VIGICARIB NEWS

17TH NOVEMBER, 2022

OVERVIEW

This issue includes:

- Case Safety Reports to VigiCarib Network
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Image by: Polina Tankilevitch, Source: pexels.com

Note to Reader:

The following summary presents data on case reports of adverse events following immunization (AEFIs) 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 given outcome requires additional investigation to get full information*.*

CASE SAFETY REPORTS TO VIGICARIB NETWORK

Between 16th October 2022 and 15th November 2022, the CRS received twelve (12) case reports of: 9 suspected adverse drug reactions (ADRs) and 3 adverse events following immunization (AEFIs) through its online reporting forms:

- Suspected ADRs: Saint Vincent and the Grenadines (6); Saint Lucia (1); British Virgin Island (1) and; Trinidad and Tobago (1).
- AEFIs: Trinidad and Tobago (1); Saint Vincent and the Grenadines (1) and; Antigua and Barbuda (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, 525 case reports have been shared with VigiCarib network since its inception in November 2017, consisting of suspected adverse drug reactions (338 – 64.4%), substandard / falsified medical products (102 – 19.4%), and adverse events following immunization (85 – 16.2%) – Table A1 (See Appendix I – restricted circulation).

CARICOM COVID-19 VACCINE SAFETY REPORTS IN GLOBAL DATABASE

As of 15th November 2022, there have been 1,578 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 (85%), and females (74.1%). The month with the greatest reporting activity for events occurring in April 2021: Figure 1. Two hundred and ninety-nine reports (18.9%) were classified as Serious, including 67 where deaths were reported outcomes – Figure 2, Table 3.

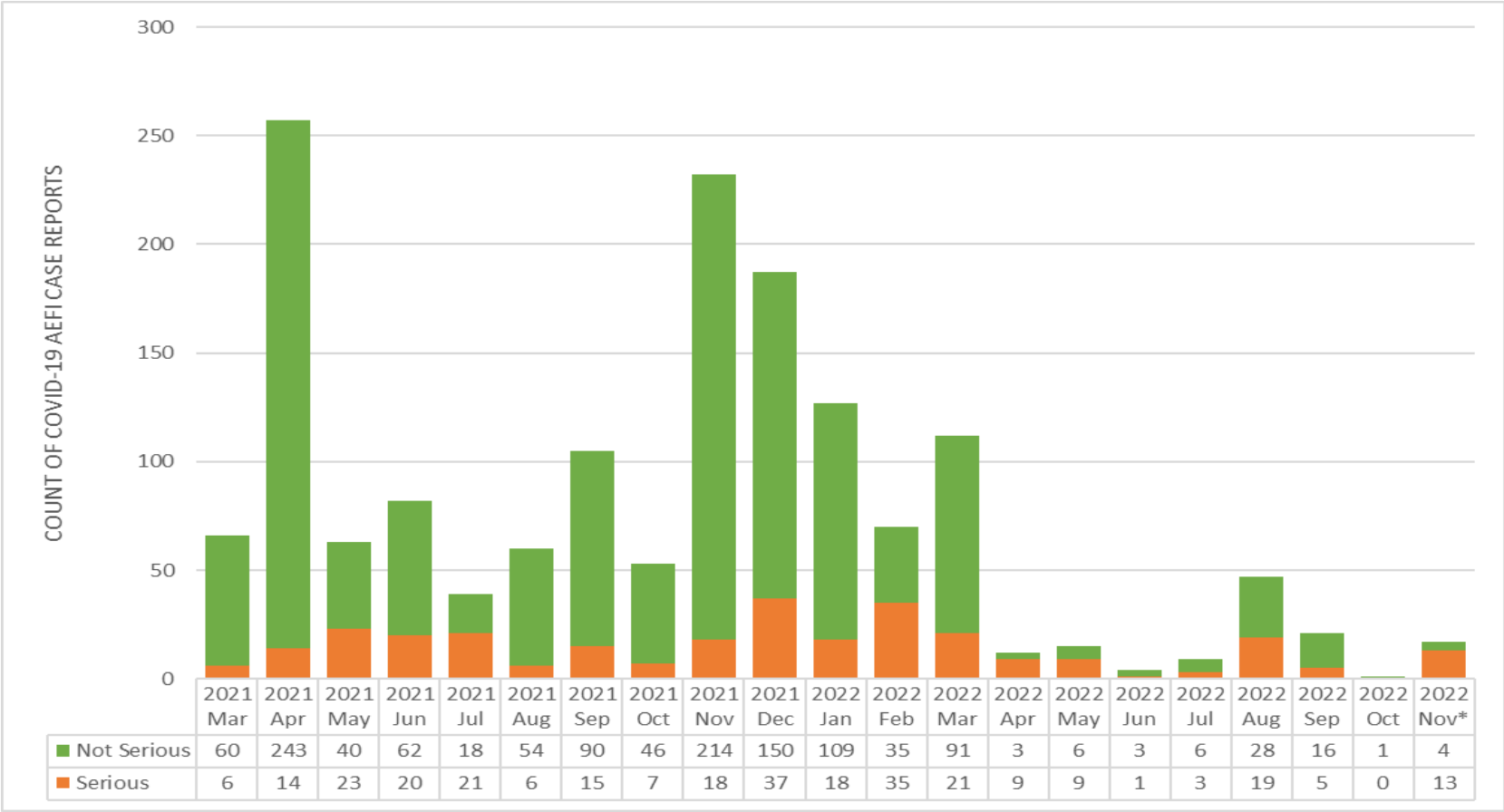
Eighteen (18) additional COVID-19 AEFI case reports were submitted between 16th October and 15th November 2022 to the global database. The most commonly reported reactions were: headache, fever, dizziness, fatigue, chills and myalgia – Table 3. The downward trend of reporting of AEFIs may be due to multiple 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).

Note: *The case reports describe events that occurred after vaccination, which may include coincidental events that are not attributed to the vaccine(s).*

Figure 1: Case reports of adverse events following immunization (AEFIs) with COVID-19 vaccines from 1st March 2021 to 15th November 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*
Not Serious	60	243	40	62	18	54	90	46	214	150	109	35	91	3	6	3	6	28	16	1	4
Serious	6	14	23	20	21	6	15	7	18	37	18	35	21	9	9	1	3	19	5	0	13

* AEFI case counts presented for the each month for March 2021 to October 2022, except for November 2022 (up to 15th Nov).

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 AEFI reports per 100,000 doses of COVID-19 vaccines administered, with approximately 12 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 15th November 2022.

Country	Total Doses	Total AEFIs*	AEFIs per 100,000 doses¥	Total Serious AEFIs	Serious AEFIs per 100,000 doses
Barbados	380,826	604	158.6	85	22.3
Haiti	509,500	1	0.2	0	0
Jamaica	1,495,377	951	63.6	208	13.9
St Vincent and the Grenadines	72,943	22	30.2	6	8.2
Total	**2,458,646**	**1,578**	**64.2**	**299**	**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 15th November 2022 (N=1,578)

Patient age	Count	Percent
12 - 17 years	100	6.3%
18 - 44 years	739	46.8%
45 - 64 years	504	31.9%
65 - 74 years	108	6.8%
≥ 75 years	84	5.3%
Unknown	43	2.7%

Table 3: Top Reported Reactions for AEFIs in VigiBase to 15th November 2022 (N=1,578)

Top Reported Reactions	Count	Percent
PT: Headache	461	29.2%
PT: Pyrexia	306	19.4%
PT: Dizziness	304	19.3%
PT: Fatigue	249	15.8%
PT: Chills	244	15.5%
PT: Myalgia	223	14.1%
PT: Arthralgia	211	13.4%
PT: Nausea	178	11.3%
PT: Vaccination site pain	160	10.1%
PT: Malaise	150	9.5%

Figure 2: Total AEFI Case Reports by Seriousness (N = 1, 578)

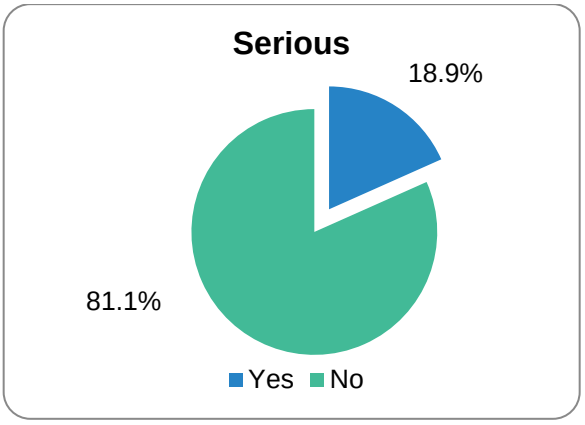


Table 4: Seriousness of Cases (n = 299)

Seriousness criteria	Count	Percent
Death	67	4.2%
Life threatening	21	1.3%
Caused/prolonged hospitalization	112	7.1%
Disabling/incapacitating	52	3.3%
Other medically important condition	106	6.7%

Note: Total exceeds 299 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 4,252 case reports from CARICOM countries with membership in the WHO Programme for International Drug Monitoring (PIDM): 1,578 COVID-19 AEFI case reports, 154 non-COVID AEFI case reports, and 2,520 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 15th November 2022, inclusive of reports submitted by the CRS on behalf of Member States. Most of the case reports involved adults – Table 6.

Between 16th October and 15th November 2022, twenty-seven (27) additional case reports were submitted to VigiBase from CARICOM: 21 AEFI reports, 6 ADR reports.

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

Countries	Count	Percent
Barbados	1,398	32.9%
Dominica	14	0.3%
Guyana	14	0.3%
Haiti	19	0.4%
Jamaica	2,075	48.8%
Saint Vincent and the Grenadines	502	11.8%
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	119	2.8%
2 - 11 years	96	2.3%
12 - 17 years	145	3.4%
18 - 44 years	1,360	32.0%
45 - 64 years	1,202	28.3%
65 - 74 years	429	10.1%
≥ 75 years	311	7.3%
Unknown	580	13.6%

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 1st November, 2022, the Center for the State Control of Medicines, Equipment and Medical Devices (CECMED), Cuba issued a health alert based on a query to the Drug Information Service of the Surveillance Section, from a citizen enquiring if the product Clonazepam, attributed to the manufacturer Mylan, is falsified.

Four alerts of falsified products were issued by the Federal Commission for the Protection against Sanitary Risk (COFEPRIS), Mexico in November, 2022 for: Flor Essence, Rantudil® (acemetacin 60mg), Rosel 3.0g/0.5g/0.02g (amantadine, chlorphenamine, paracetamol) and Desenfriol-ito® (acetaminophen, chlorpheniramine, phenylephrine), which were detected in Mexico.

Table 7: Medical Product Alert 2022

Date	Product	Company/ Manufacturer	Alert summary
10th November, 2022 (Colombia)	Desenfriol-ito® (Paracetamol/ Chlorphenamine/ Phenylephrine) chewable tablet. Lot number: X23V7X Expiry date: DEC/23	Bayer Mexico S.A. de C.V.	Lot number X23V7X has expired since the original expiration date was APR/21.
10th November, 2022 (Colombia)	Flor Essence 500ml and 1000ml. Lot numbers: 2561 and L08070112561D Expiry date: 11 08 24 and 08/2023	Kokusai Naturista SA de CV/ Flora Health	The company does not recognize batch 2561 with expiration date 08 11 24. The counterfeit product has a white plastic lid and phrase "KEEPING HOPE". The 1000ml presentation is not marketed, and lot L08070112561D does not match any original product.
10th November, 2022 (Colombia)	Rantudil Acemetacin 60mg Lot numbers: EAH5186, 5083817 and 4004731.	Meda Pharma S. de RL de CV	Batches were not manufactured, packaged and released by the company and manufacture of the product is currently suspended. Lot EAH5186 with expiration date Dec 2021, has dot-shaped engravings on blister. Lot 5083817 with expiration date Jan 2022, the lot data cannot be found engraved on the blister.
10th November, 2022 (Colombia)	Rosel Children's solution 3.0g/0.5g/0.02g (amantadine, chlorphenamine, paracetamol) Lot number: 200413 Expiry date: DEC 24	Wermar Pharmaceuticals SA de CV	Batch number 200413 was manufactured by the company, but with an expiration date of MAY 2022. The company has not manufactured the product since April 2021. The counterfeit product has expiration date with dotted print.
19th October, 2022 (Cuba)	Clonazepam Tablets USP 2mg	Mylan Pharmaceuticals	The number referred to on the label does not correspond to any drug included in the NDC Code List. The product is not currently within the company product portfolio. Based on analysis of the photographic evidence and the definition of the WHO, the product is a falsified.

Global Medical Product Alerts

In November 2022, the WHO issued an additional medical product alert for eight substandard products, identified in Indonesia and publicly reported by the national regulatory authority (Badan POM) on 20 and 30 October 2022. Substandard medical products are products that fail to meet either their quality standards or specifications and are, therefore "out of specification". The eight products are Termorex syrup (batch AUG22A06 only), Flurin DMP syrup, Unibebi Cough Syrup, Unibebi Demam Paracetamol Drops, Unibebi Demam Paracetamol Syrup, Paracetamol Drops (manufactured by PT Afi Farma), Paracetamol Syrup (mint) (manufactured by PT Afi Farma) and Vipcol Syrup. To date, these products have only been identified in Indonesia. They may however have marketing authorizations in other countries. These products may have been distributed, through informal markets, to other countries or regions – Table 8.

Table 8: Medical Product Alerts 2022

Alert number and date	Product	Manufacturer	Alert summary
N°7/2022 **2nd November, 2022**	1. Termorex syrup (Paracetamol) 2. Flurin DMP syrup (Paracetamol, Pseudoephedrine HCl, Dextromethorphan HBr, Chlorpheniramine Maleate) 3. Unibebi Cough Syrup (Paracetamol, Guaifenesin, Chlorphenamine Maleate) 4. Unibebi Demam Paracetamol Drops 5. Unibebi Demam Paracetamol Syrup 6. Unibebi Demam Paracetamol Drops 7. Paracetamol Syrup (mint) 8. Vipcol Syrup (Paracetamol, Guaifenesin, Chlorphenamine Maleate)	PT Konimex; PT Yarindo Farmatama; PT Universal Pharmaceutical Industries; PT Afi Farma	These products contain unacceptable amounts of ethylene glycol and/or diethylene glycol as contaminants: this has been confirmed by laboratory analysis of samples by the authorities in Indonesia.

Risks of Diethylene glycol and ethylene glycol are toxic to humans when consumed and can prove fatal:

The substandard products referenced in the annex of this Alert are unsafe and their use, especially in children, may result in serious injury or death. Toxic effects can include abdominal pain, vomiting, diarrhoea, inability to pass urine, headache, altered mental state, and acute kidney injury which may lead to death.

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

- 172 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).
- 49 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 11 of 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) — Table 9 (See List of CRS Recommended products).
- On 19th October, the WHO announced its validation of an additional COVID-19 vaccine: COMIRNATY Original/Omicron BA.1, a bivalent vaccine manufactured by BioNTech Manufacturing GmbH. See the product overview here: https://extranet.who.int/pqweb/vaccines/comirnaty-originalomicron-ba1. This brings the total of WHO EUL vaccines to 12 (counting AstraZeneca vaccine by SK Bio as one with Vaxzevria).
- On 11th November, the WHO announced its validation of an additional COVID-19 vaccine: COMIRNATY Original/Omicron BA.4-5, a bivalent vaccine manufactured by BioNTech Manufacturing GmbH. See the product overview here: https://extranet.who.int/pqweb/vaccines/comirnaty-originalomicron-ba4-5.
- COVID-19 primary series and first booster vaccines' performance against Omicron variant of concern (VOC) is provided from WHO's Weekly Epidemiology Update (26th October, 2022): Figure 5 and Table 3. *No table or updated information was published in the supplement dated 16th November.*

- On 4th November 2022, Health Canada authorized the second bivalent COVID-19 booster targeting the Omicron BA.4/5 variants in individuals 18 years of age or older. The booster is expected to trigger a strong immune response against both the original SARS-CoV-2 strain as well as the Omicron BA.4/BA.5 subvariants.
- On 8th November, 2022 the U.S. Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the use of Kineret (anakinra) for the treatment of COVID-19 in hospitalized adults with positive results of direct SARS-CoV-2 viral testing with pneumonia requiring supplemental oxygen (lower high-flow oxygen) at risk of progressing to severe respiratory failure and likely to have an elevated plasma soluble urokinase plasminogen activator receptor (suPAR).
- The Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom on 9th November, 2022 approved the Pfizer/BioNTech 'bivalent' Covid vaccine that targets both the Original strain of SARS-CoV-2 and the Omicron BA.4 and BA.5 sub-variants. The updated booster vaccine is the second bivalent vaccine from Pfizer/BioNTech to receive MHRA approval.

Overview of COVID-19 Medicines: Regulatory Approvals and Prequalification

- 43 potential COVID-19 medicines: 5 Prequalified medicines, 19 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). 16 November 2022.
- WHO World Antimicrobial Awareness Week 2022 Campaign Guide.
- 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

Resource	Description and Link
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 9: 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
Pending CRS review				
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 adolescents ≥12 years old	European Medicines Agency	19th October, 2022
Tozinameran/Riltozinameran; 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 adolescents ≥12 years old	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

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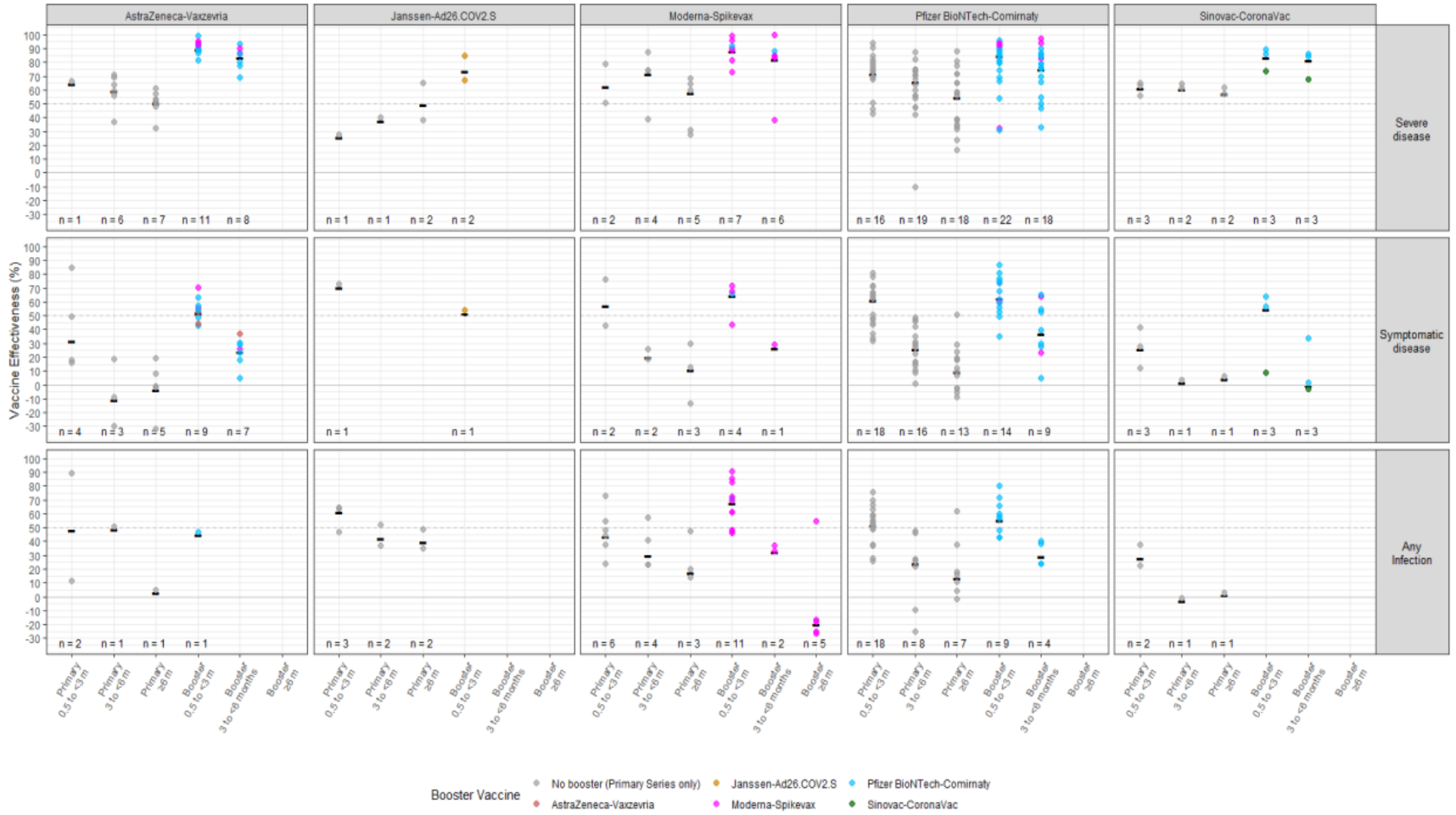
World Health Organization.

Table 4: 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 is from a systematic review of COVID-19 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%) and Gamaleya-Gam-Covid Vac (64%, 95% CI: -45 to 92.2%). Additional details on the methods for inclusion of the estimates in the plots provided in text.

Figure 5 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 5 are vaccines based on the ancestral SARS-CoV-2 strain; no VE data is yet available for variant-based vaccines. Additional information on Methods for Figure 5 and Interpretation of Results are provided at: https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---26-october-2022

Table 4: 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_{13}	HNR_2	HNR_1			HNR_1
	Beijing CNBG-BBIBP-CorV	HNR9	HNR_3	HNR_2		HNR_1	HNR_2
	Bharat-Covaxin	$\downarrow\downarrow_1$					
	Cansino-Covidecia						
	Janssen-Ad26-COV2.S	HNR_9	HNR_1	HNR_1			HNR_1
	Moderna-Spikevax	$\downarrow\downarrow\downarrow_{11}$	$\downarrow\downarrow$to$\downarrow\downarrow\downarrow_2$	HNR_1			HNR_1
	Novavax-Nuvaxovid/SII - Covavax	HNR_2	HNR_1	HNR_1			HNR_1
	Pfizer BioNTech-Comirnaty	HNR_{55}	HNR_8	HNR_1	HNR_1	HNR_1	HNR_3
	Sinovac-CoronaVac	HNR_9	$\downarrow\downarrow\downarrow_1$				$\downarrow\downarrow\downarrow_1$
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			$\downarrow\downarrow_1$	$\downarrow\downarrow\downarrow_1$
	AstraZeneca-Vaxzevria/SII-Covishield + Moderna-Spikevax	$\downarrow_1$					
	AstraZeneca-Vaxzevria/SII-Covishield + Pfizer BioNTech-Comirnaty	$\downarrow\downarrow$to$\downarrow\downarrow\downarrow_2$	$\downarrow\downarrow_1$			$\downarrow\downarrow_1$	
	Beijing CNBG-BBIBP-CorV + Beijing CNBG-BBIBP-CorV	$\downarrow\downarrow$to$\downarrow\downarrow\downarrow_4$	$\downarrow$to$\downarrow\downarrow_3$	HNR_1		$\downarrow\downarrow_1$	$\downarrow_4$
	Janssen-Ad26-COV2.S + Janssen-Ad26-COV2.S	HNR_2					
	Janssen-Ad26-COV2.S + Moderna-Spikevax	$\downarrow\downarrow\downarrow_1$					

	Janssen-Ad26-COV2.S + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_2$					
	Moderna-Spikevax + Moderna-Spikevax	↓to↓↓↓$_{10}$	↓↓$_2$	↓↓$_1$	↓$_1$	↓↓$_1$	↓↓↓$_3$
	Moderna-Spikevax + Pfizer BioNTech-Comirnaty	↓↓↓$_1$					
	Novavax-Nuvaxovid/SII – Covavax + Novavax-Nuvaxovid/SII - Covavax	↓↓$_1$					
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_{48}$	↓to↓↓↓$_{19}$	↓to↓↓$_5$	↓↓$_2$	↓to↓↓$_5$	↓↓↓$_{10}$
	Pfizer BioNTech-Comirnaty + Janssen-Ad26-COV2.S	↓$_2$					
	Pfizer BioNTech-Comirnaty + Moderna-Spikevax	↓to↓↓$_3$			↓↓↓$_1$		↓↓↓$_1$
	Sinovac-CoronaVac + Sinovac-CoronaVac	↓↓to↓↓↓$_7$	↓↓to↓↓↓$_5$	HNR$_2$		↓↓$_1$	HNR$_4$
	Sinovac-CoronaVac + Pfizer BioNTech-Comirnaty	↓↓$_5$	↓↓to↓↓↓$_3$	↓↓$_1$			↓↓↓$_2$
Other Vaccines (non-EUL)	Anhui ZL-Recombinant + Anhui ZL-Recombinant	↓to↓↓$_2$	↓↓$_1$	↓↓$_1$		↓↓↓$_1$	↓↓↓$_1$
	Beijing CNBG-BBIBP-CorV + Anhui ZL - Recombinant	↓↓to↓↓↓$_4$	HNR$_2$	HNR$_1$		↓↓↓$_1$	HNR$_1$
	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 21st October 2022

Abbreviations: HNR=high non-response. Arrows generalize the magnitude of reduction in VE or neutralization: "↔" indicates <2-fold reduction; "↓" 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/sublineage 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:

- o Samples collected <7 days or ≥6 months after final dose
- o Strain other than ancestral SARS-CoV-1 strain used as the reference
- o Samples collected from immunocompromised persons
- o 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.

Extracted from WHO Weekly Epidemiological Update: Edition 115, published 26th October, 2022. Available at: https://www.who.int/publications/m. See updated issue for references and additional information. *No table or updated information was published in the supplement dated 16th November.*

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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