina Tankilevitch, Source: pexels.com

HIGHLIGHTS OF XVII INTERNATIONAL PHARMACOVIGILANCE MEETING OF THE AMERICAS

The XVII International Pharmacovigilance Meeting of the Americas was held in Bogotá, Colombia from 5th – 9th December, 2022, as the first face-to-face meeting since the global pandemic. Three national regulatory authorities of the English-speaking Caribbean, and the Caribbean Regulatory System shared lessons learned (Appendix III), exchanged ideas, and learned from other pharmacovigilance personnel over the five day period.

Tools and topics included Evaluation of Risk Management Plans, Causality Assessment, Active Pharmacovigilance, and digital tools and bridges for reporting of adverse events following immunization (AEFIs) / events supposedly attributable to vaccination or immunization (ESAVIs).

***Pharmacovigilance focal points of the English-speaking Caribbean**. L-R: Rian Marie Extavour (CARPHA-CRS), Gina Archer (Bahamas), Julie-Ann Jemmott (Jamaica), Kristen Waight (Belize), Chrystal Samouge (Belize). Photo by Rian M. Extavour.*

CASE SAFETY REPORTS TO VIGICARIB NETWORK

Between 16th November 2022 and 14th December 2022, the CRS received three (3) case reports of: 2 suspected adverse drug reactions (ADRs), 0 adverse events following immunization (AEFIs) and 1 substandard and falsified medical product (SF) through its online reporting forms:

- Suspected ADRs: Bahamas (1) and Dominica (1)
- SFs: Dominica (1)

All case reports that were received from health professionals, pharmacovigilance officers or patients / caregivers were submitted to the national focal points for local verification and follow-up. In all, 528 case reports have been shared with VigiCarib network since its inception, consisting of suspected adverse drug reactions (340 – 64.4%), substandard / falsified medical products (103 – 19.5%), and adverse events following immunization (85 – 16.1%) – Table A1 (See Appendix I – restricted circulation).

Note to Reader:

This summary describes characteristics of case reports of adverse events following immunization (AEFIs / ESAVIs) with COVID-19 vaccines, and suspected adverse drug reactions, based on Individual Case Safety Reports (ICRSs) in regional (CRS) and global (WHO) databases. The ICSRs in the global database have been submitted by national pharmacovigilance centres in CARPHA Member States with membership in the WHO Programme for International Drug Monitoring (PIDM). The information provided is ***for descriptive purposes*** *only, e.g. reporting trends. Some of the ICSRs may not have been clinically reviewed or may be pending investigation.*

Any assessment of an association between COVID-19 vaccines and an increased risk of a

CARICOM COVID-19 VACCINE SAFETY REPORTS IN GLOBAL DATABASE

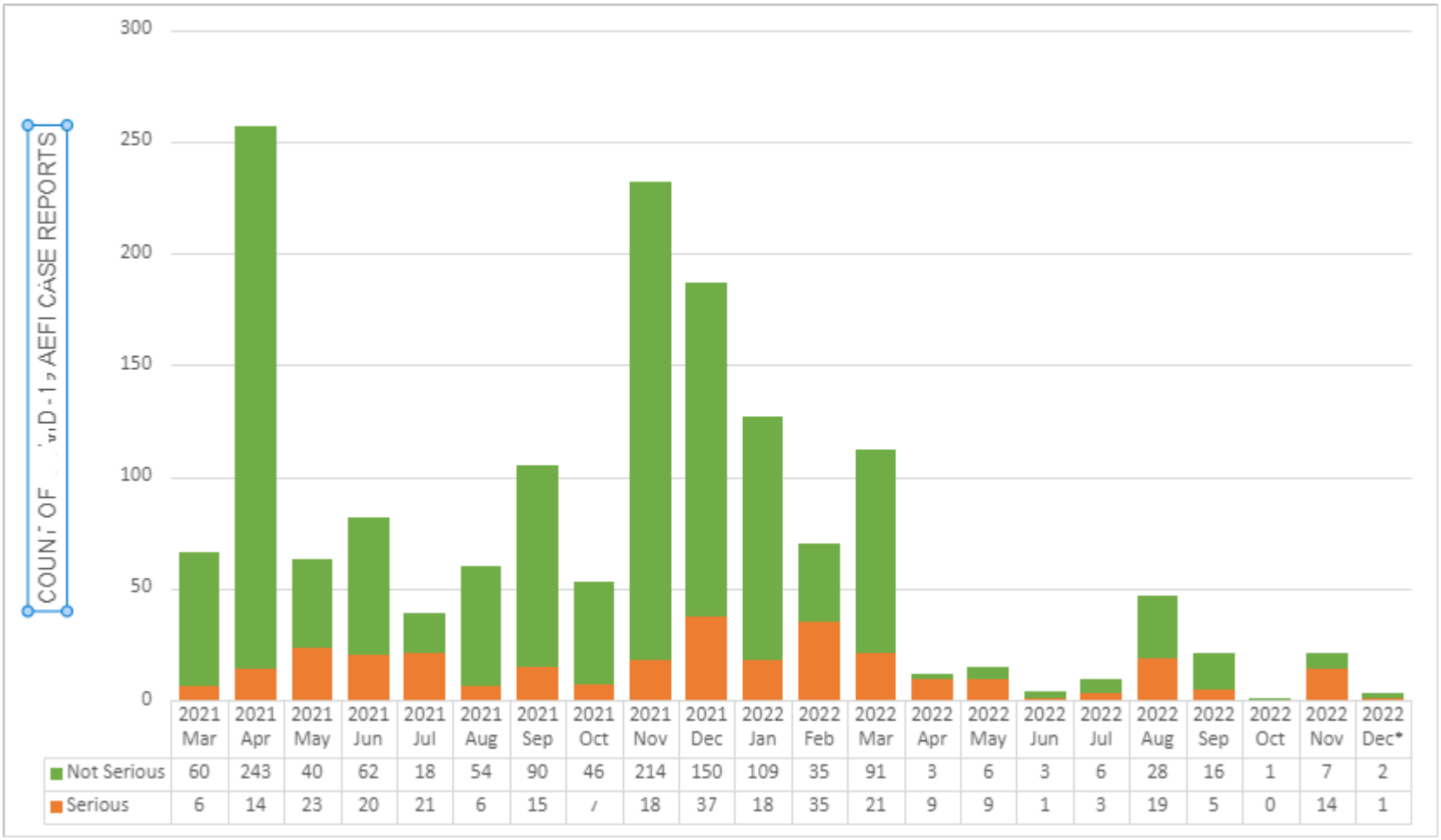
As of 14th December 2022, there have been 1,582 case reports of AEFIs involving COVID-19 vaccines submitted to the global database, VigiBase from Barbados, Haiti, Jamaica and St Vincent and the Grenadines, mostly non-serious events, involving persons under 65 years (84.9%), and females (74.1%). The month with the greatest reporting activity for events occurring in April 2021: Figure 1. Three hundred (19.0%) were classified as Serious, including 67 where deaths were reported outcomes – Figure 2, Table 3.

Three (3) additional COVID-19 AEFI case reports were submitted between 16th November and 14th December 2022 to the global database. The most commonly reported reactions were: headache, fever, dizziness, fatigue, chills and myalgia – Table 3. The downward trend of reporting of AEFIs may be due to multiple factors including reduction in vaccinations, lack of visibility of reporting systems, and reduced risk perception. However, further study at the national level would be needed to verify case reports, confirm causality and identify other possible factors that may influence reporting.

The reported ICSRs involved the following vaccines:

- COVID-19 vaccine NRVV Ad (ChAdOx1-S recombinant) by AstraZeneca or Serum Institute of India (COVISHIELD)
- COVID-19 vaccine NRVV Ad26 (Gam-Covid-Vac – Sputnik V)
- Tozinameran (Pfizer-BioNTech COVID-19 vaccine)
- COVID-19 vaccine NRVV Ad26 (JNJ 78436735) Johnson & Johnson
- COVID-19 vaccine inactivated (Vero cell) HB02 – BIBP-Sinopharm
- COVID-19 vaccine inactivated (Vero cell) WIV04- Sinopharm-Wuhan
- Elasomeran, COVID-19 Vaccine Moderna
- Covid-19 Vaccine (unspecified).

Figure 1: Case reports of adverse events following immunization (AEFIs) with COVID-19 vaccines from 1st March 2021 to 14th December 2022*



	2021 Mar	2021 Apr	2021 May	2021 Jun	2021 Jul	2021 Aug	2021 Sep	2021 Oct	2021 Nov	2021 Dec	2022 Jan	2022 Feb	2022 Mar	2022 Apr	2022 May	2022 Jun	2022 Jul	2022 Aug	2022 Sep	2022 Oct	2022 Nov	2022 Dec*
Not Serious	60	243	40	62	18	54	90	46	214	150	109	35	91	3	6	3	6	28	16	1	7	2
Serious	6	14	23	20	21	6	15	/	18	37	18	35	21	9	9	1	3	19	5	0	14	1

* AEFI case counts presented are for the entirety of each month from March 2021 to October 2022, except for December 2022 (up to 14th December).

Reporting Rates by Doses Administered

Data from the Pan American Health Organization's (PAHO) dashboard on COVID-19 vaccines administered in various Caribbean countries was used in the estimation of the reporting rate of AEFIs per 100,000 doses for countries reporting to the global database. Among the countries with reports in the global database, there were approximately 64.1 AEFI reports per 100,000 doses of COVID-19 vaccines administered, with approximately 12.2 reports of serious adverse events per 100,000 doses. These estimates include coincidental and/or unconfirmed reports. The reporting rates provide an overview of reporting in the given country, which may be influenced by various factors, including access to local reporting systems and vaccine campaigns.

Table 1: Consolidated number of reported COVID-19 AEFI and reporting rate, by country as of 9th December 2022.

Country	Total Doses	**Total Adv. Events***	Total AEFIs per 100,000 doses ¥	Total Serious AEFIs	Total Serious AEFIs per 100,000 doses
Barbados	380,962	606	159.1	86	22.6
Haiti	510,611	1	0.2	0	0
Jamaica	1,503,943	952	63.3	208	13.8
St Vincent and the Grenadines	72,979	23	31.5	6	8.2
Total	2,468,495	1,582	64.1	300	12.2

*Key: *- Includes 5 reports where the vaccine was reported using multiple names: brand and the generic name or platform.*
¥ - Calculated using counts of reports and doses administered.

Table 2: Patient Age Groups Reported for AEFIs in VigiBase to 14th December 2022 (N = 1,582)

Patient age	Count	Percent
12 - 17 years	100	6.3%
18 - 44 years	737	46.6%
45 - 64 years	506	32.0%
65 - 74 years	108	6.8%
≥ 75 years	84	5.3%
Unknown	45	2.9%

Table 3: Top Reported Reactions for AEFIs in VigiBase to 14th December 2022 (N = 1,582)

Top Reported Reactions	Count	Percent
PT: Headache	463	29.3%
PT: Pyrexia	306	19.3%
PT: Dizziness	305	19.3%
PT: Fatigue	250	15.8%
PT: Chills	244	15.4%
PT: Myalgia	224	14.2%
PT: Arthralgia	211	13.3%
PT: Nausea	178	11.3%
PT: Vaccination site pain	161	10.2%
PT: Malaise	150	9.5%

Figure 2: Total AEFI Case Reports by Seriousness (N = 1, 582)

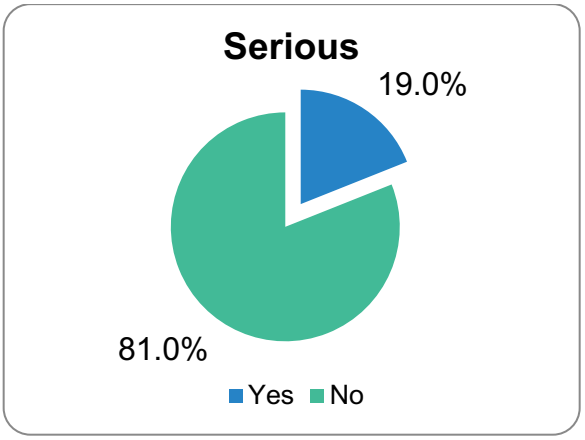


Table 4: Seriousness of Cases (n = 300)

Seriousness criteria	Count	Percent
Death	67	4.2%
Life threatening	21	1.3%
Caused/prolonged hospitalization	113	7.1%
Disabling/incapacitating	53	3.4%
Other medically important condition	106	6.7%

Note: Total exceeds 300 due to selection of multiple seriousness criteria in individual case reports

SUMMARY OF CASE SAFETY REPORTS FROM CARICOM TO WHO PIDM

A review of the Uppsala Monitoring Centre's VigiBase identified 4,279 case reports from CARICOM countries with membership in the WHO Programme for International Drug Monitoring (PIDM): 1,582 COVID-19 AEFI case reports, 157 non-COVID AEFI case reports, and 2,476 reports of suspected adverse drug reactions (ADRs). Table 5 identifies the number of case reports of suspected ADRs and AEFIs submitted by Member States between April 2007 and 14th December 2022, inclusive of reports submitted by the CRS on behalf of Member States. Most of the case reports involved adults – Table 6.

Between 16th November and 14th December 2022, eighteen (18) additional case reports were submitted to VigiBase from CARICOM: 3 AEFI reports, 15 ADR reports.

Table 5: All VigiBase Reports from CARICOM: suspected ADRs/AEFIs

Countries	Count	Percent
Barbados	1,404	32.8%
Dominica	14	0.3%
Guyana	14	0.3%
Haiti	19	0.4%
Jamaica	2,089	48.8%
Saint Vincent and the Grenadines	509	11.9%
Suriname	221	5.2%
Virgin Islands (British)	9	0.2%

Table 6: ICSR Patient Ages Reported

Patient age	Count	Percent
0 - 27 days	10	0.2%
28 days to 23 months	121	2.8%
2 - 11 years	97	2.3%
12 - 17 years	145	3.4%
18 - 44 years	1,370	32.0%
45 - 64 years	1,207	28.2%
65 - 74 years	429	10.0%
≥ 75 years	314	7.3%
Unknown	586	13.7%

GLOBAL ALERTS OF SUBSTANDARD / FALSIFIED VACCINES AND MEDICINES

Regional Medical Product Alerts

The following product alerts were provided through the PAHO network for substandard / falsified medical products from national regulatory authorities in the Americas. On 2nd and 14th November, 2022, the Center for the State Control of Medicines, Equipment and Medical Devices (CECMED), Cuba issued health alerts based on a queries to the Drug Information Service of the Surveillance Section, from citizens enquiring if the following products ABEXOL®, Chlordiazepoxide and Alprazolam are falsified.

Table 7: Medical Product Alert 2022

Date	Product	Company/ Manufacturer	Alert summary
14th November, 2022 (Cuba)	ABEXOL®	MEDSOL Laboratories, HAVANA, CUBA	The name contains a spelling error. Indicates used for the treatment of HERPES, which does not correspond to the uses declared by the Holder. Refers to a dose of 1000 mL per 60 tablets. The composition refers to the capsule however, original product is 50 mg tablets. States this medicine is produced by LABORATORIOS MEDSOL, Havana, Cuba. However, AVEXOL is not included in its product portfolio.
2nd November, 2022 (Cuba)	Chlordiazepoxide Tablets 10mg	Mylan Pharmaceuticals Inc	The NDC code 0378-5512 corresponds to the product Olanzapina, 15 mg, Mylan Pharmaceuticals Inc. Barcodes indicate phenylalanine as a component, and it is not a commonly used ingredient in this product. The bottle, country of origin, manufacturer to whom the product is attributed, type of label and information contained therein are very similar to Alprazolam, another product recently classified as a Counterfeit Medicine. CECMED has only registered chlordiazepoxide under brand name CHLORDIAZEPOXIDE-10, owned by the MEDSOL Laboratories.
2nd November, 2022 (Cuba)	Alprazolam Tablets 5mg Alprazolam Tablets 0.5mg	Boehringer Ingelheim. Promeco SA Xochimilico, Mexico;	Boehringer Ingelheim has confirmed that this product is not part of the medicine portfolio. The usual strengths of this medication are 0.25 mg; 0.5mg; 1mg and 2 mg. The label refers to tablets as pharmaceutical form, however they indicate that it contains elixir (liquid pharmaceutical form), of Bromhexine hydrochloride. The dose is indicated in tablespoons, the pharmaceutical form being a tablet. The product is a bronchial mucolytic, which is not an approved indications for Alprazolam. The NDC code 0228-2620-11 corresponds to the product Isosorbide Mononitrate, 20 mg/ 1, tablets, from Actavis Pharma Inc. They have the same lot number (3062571) and expiration date (May 2025). They indicate phenylalanine as a component. This is not a commonly used ingredient.

Global Medical Product Alerts

There have been no medical product alerts issued by the WHO in the past month. Given that medical products for the diagnosis, treatment and prevention of COVID-19 are in demand globally, this along with supply chain vulnerabilities and limited capacities in some countries creates opportunities for illicit goods (e.g. falsified test kits, vaccines and medicines), and diversion of legitimate products. We remind regulators in our Member States to remain vigilant and to work closely with national security agencies to assist to prevent, detect and respond to threats of falsified COVID-19 medical products.

PRACTICAL TIPS AND REMINDERS

National regulatory authorities and the public are advised to increase vigilance within the supply chains of countries and regions likely to be affected by these falsified products. Increased vigilance should include hospitals, clinics, health centers, wholesalers, distributors, pharmacies, and any other suppliers of medical products.

All medical products must be obtained from authorized/licensed suppliers. The products' authenticity and physical condition should be carefully checked. Seek advice from a healthcare professional in case of doubt.

The detection and response to substandard, falsified and/or unregistered medical products is a challenge to regulatory authorities and national systems with limited capacity. The presence of substandard and/or falsified and/or unregistered medicines, vaccines or test kits for COVID-19 poses a threat to the prevention of deaths and hospitalization and undermines the needed efficacy in the treatment of the disease. Poorly treated infections also create opportunities for antimicrobial resistance, and more severe disease and death.

The following is a brief list that technical officers in regulatory divisions may keep on hand for their own use or for patient education.

Reminders:

We remind regulators in our Member States to remain vigilant and to work closely with national security agencies to assist to prevent, detect and respond to threats of falsified COVID-19 medical products. For ease of reference and to assist with the identification of substandard / falsified medical products, we include the following reminders:

- Ensure that the supplier or donor is duly authorized by the emergency authorization holder of the vaccine or medicine to distribute the product in your country.
- Request quality documentation, such as: authorization letters, product dossiers, and lot release certificates for the proposed batches.

Identifying a Substandard or Falsified Medical Product (WHO SF products)

Some falsified medical products are almost visually identical to the genuine product and very difficult to detect. However, many can be identified by:

- Examining the packaging for condition, spelling mistakes or grammatical errors;
- Checking the manufacture and expiry dates and ensuring any details on the outer packaging match the dates shown on the inner packaging; and

- Ensuring the medicine looks correct, is not discoloured, degraded, or has an unusual smell.

Patients or consumers should be advised to:

- Discuss anomalies with a doctor or pharmacist as soon as possible if he or she suspects the product is not working properly or he or she has suffered an adverse reaction;
- Refrain from buying, receiving or using medicines or vaccines from unauthorized or unregulated sources; and
- Report suspicious medical products to the National Medicines Regulatory Authority.

COVID-19 VACCINES AND THERAPEUTICS: REGULATORY UPDATES

Overview of COVID-19 Vaccine Development and Approvals

- 175 candidate vaccines are in clinical development: 49 in Phase 3 trials, and 11 in Phase 4 trials; Figure in COVID-19 Vaccines and Therapeutics Regulatory Tracker (Phases tab).
- 50 vaccines are approved in various countries, and 39 are at various stages of engagement with WHO for emergency use listing (EUL).
- CARPHA-CRS has recommended all 13 COVID-19 vaccines approved for emergency use listing by the WHO to Member States to date (counting AstraZeneca vaccine by SK Bio as one with Vaxzevria).
- The most recent recommendations were Pfizer-BioNTech Tozinameran/ Riltozinameran – COVID-19 mRNA Vaccine (nucleoside modified)- COMIRNATY® Original/ Omicron BA.1 and Tozinameran/ Famtozinameran – COVID-19 mRNA Vaccine (nucleoside modified)- COMIRNATY® Original/ Omicron BA.4-5— Table 8 (See List of CRS Recommended products).
- COVID-19 primary series and first booster vaccines' performance against Omicron variant of concern (VOC) is provided from WHO's Weekly Epidemiology Update (23rd November, 2022): Figure 3; Table 9. *No table or updated information was published in the supplement dated 14th December.*

- The Medicines and Healthcare Products Regulatory Agency (MHRA) on 6th December, 2022 has authorised the Pfizer/BioNTech COVID-19 vaccine for use in infants and children aged 6 months to 4 years. The MHRA's experts carefully reviewed data from an ongoing clinical trial involving 4,526 participants. This decision has been endorsed by the Commission on Human Medicines, after a careful review of the evidence.
- On 9th December, 2022 Health Canada authorized the booster dose of Comirnaty® Original & Omicron BA.4/BA.5 after completion of the primary series of Comirnaty in individuals 5 through <12 years of age. The safety and effectiveness of a booster dose is inferred from preliminary supportive descriptive clinical data from studies of a booster dose of Comirnaty Original & Omicron BA.4/BA.5 at 30mcg in adults and clinical data from the studies of a booster dose of Comirnaty Original & Omicron BA.1 vaccine at 30mcg in adults >55 years of age.
- As of 16th November, 2022, U.S. Food and Drug Administration (FDA) authorized bivalent formulations of the Moderna amd Pfizer-BioNTech COVID-19 vaccines for use as a single booster dose at least two months after completion of the primary series or booster vaccination. The Moderna COVID-19 Vaccine, Bivalent is authorized for use as a single booster dose in individuals 6 years of age and older. The Pfizer BioNTech COVID-19 Vaccine, Bivalent is for use as a single booster in individuals 5 years of age or older.

Overview of COVID-19 Medicines: Regulatory Approvals and Prequalification

- 44 potential COVID-19 medicines: 5 Prequalified medicines, 20 PAHO evidence summary, and 19 Regulatory approval (U.S. FDA; Health Canada; EMA; Swissmedic; TGA; ANVISA; MHRA; PMDA); Table in COVID-19 Vaccines and Therapeutics Regulatory Tracker (Medicine tab).
- Ongoing Living Update of Potential COVID-19 Therapeutics Options: Summary of Evidence. Rapid Review (7th November, 2022).

Additional Resources

- UMC New Course 2022 available to national and regional PV centre staff: Practical exercises in individual case causality assessment
- WHO Managing conflicts of interest, a how-to guide for public pharmaceutical-sector committees in low- and middle-income countries 22 September 2022.
- WHO Training on handling, storing and transporting Pfizer-BioNTech COVID-19 mRNA Vaccine COMIRNATY® (Tozinameran). Updated 3 October 2022.
- WHO. Status of COVID-19 Medicines and Active Pharmaceutical Ingredients (APIs). 14 December 2022.
- Health Canada: Guidance on releasing information from adverse reaction and medical device incident reports to the public.

COVID-19 RESOURCES FOR REGULATION, CAPACITY-BUILDING AND VIGILANCE

Resource	Description and Link
CARPHA COVID-19 Webpage	This page provides media releases on regional responses to COVID-19, CARPHA Situation Reports, and Technical Guidance: https://www.carpha.org/What-We-Do/Public-Health/Novel-Coronavirus.
CARPHA CRS VigiCarib Online Reporting Forms	Adverse Events Following Immunization: VigiCaribVaccine Reporting Form Adverse Drug Reactions, and Substandard / Falsified / Unregistered Medical Products: VigiCarib Reporting Form
PAHO COVID-19 Webpage	URL: https://www.paho.org/en/topics/coronavirus-infections/coronavirus-disease-covid- 19-pandemic
PAHO Technical Documents	URL: https://www.paho.org/en/technical-documents-coronavirus-disease-covid-19.
PAHO Ongoing Living Update of Potential COVID-19 Therapeutics	A summary of evidence on potential therapeutic options for COVID-19, examines 239 therapeutic options. 7th November, 2022 (41st edition) URL: https://iris.paho.org/handle/10665.2/52719
PAHO Periodic Updates on AEFIs	Consolidated regional and global information on adverse events following immunization (AEFI) against COVID-19 and other updates. 12th September, 2022 (38th Edition): URL: https://covid-19pharmacovigilance.paho.org/img/recursos/634743d0dd6dc20afce6cbd4e.pdf
WHO Strategic Advisory Group of Experts on Immunization (SAGE)	COVID-19 Vaccine Technical Documents URL: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials
WHO Technical Documents for Vaccines and Biologicals	Relevant WHO documents for SARS-CoV-2 vaccines and other biologicals URL: https://www.who.int/biologicals/Relevant_WHO_documents_for_SARS-CoV-2_vaccines_and_other_biologicals.TZ.IK.7_Apr_2020.pdf
WHO COVID-19 Vaccines Safety Surveillance Manual	The COVID-19 vaccine safety guidance manual of Global Advisory Committee on Vaccine Safety (GACVS). URL: https://www.who.int/publications/i/item/10665338400
WHO Regulatory Updates on COVID-19	URL: https://www.who.int/teams/regulation-prequalification/eul/covid-19
WHO Guidelines for MedicineDonations	URL: https://www.who.int/selection_medicines/emergencies/guidelines_medicine_donations/en/
WHO Lot Release of Vaccines by NRAs	URL: https://www.who.int/biologicals/areas/vaccines/lot_release/en/
WHO Model packaging for COVID-19 vaccines	URL: https://www.who.int/teams/regulation-prequalification/eul/covid-19/covid-19-model-packaging

Table 8: COVID-19 Vaccines with WHO EUL and Other Regulatory Approvals Consideration

Vaccine/ WHO EUL Holder	Vaccine Platform	Dosing/ Storage ¥/ Approvals	NRA of record	Recommendation issued
WHO EUL status – Approved				
Recommended by CARPHA-CRS				
Tozinameran; COMIRNATY®; Pfizer-BioNTech COVID-19 Vaccine COVD-19 mRNA Vaccine (nucleoside modified)/ BioNTech Manufacturing GmbH §: Ready-to-Use formulation	mRNA (nucleoside modified)	2 doses I.M. -90°C to -60°C [15 mo. (PBS/Sucrose) and 12 mo. (Tris/Sucrose)]; 2°C to 8°C (31 days / 10 wks§) WHO EUL For: Adults; ≥12 yrs; 5-11 yrs	European Medicines Agency	31st December 2020
			United States Food and Drug Administration	16th July, 2021
VAXZEVRIA® COVID-19 Vaccine (ChAdOx1-S [recombinant])/ AstraZeneca AB + SK Bioscience Co. Ltd and AstraZeneca AB	Recombinant ChAdOx1-S adenoviral vector	2 doses I.M. 2°C to 8°C (6 mo.) WHO EUL For: Adults ≥18 yrs old	Ministry of Food and Drug Safety, Korea	15th February 2021
			European Medicines Agency	16th April 2021
			Ministry of Health, Labour and Welfare, Japan	9th July 2021
			Therapeutic Goods Administration, Australia	9th July 2021
			Health Canada	27th August 2021
			COFEPRIS (DP), Mexico ANMAT (DS), Argentina	23rd December 2021
COVISHIELD™ COVID-19 Vaccine (ChAdOx1-S [recombinant])/ Serum Institute of India Pvt. Ltd	Recombinant ChAdOx1-S adenoviral vector	2 doses I.M. 2°C to 8°C (6 mo.) WHO EUL for: Adults ≥18 yrs old	Central Drugs Standard Control Organization, India	15th February 2021
COVID-19 Vaccine Janssen (Ad26.COV2-S [recombinant])/ Janssen–Cilag International NV	Viral vector (non-replicating)	1 dose I.M. -25°C to -15°C (24 mo.) 2-8°C (11 mo. within shelf-life) WHO EUL For: Adults ≥18 yrs old	European Medicines Agency	12th March 2021;
Elasomeran; SPIKEVAX™ COVID-19 mRNA Vaccine (nucleoside modified)/ Moderna Biotech and ModernaTX, Inc	mRNA-based in lipid nanoparticle (LNP)	2 doses I.M. -25°C to -15°C (9 mo.); 2-8°C (30d) or 9-25°C (12h) WHO EUL For: Adults and adolescents ≥12 years old; Children 6-11 yrs old	European Medicines Agency	30th April 2021
			United States Food and Drug Administration	6th August, 2021
			Ministry of Food and Drug Safety (MFDS), Rep. of Korea	23rd December 2021
Inactivated COVID-19 Vaccine (Vero Cell)/ Beijing Institute of Biological Products Co., Ltd. (BIBP)	Inactivated virus	2 doses I.M. 2°C to 8°C (24 mo.) WHO EUL For: Adults ≥18 yrs old	National Medical Products Administration, China	7th May 2021

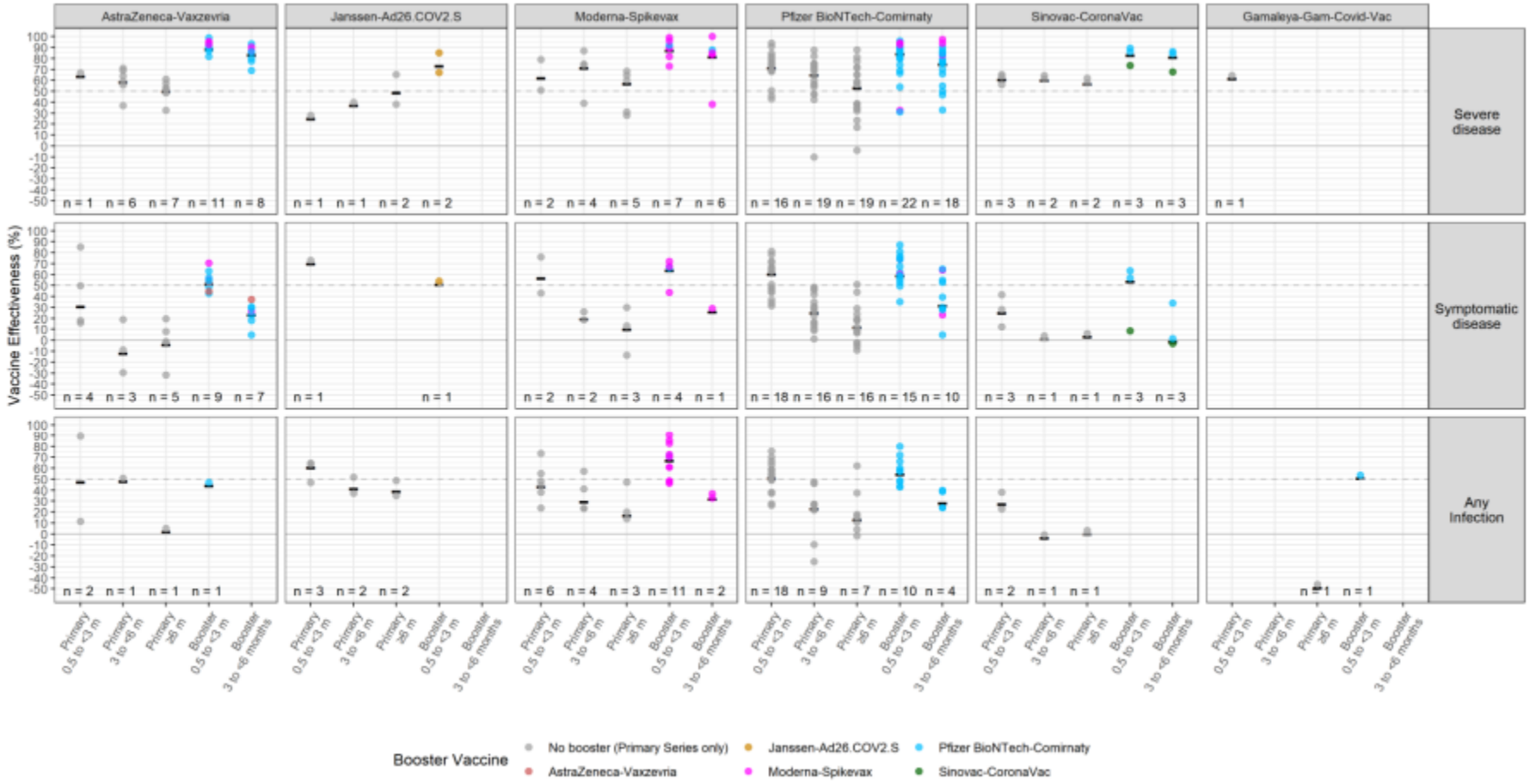
CoronaVac™ COVID-19 Vaccine (Vero Cell), Inactivated/ Sinovac Life Sciences Co., Ltd	Inactivated virus	2 doses I.M. 2°C to 8°C (12 mo.) WHO EUL For: Adults and adolescents ≥12 years old; Children 3-11 yrs old	National Medical Products Administration, China	1st June 2021
COVAXIN® Covid-19 vaccine (Whole Virion Inactivated Corona Virus vaccine)/ Bharat Biotech International Ltd	Whole virion inactivated	2 Doses I.M. 2°C to 8°C (9 mo.) WHO EUL For: Adults ≥18 yrs old	Central Drugs Standard Control Organization, India	3rd November 2021 **Supplies suspended**
COVOVAX™ COVID-19 vaccine (SARS-CoV-2 rS Protein Nanoparticle [Recombinant])/ Serum Institute of India Pvt. Ltd	Protein subunit	2 doses I.M. 2°C to 8°C WHO EUL For: Adults ≥18 yrs old	Central Drugs Standard Control Organization, India	17th December 2021
NUVAXOVID™ COVID-19 vaccine (SARS-CoV-2 rS [Recombinant, adjuvanted])/ Novavax CZ a.s.	Protein subunit	2 doses I.M. 2°C to 8°C WHO EUL For: Adults ≥18 yrs old	European Medicines Agency	20th December 2021
CONVIDECIA™ COVID-19 Vaccine, (Ad5.CoV2-S [Recombinant])/ CanSino Biological Inc	Adenovirus; Viral vector (non-replicat)	1 dose I.M. 2°C to 8°C WHO EUL for: Adults 18 to 59 yrs old	National Medical Products Administration	19th May 2022
Tozinameran/ Riltozinameran; COMIRNATY Original/Omicron BA.1 COVID-19 mRNA Vaccine/ BioNTech Manufacturing GmbH	mRNA (nucleoside modified)	1 booster dose I.M. -90°C to -60°C (12 mo); 2°C to 8°C (10 wks) WHO EUL For: Adults and adol. ≥12 yrs as a booster	European Medicines Agency	19th October, 2022
Tozinameran/ Famtozinameran; COMIRNATY Original/Omicron BA.4-5 COVID-19 mRNA Vaccine/ BioNTech Manufacturing GmbH	mRNA (nucleoside modified)	1 booster dose I.M. -90°C to -60°C (12 mo); 2°C to 8°C (10 wks) WHO EUL For: Adults and adol. ≥12 years as a booster	European Medicines Agency	11th November, 2022

¥ - Storage information is provided primarily for sealed vials. See product information for additional details on storage and handling.

References:

World Health Organization. **Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process**. Updated 8th November, 2022. WHO, Geneva, 2020. Available at: https://www.who.int/teams/regulation-prequalification/eul/covid-19.
World Health Organization. **COVID-19 vaccines WHO EUL issued**. Available at: https://extranet.who.int/pqweb/vaccines/vaccinescovid-19-vaccine-eul-issued
World Health Organization. **COVID-19 vaccine tracker and landscape**. WHO, Geneva, 6th December, 2022. *No tracker and landscape was published on 9th December.* Available at: Draft landscape of COVID-19 candidate vaccines (who.int).
World Health Organization. **Emergency Use Listing Procedure for Vaccines**. WHO, Geneva 2021. Available at: https://www.who.int/teams/regulation-prequalification/eul/eul-vaccines.

Figure 3: WHO Summary of Neutralization Studies of Primary series and First booster vaccine performance against Omicron variant of concern



Dots represent point estimates of VE from each study; dark black horizontal lines represent median VE across all studies in stratum. All data are from a systematic review of COVID19 VE studies; methods and summary tables of VE studies can be found on view-hub.org. Vertical panels represent VE for full primary series (grey dots) and VE for homologous or heterologous booster vaccination (other colored dots) following completion of primary series vaccination with vaccine of primary series noted in column header. All booster VE estimates are for first booster dose. Severe disease includes hospitalization; symptomatic disease includes disease of any severity level; any infection can include symptomatic and asymptomatic infection. Not shown in plot: VE against severe disease at 0.5-<3 month post primary series of Beijing CNBG-BBIBP-CorV (59%, 95% CI: 4 to 80%). Additional details on the methods for inclusion of the estimates in the plots provided in text.

Figure 3 shows the absolute vaccine effectiveness (VE) over time against the Omicron variant, grouped by the primary series vaccine; booster doses may have been a different vaccine (i.e., both homologous and heterologous booster vaccination VEs are shown). All vaccines included in Figure 3 are vaccines based on the ancestral SARS-CoV-2 strain; no VE data are yet available for variant-based vaccines. Additional information on vaccine performance against VOCs and Interpretation of Results are provided at: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---23-november-2022

Table 9: WHO Summary of Neutralization Studies of Primary series and First booster vaccine performance against Omicron variant of concern

		Omicron Sub-Lineage					
		BA.1	BA.2	BA.2.12.1	BA.2.75	BA.3	BA.4/BA.5
Primary Series Vaccination							
WHO Emergency Use Listing (EUL) Qualified Vaccines	AstraZeneca-Vaxzevria/SII-Covishield	HNR_{15}	HNR_{2}	HNR_{1}			HNR_{1}
	Beijing CNBG-BBIBP-CorV	HNR_{9}	HNR_{3}	HNR_{2}		HNR_{1}	HNR_{2}
	Bharat-Covaxin	↓↓$_{1}$					
	Cansino-Covidecia						
	Janssen-Ad26-COV2.S	HNR_{10}	HNR_{1}	HNR_{1}			HNR_{1}
	Moderna-Spikevax	↓↓↓$_{11}$	↓↓to↓↓↓$_{2}$	HNR_{1}			HNR_{1}
	Novavax-Nuvaxovid/SII - Covavax	HNR_{2}	HNR_{1}	HNR_{1}			HNR_{1}
	Pfizer BioNTech-Comirnaty	HNR_{57}	HNR_{10}	HNR_{3}	HNR_{1}	HNR_{1}	HNR_{5}
	Sinovac-CoronaVac	HNR_{11}	HNR_{2}	HNR_{1}			HNR_{2}
Other Vaccines (non-EUL)	Anhui ZL-Recombinant						
	Gamaleya-Sputnik V	HNR_{3}	HNR_{1}	HNR_{1}			HNR_{1}
	Chumakov-Covi-Vac	HNR_{2}					
First Booster Vaccination (Primary Series Vaccine + Booster Vaccine)							
WHO Emergency Use Listing (EUL) Qualified Booster Vaccines	AstraZeneca-Vaxzevria/SII-Covishield + AstraZeneca-Vaxzevria/SII Covishield	HNR_{2}	HNR_{2}			↓↓$_{1}$	↓↓↓$_{1}$
	AstraZeneca-Vaxzevria/SII-Covishield + Moderna-Spikevax	↓$_{1}$					
	AstraZeneca-Vaxzevria/SII-Covishield + Pfizer BioNTech-Comirnaty	↓↓to↓↓↓$_{2}$	↓↓$_{1}$			↓↓$_{1}$	
	Beijing CNBG-BBIBP-CorV + Beijing CNBG-BBIBP-CorV	↓↓to↓↓↓$_{6}$	↓$_{4}$	HNR_{2}	↓$_{1}$	↓↓$_{2}$	↓$_{5}$
	Cansino-Convidecia + Cansino-Convidecia	↓$_{1}$					
	Janssen-Ad26-COV2.S + Janssen-Ad26-COV2.S	HNR_{3}					
	Janssen-Ad26-COV2.S + Moderna-Spikevax	↓↓↓$_{1}$					
	Janssen-Ad26-COV2.S + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_{2}$					
	Moderna-Spikevax + Moderna-Spikevax	↓to↓↓↓$_{11}$	↓↓to↓↓↓$_{4}$	↓↓$_{1}$	↓$_{2}$	↓↓$_{1}$	↓↓↓$_{4}$
	Moderna-Spikevax + Pfizer BioNTech-Comirnaty	↓↓↓$_{1}$					
	Novavax-Nuvaxovid/SII – Covavax + Novavax-Nuvaxovid/SII - Covavax	↓↓$_{1}$					
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_{52}$	↓to↓↓$_{24}$	↓to↓↓$_{9}$	↓↓$_{3}$	↓to↓↓$_{5}$	↓↓to↓↓↓$_{15}$
	Pfizer BioNTech-Comirnaty + Janssen-Ad26-COV2.S	↓$_{2}$					
	Pfizer BioNTech-Comirnaty + Moderna-Spikevax	↓to↓↓$_{3}$	↓↓$_{1}$		↓↓↓$_{1}$		↓↓↓$_{1}$

	Sinovac-CoronaVac + Sinovac-CoronaVac	HNR_{11}	↓↓to↓↓↓$_6$	HNR_3	↓↓$_1$	↓↓$_1$	HNR_5
	Sinovac-CoronaVac + AstraZeneca-Vaxzevria	↓↓$_1$					
	Sinovac-CoronaVac + Pfizer BioNTech-Comirnaty	↓↓$_6$	↓to↓↓$_4$	↓to↓↓$_2$			↓to ↓↓↓$_3$
Other Vaccines (non-EUL)	Anhui ZL-Recombinant + Anhui ZL-Recombinant	↓to↓↓$_3$	↓↓$_1$	↓↓$_1$		↓↓↓$_1$	↓↓↓$_1$
	Beijing CNBG-BBIBP-CorV + Anhui ZL - Recombinant	↓↓to↓↓↓$_5$	↓↓to↓↓↓$_2$	HNR_2	↓↓↓$_1$	↓↓↓$_2$	HNR_2
	Cansino-Convidecia + Anhui ZL - Recombinant	↓$_1$					
	Gamaleya-Sputnik V + Gamaleya Sputnik Light	↓↓$_1$					
	Sinovac-CoronaVac + Anhui ZL - Recombinant	↓to↓↓$_2$	↓to↓↓$_2$	↓ to ↓↓↓$_2$		↓to↓↓↓$_2$	↓↓$_1$
	Sinovac-CoronaVac + Cansino-Ad5-nCoV-IH	↓↓↓$_1$					
Second Booster Vaccination (Primary Series + First Booster Vaccine + Second Booster Vaccine)							
WHO Emergency Use Listing (EUL) Qualified Booster Vaccines	Moderna-Spikevax + Moderna-Spikevax + Moderna-Spikevax	↓$_1$					
	Moderna-Spikevax + Moderna-Spikevax + Moderna-Spikevax Bivalent Original/Omicron BA.1	↓$_1$					↓↓$_1$
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty	↓↓↓$_1$					
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty + Moderna-Spikevax	↓↓↓$_1$					

Data as of 20th November 2022

Abbreviations: HNR=high non-response. Arrows generalize the magnitude of reduction in VE or neutralization: "↔" indicates <2-fold reduction in neutralization relative to the ancestral strain; "↓" indicates 2 to <5-fold reduction; "↓↓" indicates 5 to <10-fold reduction; "↓↓↓" indicates ≥10-fold reduction. When more than one neutralization study is available, the interquartile range (25th and 75th percentiles) of fold-reductions across all studies for specific vaccine/sub-lineage was used. HNR indicates a median percent response across all studies of <75%; in these instances, fold-reductions can be biased, and thus are not presented. The number of studies is shown as subscripts

Additional notes

- Studies contributing to the table are identified from an ongoing review of the preprint and published literature on neutralization of SARS-CoV-2 variants by COVID-19 vaccines.
- The following sets of results are excluded from the table:
    - Samples collected <7 days or ≥6 months after final dose
    - Strain other than ancestral SARS-CoV-1 strain used as the reference
    - Samples collected from immunocompromised persons
    - More than 20% of samples collected from persons previously infected with SARS-CoV-2
- It is important to note that studies vary in population and other methodological considerations, which may in part explain some differences when comparing products between different studies. In addition, the reductions summarized in the table do not incorporate uncertainty intervals around the degree of reductions, which can vary substantially across studies when reported.

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INFORMATION

This newsletter is produced by the technical team of the CARPHA Caribbean Regulatory System **for the focal points of CARPHA Member States, drug safety officers, immunization programme managers, public health administrators, public sector procurement agencies, and CARPHA staff** with an interest in the safety and quality of medicines and vaccines. A public version may be posted occasionally, however not all content shared with focal points will be publicized.

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