VIGICARIB NEWS

19TH OCTOBER, 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

No reports of suspected adverse drug reaction, (ADRs), adverse events following immunization (AEFIs), or of substandard/ falsified / unregistered medical products were received by the Caribbean Regulatory System between 16th September and 15th October 2022, from Member States.

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 October 2022, there have been 1,560 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 (85.1%), and females (74.3%). The month with the greatest reporting activity for events occurring in December 2021: Figure 1. Two hundred and eighty-six reports (18.3%) were classified as Serious, including 59 where deaths were reported outcomes – Figure 2, Table 3.

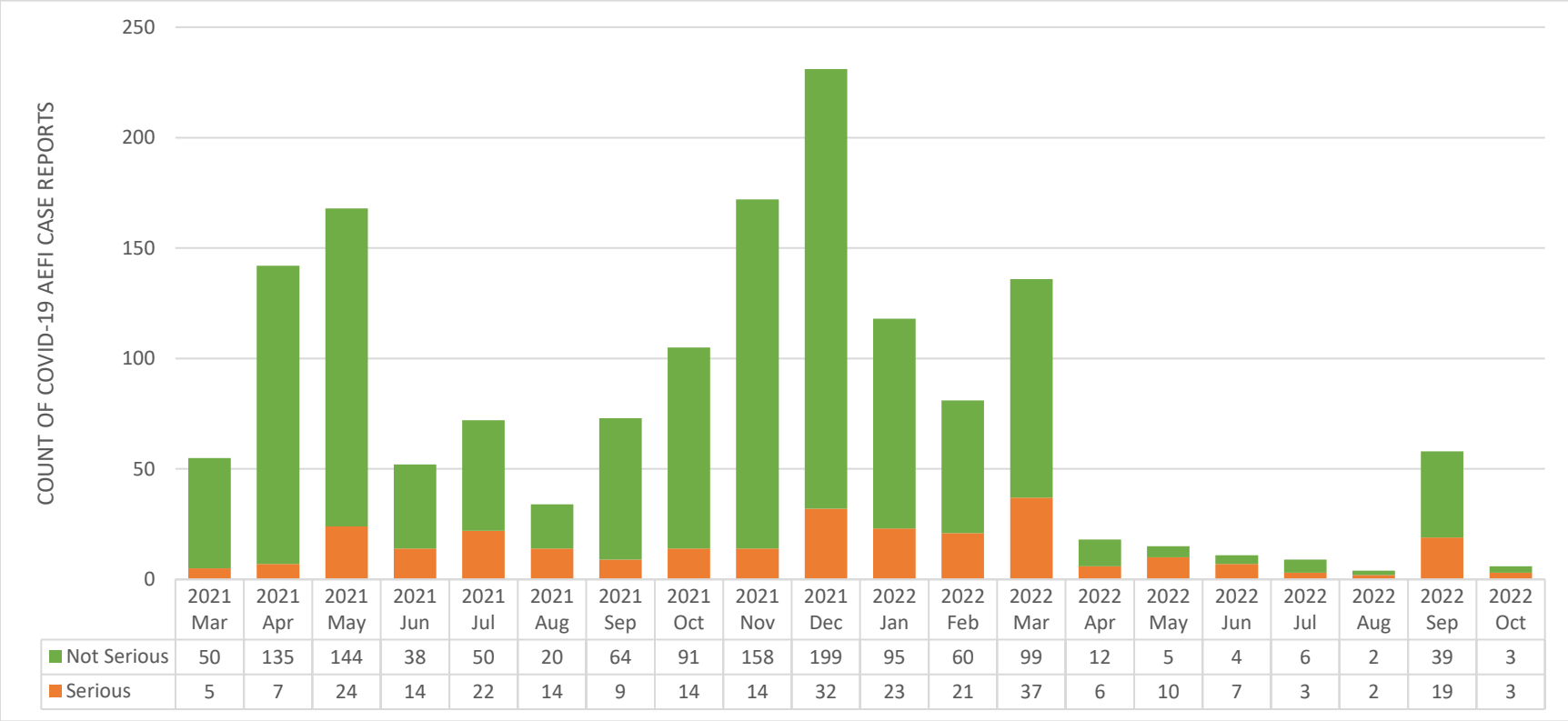
Six (6) additional COVID-19 AEFI case reports were submitted between 16th September and 15th October 2022 to the global database. The most commonly reported reactions were: headache, fever, dizziness, fatigue, chills and myalgia – Table 3. The downward trend of reporting of AEFIs may be due to multiple 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 October 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
Not Serious	50	135	144	38	50	20	64	91	158	199	95	60	99	12	5	4	6	2	39	3
Serious	5	7	24	14	22	14	9	14	14	32	23	21	37	6	10	7	3	2	19	3

* - *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 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 14th October 2022.

Country	Total Doses	Total AEFIs*	AEFIs per 100,000 doses¥	Total Serious AEFIs	Serious AEFIs per 100,000 doses
Barbados	379,843	603	158.7	85	22.4
Haiti	476,304	1	0.2	0	0
Jamaica	1,493,518	934	62.5	195	13.1
St Vincent and the Grenadines	72,875	22	30.2	6	8.2
Total	**2,422,540**	**1,560**	**64.4**	**286**	**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 October 2022 (N=1,560)

Patient age	Count	Percent
12 - 17 years	98	6.3%
18 - 44 years	729	46.7%
45 - 64 years	500	32.1%
65 - 74 years	108	6.9%
≥ 75 years	79	5.1%
Unknown	46	2.9%

Table 3: Top Reported Reactions for AEFIs in VigiBase to 15th October 2022 (N=1,560)

Top Reported Reactions	Count	Percent
PT: Headache	460	29.5%
PT: Pyrexia	304	19.5%
PT: Dizziness	303	19.4%
PT: Fatigue	249	16.0%
PT: Chills	244	15.6%
PT: Myalgia	223	14.3%
PT: Arthralgia	210	13.5%
PT: Nausea	177	11.3%
PT: Vaccination site pain	160	10.3%
PT: Malaise	149	9.6%

Figure 2: Total AEFI Case Reports by Seriousness (N = 1, 560)

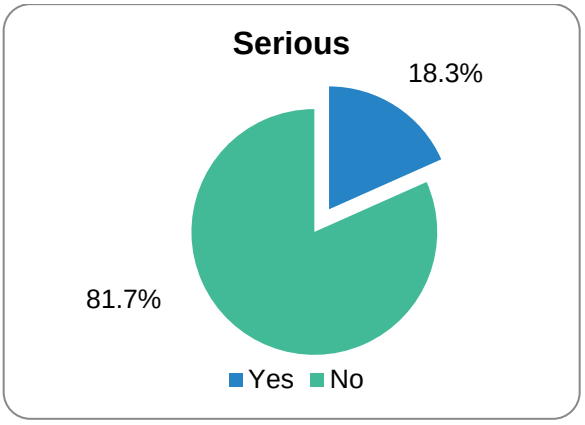


Table 4: Seriousness of Cases (n = 286)

Seriousness criteria	Count	Percent
Death	59	3.8%
Life threatening	20	1.3%
Caused/prolonged hospitalization	103	6.6%
Disabling/incapacitating	52	3.3%
Other medically important condition	104	6.7%

Note: Total exceeds 286 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 4,255 case reports from CARICOM countries with membership in the WHO Programme for International Drug Monitoring (PIDM): 1,560 COVID-19 AEFI case reports, 152 non-COVID AEFI case reports, and 2,449 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 October 2022, inclusive of reports submitted by the CRS on behalf of Member States. Most of the case reports involved adults – Table 6.

Between 16th September and 15th October 2022, fifteen (15) additional case reports were submitted to VigiBase from CARICOM: 6 AEFI reports, 9 ADR reports.

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

Countries	Count	Percent
Barbados	1,394	33.0%
Dominica	14	0.3%
Guyana	12	0.3%
Haiti	19	0.4%
Jamaica	2,055	48.6%
Saint Vincent and the Grenadines	502	11.9%
Suriname	221	5.2%
Virgin Islands (British)	8	0.2%

Table 6: ICSR Patient Ages Reported

Patient Age	Count	Percent
0 - 27 days	10	0.2%
28 days to 23 months	117	2.8%
2 - 11 years	96	2.3%
12 - 17 years	142	3.4%
18 - 44 years	1,352	32.0%
45 - 64 years	1,198	28.4%
65 - 74 years	429	10.2%
≥ 75 years	303	7.2%
Unknown	578	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 7th October, 2022, the Center for the State Control of Medicines, Equipment and Medical Devices (CECMED), Cuba issued a health alert of based on query to the Information Service is received via email on Medications, of the Medicines Surveillance Section of the CECMED, of a resident in Colombia, referring to a product marketed in Colombia, Eagle Eye Cuban eye drops, from the manufacturer LABORATORIOS FERCHOP SA, Havana, Cuba.

Four alerts from the Federal Commission for the Protection against Sanitary Risk (COFEPRIS), Mexico were issued between 3rd and 5th October, 2022, involving Substandard / Falsified / Unregistered Medical Products (SF) for: Limustin® (tacrolimus) 1mg capsules, Brospina® (buprenorphine) 0.3 mg/1 mL, injectable solution, Avastin® (bevacizumab) 400 mg/16 mL solution, Bedoyecta® Tri, FF injectable solution and Bedoyecta® FF capsules, which were detected in Mexico. The authority confirmed that products were either falsified, or had been adulterated (substandard).

Table 7: Medical Product Alert 2022

Date	Product	Company/ Manufacturer	Alert summary
3rd October, 2022 (Mexico)	Limustin® (tacrolimus) 1mg capsules	Landsteiner Scientific SA de CV	Lot numbers are not recognized: • 129B0219 expiration DEC 23 • I20J0121 expiration OCT 2023
5th October, 2022 (Mexico)	Brospina® (buprenorphine) 0.3 mg/1 mL, injectable solution	Laboratorios PISA, SA de CV	• The product with batch number B20J426 and expiration date JUN 23 is counterfeit, since it does not contain the active ingredient buprenorphine while the primary packaging it is original. • The product is characterised as falsified due to deficiency in the affixing of the label and amber vials with gray lines.
5th October, 2022 (Mexico)	Avastin® (bevacizumab) 400 mg/16 mL solution	Productos Roche, SA de CV	• H0209B01- counterfeit, it was not imported for sale in Mexico. Batch H0209B01 has the number 10140912 on the front face and a barcode with the number 7501009071815 on the side face of the secondary packaging. • B8607H03 and B8607H01- tampered with, original packaging, unknown content and use of removable cover glued with glue. • H02315B14- counterfeit, lot number not recognized as original.
5th October, 2022 (Mexico)	1. Bedoyecta® Tri, FF injectable solution, box with 5 prefilled syringes with 2 mL and 5 disposable needles. 2. Bedoyecta® FF capsules, box with 30 capsules	Laboratorios GROSSMAN, SA	• Bedoyecta® Tri, FF injectable solution with lot 179367, the batch number is not identified as manufactured by the company. • Bedoyecta® FF capsules with lot 318783, the number batch has an altered expiration date.

Date	Product	Company/ Manufacturer	Alert summary
7th October, 2022 (Cuba)	Eagle Eye Cuban eye drops	LABORATORIOS FERCHOP SA, Havana, Cuba	The product nor the manufacturer are registered by the drug regulatory authorities in Cuba and Colombia; the analysis of the evidence photographic; Falsified medication.

Global Medical Product Alerts

In October 2022, the WHO issued an additional medical product alert for four substandard products, identified in The Gambia. Substandard medical products are products that fail to meet either their quality standards or specifications and are, therefore "out of specification" The four products are Promethazine Oral Solution, Kofexmalin Baby Cough Syrup, Makoff Baby Cough Syrup and Magrip N Cold Syrup. To date, the stated manufacturer has not provided guarantees to WHO on the safety and quality of these products. The four 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°6/2022 **5th October, 2022**	1. Promethazine Oral Solution BP® (Promethazine) 2. Kofexmalin Baby Cough Syrup® (Pheniramine Maleate, Ammonium chloride, Menthol) 3. Makoff Baby Cough Syrup® (Chlorphenamine Maleate, Phenylephrine HBR, Dextromethorphan) 4. Magrip N Cold Syrup® (Paracetamol Phenylephrine HCL, Chlorphenamine Maleate)	Maiden Pharmaceuticals Limited (Haryana, India)	Laboratory analysis confirms that the products contain unacceptable amounts of diethylene glycol and ethylene glycol as contaminants.

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

- 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.
- All batches of these products should be considered unsafe until they can be analyzed by the relevant National Regulatory Authorities.
- The substandard products referenced in this alert are unsafe and their use, especially in children, may result in serious injury or 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: 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).
- 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).
- On 21st September, 2022 the WHO Prequalification Unit (PQT) added the first generic Molnupiravir to its prequalified medicine list, CV008 (molnupiravir 200mg hard capsules) manufactured by Hetero Labs Ltd, India.

- On 27th September, 2022 WHO updated its interim recommendations for the Novavax NVX-CoV2373 vaccine based on advice issued by the Strategic Advisory Group of Experts on Immunization (SAGE). Key updates include:
    - o Vaccine performance- Post authorization surveillance data for safety including myocarditis and pericarditis, angioedema, GBS and paranesthesia and hypoesthesia, data for adolescents and booster administration
    - o Intended use- Change in authorization of the age indication from age 12 years upwards o New sub-section for the inclusion of the adolescent age group
    - o Administration- Potential 8-week gap between primary doses
    - o Updated wording for additional doses to the primary series
    - o Booster doses- Updated wording. New booster data, and for clarification that no data for booster doses for adolescents is currently available
    - o Interchangeability with other COVID-19 vaccines in (heterologous schedules)- Updated wording.

- On 7th October, 2022, Health Canada authorized a second bivalent COVID-19 vaccine booster, the updated version of the Pfizer-BioNTech Comirnaty COVID-19 vaccine, targeting the Omicron BA.4 and BA.5 subvariants. It is authorized for use as a booster dose in individuals 12 years of age and older. Health Canada conducted an independent scientific review of the evidence that has determined that this booster is safe and effective.

- Swissmedic, Switzerland on 10th October, 2022 has temporarily authorised Comirnaty Bivalent Original / Omicron BA.1 (tozinameran / riltozinameran), containing messenger ribonucleic acid (mRNA) against two coronavirus variants. A booster vaccination with this vaccine showed higher antibody concentrations against Omicron variant BA.1 than one with original Comirnaty in studies. The side effects profile in the study was similar to that of the original vaccine.

- On 12th October, 2022, the U.S. Food and Drug Administration to authorize the use of the Moderna COVID-19 Vaccine, Bivalent and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent as a single booster dose in younger age groups. The Moderna COVID-19 Vaccine, Bivalent is authorized in children down to six years of age and the Pfizer-BioNTech COVID-19 Vaccine, Bivalent in children down to five years of age. FDA relied on immune response and safety data that it had previously evaluated from a clinical study in adults of a booster dose of a bivalent COVID-19 vaccine that contained a component of the original strain of SARS-CoV-2 and a component of omicron lineage BA.1. The FDA considers such data as relevant and supportive of vaccines containing a component of the omicron variant BA.4 and BA.5 lineages.

- Health Canada on 13th October, 2022, approved Actemra (tocilizumab) for treating adults with severe COVID-19 for treating adults with severe COVID-19 who are in hospital who are receiving systemic corticosteroids and need supplemental oxygen, mechanical ventilation (non-invasive or invasive) or extracorporeal membrane oxygenation (ECMO). The authorization was based on one pivotal clinical study, RECOVERY, which met its primary outcome by demonstrating a clinically and statistically significant reduction in the risk of death by day 28 after treatment.

- COVID-19 primary series and first booster vaccines' performance against Omicron variant of concern (VOC) is provided from WHO's Weekly Epidemiology Update (21st September, 2022): Figure 5 and Table 3. *No table or updated information was published in the supplement dated 12th October.*

Overview of COVID-19 Medicines: Regulatory Approvals and Prequalification

- 43 potential COVID-19 medicines: 4 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 (3rd October, 2022).

Additional Resources

- UMC New Course 2022 available to national and regional PV centre staff: Practical exercises in individual case causality assessment
- WHO Virtual meeting of the WHO Programme for International Drug Monitoring (PIDM) and other partners: 20 October 2022.
- 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.
- EMA. Codeine with ibuprofen: PRAC adds warning for serious renal and gastrointestinal harms. 30 September 2022.
- WHO. Status of COVID-19 Medicines and Active Pharmaceutical Ingredients (APIs). 7 October 2022.
- WHO World Antimicrobial Awareness Week 2022 Campaign Guide.
- PAHO News: Countries approve policy to strengthen regulatory systems for medicines and other health technologies in the Americas
- Health Canada: Guidance on releasing information from adverse reaction and medical device incident reports to the public.
- Publication: Regulatory work-sharing initiative in Africa: ZaZiBoNa, past, present and future
- Article: Missing data on accessibility of children's medicines

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 237 therapeutic options. 3rd October, 2022 (40th edition) URL: https://iris.paho.org/handle/10665.2/52719?locale-attribute=pt
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 9: COVID-19 Vaccines with WHO EUL and Other Regulatory Approvals

Vaccine/ WHO EUL Holder	Vaccine Platform	Dosing/ Storage ¥/ Approvals	NRA of record	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**. (PBS/Sucrose) and **12 mo**. (Tris/Sucrose)]; 2°C to 8°C (31 days / 10 wks§) CARPHA + 149 countries Full Market authorization by US FDA (16yrs+) 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.) CARPHA + 149 countries WHO EUL For: Adults ≥18 years 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.) CARPHA + 49 countries WHO EUL for: Adults ≥18 years 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) CARPHA + 113 countries Full market approval by Health Canada WHO EUL For: Adults ≥18 years old	European Medicines Agency	12th March 2021;
Elasomeran; SPIKEVAX™ **COVID-19 mRNA Vaccine (nucleoside**	mRNA-based in lipid nanoparticle (LNP)	2 doses I.M. -25°C to -15°C (9 mo.);	European Medicines Agency	30th April 2021

modified)/ Moderna Biotech and ModernaTX, Inc		2-8°C (30d) or 9-25°C (12h) CARPHA + 88 countries WHO EUL For: Adults and adolescents ≥12 years old; Children 6-11 years old	United States Food and Drug Administration Ministry of Food and Drug Safety (MFDS), Rep. of Korea	6th August, 2021 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 For: Adults ≥18 years 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.) CARPHA + 56 countries WHO EUL For: Adults ≥18 years 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.) CARPHA + 14 countries WHO EUL For: Adults ≥18 years 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 CARPHA + 6 countries WHO EUL For: Adults ≥18 years 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 CARPHA + 40 countries WHO EUL For: Adults ≥18 years 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 CARPHA + 10 countries WHO EUL for: Adults 18 to 59 years old	National Medical Products Administration	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 12th October, 2022. Available at: https://covid19.trackvaccines.org/

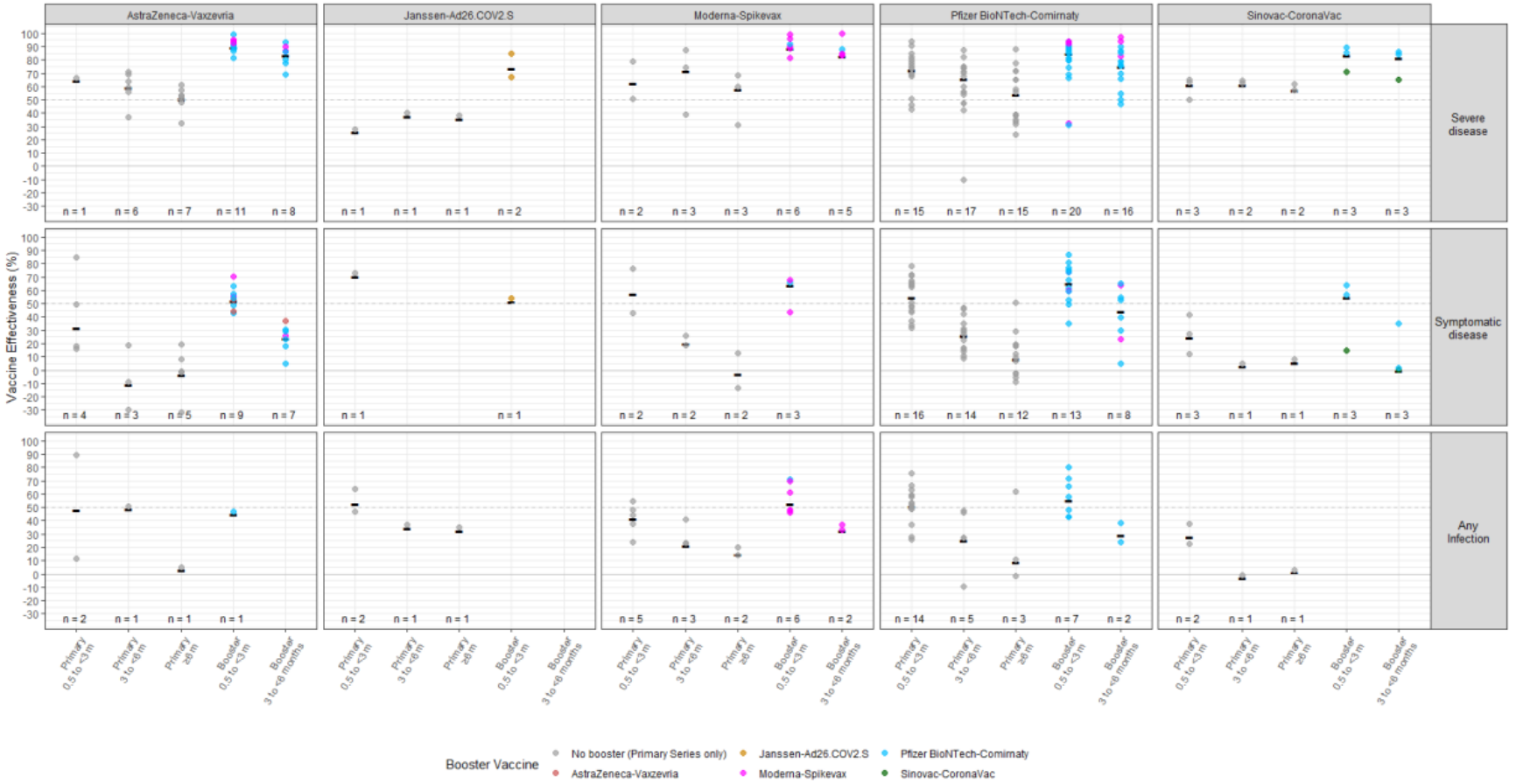
World Health Organization. **Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process**. Updated 21st September, 2022. WHO, Geneva, 2020. Available at: https://www.who.int/teams/regulation-prequalification/eul/covid-19

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, 14th October, 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 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 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---21-september-2022

Table 4: WHO Summary of Neutralization Studies of Primary series and First booster vaccine performance against Omicron variant of concern

		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_{53}	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$\downarrow\downarrow\downarrow_{4}$	HNR_{2}	HNR_{1}		$\downarrow\downarrow_{1}$	HNR_{1}
	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	$\downarrow$to$\downarrow\downarrow\downarrow_{2}$					
	Moderna-Spikevax + Moderna-Spikevax	$\downarrow$to$\downarrow\downarrow\downarrow_{9}$	$\downarrow\downarrow_{1}$	$\downarrow\downarrow_{1}$		$\downarrow\downarrow_{1}$	$\downarrow\downarrow\downarrow_{2}$
	Moderna-Spikevax + Pfizer BioNTech-Comirnaty	$\downarrow\downarrow\downarrow_{1}$					
	Novavax-Nuvaxovid/SII – Covavax + Novavax-Nuvaxovid/SII - Covavax	$\downarrow\downarrow_{1}$					
	Pfizer BioNTech-Comirnaty + Pfizer BioNTech-Comirnaty	$\downarrow$to$\downarrow\downarrow\downarrow_{44}$	$\downarrow$to$\downarrow\downarrow\downarrow_{15}$	$\downarrow$to$\downarrow\downarrow\downarrow_{3}$	$\downarrow\downarrow_{1}$	$\downarrow$to$\downarrow\downarrow_{4}$	$\downarrow\downarrow$to$\downarrow\downarrow\downarrow_{7}$
	Pfizer BioNTech-Comirnaty + Janssen-Ad26-COV2.S	$\downarrow_{2}$					

		BA.1	BA.2	BA.2.12.1	BA.2.75	BA.3	BA.4/BA.5
	Pfizer BioNTech-Comirnaty + Moderna-Spikevax	↓to↓↓$_2$			↓↓↓$_1$		↓↓↓$_1$
	Sinovac-CoronaVac + Cansino-Convidecia	↓↓$_1$					
	Sinovac-CoronaVac + Sinovac-CoronaVac	↓↓to↓↓↓$_7$	↓↓to↓↓↓$_3$	↓↓$_1$		↓↓$_1$	↓↓to↓↓↓$_3$
	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↓↓↓$_2$	↓↓$_1$
	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 Orig/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 19th September2022

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 110, published 21st September, 2022. Available at: https://www.who.int/publications/m. *No table or updated information was published in the supplement dated 12th October.* 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.

Editor: Dr. Rian Marie Extavour
Contributions by: Mrs. Kerrine Ottley, Mrs. Cadell Monrose-Forde

Email: VigiCarib@carpha.org

Website: https://carpha.org/What-We-Do/CRS/VigiCarib