

COVID-19

CONSOLIDATED REGIONAL AND GLOBAL INFORMATION ON ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI) AGAINST COVID-19 AND OTHER UPDATES

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ARGENTINA

- As of 2 June 2021, a total of 12,801,115 doses of the Sputnik V (6,964,344 doses), Covishield/AstraZeneca (2,305,351 doses) and Sinopharm (3,531,420 doses) vaccines had been administered. A total of 45,728 adverse events following immunization (AEFI) had been reported, equivalent to 357.22 AEFI per 100,000 doses of vaccines administered.
- Of total AEFI reported, 40,445 were associated with the Sputnik V vaccine (580.74 per 100,000 doses administered), 3,543 with the Covishield/AstraZeneca vaccine (153.69 per 100,000 doses administered), and 1,740 with the Sinopharm vaccine (49.27 per 100,000 doses administered).
- More than 99% of AEFI were mild or moderate. Only 307 of the reported events (0.67%) were considered serious (cases requiring hospitalization), a rate of 2.39 per 100,000 doses administered.
- The most frequently diagnosed events were fever, headache, myalgia, and arthralgia.
- Among the serious events, there were 2 cases of immune thrombocytopenia and 2 cases of Guillain-Barré syndrome, which were classified as associated with the Sputnik V vaccine, while one case of Guillain-Barré syndrome was associated with the Covishield/AstraZeneca vaccine. Nine cases of anaphylaxis were reported with the Sputnik V vaccine, two with Covishield/AstraZeneca, and two with the Sinopharm vaccine.

Link: <https://www.argentina.gob.ar/coronavirus/vacuna/equipos-salud/informes-seguridad>

CANADA

- As of 2 July 2021, 38,297,511 doses of Covishield (AstraZeneca manufactured by the Serum Institute of India), Pfizer-BioNTech, and Moderna COVID-19 vaccines had been administered.
- There were 8,972 individual reports of one or more adverse events (0.023% of doses administered). Of these, 2,056 were considered serious events (0.005% of doses administered).
- Of total reports, there were 3,614 non-serious and 1,350 serious events associated with the Pfizer-BioNTech vaccine. For the Moderna vaccine, 2,438 non-serious and 255 serious events were reported, while for Covishield/AstraZeneca, 841 non-serious and 359 serious events were reported.
- A total of 24,301 AEFI were reported (including 8,972 reports of one or more events), of which the majority were non-serious events, such as injection-site reactions, paresthesia, itching, hives, headache, hypoesthesia, and nausea. A total of 94 cases of anaphylaxis were reported (79 for the Pfizer-BioNTech vaccine and 15 for the Moderna vaccine).

- As of 2 July, there were 59 reported cases of thrombosis with thrombocytopenia syndrome (TTS), of which 55 involved patients who had been vaccinated with the Covishield/AstraZeneca vaccine, three who had received the Pfizer-BioNTech vaccine, and one who had received the Moderna vaccine. Onset of symptoms occurred from one to 34 days after vaccination. Of these cases, 22 were women (ages 44 to 88), 32 were men (ages 34 to 73), and in one case the sex of the individual was not specified.
- A total of 130 post-vaccination deaths were reported. Following a medical review, it was determined that 55 of these deaths were not linked to administration of the COVID-19 vaccine; 31 are still under investigation; six were determined to be potentially attributable to the vaccination (cases of TTS); while in 38 cases the cause of death could not be determined due to insufficient information.
- As of 2 July, 105 cases of myocarditis/pericarditis had been reported. Of these, 70 were individuals who had received the Pfizer-BioNTech vaccine, 26 had received the Moderna vaccine, 8 had received the Covishield/AstraZeneca vaccine, and in one case the vaccine was not specified. Of the cases associated with the Pfizer-BioNTech vaccine, 37 involved women (ages 17 to 86) and 33 involved men (ages 15 to 78). In 45 of these cases, the events occurred after the first dose, 14 after the second dose, and in 11 cases there was no indication whether the occurrence followed the first or second dose. Onset of symptoms occurred between 5 hours and 94 days after administration of the vaccine. No clear association between myocarditis/pericarditis and COVID-19 vaccines has yet been established, though such an association has not been ruled out.
- As of 2 July, one case of capillary leak syndrome had been reported following the first dose of the Covishield/AstraZeneca vaccine. In addition, 37 cases of Guillain-Barré syndrome were reported, of which 20 occurred after administration of the Covishield/AstraZeneca vaccine, 12 after administration of the Pfizer-BioNTech vaccine, 4 after administration of the Moderna vaccine, and in one case the vaccine was not specified.

Source: <https://health-infobase.canada.ca/covid-19/vaccine-safety/>

PARAGUAY

- Paraguay's Expanded Immunization Program (PAI), through its AEFI Surveillance System, reports AEFI related to Sputnik V, Sinovac (CoronaVac), Sinopharm, AstraZeneca, Covaxin, Hayat-Vax,* and Moderna vaccines administered between 22 February 2021 and 25 June 2021.
- A total of 1,503 AEFI were reported between the start of the COVID-19 vaccination program (22 February) and 25 June, representing 0.19% of total doses administered; 118 reported cases are still under investigation.
- Of total AEFI reports, 75.1% (1,129) involved women and 24.8% (374) involved men. Most reported cases of AEFI (962) were in people under 40 years of age.

- The most frequent clinical manifestations of AEFI reported were myalgia (69%), fever (56%), headache (56%), injection-site pain (53%), and fatigue (46%). The majority of reports cited more than one clinical manifestation.
- The AEFI reporting rate for the Coronavac vaccine was 916.18 per 100,000 doses administered, while for the Sinopharm, AstraZeneca, and Sputnik V vaccines the rates per 100,000 doses administered were 510.73, 292.61, and 244.06, respectively. For the Covaxin vaccine, the AEFI reporting rate was 64.47 per 100,000 doses administered.
- * Vaccine produced as the result of a joint project between Sinopharma CNBG and G42, of the United Arab Emirates, in Abu Dhabi.

Source: <http://pai.mspbs.gov.py/article/vigilancia-esavi>

AEFI and serious adverse events reported for vaccines being used in the Region of the Americas, by doses administered, as of 30 June 2021

Vaccines	Total doses administered*	Total events	Serious events	Total events/100,000 doses	Range	Serious events/100,000 doses	Range
AstraZeneca	25,826,881	52,570	1,914	203.5	(0.5–652.1)	7.4	(0.4–24.8)
CanSino	3,624,525	1,049	46	28.9		1.3	
Gamaleya	6,258,470	25,814	30	412.5	(5.3–739.5)	0.5	(0.3–4.6)
Janssen	12,838,245	41,022	3,367	319.5		26.2	
Moderna	140,332,167	178,493	13,507	127.2	(40.0–130.8)	9.6	(3.7–36.9)
Pfizer	222,529,848	189,192	18,439	85.0	(0.8–201.5)	8.3	(0.2–9.7)
Sinopharm	3,203,512	8,340	61	260.3	(10.7–807.3)	1.9	(0.1–6.2)
Sinovac	57,486,521	36,340	3,353	63.2	(5.1–603.5)	5.8	(0.0–10.3)
Totals	472,100,169	532,820	40,717	112.9	(7.1–504.3)	8.6	(0.0–5.7)

* Represents administered doses for which adverse events were reported. The total number of doses administered as of 30 June in the Region of the Americas was 556,178,770.

Source: Number of doses is derived from reports by the countries to the Vaccination Dashboard for the Americas (https://ais.paho.org/imm/IM_DosisAdmin-Vacunacion.asp) as of 30 June 2021, supplemented by country reports.

For AEFI: Information is from the Upsala Monitoring Centre, public sources in the countries (e.g. Epidemiological Bulletins), and country-specific reports provided to PAHO.

Update on SARS-CoV-2 variants of interest

On 14 June 2021, the World Health Organization (WHO) reported that a variant assigned to the Pango C.37 lineage (GISAID clade GR/452Q. V1, Nextstrain clade 20D) was designated as a variant of interest (VOI), and was given the designation "Lambda."

The Lambda variant has been associated with substantial rates of community transmission in multiple countries, with an increasing prevalence over time and a higher incidence of COVID-19. The earliest sequenced samples of Lambda were reported from Peru in August 2020.

Lambda has a series of mutations in the spike protein, including G75V, T76I (with the 247-253 deletion), L452Q, F490S, D614G, and T859N; with possible phenotypic implications, such as a potential increase in transmissibility and a possible increase in resistance to neutralizing antibodies. At present, however, the evidence is limited, and more studies are being conducted to determine the impact of these phenotypic changes.

Source: <https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---23-march-2021>

CECMED grants emergency use authorization (EUA) to the Cuban vaccine candidate Abdala

On 9 July 2021, the Center for State Control of Medicines and Medical Equipment and Devices (CECMED) granted emergency use authorization (EUA) to the Cuban vaccine ABDALA 50 µg, developed by the Cuba's Center for Genetic Engineering and Biotechnology (CIGB).

The authorization was granted once an evaluation of the file submitted by CECMED for the EUA had been completed, inspection of the plants involved in the production process had been carried out, and compliance with the official requirements had been confirmed. Data from Phase I and Phase II clinical trials, with a Phase III clinical trial now in progress, demonstrated 92.28% efficacy in preventing symptomatic forms of the disease, as well as an adequate safety profile, supported by the number of doses administered in the clinical trials to date, the intervention study in at-risk populations, and the health intervention conducted in the country.

Source: <https://www.cecmecd.cu/noticias/aprueba-cecmecd-autorizo-uso-emergencia-candidato-vacunado-cubano-abdala>

Preliminary results of the CombiVacS study conducted in Spain

To date, the administration of different COVID-19 vaccines has been homologous in nature in the vast majority of cases, with administration of the same vaccine according to its authorized regimen. Adopting a heterologous vaccination regimen – administering the second dose of vaccine using a vaccine different from the one used for the initial dose – could give vaccination programs greater flexibility and make it possible to deal with shortages in a given vaccine. There has also been speculation that a heterologous regimen could result in an even better immune response, in both antibody levels and cellular immune response.

The CombiVacS study is a Phase 2, multicenter randomized controlled study being conducted at five university hospitals in Spain. A group of volunteers who had received one dose of the AstraZeneca vaccine received a second dose of the Pfizer-BioNTech vaccine between 8 and 12 weeks after the first dose. Immunogenicity was measured 14 days after the second dose, and preliminary results appear to indicate a marked immune response, as well as an acceptable safety profile.

One limitation of the study was the absence of a control group with a complete homologous vaccination regimen, using the initial vaccine for the second dose; this was not possible because at that time, use of the AstraZeneca vaccine had been suspended in Spain.

Source: Borobia AM, Carcas AJ, Pérez-Olmeda M, et al. Immunogenicity and reactogenicity of BNT162b2 booster in ChAdOx1-S-primed participants (CombiVacS): a multicentre, open-label, randomised, controlled, phase 2 trial. *Lancet* 2021; published online June 25. [http://dx.doi.org/10.1016/S0140-6736\(21\)01420-3](http://dx.doi.org/10.1016/S0140-6736(21)01420-3)

Warning about possible risk of myocarditis/pericarditis with mRNA vaccines

- The European Medicines Agency's Safety Committee

On 9 July 2021, the Pharmacovigilance Risk Assessment Committee (PRAC), of the European Medicines Agency (EMA), concluded that myocarditis and pericarditis can occur in very rare instances after administration of the Comirnaty (Pfizer-BioNTech) and Spikevax (Moderna) COVID-19 vaccines. The Committee is therefore recommending that myocarditis and pericarditis be incorporated as new side effect of these vaccines, along with a warning to raise awareness among health professionals and people receiving these vaccines.

The Committee reached this conclusion after reviewing 321 cases that occurred in the European Economic Area (EEA, consisting of the European Union countries plus Iceland, Liechtenstein, and Norway), involving 145 cases of myocarditis and 138 cases of pericarditis in people who received the Comirnaty vaccine, in addition to 19 cases of myocarditis and 19 of pericarditis in people who received the Spikevax vaccine. As of 31 May 2021, approximately 177 million doses of Comirnaty and 20 million doses of Spikevax had been administered in the EEA. The Committee also reviewed information on cases reported in the rest of the world.

PRAC concluded that most of the cases occurred within 14 days of vaccination, most often in young men, after the second dose. In five of the cases that occurred in the EEA, subsequent deaths were reported; these occurred in individuals who were elderly or who had concomitant diseases.

The Committee is recommending that healthcare professionals be alert to the signs and symptoms of myocarditis and pericarditis in individuals who received mRNA vaccines, and that people receiving these vaccines be told to seek immediate medical attention if they experience symptoms indicative of myocarditis or pericarditis, such as shortness of breath, an unusually strong and sometimes irregular heartbeat, and chest pain.

The EMA confirms that the benefits of all licensed COVID-19 vaccines outweigh the risks of contracting COVID-19 and the associated complications.

Source: <https://www.ema.europa.eu/en/news/comirnaty-spikevax-possible-link-very-rare-cases-myocarditis-pericarditis>

- COVID-19 subcommittee of the Global Advisory Committee on Vaccine Safety (GACVS)

On 9 July 2021, WHO published an update to the guidance issued by the COVID-19 subcommittee of WHO's Global Advisory Committee on Vaccine Safety (GACVS). After reviewing all information available to date, including actions taken by the United States FDA and the EMA, it notes the following:

- The benefits of mRNA COVID-19 vaccines in reducing hospitalizations and deaths from COVID-19 infections outweigh the risks.
- Very rare cases of myocarditis and pericarditis have been reported after administration of mRNA COVID-19 vaccines; these occurred more frequently in young men, after the second dose of the vaccine, usually within a few days after vaccination. Current evidence suggests a probable causal association between myocarditis and the mRNA vaccines.
- Available data suggest that cases of myocarditis and pericarditis after vaccination are generally mild and respond to conservative treatment (e.g., rest, treatment with non-steroidal anti-inflammatory drugs, etc.). Monitoring is being carried out to determine the long-term outcomes.

The GACVS subcommittee will continue to review this signal as more data become available.

Source: <https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines>

- [U.S. Food and Drug Administration](#)

On 25 June 2021, the U.S. Food and Drug Administration (FDA) announced that, having reviewed the existing information and taken into account the discussion at the meeting of the Advisory Committee on Immunization Practices, of the Centers for Disease Control and Prevention (CDC), it decided to include in the Moderna and Pfizer-BioNTech COVID-19 vaccine fact sheets a warning concerning the possible increased risk of myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the tissue surrounding the heart) following vaccination.

The warning in the fact sheets for health professionals will indicate that reports of adverse event suggest that there is an increased risk of myocarditis and pericarditis, particularly after the second dose, with the onset of symptoms occurring a few days after vaccination. The fact sheets for the general population will emphasize that people who receive these vaccines should seek immediate medical attention if they experience chest pain, shortness of breath, or heart palpitations following vaccination.

Source: <https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-june-25-2021>

The European Medicines Agency adds capillary leak syndrome as a contraindication to Janssen's COVID-19 vaccine

The Safety Committee of the European Medicines Agency (EMA), the Pharmacovigilance Risk Assessment Committee (PRAC), evaluated three cases of capillary leak syndrome, which occurred within two days of vaccination in people who had received the Janssen COVID-19 vaccine. One of the affected individuals had a history of capillary leak syndrome and two of them subsequently died. As of 21 June 2021, more than 18 million doses of the Janssen COVID-19 vaccine had been administered worldwide.

On 9 July 2021, the EMA reported that PRAC is recommending that people who have previously been diagnosed with capillary leak syndrome should not be vaccinated with the Janssen COVID-19 vaccine. Capillary leak syndrome will be added, as a new side effect, to the product information for this vaccine, along with a warning to raise awareness among health professionals and patients about this risk.

Capillary leak syndrome is a serious, very rare condition that causes fluid to leak from small blood vessels (capillaries) into neighboring body cavities, resulting in swelling mainly in the arms and legs, low blood pressure, thickening of the blood, and low blood albumin levels. Healthcare professionals should be aware of the signs and symptoms of capillary leak syndrome and its risk of recurrence in people who have been previously diagnosed with the disease.

People who have been vaccinated with the Janssen Covid-19 vaccine should seek immediate medical attention if they experience rapid swelling of the arms and legs or sudden weight gain in the days following vaccination. These symptoms are usually associated with feeling faint (due to low blood pressure).

Source: <https://www.ema.europa.eu/en/news/ema-advises-against-use-covid-19-vaccine-janssen-people-history-capillary-leak-syndrome>

A similar measure was taken previously by the European Medicines Agency for the Vaxzevria vaccine. Additional information at: <https://www.ema.europa.eu/en/news/vaxzevria-ema-advises-against-use-people-history-capillary-leak-syndrome>

European Medicines Agency guidance for variant strain(s) update to COVID-19 vaccines

The European Medicines Agency (EMA) issued its “Procedural guidance for variant strain(s) update to vaccines intended for protection against Human coronavirus.” This guide sets forth matters related to modifying the composition of previously authorized COVID-19 vaccines. These changes include the replacement or addition of a serotype, strain, antigen, or coding sequence, or combination of serotypes, strains, antigens, or coding sequences, provided the technological platform of the vaccine remains similar.

The guide also describes the rules for establishing the names assigned to modified vaccines, including modification of the international non-proprietary name (INN) for the variant, where appropriate, and inclusion of the assigned name for the variant(s) in the name of the modified vaccine.

Source: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/procedural-guidance-variant-strains-update-vaccines-intended-protection-against-human-coronavirus_en.pdf

WHO EUL recommendation for BIBP's COVID-19 vaccine risk management plan and vaccine pharmacovigilance plan

The WHO's emergency use listing (EUL) recommendations for SINOPHARM's COVID-19 vaccine, published on 4 June 2021, discuss the risk management plan and pharmacovigilance plan for this vaccine, as summarized below.

Risk management plan:

- Major risks identified: With regard to anaphylaxis, observation time after vaccination should be at least 15 minutes, given the life-threatening risk of anaphylactic/anaphylactoid reactions.
- Potential risks: The manufacturer considered the risk of vaccine-associated enhanced disease (VAED); WHO includes, in addition, the risk of vaccine-associated enhanced respiratory disease (VAERD), and notes that there is a theoretical concern that vaccination against SARS-CoV-2 may be associated with enhanced severity of COVID-19 episodes which would manifest as VAED, which can be life-threatening, and requires early detection, careful monitoring, and timely medical intervention.

Programmatic errors: WHO requested the inclusion of risks related to programmatic errors under real use conditions, which should be monitored via routine pharmacovigilance activities and be presented in each PBRER/PSUR.

Reactogenicity: Overview of safety information is limited to written descriptions of adverse events, without information on number of exposed or the description of relevant cases. The identified risks need to consider frequency, but also the importance of seriousness, severity, and impact.

- Missing information: WHO requested inclusion of the following:

Use during pregnancy and while breastfeeding. Pregnant and lactating women were not included in the clinical trials.

Current or past SARS-CoV-2 infection: To be assessed in a post-emergency use or post-marketing study.

Use in immunocompromised patients, including people living with HIV. This population was excluded from the clinical trials.

Subjects aged 60 and above. Current ongoing clinical trials include only a small proportion of participants aged 60 and above.

Use in patients with comorbidities (e.g., chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders).

In addition to interaction with other vaccines, WHO incorporated interchangeability or sequential use with other vaccines.

Use in pediatric population. WHO noted that no efficacy data are available from participants <18 years of age.

Use in patients with autoimmune or inflammatory disorders. There is a theoretical concern that the vaccine may exacerbate their underlying disease.

Long-term safety: WHO indicated that it is taking additional steps to learn more in this regard.

Impact of the emergence of variants on vaccine efficacy/effectiveness and safety: WHO requested that BIBP provide it with any relevant data as soon as available, irrespective of source.

Pharmacovigilance plan:

WHO recommended monitoring of the following adverse events of interest: facial paralysis; Guillain-Barré syndrome and neurological disorders; coagulation disorders (thromboembolism, hemorrhage); reactogenicity following vaccination, and all serious adverse events. In addition, it emphasizes that routine pharmacovigilance activities should be implemented in all WHO regions, taking into account the regulations and particularities of each country.

Source: <https://extranet.who.int/pqweb/file/4960602/download>

COVID-19 vaccine traceability initiative

UNICEF will be responsible for implementing the Global Trust Repository (GTR) information system, a database that will allow countries to validate information on a given vaccine, using the barcodes on the packaging.

The GTR initiative will strengthen traceability and verification of the COVID-19 vaccines being used, and will have the ability to store information from the different vaccine lots distributed through legitimate supply chains.

Source: <https://www.who.int/publications/m/item/36th-who-regulatory-update-on-covid-19>

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