CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AND OTHER UPDATES

L Report

WASHINGTON, D.C.

Updated: 18 October 2024

OPS Organización Panamericana de la Salud
Organización Mundial de la Salud Oficina Regional para las Américas
En colaboración con Canadá

CONTENTS

EDITORIAL

Dear Readers:

We are pleased to share with you that we have reached the 50th edition of the newsletter *Consolidated Regional and Global Information on Adverse Events Following Immunization (AEFI) and Other Updates*

This newsletter came about as part of Pan American Health Organization/World Health Organization (PAHO/WHO) support for the regulatory systems of the Americas region during the COVID-19 pandemic, to technically support the proper introduction and surveillance of the safety and efficacy of vaccines and medications.

The first newsletter was published on 11 February 2021; on an initially weekly basis and with outreach specifically targeting COVID-19 vaccines. In 2024, after 46 editions, the scope was expanded to include other vaccines relevant to the region.

Many people have contributed to the success of this newsletter since its inception, and we are infinitely grateful for their collaboration. We would particularly like to highlight the invaluable and ongoing support of the following PAHO/WHO advisors, technical officers, and consultants: María Teresa Ibarz, José Luis Castro, María José Alfonso, Carolina Rancaño, Diego Macías, Gabriela Carrasco, Robin Rojas Cortés, María Luz Pombo, Tomás Pippo, María Almirón, Desirée Pastor, Felipe Molina, Gabriely Mota, Katia Uchimura, and Rayane Barbosa.

This initiative was financially supported by *Global Affairs Canada (GAC)* as part of the project “Strengthening Local Manufacturing Capacities to Improve Equitable Access to Vaccines in Latin America and the Caribbean."

We are committed to continuing to provide consolidated regional and global information on AEFIs and other relevant updates on the efficacy and safety of vaccines used in our region.

Editorial Team

Mexico

COVID-19 vaccines

As of 7 September 2024, 133,982,641 doses of COVID-19 vaccine had been administered in Mexico since the start of vaccination. During this period, a total of 40,223 AEFIs were reported, of which 3.20% (1,285) were classified as serious. Most serious (57%) and non-serious (71%) AEFIs occurred in women. Non-serious AEFIs occurred mainly in the age group 30-39, while serious AEFIs occurred mostly in people over age 60. The main signs and symptoms presented in serious AEFIs were headache (43.19%), asthenia (37.48%), and dyspnea (28.90%).

Number and Notification Rate of AEFIs by Vaccine through 07 September 2024 (n= 40 223).

Vaccine	Total Doses Given	Non-serious AEFIs		Serious AEFIs		Total AEFIs	
		No.*	Rate**	No.*	Rate**	No.*	Rate**
Pfizer-BioNTech	35,874,667	19 951	0.56	460	0.01	20 411	0.57
SERUM-AstraZeneca	49,783,383	12,800	0.26	486	0.01	13,286	0.27
SINOVAC	18,456,001	1,681	0.09	110	0.01	1,791	0.10
Sputnik-V	15,177,016	1,220	0.08	63	000	1,183	0.08
Cansino	10,257,589	1,663	0.16	72	0.01	1,735	0.17
Janssen	1,242,211	830	0.67	9	0.01	839	0.68
Moderna	3,181,399	630	0.20	54	0.02	684	0.21
CIGB-66* **	10,375	222	21.40	21	2.02	243	23.42
Unknown	-	7	-	2	-	9	-
Vaccination abroad	-	34	-	8	-	42	-
Total	**133,982,641**	**39 038**	**0.29**	**1,285**	**0.01**	**40 ,23**	**0.30**

*Number of AEFIs
**Rate per 1 000 doses administered
***The Abdala COVID-19 vaccine is based on the recombinant protein of the receptor-binding domain (RBD) of the SARS-CoV-2 virus, expressed in *Pichia pastoris* yeast and adjuvanted with aluminum hydroxide.

Source: Epidemiología, Dirección de Vigilancia Epidemiológica de Enfermedades Transmisibles. Reporte ESAVI COVID-19 Agosto 2024. 19 September 2024. Available from: https://www.gob.mx/cms/uploads/attachment/file/944580/REPORTEESAVIDVEETAGOSTO2024.pdf. Data reproduced by PAHO/WHO.

Mpox vaccines

Vaccine effectiveness of 3rd generation Mpox vaccines against mpox and disease severity: a systematic review and meta-analysis

On 21 June, this systematic review was released, with the objective of measuring vaccine effectiveness (VE) of 3rd and 4th generation mpox vaccines (MVA-BN: Modified vaccinia Ankara, LC16m8, OrthopoxVac) in the global population in preventing infection, hospitalization, and death.

VE was stratified by 1-dose and 2-doses and post-exposure prophylaxis (PEP). Human studies of vaccine effectiveness for any vaccine with protection against mpox including outbreak investigations, case-series, prospective cohorts, retrospective cohorts and randomized control trials since 1970 that measured vaccine efficacy or effectiveness in humans.

The review identified 33 studies of 3rd generation vaccines, 32 of which were MVA-BN. Two additional studies re-analyzed existing data. Most of these studies were focused on gay, bisexual, or other men who have sex with men between the ages of 18-49, between May and October of 2022.

VE for disease prevention of 1 dose of MVA-BN was 76% (95% CI 64–88%) from 12 studies. VE of two doses was 82% (95% CI 72–92%) from six. Additionally, vaccination may also have some benefit in preventing hospitalization with a VE of 67%.

VE of PEP with MVA-BN against mpox was 20% (95% CI -24–65%) from seven studies. All VE are calculated from random effects estimates.

Eighteen of the 33 studies (55%) were rated as poor, three (9%) as fair and 12 (36%) as good quality. Studies included in the meta-analysis had higher quality: 11 of the 16 (69%) were rated as good quality.

All the above studies dealt with MVA-BN; there were no studies published for OrthopoxVac or LC16. There were not enough events to evaluate impact on mortality. It appears the VE is not impacted by route of administration, though only two studies addressed this. Most of these studies were from May to October 2022, in young cisgender-men who are gay, bisexual, or other men who have sex with men, and this limits the generalizability of these findings.

The authors conclude that one and two doses of MVA-BN would be highly effective at preventing mpox. However, PEP may have low effectiveness, which could be related to its time of administration. The effectiveness of vaccines remains an important topic of study, especially in immunocompromised groups and children.

Source: Pischel L, Martini BA, Yu N, Cacesse D, Tracy M, Kharbanda K, Ahmed N, Patel KM, Grimshaw AA, Malik AA, Goshua G, Omer SB. Vaccine effectiveness of 3rd generation mpox vaccines against mpox and disease severity: A systematic review and meta-analysis. Vaccine. 2024 Nov 14;42(25):126053. doi: 10.1016/j.vaccine.2024.06.021. Epub 2024 Jun 21. PMID: 38906763.

Prospective Monitoring of Adverse Events Following Vaccination with the Vaccine MVA-BN Administered to a Canadian Population At Risk of Mpox: A Canadian Immunization Research Network study

The Canadian National Vaccine Safety Network (CANVAS) conducted prospective safety surveillance during public health vaccination campaigns with the mpox vaccine MVA-BN (Modified Vaccinia Ankara – Bavarian Nordic) in Toronto, Ontario, and British Columbia from 15 September 2022 to 14 April 2023, in at-risk populations including men who have sex with men and sex workers.

Vaccinated individuals were eligible if they received a first or second dose of MVA-BN within the preceding 8 days and had not received other vaccines within two weeks. Control participants were eligible if they had never received any dose of MVA-BN and had not received any other vaccine within two weeks and were recruited from a concurrent CANVAS project evaluating COVID-19 boosters and influenza vaccination, conducted over the fall of 2022.

A questionnaire was emailed to participants eight days after vaccination to collect demographic data, medical history, and document new or worsening symptoms. All vaccinated participants were asked about the occurrence of local injection site reactions. The other primary outcome was any other symptom or health event that prevented work/school or required medical assessment.

Those who reported a health event that prevented work/school or required medical assessment were then asked about a list of potential symptoms. Vaccinated and control participants that reported the need for a medical assessment were contacted by telephone to collect additional data on their clinical presentation, diagnosis received, and whether it was felt to be related to vaccination. A follow-up questionnaire was sent to all vaccinated participants 30 days after vaccination to document health events resulting in an emergency department visit or hospitalization occurring out to 30 days post vaccination. Controls completed one questionnaire that collected similar information over the preceding seven days.

In a subgroup analysis, baseline characteristics and outcomes were compared between HIV infected and uninfected vaccinated participants, with symptom frequency compared using the Chi-squared or Fisher's exact test, as appropriate.

For the matched analysis, vaccinated cases and controls were matched 1:1 based on sex, gender, age group and province. Participants that could not be matched were excluded. Symptom frequency was compared between matched cases and controls using the Chi-squared test or Fisher's exact test, as appropriate.

Cutaneous reactions were defined as any vesicular or non-vesicular rash, other than reports of bruising. Cardiac reactions were defined as chest pain, tightness or pressure, or palpitations. Neurological reactions were defined as seizures; face, arm, or leg paralysis, or weakness or new difficulty walking; confusion or acute change in personality or behavior; or trouble urinating or defecating. Headache or migraine, and paresthesia (numbness or tingling), were considered separately.

A total of 1173 vaccinated participants completed a questionnaire at seven days. Of these participants, 75% (n = 878) went on to complete a 30-day questionnaire. Mild to moderate pain at the injection site was reported by 60% of vaccinated participants.

Among vaccinated participants, 8.4% were HIV positive and when compared to HIV negative vaccinated individuals, local injection site reactions were less frequent in those with HIV (48% vs 61%, p = 0.021), but health events preventing work/school or requiring medical assessment were more frequent (7.1% vs 3.1%, p = 0.040).
Health events interfering with work/school, or requiring medical assessment were less common in the vaccinated group than controls (3.3% vs. 7.1%, p < 0.010). No participants were hospitalized within seven or 30 days of vaccination. No cases of severe neurological disease, skin disease, or myocarditis were identified.

The authors conclude that these results would demonstrate that the MVA-BN vaccine appears safe when used for mpox prevention, with a low frequency of severe adverse events and no hospitalizations observed.

Source: Muller MP, Navarro C, Wilson SE, Shulha HP, Naus M, Lim G, Padhi S, McGeer A, Finkelstein M, Liddy A, Bettinger JA; for CANVAS. Prospective monitoring of adverse events following vaccination with Modified vaccinia Ankara - Bavarian Nordic (MVA-BN) administered to a Canadian population at risk of Mpox: A Canadian Immunization Research Network study. Vaccine. 2024 Jan 25;42(3):535-540. doi: 10.1016/j.vaccine.2023.12.068. Epub 2024 Jan 9. PMID: 38199921.

Respiratory Syncytial Virus (RSV) vaccines

Efficacy and safety of bivalent RSVpreF maternal vaccination to prevent RSV Illness in Japanese infants: subset analysis from the pivotal randomized phase 3 MATISSE trial

On 8 June, this subgroup analysis was released from the global, phase 3, randomized, double-blind, placebo-controlled MATISSE (Maternal Immunization Study for Safety and Efficacy) trial that evaluated participants enrolled in Japan.
Pregnant women 24–36 weeks' gestation were randomized 1:1 to receive RSVpreF or placebo. Maternal safety endpoints included local reactions/systemic events within seven days, adverse events (AEs) through one month, and serious AEs (SAEs) through six months after vaccination. In infants born to participants, safety endpoints included specific birth outcomes, AEs through one month after birth, and SAEs and newly diagnosed chronic medical conditions through 12 or 24 months after birth.
Vaccine efficacy in infants was assessed against RSV-positive, medically attended LRTI (RSV-MA-LRTI) and severe RSV-MA-LRTI through 180 days after birth.
The results of this subgroup in Japan report that 230 maternal participants received RSVpreF and 232 received placebo; 218 and 216 infants born to these mothers, respectively, were analyzed. Observed vaccine efficacy (95% CIs) against infant RSV-MA-LRTI within 90 and 180 days after birth was 100.0% (30.9, 100.0; RSVpreF, 0 cases; placebo, 7 cases) and 87.6% (7.2, 99.7; RSVpreF, 1 case; placebo, 8 cases), respectively. Vaccine efficacy (95% CIs) against severe RSV-MA-LRTI within 90 and 180 days was 100.0% (−140.9, 100.0; RSVpreF, 0 cases; placebo, 3 cases) and 75.1% (−151.5, 99.5; RSVpreF, 1 case; placebo, 4 cases), respectively. No safety concerns

were identified. AE rates ≤1 month after vaccination/birth were similar in the RSVpreF (maternal, 16.1%; infant, 48.6%) and placebo (19.8%; 50.5%) groups. Preterm birth rates were also similar (RSVpreF, 3.2%; placebo, 6.0%).
The authors conclude that the safety and efficacy data in Japanese participants were consistent with overall MATISSE results, supporting the efficacy of maternal RSVpreF vaccination against severe MA-RSV-LRTI/MA-RSV-LRTI in infants, with no safety concerns.

Source: Otsuki T, Akada S, Anami A, Kosaka K, Munjal I, Baber J, Shoji Y, Aizawa M, Swanson KA, Gurtman A. Efficacy and safety of bivalent RSVpreF maternal vaccination to prevent RSV illness in Japanese infants: Subset analysis from the pivotal randomized phase 3 MATISSE trial. Vaccine. 2024 Sep 17;42(22):126041. doi: 10.1016/j.vaccine.2024.06.009. Epub 2024 Jun 8. PMID: 38853036.

Dengue vaccine

Safety signal detected: anaphylaxis after attenuated dengue vaccine (TAK-003) - Brazil, 1 March 2023-11 March 2024

On 4 October, a study was released with the aim of describing cases of anaphylaxis following administration of the attenuated dengue vaccine (TAK-003) in Brazil, from 1 March 2023 to 11 March 2024. A descriptive study of anaphylaxis cases following TAK-003 was conducted, as reported in the National System for Surveillance of Adverse Events Following Immunization (AEFI). Percentages and notification rates of AEFI per million doses administered (DA) were calculated.

In total, 380 358 doses of TAK-003 were administered, and 626 AEFIs were reported. Of these, 85 were cases of immediate hypersensitivity, with 24 (63.1 cases per million DA) being anaphylaxis, including three anaphylactic shocks. For 10 (41.7 %) cases, reactions began within 15 min after vaccination. No deaths related to anaphylaxis were reported.

The authors state that the observed value exceeds estimates of vaccine allergic reactions, including immediate hypersensitivity reactions, which range from 1 in 50 000 to 1 in 1 000 000 doses administered.

The first clinical studies of TAK-003 did not indicate the occurrence of anaphylaxis or anaphylactic shock after 18 273 doses administered. In its 2022 Risk Management Plan, the pharmaceutical company reported that the vaccine contains human serum albumin, a component that has been associated with cases of hypersensitivity reactions, such as urticaria, in certain situations. These reactions have been observed primarily following the administration of rabies vaccines

The authors mention that human serum albumin could be a component to evaluate in the occurrence of anaphylaxis in the present study, as individuals with a history of allergic reactions to albumin-containing products may have a higher risk of an allergic reaction to TAK-003. To date, no scientific evidence has been published identifying other components of TAK-003 with the potential to cause hypersensitivity reactions through IgE-mediated or non-IgE-mediated mechanisms

Although post-vaccination anaphylaxis may occur more frequently than with other vaccines, no deaths have been reported. The Ministry of Health has continued the vaccination campaign, reinforcing guidelines to ensure its safety and publishing recommendations for intensifying actions for safe vaccination, including healthcare professional training and post-vaccination observation.

Source: Percio J, Kobayashi CD, Silva RMA, Marinho AKBB, Capovilla L, Andrade PHS, da Nóbrega MEB, Cabral CM, de Moraes MB, Werneck GL, Fernandes EG. Safety signal detected: Anaphylaxis after attenuated dengue vaccine (TAK-003) - Brazil, March 1, 2023-march 11, 2024. Vaccine. 2024 Oct 4;42(26):126407. doi: 10.1016/j.vaccine.2024.126407.

COVID-19 Vaccine

Brazil's National Health Surveillance Agency approves standard for updated COVID-19 vaccines

On 18 September, Brazil's National Health Surveillance Agency (ANVISA) reported the approval of Normative Instruction 316/2024, which specifically provides for the updating of COVID-19 vaccines to be used in Brazil. This standard aligns with international standards regarding the strains that should be included, in accordance with the "WHO Statement on the antigen composition of COVID-19 vaccines" published on 26 April 2024 and establishes the rules for updating these vaccines.

The regulatory process began at the end of May of this year, and the public consultation period ended on 5 August.

Additional information available from: https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2024/anvisa-aprova-normas-sobre-atualizacao-das-vacinas-contra-covid-19

European Medicines Agency Authorizes COVID-19 Vaccine Comirnaty KP.2

On 26 September, the European Medicines Agency (EMA) licensed the Comirnaty KP.2 vaccine, which contains an mRNA molecule with instructions to produce a protein of the Omicron KP.2 subvariant of SARS-CoV-2.

In the product information released by the EMA, it is indicated that the three previous Comirnaty adapted vaccines are still available:

- Comirnaty Original/Omicron BA.4-5 contains tozinameran and famtozinameran,
- Comirnaty Omicron XBB.1.5 contains raxtozinameran.
- Comirnaty JN.1 contains bretovameran.

The indication for Comirnaty is still the prevention of coronavirus disease 2019 (COVID-19) in people from the age of 6 months.

Additional information available from: https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/coronavirus-disease-covid-19/covid-19-medicines and

https://www.ema.europa.eu/en/documents/overview/comirnaty-epar-medicine-overview_en.pdf

Influenza vaccine

Recommendations announced for influenza vaccine composition for the 2025 southern hemisphere influenza season

On 27 September, the WHO released the recommendations for the viral composition of influenza vaccines for the 2025 influenza season in the southern hemisphere, which are summarized below.

- **Egg-based vaccines:**
  - an A/Victoria/4897/2022 (H1N1)pdm09-like virus,
  - an A/Croatia/10136RV/2023 (H3N2)-like virus; and
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

- **Cell culture-, recombinant protein- or nucleic acid-based vaccines**
  - an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
  - an A/District of Columbia/27/2023 (H3N2)-like virus; and
  - a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

- **Tetravalent vaccines:**
  The recommendation for the B/Yamagata lineage component of quadrivalent influenza vaccines remains unchanged from previous recommendations:
  - a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Additional information available from: https://www.who.int/news/item/27-09-2024-recommendations-announced-for-influenza-vaccine-composition-for-the-2025-southern-hemisphere-influenza-season

Mpox vaccine

Mexico's Federal Commission for Protection against Health Risks authorized the Smallpox and Mpox vaccine Jynneos

On 12 September, the Federal Commission for Protection against Health Risks (COFEPRIS) announced that after a proactive regulatory monitoring process with the company Bavarian Nordic, it had authorized the registration of the smallpox and mpox vaccine Jynneos, concluding that the vaccine meets the quality, safety, and efficacy requirements to issue the registration allowing it to be marketed in Mexico. The product was authorized for primary vaccination or revaccination of persons 18 years of age and older at high risk of exposure to the virus. It is not recommended for use in the general population, including children and pregnant or breastfeeding women.

Additional information available from: https://www.gob.mx/cofepris/es/articulos/cofepris-autoriza- registro-sanitario-a-vacuna-contra-mpox?idiom=es

Vaccines

Upcoming meeting of WHO's Global Advisory Committee on vaccine safety

The Global Advisory Committee on Vaccine Safety (GACVS) will hold its next meeting in Geneva on 12–14 November 2024. The last GACVS meeting, the 47th, was held virtually on 15–17 May 2024.

At this next meeting, the members of the GACVS Will discuss key aspects related to vaccine safety and policies.

Additional information available from: https://www.who.int/publications/i/item/who-wer-9932-407-414#:~:text=The%20next%20GACVS%20meeting%20will,on%2012%E2%80%9314%20November%202024

COVID-19 vaccine

Next meeting of the WHO Technical Advisory Group on COVID-19 vaccine composition

The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) announced that its next decision-making meeting is scheduled for December 2024, after which a statement on COVID-19 vaccine antigen composition and an accompanying data annex will be published on the WHO website.

To inform decisions on COVID-19 vaccine antigen composition, the TAG-CO-VAC reviews data on the genetic evolution of SARS-CoV-2 and the antigenic characteristics of previously and currently circulating variants. In addition, it reviews available data from vaccine manufacturers, including animal and/or human studies demonstrating the breadth and durability of immune responses elicited by currently authorized vaccines, as well as any vaccine candidates in development. Vaccine manufacturers are also asked to provide observational epidemiological data that demonstrate the effectiveness of their authorized COVID-19 vaccines.

Additional information available from: https://www.who.int/news/item/07-10-2024-types-of-data-requested-to-inform-december-2024-covid-19-vaccine-antigen-composition-deliberations

Mpox vaccine

WHO extends the indication for use of the prequalified vaccine Imvanex to age 12 years and older

In October, the WHO extended the conditions of use of the mpox vaccine Imvanex®, approved under the trade name JYNNEOS by the US FDA and as IMVAMUNE by Health Canada, to extend it to people aged 12 years and older.

On 13 September, the mpox vaccine Imvanex® was prequalified for use in people over 18 years of age.

Additional information available from: https://extranet.who.int/prequal/vaccines/p/imvanexr

Human Papilloma Virus (HPV) vaccine

WHO prequalified fifth HPV vaccine

On August 2, the WHO announced the prequalification of the fifth HPV vaccine Walrinvax®, with a two-dose schedule for use. Subsequently, when more data are available, they will evaluate whether this vaccine can be recommended for a single-dose schedule. Key characteristics of these vaccines are summarized below:

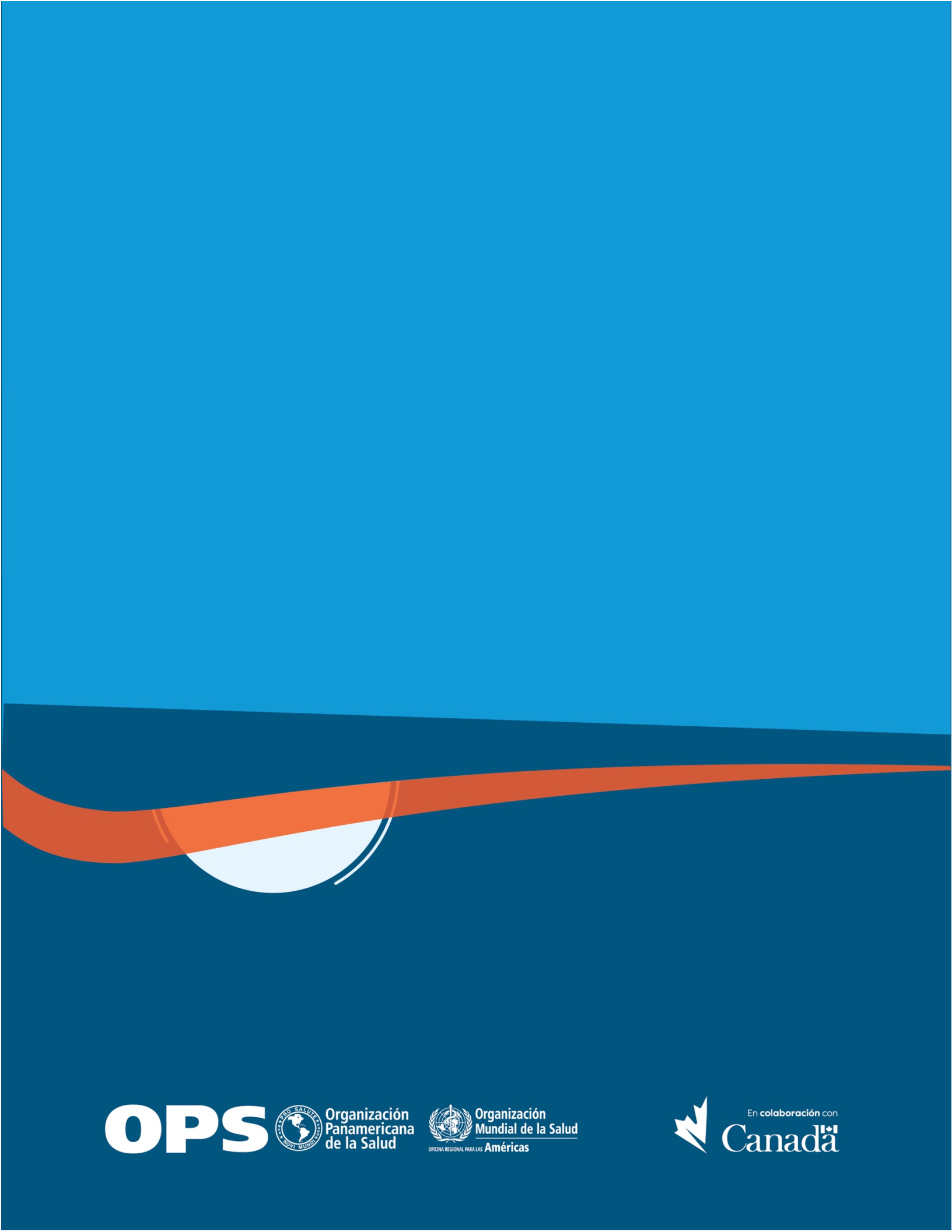
Vaccine	Commercial name	Manufacturer	Responsible NRA	Pharmaceutical form	Presentation / storage
Bivalent recombinant vaccine (Types 16 and 18) against human papillomavirus (HPV) (produced in *Pichia pastoris*) (adsorbed onto aluminum phosphate as an adjuvant)	Walrinvax®	Yuxi Zerun Biotechnology Co., Ltd, China	National Medical Products Administration, China	Injectable suspension	Single dose vial 2° - 8°C

Additional information available from: https://extranet.who.int/prequal/vaccines/p/walrinvaxr

WHO adds prequalified HPV vaccine for single-dose use

On 4 October, the WHO announced that a fourth WHO-prequalified HPV vaccine, Cecolin®, has been confirmed for use in a single-dose schedule. The decision was made based on new data on the vaccine that fulfilled the criteria set out in the WHO's 2022 recommendations for alternative, off-label use of HPV vaccines in single-dose schedules.

Additional information available from: https://www.who.int/news/item/04-10-2024-who-adds-an-hpv-vaccine-for-single-dose-use


OPS
Organización Panamericana de la Salud
Organización Mundial de la Salud
OFICINA REGIONAL PARA LAS Américas
En colaboración con
Canadá