COVID-19

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

Twenty-seventh report

WASHINGTON, DC

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CONTENTS

CANADA

As of 24 September 2021, 38,472,075 doses of the COVID-19 vaccine of Pfizer-BioNTech, 13,592,652 doses of the Moderna vaccine, and 2,787,374 doses of the AstraZeneca/Covishield vaccine (AstraZeneca vaccine manufactured by the Serum Institute of India) had been administered.

A total of 17,124 individual reports of one or more adverse events (0.031% of doses administered) were received. Of these, 4,505 reports involved serious events (0.008% of doses administered).

There were 46,000 reports of adverse events following immunization (AEFI), of which 17,124 involved one or more events. The most frequently reported adverse events were injection-site reactions, paresthesia, headache, pruritis, dyspnia, fatigue, nausea, etc.

Number of reports and reporting rate of adverse events (per 100,000 doses administered) as of 24 September 2021

Vaccine	Number of reports of non-serious AEFI		Number of reports of serious AEFI		Total number of reports of AEFI	
	N	Rate/ 100,000 doses administered	N	Rate/ 100,000 doses administered	N	Rate/100,000 doses administered
Pfizer-BioNTech	6,471	16.82	2,952	7.67	9,423	24.49
Moderna	4,465	32.85	774	5.69	5,239	38.54
Covishield and AstraZeneca	1,654	59.34	620	22.24	2,274	81.58
Unknown	29	-	159	-	188	-
Total	12,619	22.72	4,505	8.11	17,124	30.84

Number of reports and reporting rate of serious AEFI (per 100,000 doses administered), by vaccine, as of 24 September 2021

Vaccine	***Pfizer-BioNTech***	***Moderna***	***Covishield and AstraZeneca***
Anaphylaxis	202 (0.52/100,000)	54 (0.40/100,000)	12 (0.43/100,000)
Thrombosis with thrombocytopenia syndrome (TTS)	16 (0.04/100,000)	5 (0.04/100,000)	61 (2.19/100,000)
Guillain-Barré syndrome	33 (0.09/100,000)	18 (0.13/100,000)	31 (1.11/100,000)
Capillary leak syndrome	-	-	2 (0.07/100,000)
Myocarditis/pericarditis	466 (1.21/100,000)	321 (2.36/100,000)	21 (0.75/100,000)
Bell's palsy/facial paralysis	364 (0.94/100,000)	117 (0.86/100,000)	44 (1.58/100,000)
Fatal events	194* post-vaccination deaths		

**Following a medical review of the 194 deaths, it was determined that 74 were not linked to administration of the COVID-19 vaccine, while 44 are still under investigation; 6 (cases of TTS) are considered to be potentially attributable to the vaccination, and 70 could not be classified due to insufficient information.*

An analysis of 808 of the 812 cases of myocarditis/pericarditis, with indication of the vaccine administered, is shown below:

Vaccine	Total number of cases (rate per 100,000 doses administered)	By sex (median age)		Number of reports, by dose administered		
		Number of women (median age)	Number of men (median age)	1st	2nd	Unknown
Pfizer-BioNTech*	466 (1.21)	168 (39 years)	294 (22 years)	196	211	59
Moderna**	321 (2.36)	81 (34 years)	235 (26 years)	69	217	35
Covishield and AstraZeneca	21 (0.75)	N/A	N/A	N/A	N/A	N/A

* In four cases, the sex of the individual was not specified.

** In three cases, the sex of the individual was not specified, and in one case the sex was indicated as "other."

Source: Public Health Agency of Canada. Canadian COVID-19 vaccination safety report. Ottawa: Public Health Agency of Canada; 4 October 2021. https://health-infobase.canada.ca/covid-19/vaccine-safety/. Data reproduced by PAHO/WHO.

CARIBBEAN PUBLIC HEALTH AGENCY (CARPHA)

The Caribbean Regulatory System (CRS), through the Caribbean Public Health Agency (CARPHA), in the latest update published on its website, indicates that as of 24 September 2021 approximately 4,507,347 doses of COVID-19 vaccines, included in the WHO Emergency Use Listing (EUL), had been administered in the CARPHA member countries (Anguilla, Antigua and Barbuda, Aruba, Bahamas, Barbados, Belize, Bermuda, Bonaire, St. Eustatius, Saba, British Virgin Islands, Cayman Islands, Curacao, Dominica, Grenada, Guyana, Haiti, Jamaica, Montserrat, Saint Kitts and Nevis, Saint Lucia, Saint Martin, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, and Turks and Caicos Islands). As of the same date, 38 reports of AEFI had been received through an online reporting form since August 2021, the date on which the form was instituted. Of these reported cases, 13 were serious, including one death.

These reports are being verified and/or investigated by local authorities.

Source: CARPHA_COVID-19_Vaccine_Update_038_September_27,_2021.pdf

COVID-19 vaccination for pregnant women, and pregnancy outcomes

On 1 October, one of the largest ever observational cohort studies of pregnant women was published. Its objective was to study the association between prenatal Pfizer-BioNTech COVID-19 vaccination, pregnancy course, and outcomes. A retrospective cohort study was performed, including all women who delivered between January and June 2021 at Soroka University Medical Center, in Israel. Excluded were women diagnosed with COVID-19 in the past, multiple gestations, or unknown vaccination status. Pregnancy, delivery, and newborn complications were compared between women who had received one- or two-dose vaccines during pregnancy and unvaccinated women. A total of 4,399 women participated in this study, of whom 913 (20.8%) were vaccinated during pregnancy. All vaccinations occurred during the second or third trimester. As compared to the unvaccinated women, the vaccinated women were older, more likely to conceive following fertility treatments and to have sufficient prenatal care, and were of higher socioeconomic position. In both crude and multivariable analyses, no differences were found between groups, in terms of pregnancy, delivery, and newborn complications, including gestational age at delivery, incidence of small for gestational age, and newborn respiratory complications. The authors conclude that prenatal maternal COVID-19 vaccination with the Pfizer-BioNTech vaccine has no adverse effects on pregnancy course and outcomes.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8421099/pdf/main.pdf

Declining mortality from cerebral venous sinus thrombosis with thrombocytopenia (CVST) after SARS-CoV-2 vaccination

On 18 September, an observational study was published evaluating whether the mortality of patients with cerebral venous sinus thrombosis (CVST) due to vaccine-induced immune thrombotic thrombocytopenia (VITT) has decreased over time.

The EudraVigilance database, of the European Medicines Agency, was used to identify cases of CVST with concomitant thrombocytopenia that occurred within 28 days of vaccination against SARS-CoV-2. Vaccines were grouped based on vaccine type (adenoviral or mRNA). Cases with CVST onset up to 28 March were compared with cases after 28 March 2021 – the day when the first scientific paper on VITT was published. A total of 270 cases of CVST with thrombocytopenia were identified, of which 266 (99%) occurred after adenoviral vector SARS-CoV-2 vaccination (ChAdOx1 nCoV-19, n = 243; Ad26.COV2.S, n = 23). The reported mortality among adenoviral cases with onset up to 28 March 2021 was 47/99 (47%, 95% CI 37%–58%), compared with 36/167 (22%, 95% CI 16%–29%) in cases with onset after 28 March (p = <0.001). None of the four cases of CVST with thrombocytopenia that occurred following mRNA vaccination died. The authors conclude that the reported mortality of CVST with thrombocytopenia following vaccination with adenoviral vector-based SARS-CoV-2 vaccines has significantly

decreased over time, which may indicate a beneficial effect of earlier recognition and/or improved treatment on outcome after VIIT.

Source: https://onlinelibrary.wiley.com/doi/epdf/10.1111/ene.15113

Cerebral venous thrombosis after vaccination against COVID-19 in the UK: a multicenter cohort study

On 25 September, a multicenter cohort study of cerebral venous thrombosis following COVID-19 vaccination, perhaps the largest such study to date, was published. The authors were able, for the first time, to make a direct comparison between 70 patients with VIIT-associated cerebral venous thrombosis and 25 patients who developed cerebral venous thrombosis without evidence of VITT following vaccination, as well as with historical data from a large cohort of patients with cerebral venous thrombosis. The results show, for what appears to be the first time, that when compared to patients without VITT, patients with VITT-associated cerebral venous thrombosis were younger, had fewer risk factors for venous thrombosis, and were more likely to have received the ChAdOx1 vaccine. The group with VITT-associated CVT had more extensive venous thrombosis, and higher rates of thrombosed veins or sinuses. Compared with non-VITT patients, those with VITT-associated cerebral venous thrombosis had more extensive venous thrombosis and higher rates of multiple infarcts, multiple intracerebral hemorrhages, and extracranial thrombosis. Their outcomes, at the end of hospital admission, were worse, with higher rates of death and dependency. Although the treatment response of patients with VITT-associated cerebral venous thrombosis is difficult to assess in a purely observational study, nonheparin anticoagulants and intravenous immune globulin were associated with better outcomes. The initial criteria for VITT, based on low platelet count and high D-dimers, appeared to overlook two patients who had typical characteristics for this condition, leading the authors to suggest new, more appropriate diagnostic criteria.

VITT is specifically associated with adenovirus vector COVID-19 vaccines. Urgent work is needed to determine the trigger for this reaction, in hopes that future vaccines can be designed to prevent it. Physicians should be aware of the clinical, laboratory, and radiological markers of this condition, since without timely treatment the prognosis is poor.

Source: Perry RJ, Tamborska A, Singh B et al. Cerebral venous thrombosis after vaccination against COVID-19 in the UK: a multicenter cohort study. (2021) The Lancet, 398 (10306), 1147–1156. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)01608-1/fulltext

Myocarditis and pericarditis after vaccination for COVID-19

On 4 August, an observational study was published that included forty hospitals in Washington, Oregon, Montana, and Los Angeles County, California, that were part of the Providence health care system in the United States, all of which used the same electronic medical record (EMR) system. The aim of the study was to identify vaccinated

patients who were seen in the emergency room and were diagnosed with myocarditis, myopericarditis, or pericarditis. All patients with documented COVID-19 vaccinations administered inside the system or recorded in state registries at any time through 25 May 2021, a total of 2,000,287 people, were identified. Vaccinated patients who subsequently had emergency department or inpatient encounters, with diagnoses of myocarditis/myopericarditis (20 cases) or pericarditis (37 cases), were ascertained from EMRs.

Monthly baseline rates of first-time hospital diagnoses between January 2019 and January 2021 (pre-vaccine period) and February through May 2021 (vaccine period) were compared. The mean monthly number of cases of myocarditis or myopericarditis during the pre-vaccine period was 16.9 (95% CI, 15.3-18.6) vs 27.3 (95% CI, 22.4-32.9) during the vaccine period ($p < .001$). The mean numbers of pericarditis cases during the same periods were 49.1 (95% CI, 46.4-51.9) and 78.8 (95% CI, 70.3-87.9), respectively ($p < .001$).

Two distinct self-limited syndromes, myocarditis and pericarditis, were observed after COVID-19 vaccination. Myocarditis developed rapidly in younger patients, mostly after the second vaccination. Pericarditis affected older patients later, after either the first or second dose.

Some vaccines are associated with myocarditis, including mRNA vaccines, and the Centers for Disease Control and Prevention (CDC) recently reported a possible association between COVID-19 mRNA vaccines and myocarditis, primarily in younger male individuals within a few days after the second vaccination, at an incidence of about 4.8 cases per million. This study shows a similar pattern, although at higher incidence, suggesting underreporting of vaccine-related adverse events. Additionally, pericarditis may be more common than myocarditis among older patients.

Study limitations include cases missed in outside care settings, and missed diagnoses of myocarditis or pericarditis (which would underestimate the incidence), as well as inaccurate EMR vaccination information. Temporal association does not prove causation, although the short span between vaccination and myocarditis onset, and the elevated incidence of myocarditis and pericarditis in the study hospitals, lend support to a possible relationship.

Source: Diaz GA, Parsons GT, Gering SK, et al. Myocarditis and Pericarditis After Vaccination for COVID-19. JAMA. 2021;326(12):1210–1212. doi:10.1001/jama.2021.13443. https://jamanetwork.com/journals/jama/fullarticle/2782900

Update to the WHO interim statement of the Strategic Advisory Group of Experts on Immunization regarding booster doses for COVID-19 vaccination

On 4 October 2021, the Strategic Advisory Group of Experts (SAGE) on Immunization and its COVID-19 Vaccines Working Group updated the interim statement on COVID-19 booster doses for the vaccines included in the Emergency Use Listing (EUL).

They note that, at present, the main purpose of immunization against COVID-19 continues to be to protect against hospitalization, serious illness, and death. Booster doses may only be needed if there is evidence of insufficient protection against these disease outcomes over time. In a period of continued global vaccine supply shortage, equity considerations at the country, regional, and global levels remain an essential factor in assuring vaccination of high-priority groups in all countries, and indicate that the following factors should be considered:

1. Waning immunity: Neither an immune correlate of protection nor of duration of protection has been established to date. Although there may be a loss of protection against infections by SARS-CoV-2, protection against severe disease is more durably retained due to anamnestic humoral and cell-mediated immunity.
2. Vaccine effectiveness: Emerging data from observational studies consistently show a decline in vaccine effectiveness against infection and milder forms of COVID-19 over time. With respect to duration of protection against disease requiring hospitalization, current data show an overall continued high level of effectiveness, although data vary according to type of vaccine, age group, and target population. The vast majority of current infections are observed in unvaccinated populations, and if breakthrough infections occur in vaccinated persons, they are in most cases less severe than those seen in unvaccinated persons.
3. Global vaccine supply and global and national equity: National vaccination program policy decisions to add a booster dose should take into account the strength of evidence regarding the need for these doses, their safety and effectiveness, as well as the global availability of vaccines. Prioritizing booster doses over speed and breadth in the initial dose coverage may also damage the prospects for global mitigation of the pandemic, with severe implications for the health and social and economic well-being of people globally.

In assessing the need for booster doses, the following should be taken into account:

- Epidemiology and burden of disease: Epidemiology of breakthrough cases, by disease severity, age, co-morbidity, risk group, exposure, type of vaccine, time since vaccination, and context with regard to VoCs.
- Vaccine-specific data: Efficacy, effectiveness, duration of protection of vaccines, in the context of circulating VoCs, based on observational studies and, if possible, randomized controlled trials. Supplementary evidence from immunological studies assessing binding and neutralizing antibodies over time, as well as biomarkers of cellular and durable humoral immunity, when possible, should also be considered.

- Assessing the performance of booster doses: While preliminary data on effectiveness of booster vaccinations have been obtained only for the Pfizer-BioNTech vaccine (1), additional data on efficacy, effectiveness, and duration of protection of original and variant-adapted vaccine booster doses in the context of SARS-CoV-2 wild-type and VOCs would be helpful. Safety and reactogenicity of booster vaccination, including heterologous boosting, also need to be studied.
- Additional considerations: Optimal timing of the booster dose; homologous versus heterologous boosters; possibility of dose-sparing for booster doses; booster needs in previously infected individuals; specification and prioritization of high-risk populations; programmatic feasibility and sustainability; community perception and demand, as well as equity considerations.

SAGE will deliberate on the evidence for a booster dose during an upcoming extraordinary meeting of SAGE in November 2021.

Source: https://www.who.int/news/item/04-10-2021-interim-statement-on-booster-doses-for-covid-19-vaccination

(1) Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Freedman L, Kalkstein N et al. Protection of BNT162b2 Vaccine Booster against Covid-19 in Israel. N Engl J Med. 2021. doi: 10.1056/NEJMoa2114255.

Meeting highlights from the Pharmacovigilance Risk Assessment Committee of the European Medicines Agency, from 27 to 30 September 2021

- Assessment of rare cases of venous thromboembolism with the Janssen COVID-19 vaccine

The Pharmacovigilance Risk Assessment Committee (PRAC) has concluded that there is a possible link between rare cases of venous thromboembolism (VTE) and the Janssen COVID-19 vaccine.

VTE is a condition in which a blood clot forms in a deep vein, usually in a leg, arm, or groin, and may travel to the lungs causing a blockage of the blood supply, with possible life-threatening consequences. This safety issue is distinct from the very rare side effect of thrombosis with thrombocytopenia syndrome (TTS) (i.e. blood clots with low blood platelets).

VTE was included in the risk management plan for the Janssen COVID-19 vaccine, as a safety concern to be investigated, based on a higher proportion of cases of VTE observed within the vaccinated group versus the placebo group, in the large clinical study that was used to authorize this vaccine. The issue has been closely monitored.

The PRAC also reviewed evidence from the post-marketing setting – that is, data gathered while the vaccine is being used in vaccination campaigns. When taking all evidence into account, the committee concluded that there is a reasonable possibility that rare cases of VTE are linked to vaccination with the Janssen COVID-19 vaccine.

The committee is therefore recommending that VTE be listed in the product information as a rare side effect of the Jansen COVID-19 vaccine, together with a warning to raise awareness among healthcare professionals and people receiving the vaccine, especially those who may have an increased risk of VTE.

- PRAC assessment of cases of immune thrombocytopenia with the Vaxzevria and Janssen COVID-19 vaccines

The PRAC assessed cases of immune thrombocytopenia (ITP) reported following vaccination with the Vaxzevria vaccine (formerly AstraZeneca COVID-19 vaccine), as well as with the Janssen COVID-19 vaccine.

ITP is a condition in which the immune system mistakenly targets blood cells called platelets, which are needed for normal blood clotting. Very low levels of blood platelets can be associated with bleeding, and have serious health consequences.

The committee assessed all of the available data, and recommended updating the product information of both vaccines to include ITP as an adverse reaction with unknown frequency.

Furthermore, a warning statement has been agreed upon to highlight the fact that cases of very low levels of blood platelets have been reported very rarely, usually within the first four weeks following vaccination with the Janssen or Vaxzevria COVID-19 vaccine.

If an individual has a history of ITP, the risk of developing low platelet levels should be considered before vaccination, and platelet monitoring is recommended after vaccination with either of these vaccines.

The PRAC will continue to monitor new information, and will take any further actions that may be necessary.

Source: https://www.ema.europa.eu/en/news/meeting-highlights-pharmacovigilance-risk-assessment-committee-prac-27-30-september-2021

CLARIFICATIONS/CONCLUSIONS ON EVENTS PRESENTED IN PREVIOUS COMMUNICATIONS

Safety and efficacy of the NVX-CoV2373 COVID-19 vaccine

Early clinical studies of the Novavax COVID-19 vaccine, NVX-CoV2373, consisting of 5 mg of a recombinant nanoparticle spike protein plus 50 mg of Matrix-M adjuvant, have shown that a two-dose regimen administered 21 days apart was safe and was associated with a robust immune response in healthy adult participants.

The publication cited presents data from the 2019nCoV-302 study, a phase 3, randomized, observer-blinded, placebo-controlled trial to evaluate the efficacy, immunogenicity, and safety of NVX-CoV2373 in preventing Covid-19 in participants between the ages of 18 and 84 in the United Kingdom.

A total of 15,187 participants were randomly selected, and 14,039 were included in the per-protocol efficacy population. Of the participants, 27.9% were 65 years of age or older, and 44.6% had coexisting illnesses. A two-dose regimen of the NVX-CoV2373 vaccine administered to adult participants conferred 89.7% protection against SARS-CoV-2 infection, and showed high efficacy against the B.1.1.7 variant.

The results of this trial provide further evidence that immunization with a protein-based, adjuvanted vaccine such as NVX-CoV2373 can prevent Covid-19 caused by either B.1.1.7 or non-B.1.1.7 variants. In addition, NVX-CoV2373 can be stored at standard refrigeration temperatures and has the potential to induce a broad epitope response to the spike protein antigen. Both of these attributes are important for the efficient implementation of this vaccine globally.

Source: Heath PT, Galiza EP, Baxter DN, et al. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. N Engl J Med. (2021) doi: 10.1056/NEJMoa2107659.

Co-administration of COVID-19 vaccines with other vaccines

Argentina: The National Commission on Immunizations (CoNaIn) of Argentina's Ministry of Health, in furtherance of the goals set forth in its national vaccination strategy, issued a recommendation on the co-administration of vaccines, providing for co-administration of COVID-19 vaccines with any other vaccine in the National Vaccination Schedule. The recommendation allows for administering the vaccines on the same or different days, and does not require an interval between doses. The goal is to take advantage of all opportunities for vaccination, an approach aligned with various scientific societies, agreed to by ministers of the country's 24 jurisdictions, and consistent with available evidence and the recommendations issued by other countries.

Source: https://bancos.salud.gob.ar/recurso/memorandum-coadministracion-de-vacunas-contra-covid-19-con-otras-vacunas

United States: Studies are being planned and conducted to evaluate the safety and immunogenicity of co-administering COVID-19 vaccines with other vaccines. Extensive research on the simultaneous administration of the most widely used live and inactivated vaccines has demonstrated seroconversion rates and rates of adverse reactions similar to those observed when the vaccines are administered separately.

It is not known whether the reactogenicity of COVID-19 vaccines is increased with co-administration, including with other vaccines known to be more reactogenic, such as adjuvanted vaccines. The CDC believes that COVID-19 vaccines can be administered without regard to the timing for administering other vaccines. This includes simultaneous administration of COVID-19 vaccine and other vaccines on the same day.

When deciding whether to administer one or more vaccines with a COVID-19 vaccine, vaccination providers should consider whether the patient is behind or at risk of becoming behind on recommended vaccines, the risk to the patient of vaccine-preventable disease (e.g., during an outbreak or occupational exposures), and the reactogenicity profile of the vaccines. If multiple vaccines are administered at a single visit, each injection should be administered in a different injection site. For adolescents and adults, the deltoid muscle can be used for more than one intramuscular injection administered at different sites in the muscle. It is important to document the vaccines given, along with the dosage, batch number, and expiration date of each vaccine.

In administering the vaccines, it is recommended that the injection sites be separated, if possible, by at least one inch (2.5 cm), and that vaccines that are more likely to cause local reactions be administered in different limbs.

Source: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fvaccines%2Fcovid-19%2Finfo-by-product%2Fclinical-considerations.html#Coadministration

United Kingdom: In the absence of information on the co-administration of COVID-19 vaccines with other vaccines, first principles would suggest that interference between inactivated vaccines with different antigenic content is likely to be limited. Based on experience with other vaccines, any potential interference is most likely to result in slightly attenuated immune response to one of the vaccines. There is no evidence of any safety concerns, although it may make the attribution of any adverse events more difficult.

Considering that the COVID-19 vaccines of Pfizer-BioNTech, AstraZeneca, and Moderna are considered inactivated, where individuals in an eligible cohort present with having recently received another inactivated or live vaccine, COVID-19 vaccination should still be given. The same applies for most other live and inactivated vaccines where COVID-19 vaccination has been administered first, or where a patient presents requiring two vaccines. It is generally better for vaccination to proceed in order to avoid any further delay in protection, and to avoid the risk of the patient not returning for a subsequent appointment.

An exception to this is the live attenuated shingles vaccination, where a seven-day interval should ideally be observed, given the possibility that an inflammatory response to the COVID-19 vaccine may reduce the response to the live virus.

Studies are currently underway to support co-administration of COVID-19 vaccines in the 2021–2022 season.

When co-administration of vaccines does occur, patients should be informed about the likely timing of potential adverse events relating to each vaccine.

Source:
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1009174/COVID-19_vaccination_programme_guidance_for_healthcare_workers_6_August_2021_v3.10.pdf

Booster doses of Janssen's and Moderna's COVID-19 Vaccines: Meeting of the U.S. Food and Drug Administration (FDA) Vaccines and Related Biological Products Advisory Committee

The Vaccines and Related Biological Products Advisory Committee (VRBPAC) is due to meet on 14 and 15 October to discuss the use of booster doses of the Moderna and Janssen COVID-19 vaccines. Both vaccines are currently licensed in the U.S. for emergency use to prevent COVID-19 in people 18 years of age and older. The committee will also hear presentations and discuss the available data on the use of a booster consisting of a vaccine different from the one used for the primary authorized or approved COVID-19 vaccination series (heterologous or “mix and match” booster).

The committee will discuss, on separate days, amendments to the emergency use authorization, to allow boosters of the Moderna and of the Janssen COVID-19 vaccines in individuals 18 years of age and older.

Additionally, the committee will hear a presentation from the National Institute of Health's National Institute of Allergy and Infectious Diseases, on the heterologous use of booster doses following primary series of the three COVID-19 vaccines currently authorized for use in the United States.

Source: https://www.fda.gov/news-events/press-announcements/fda-hold-advisory-committee-meetings-discuss-emergency-use-authorization-booster-doses-and-covid-19

Adverse Events of Special Interest (AESI) and Related Risks: Multisystem Inflammatory Syndrome in Children

About AESI: Children and adolescents are just as susceptible to SARS-CoV-2 infection as adults, but they develop primary symptomatic COVID-19 infection at significantly lower rates and rarely develop severe illness. However, it has become clear that a small proportion of children develop a life-threatening hyperinflammatory condition four to six weeks after infection with primary COVID-19, known as Multisystem Inflammatory Syndrome in Children (MIS-C). Patients with MIS-C experience persistent fever, fatigue, and a variety of signs and symptoms (e.g., cardiac, gastrointestinal, renal, hematological, dermatological, neurological) involving multiple organs, in addition to elevated inflammatory markers.

A similar condition has also been reported since June 2020 as a rare complication of COVID-19 in adults (MIS-A), which can, however, be more complicated than in children. Adults with MIS-A may experience fever, low blood pressure, abdominal (intestinal) pain, vomiting, diarrhea, neck pain, rash, tightness/pain in the chest, and fatigue. MIS-A can be very serious, so it is important to seek medical attention as soon as possible. It requires hospitalization if, in the absence of severe respiratory disease, there is laboratory evidence of current or previous SARS-CoV-2 infection (within 12 weeks), severe extrapulmonary organ dysfunction (including thrombosis), or laboratory evidence of severe inflammation. There have been reports of patients with MIS-A up to the age of 50 and, compared with MIS-C, they are more likely to have underlying health problems and an identifiable background of respiratory disease.

Patients with MIS-A have clinical features that overlap markedly with MIS-C, although the severity of cardiac dysfunction, incidence of thrombosis, and mortality can be higher in the case of MIS-A.

Differential diagnoses for MIS-C/A include Kawasaki Disease (KD), Kawasaki Shock Syndrome (KSS), Hemophagocytic Lymphohistiocytosis (HLH), Toxic Shock Syndrome (TSS), Macrophage Activation Syndrome (MAS), and a variety of other conditions, particularly those that cause myocarditis or hyperinflammation.

Diseases and other factors: According to the CDC, research on MIS-C and MIS-A, and on how they affect children and adults, is continuing. It is not known why some children and adults develop MIS-C or MIS-A and others do not, and whether children with certain health conditions are more likely to develop MIS-C.

Medications: There are no medications associated with MIS C/A.

Vaccines in general: There have been reports, following vaccination with DTaP and DTaP-IPV/PRP-T, of cases of Kawasaki disease (KD), however it is unknown whether MIS-C/A could occur after routine immunization.

COVID-19 vaccines: At present it is not known whether MIS-C/A could occur following SARS-CoV-2 vaccination, however this condition, as a potential adverse event following immunization (AEFI), needs to be explored. MIS-C is a novel syndrome in children, one that is temporally associated with SARS-CoV-2 infection, and has not previously been described in association with any vaccine. To date, MIS-A has not been reported in adult participants in SARS-CoV-2 vaccine trials, and so far few children have been included in these trials.

Sources:

Black SB, Law B, Chen RT, et al. The critical role of background rates of possible adverse events in the assessment of COVID-19 vaccine safety. Vaccine, 39(19), 2021, 2712–2718. https://doi.org/10.1016/j.vaccine.2021.03.016

Multisystem Inflammatory Syndrome in Adults (MIS-A) | CDC. https://www.cdc.gov/mis-c/hcp/index.html