VIGICARIB NEWS

23RD SEPTEMBER, 2022

OVERVIEW

This issue includes:

- Case Safety Reports to VigiCarib Network
- CARICOM COVID-19 Vaccine Safety Reports in VigiBase
- Summary of Case Safety Reports from CARICOM to WHO Programme for International Drug Monitoring (PIDM)
- Global Alerts of Substandard / Falsified Medical Products
- COVID-19 Vaccines and Therapeutics: Regulatory Updates
- COVID-19 Resources for Regulation and Vigilance

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 August and 15th September 2022, the Caribbean Regulatory System received three (3) reports of suspected adverse drug reactions (ADR) from events in Member States. There were no safety case reports of adverse events following immunization (AEFI), or reports of substandard / falsified / unregistered medical products (SF).

In all, 513 case reports have been shared with the CRS and the VigiCarib network since its inception in November 2017: suspected ADRs (329 – 64.1%), SFs (102 – 19.9%), and AEFIs (82 – 16.0%) – Table A1 (See Appendix I).

CARICOM COVID-19 VACCINE SAFETY REPORTS IN GLOBAL DATABASE

As of 15th September 2022, there have been 1,554 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 (85.0%), and females (74.3%). The month with the greatest reporting activity for events occurring in December 2021: Figure 1. Two hundred and eighty-three reports (18.2%) were classified as Serious, including 59 where deaths were reported outcomes – Figure 2, Table 3.

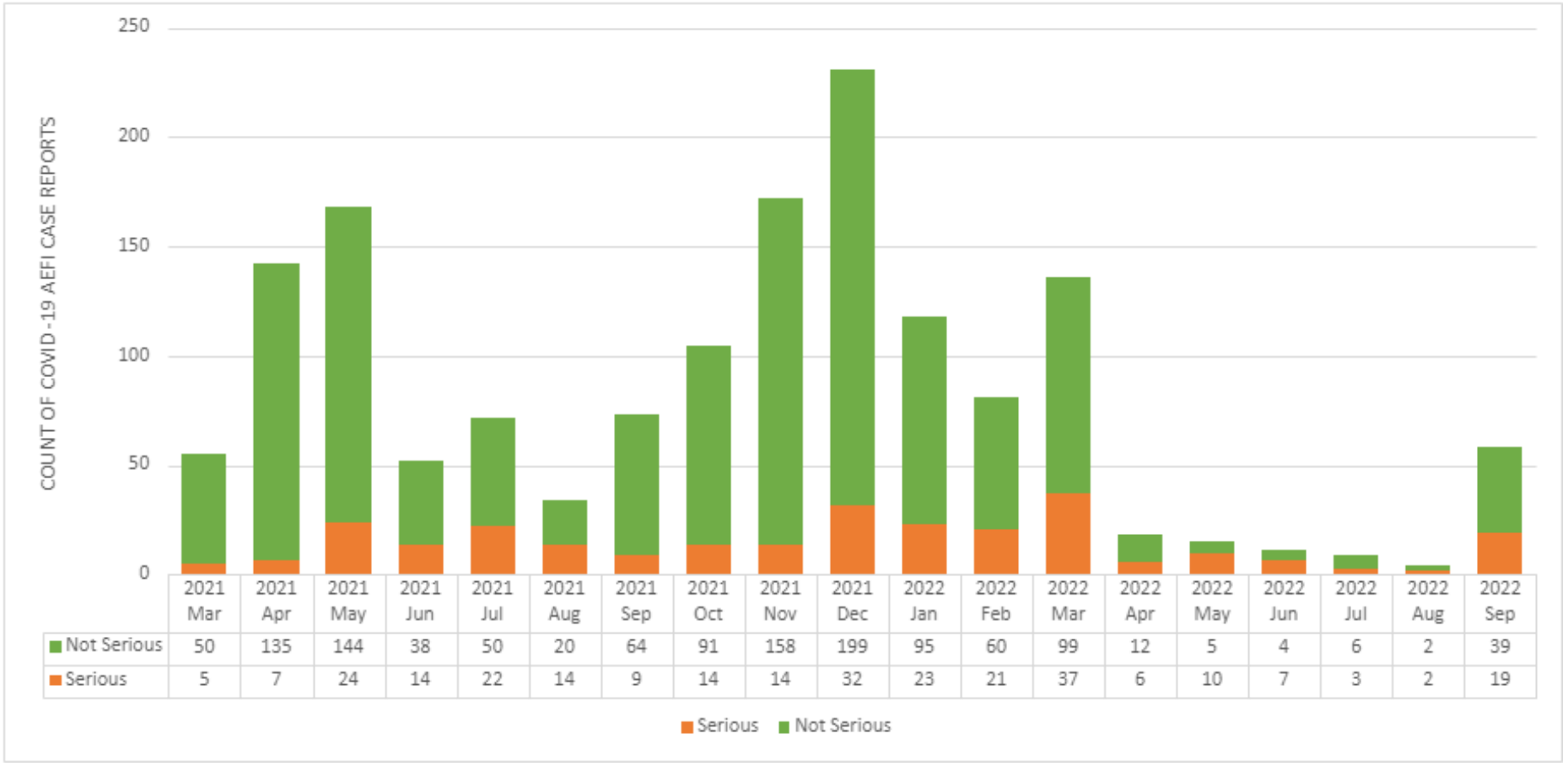
Fifty-eight (58) additional COVID-19 AEFI case reports were submitted between 16th August and 15th September 2022. The most commonly reported reactions were: headache, fever, dizziness, fatigue, chills and myalgia – Table 3. The downward trend of reporting of AEFIs may be due to multiple factors including reduction in vaccinations, lack of awareness of reporting systems, and reduced risk perception. However, further study at the national level would be needed to confirm causality and factors affecting 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 September 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
Not Serious	50	135	144	38	50	20	64	91	158	199	95	60	99	12	5	4	6	2	39
Serious	5	7	24	14	22	14	9	14	14	32	23	21	37	6	10	7	3	2	19

* - *Monthly mid-points are cut-off points for the AEFI count*

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 65 AEFI reports per 100,000 doses of COVID-19 vaccines administered, with 12 serious adverse events reported 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 AEFI and reporting rate, by country as of 16th September 2022

Country	Total Doses	Total AEFIs*	AEFIs per 100,000 doses¥	Total Serious AEFIs	Serious AEFIs per 100,000 doses¥
Barbados	374,195	603	161.1	85	22.7
Haiti	470,964	1	0.2	0	0
Jamaica	1,487,460	932	62.7	194	13.0
St Vincent and the Grenadines	7,2687	22	30.3	6	8.3
Total	**2,405,306**	**1,558**	**64.8**	**285**	**11.8**

*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 September 2022 (N=1,554)

Patient age	Count	Percent
12 - 17 years	97	6.2%
18 - 44 years	724	46.6%
45 - 64 years	500	32.2%
65 - 74 years	108	6.9%
≥ 75 years	79	5.1%
Unknown	4	3.0%

Table 3: Top Reported Reactions for AEFIs in VigiBase to 15th September 2022 (N=1,554)

Top Reported Reactions	Count	Percent
PT: Headache	460	29.6%
PT: Pyrexia	304	19.6%
PT: Dizziness	302	19.4%
PT: Fatigue	249	16.0%
PT: Chills	244	15.7%
PT: Myalgia	223	14.4%
PT: Arthralgia	210	13.5%
PT: Nausea	175	11.3%
PT: Vaccination site pain	160	10.3%
PT: Malaise	149	9.6%

Figure 2: Total AEFI Case Reports by Seriousness (N = 1, 554)

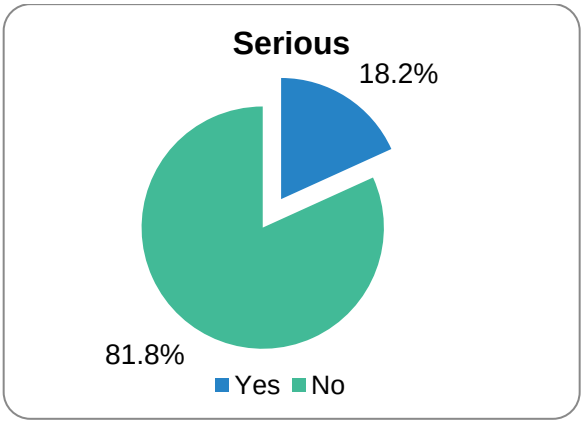


Table 4: Seriousness of Cases (n = 283)

Seriousness criteria	Count	Percent
Death	59	3.8%
Life threatening	20	1.3%
Caused/prolonged hospitalization	103	6.6%
Disabling/incapacitating	51	3.3%
Other medically important condition	102	6.6%

Note: Total exceeds 283 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 4,208 case reports from CARICOM countries with membership in the WHO Programme for International Drug Monitoring (PIDM): 1,554 COVID-19 AEFI case reports, 152 non-COVID AEFI case reports, and 2,440 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 September 2022, inclusive of reports submitted by the CRS on behalf of Member States. Most of the case reports involved adults – Table 6.

Between 16th August and 15th September 2022, seventy-seven (77) additional case reports were submitted to VigiBase from CARICOM: 58 AEFI reports, 19 ADR reports.

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

Countries	Count	Percent
Barbados	1,372	33.3%
Dominica	14	0.3%
Guyana	12	0.3%
Haiti	19	0.5%
Jamaica	1,973	47.9%
Saint Vincent and the Grenadines	502	12.2%
Suriname	221	5.4%
Virgin Islands (British)	7	0.2%

Table 6: ICSR Patient Ages Reported

Patient age	Count	Percent
0 - 27 days	10	0.2%
28 days - 23 months	111	2.7%
2 - 11 years	91	2.2%
12 - 17 years	139	3.4%
18 - 44 years	1,307	31.7%
45 - 64 years	1,176	28.5%
65 - 74 years	423	10.3%
≥ 75 years	298	7.2%
Unknown	565	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 5th September, 2022, the Ministry of Health of Costa Rica issued a health alert of theft of pharmaceutical products from different manufacturers and their possible presence in the national market. The products, mostly medicines were packed in 264 closed packages and came from different manufacturers and drugstores.

Seven alerts from the Federal Commission for the Protection against Sanitary Risk (COFEPRIS), Mexico were issued between 5th and 14th September, 2022, involving Substandard / Falsified / Unregistered Medical Products (SF) for: Ocrevus® (ocrelizumab), Nabota® (botulinum toxin type A), Keytruda® (pembrolizumab), Higlobin® (Human normal immunoglobulin), Herceptin® (trastuzumab), remdesivir, and Botox® (botulinum toxin type A), which were detected in Mexico. The authority confirmed that products were either falsified, had undergone improper commercialization or had been adulterated (substandard).

Table 7: Medical Product Alert 2022

Date	Product	Company/ Manufacturer	Alert summary
5th September (Costa Rica)	Not specified: 264 closed packages	Alcames Drug Store; Chemical Laboratories of Central America SA; Farmanova Group Intermed and Drugstore Transmedical SA	**Theft / Diversion of Product (potential substandard products)** Traceability was lost and storage and handling conditions are uncertain. Possible deterioration, adulteration and/or falsification.
7th September (Mexico)	Nabota (botulinum toxin type A) 100 U injectable solution, Batch numbers: X20050, X20027, X21056 and X21090A.	Probiomed, SA de CV	**Improper Commercialization:** Lacks the sanitary registration data, for which it does not know the origin and handling of said products.
7th September (Mexico)	Ocrevus® (Ocrelizumab 300mg/10mL) Batch numbers B1018A01, H0531B59 and A3011Z02, expiration date June 2023, February 07 2023 and April 2022	Productos Roche SA de CV	**Falsified** Batch not recognized in the company's system, has texts in English and has an incorrect QR code format. Lot not recognized in the company's system.
8th September (Mexico)	Higlobin® Normal Human Immunoglobulin Intravenous Solution for Injection 5g, Batch number: P100107626	CSL Bering SA de CV	**Substandard (adulteration)** The product does not contain the active ingredient IgG. The caps of the vial are mistreated. The plugs were tampered with. The physical appearance of the solution is yellowish.
8th September (Mexico)	KEYTRUDA® (pembrolizumab 100mg/4mL) Falsified Batch numbers: DC68976, DE68005, LT87333, NT78236, S012080, S032357, S035357, T009249, T021792, T032457, VZ01380, V011628 and W002260	Merck Sharp and Dohme Comercializadora S. de RL de CV	**Update: Falsified Product** Identification of additional falsified lots. Secondary packaging with texts in English Expiration date 11 Mar, 06 – 2022 and 09 – 2023

Date	Product	Company/ Manufacturer	Alert summary
13th September (Mexico)	Herceptin® 440mg: Lots: N7367B08 B3123 (Exp: 23 Jun 2022) Herceptin® SC 600: Lot B1082B10 (Exp: 23 Apr 2022) Herceptin® SC 600: Lot B2109B08 (Exp: 30 Jan 2023)	Productos Roche, S.A. de C.V.	**Falsified Product** **Falsified product:** The product expired in 2021 **Falsified:** Not recognized by the company
13th September (Mexico)	COROVIR, Bemsivir, Desrem, Remdesivir Batches: EN2005A2-B, EN2009D7-Q, CM2022F5, CA2023G5	Gilead Sciences México S. de R.L. de C.V.	**Falsified Products:** Remdesivir batches are not recognized by Company; Other named products are not authorized for marketing and distribution in Mexico. Characteristics: false lot numbers, fonts and legends do not correspond to those authorized for Mexico.
14th September (Mexico)	Botox® (botulinum toxin type A) Lot Nos.: C7749C3 (Exp. 24 May 2025), C7773C3 (Exp. 01 Jun 2025)	Allergan S.A. de C.V.	**Theft / Diversion of Product (potential substandard products)** Conditions of storage and handling are unknown. Possible deterioration, adulteration and/or falsification.

Global Medical Product Alerts

In August 2022, the WHO issued two additional medical product alerts for falsified DYSPORT (Clostridium botulinum type A toxin-haemagglutinin complex) and DIPRIVAN (Propofol) discovered in Europe, Eastern Mediterranean and Americas. The genuine manufacturers have confirmed that all the products referenced in this Alert are falsified on the basis that they deliberately/fraudulently misrepresent their identity and source–Table 8.

Table 8: Medical Product Alerts 2022

Alert number and date	Product	Manufacturer	Alert summary
N°4/2022 **19th August, 2022**	DYSPORT (Clostridium botulinum type A toxin-haemagglutinin complex)	IPSEN	Five **falsified** batches detected in five countries - Jordan (May 2022), Türkiye (May 2022), Kuwait (June 2022), United Kingdom (June 2022), and Poland (July 2022) Batch numbers and manufacturing-expiry dates are falsified. Discrepancies in the packaging languages, printing errors on the cartons, and discrepancies in vial types.
N°5/2022 **25th August 2022**	DIPRIVAN (Propofol)	ASTRAZENECA for ASPEN	Identified in Venezuela (Bolivarian Republic of) [July 2022] Lot numbers are **falsified** and have never been issued for DIPRIVAN. Printing and spelling errors have been identified and the fill line is potentially inconsistent among the identified vials.

Global Articles of COVID-19 Medical Product Quality Issues

Global Articles of COVID-19 Medical Product Quality Issues Equitable access to quality-assured COVID-19 vaccines is threatened by falsified, diverted and substandard (especially degraded) vaccines. The Medicines Quality Research Group has published its new Medical Product Quality Report on substandard and falsified (SF) COVID-19 vaccines, which summarizes reports in the public domain including data from the lay press, regulatory authorities, scientific literature and public alerts and warnings.

The group found 184 individual reports of diverted or substandard / falsified (SF) COVID-19 vaccines from 48 countries in the lay press between 12th March 2020 and 31st March 2022. Out of these reports, 22 were published in 2020; 156 reports were published in 2021; 6 reports were published in 2022- Figure 3. Six (6) new incidents were reported. For the first time quality issues were reported in Ireland, Rwanda, and Singapore.

Five incidents involved falsified COVID-19 vaccines including those labelled as manufactured by Covishield, Zydus Cadila, and Pfizer/BioNTech. One incident was related to diversion of COVID-19 vaccines out of the regular supply chain. Inequitable access is highly likely to fuel an increase in such incidents, negating the global good on health and economy of these remarkable vaccines. The most recent edition as of Issue 15: September 2022 (Data for January to March 2022) is available at: Medical Product Quality Report – COVID-19 vaccine issues.

Figure 3. Articles Reporting Quality Issues involving COVID-19 vaccines: Medicine Quality Monitoring Globe

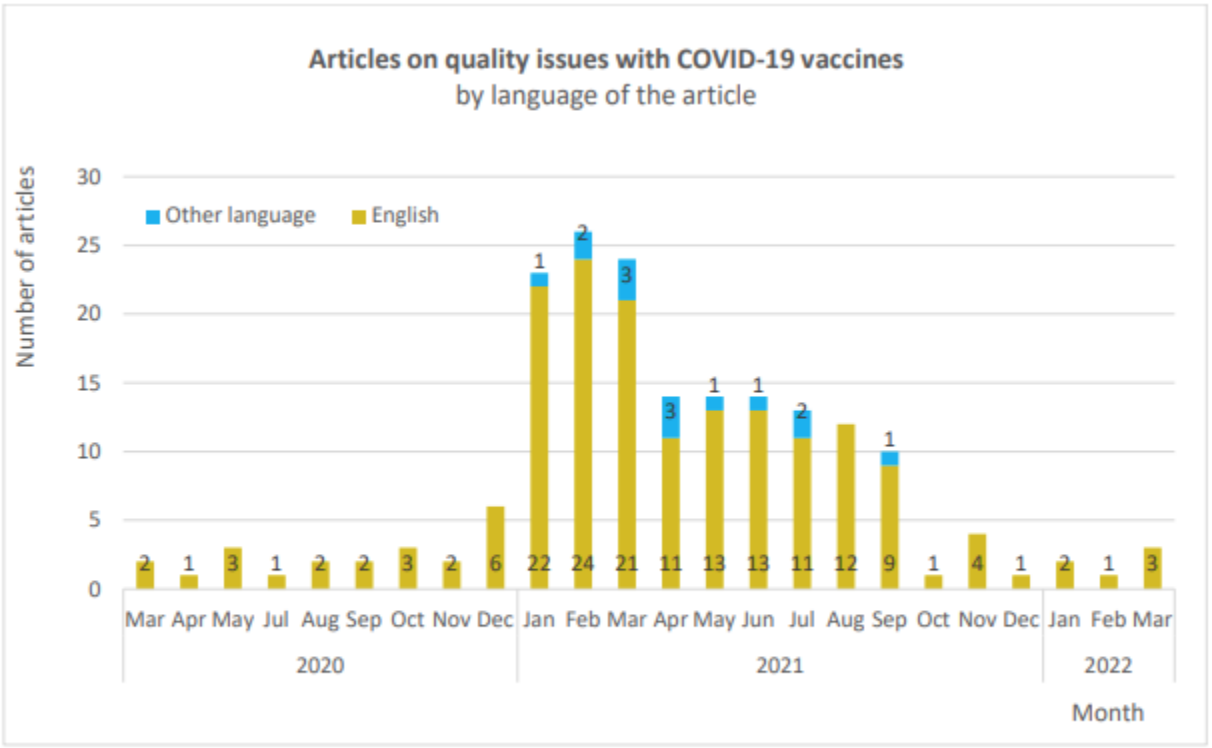


Figure 1. Number of articles on the Medicine Quality Monitoring Globe reporting quality issues with COVID-19 vaccines.

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.

Overview of COVID-19 Vaccine Development and Approvals

- 172 candidate vaccines are in clinical development: 46 in Phase 3 trials, and 11 in Phase 4 trials; Figure in COVID-19 Vaccines and Therapeutics Regulatory Tracker (Phases tab).
- 47 vaccines are approved in various countries, and 39 are at various stages of engagement with WHO for emergency use listing (EUL).
- The European Centre for Disease Prevention and Control (ECDC) and the European Medicines Agency (EMA) have issued a joint statement providing updated public health considerations on the use of the newly authorised adapted COVID-19 vaccines to support the planning of the autumn and winter vaccination campaigns.
- An adapted vaccine targeting BA.4 and BA.5 Omicron variants and original SARS-CoV-2 has been recommended for approval by EMA's human medicines committee (CHMP). The CHMP based its opinion on the clinical data available with Comirnaty Original/Omicron BA.1, which is closely related to BA.4/5. The vaccine is more effective at triggering an immune response against the BA.1 subvariant than Comirnaty and was as effective as Comirnaty against the original strain. Side effects were comparable to those seen with Comirnaty. In addition, immunogenicity data from laboratory studies provided supportive evidence that Comirnaty Original/Omicron BA.4-5 triggers adequate immunity against the strains it targets. The CHMP's opinion for Comirnaty Original/Omicron BA.4-5 is also based on data on its quality and manufacturing process, which confirmed that it meets the EU standards for quality.
- CARPHA-CRS has recommended all 11 COVID-19 vaccines approved for emergency use listing by the WHO to Member States to date — Table 9 (See List of CRS Recommended products), The team held a vaccine review webinar for country focal points to present the technical summary on Tuesday 20th September, 2022.
- COVID-19 primary series and first booster vaccines' performance against Omicron variant of concern (VOC) is provided from WHO's Weekly Epidemiology Update (17th August, 2022): Figure 5 and Table 3. *No table or updated information was published in the supplement dated 14th September.*
- On 16th September, 2022 the World Health Organization (WHO) published the twelfth version of the WHO Therapeutics and COVID-19: Living guideline which now contains 19 recommendations. This latest update provides updated recommendations for remdesivir, addresses the use of combination therapy with corticosteroids, interleukin-6 (IL-6) receptor blockers and Janus kinase (JAK) inhibitors, and modifies previous recommendations for the monoclonal antibodies sotrovimab and casirivimab-imdevimab (now strongly recommends **against** use).
- CARPHA issued a regulatory recommendation for market authorisation of casirivimab-imdevimab in July this year based on assessment by the European Medicines Agency (EMA), including clinical trials involving earlier strains of the virus. Since then, evidence has emerged where the medicine is not as effective against the Omicron variant, hence the recommendation will be reviewed by the CRS. The medicine remains authorized by the EMA for use.

Overview of COVID-19 Medicines: Regulatory Approvals and Prequalification

- 42 potential COVID-19 medicines: 4 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 (29th August 2022).

Additional Resources

- UMC New Course 2022 available to national and regional PV centre staff: Practical exercises in individual case causality assessment
- PAHO How to Make Use of Oversupply of COVID-19 Vaccine Doses to Close Gaps in Vaccination Coverage. 14 September 2022.
- CIOMS Cumulative Glossary, with a focus on Pharmacovigilance (Version 2.0)
- WHO pharmaceuticals newsletter - No. 3, 2022
- COVAX: Key learnings for future pandemic preparedness and response. 14 September 2022.
- Research: Substandard and falsified antibiotics: neglected drivers of antimicrobial resistance?
- WHO Open Short Course: Ultra-low temperature vaccine management
- UMC New Course 2022 available to national and regional PV centre staff: Regulatory aspects of pharmacovigilance
- Uppsala Reports Current Issue: Uppsala Reports - Latest issues
- EMA HUMAN MEDICINES HIGHLIGHTS Issue 161 August 2022
- PRAC Strategy on Measuring the Impact of Pharmacovigilance Activities
- WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2. 31 August 2022 Update.

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 232 therapeutic options. 29th July, 2022 (39th edition)** **URL: https://iris.paho.org/handle/10665.2/52719?locale-attribute=pt**

Resource	Description and Link
PAHO Periodic Updates on AEFIs	Consolidated regional and global information on adverse events following immunization (AEFI) against COVID-19 and other updates. 7th July, 2022 (37th Edition): URL: https://covid-19pharmacovigilance.paho.org/img/recursos/62f695e3330b6899d2b674105.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 9: COVID-19 Vaccines with WHO EUL and Other Regulatory Approvals

Vaccine/ WHO EUL Holder	Vaccine Platform	Dosing/ Storage ¥/ Approvals	NRA of record	WHO Approved Drug Product site(s)	Recommendation issued
WHO EUL status – Approved					
Recommended by 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. and 12 mo.); 2°C to 8°C (31 days / 10 wks§) CARPHA + 149 countries Full Market authorization by US FDA (16yrs+) WHO EUL For: Adults and adolescents ≥12 years old; Children 5-11 years old	European Medicines Agency	**Baxter Oncology GmbH**, Germany **BioNTech Manufacturing GmbH,** Germany **Pfizer Manufacturing Belgium NV,** Belgium **Novartis Pharma Stein AG,** Switzerland **Mibe GmbH Arzneimittel,** Germany **Delpharm Saint-Remy,** France **Sanofi-Aventis Deutschland GmbH,** Germany **Siegfried Hameln GmbH,** Germany. **Patheon Italia S.p.A**, Italy.	31st December 2020
			United States Food and Drug Administration	**Pharmacia & Upjohn Company LLC,** USA **Hospira Inc., a Pfizer company,** USA **Exelead, Inc.**, IN, United States **Exela Pharma Sciences, LLC, NC**, United States.	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.) CARPHA + 149 countries WHO EUL For: Adults ≥18 years old	Ministry of Food and Drug Safety, Korea	**SK Bioscience**, Republic of Korea **Universal Farma, S.L.** ("Chemo"), Spain **Catalent Anagni S.R.L.**, Italy. **IDT Biologika GmbH**, Germany. **Seqirus Pty Ltd.**, Australia. **CP Pharmaceuticals Limited**, UK. **Amylin Ohio LLC (AZ),** USA **Seqirus Pty Ltd.**, Australia.	15th February 2021
			European Medicines Agency	**SK Bioscience**, Republic of Korea **Universal Farma, S.L.** ("Chemo"), Spain **Catalent Anagni S.R.L.**, Italy. **IDT Biologika GmbH**, Germany. **Amylin Ohio LLC (AZ),** USA **CP Pharmaceuticals Limited**, UK.	16th April 2021
			Ministry of Health, Labour and Welfare, Japan	**Catalent Anagni S.R.L.**, Italy. **Daiichi Sankyo Biotech Co., LTD.**, Japan. **KM Biologics Co. Ltd.**, Japan. **Nipro Pharma Corporation Ise**, Japan	9th July 2021
			Therapeutic Goods Administration, Australia	**Catalent Anagni S.R.L.**, Italy. **IDT Biologika GmbH**, Germany. **Seqirus Pty Ltd.**, Australia. **CP Pharmaceuticals Limited**, UK.	9th July 2021

				Amylin Ohio LLC (AZ), USA **Siam Bioscience Co., Ltd**, Thailand	
			Health Canada	**Catalent Anagni S.R.L**., Italy. **IDT Biologika GmbH**, Germany. **Seqirus Pty Ltd**., Australia. **CP Pharmaceuticals Limited**, UK. **Amylin Ohio LLC (AZ),** USA	27th August 2021
			COFEPRIS (DP), Mexico ANMAT (DS), Argentina	**Liomont, S.A.,** Mexico	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.) CARPHA + 49 countries WHO EUL: Adults ≥18 yrs	Central Drugs Standard Control Organization, India	**Serum Institute of India Pvt. Ltd.,** S. No. 105–110, India **Serum Institute of India Pvt. Ltd.,** 212/2, India	15th February 2021
COVID-19 Vaccine (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) CARPHA + 113 countries Full market approval by Health Canada (23.Nov) WHO EUL: Adults ≥18 yrs	European Medicines Agency	**Janssen Biologics B.V**, The Netherlands **Janssen Pharmaceutica NV**, Belgium **Aspen SVP**., South Africa **Catalent Indiana LLC**., USA. **Grand River Aseptic Manufacturing Inc**., USA. **Catalent Anagni S.R.L**., Italy. **Merck Sharp & Dohme (MSD) Corp**., USA **Sanofi Pasteur,** France **Biological E Ltd,** India	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) CARPHA + 88 countries WHO EUL for: Adults and adolescents ≥12 yrs; Children 6-11 yrs	European Medicines Agency	**Rovi Pharma Industrial Services, S.A.,** Spain	30th April 2021
			United States Food and Drug Administration	**Baxter Pharmaceutical Solutions**, USA. **Catalent Indiana, LLC**, USA	6th August, 2021
			Ministry of Food and Drug Safety (MFDS), Rep. of Korea	**Samsung Biologics**, Republic 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.) CARPHA + 93 countries WHO EUL: Adults ≥18 yrs	National Medical Products Administration, China	**Beijing Institute of Biological Products Co., Ltd**., People's Republic of 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.) CARPHA + 56 countries	National Medical Products Administration, China	**Sinovac Life Sciences Co., Ltd**., People's Republic of China.	1st June 2021

		WHO EUL For: Adults ≥18 years old			
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.) CARPHA + 14 countries WHO EUL For: Adults ≥18 yrs old	Central Drugs Standard Control Organization, India	**Bharat Biotech International Limited**, 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 CARPHA + 6 countries WHO EUL: Adults ≥18 yrs	Central Drugs Standard Control Organization, India	**Serum Institute of India Pvt. Ltd.,** S. No. 105–110, India **Serum Institute of India Pvt. Ltd.,** 212/2, 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 CARPHA + 39 countries WHO EUL: Adults ≥18 yrs	European Medicines Agency	**Serum Institute of India Pvt. Ltd.,** S. No. 105–110, India	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 CARPHA + 10 countries WHO EUL: Adults 18 - 59 yrs	National Medical Products Administration, China	**CanSino Biologics Inc.,** People's Republic of China.	19th May 2022

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

References:

McGill COVID19 Vaccine Tracker. **COVID-19 Vaccines**. Updated 16th September, 2022. Available at: https://covid19.trackvaccines.org/.
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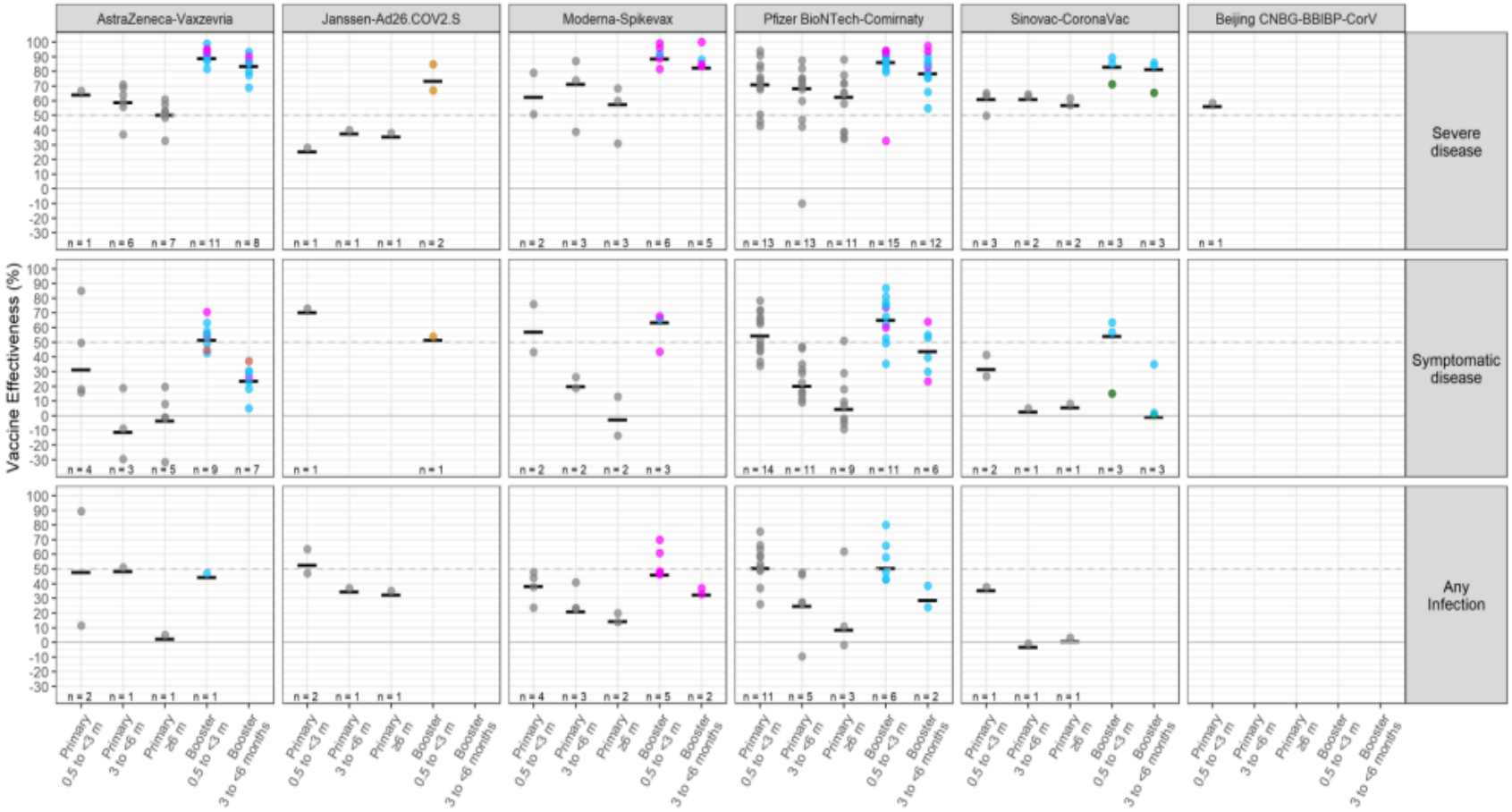
World Health Organization. **COVID-19 vaccine tracker and landscape**. WHO, Geneva, 16th September, 2022. Available at: Draft landscape of COVID-19 candidate vaccines (who.int).
World Health Organization. **Emergency Use Listing Procedure for Vaccines**. WHO, Geneva 2021. Available at: https://www.who.int/teams/regulation-prequalification/eul/eul-vaccines.

Figure 4: WHO Summary of Vaccine effectiveness (VE) of primary series and first booster vaccination against the 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 panel header. All booster VE estimates are for first booster dose. Severe disease includes hospitalization, and pneumonia; symptomatic disease includes disease of any severity level; any infection can include symptomatic and asymptomatic infection. Additional details on the methods for inclusion of the estimates in the plots provided in text.

Figure 5 summarizes the impact of the Omicron variant on absolute vaccine effectiveness (VE) over time, 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). Additional information on vaccine performance against VOCs can also be found in Annex 3.

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---17-august-2022

Table 10: WHO Summary of Neutralization Studies of Primary series and First booster vaccine performance against Omicron variant

		Omicron Sub-Lineage				
		BA.1	BA.2	BA.2.12.1	BA.3	BA.4/BA.5
Primary Series Vaccination						
WHO Emergency Use Listing (EUL) Qualified Vaccines	AstraZeneca-Vaxzevria/SII-Covishield	HNR_{12}	HNR_{2}	HNR_{1}		HNR_{1}
	Beijing CNBG-BBIBP-CorV	HNR_{8}	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_{49}	HNR_{7}	HNR_{1}	HNR_{1}	HNR_{2}
	Sinovac-CoronaVac	HNR_{8}	$\downarrow\downarrow\downarrow_{1}$			$\downarrow\downarrow\downarrow_{1}$
Other Vaccines (non-EUL)	Anhui ZL-Recombinant					
	Gamaleya-Sputnik V	HNR_{3}	HNR_{1}	HNR_{1}		HNR_{1}
	Chumakov-Covi-Vac	HNR_{2}				
Booster Vaccination (Primary Series Vaccine + Booster Vaccine)						
WHO Emergency Use Listing (EUL) Qualified	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	$\downarrow_{1}$				

Booster Vaccines	AstraZeneca-Vaxzevria/SII-Covishield + Pfizer BioNTech-Comirnaty	↓↓$_1$	↓↓$_1$		↓↓$_1$	
	Beijing CNBG-BBIBP-CorV + Beijing CNBG-BBIBP-CorV	↓↓to↓↓↓$_4$	HNR$_2$	HNR$_1$	↓↓$_1$	HNR$_1$
	Janssen-Ad26-COV2.S + Janssen-Ad26-COV2.S	HNR$_2$				
	Janssen-Ad26-COV2.S + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_2$				
	Moderna-Spikevax + Moderna-Spikevax	↓to↓↓↓$_8$	↓↓$_1$	↓↓$_1$	↓↓$_1$	↓↓↓$_1$
	Moderna-Spikevax + Pfizer BioNTech-Comirnaty	↓↓↓$_1$				
	Novavax-Nuvaxovid/SII – Covavax + Novavax-Nuvaxovid/SII - Covavax	↓↓$_1$				
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty	↓to↓↓↓$_{42}$	↓to↓↓↓$_{14}$	↓to↓↓↓$_3$	↓to↓↓$_4$	↓↓to↓↓↓$_6$
	Pfizer BioNTech-Comirnaty + Janssen-Ad26-COV2.S	↓$_2$				
	Pfizer BioNTech-Comirnaty + Moderna-Spikevax	↓to↓↓$_2$				
	Sinovac-CoronaVac + Sinovac-CoronaVac	↓to↓↓↓$_7$	↓↓to↓↓↓$_3$	↓↓$_1$	↓↓$_1$	↓↓to↓↓↓$_2$
	Sinovac-CoronaVac + Pfizer BioNTech-Comirnaty	↓↓$_2$	↓↓$_1$			
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↓↓↓$_2$	↓↓$_1$

Data as of 25 July 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.

• Studies that use samples collected more than seven days and less than six months after complete vaccination and that use an ancestral strain as the reference are included in the table.

• Studies of immunocompromised persons are excluded.

• 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 105, published 17th August, 2022. *No table or updated information was published in the supplement dated 14th September.* Available at: https://www.who.int/publications/m. See updated issue for references and additional information.

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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