Indian Academy of Pediatrics
ADVISORY COMMITTEE ON VACCINES AND IMMUNIZATION PRACTICES

Guidance on Covid-19 vaccines:
FAQs on Covid-19 vaccines for Pediatricians

Coronavirus disease (COVID-19), is an infectious disease caused by the newly discovered coronavirus (SARS-CoV-2), which has spread rapidly throughout the world. In March 2020, the World Health Organization (WHO) declared the COVID-19 outbreak a pandemic. The Covid-19 pandemic has caused, globally, as of 12 January 2021, 91,304,594 confirmed cases, including 1,952,195 deaths. In India, as on 12 January 2021, there have been 10,479,913 confirmed cases of COVID-19 with 151,364 deaths. While countries, including India, have taken strong measures to contain the spread of COVID-19 through better diagnostics and treatment, vaccines are expected to provide a lasting solution by enhancing immunity and containing the disease spread. In response to the pandemic, the vaccine development process has been fast-tracked. With vaccines based on new, never licensed platforms, concerns exist about the safety of these vaccines.

The Government of India is geared to launch the COVID 19 vaccination rollout on 16th January 2021. Two vaccines, Covishield^{TM} (Oxford-Astra-Sii) and Covaxin^{TM} (Bharat Biotech) have been granted Emergency Use Authorization (EUA). The safety and efficacy data from clinical trials of vaccine candidates have been examined by National Regulatory Authority (NRA) of our country before granting the EUA. It needs to be strongly emphasized that even after receiving the COVID 19 vaccine, precautions like use of face cover or masks, hand sanitization and maintain distancing should be continued.

This guidance document, in a FAQ format, attempts to guide the pediatricians/members of the Indian Academy of Pediatrics (IAP), regarding the usage of the available Covid vaccines.

Q.1 Which platforms are being investigated for Covid-19 vaccines?

Ans. Several platforms are being explored for Covid vaccines. These include the traditional platforms- inactivated virus, live-attenuated virus, subunit vaccines, VLPs and the newer platforms- viral vectored vaccines and the nucleic acid (DNA/mRNA) vaccines. The newer platforms are being used for the first time in humans.

Q.2 How many vaccines against Covid-19 are in development?

Ans. As of 5 January 2021, there are 172 vaccine candidates in pre-clinical development, 20 are in phase 1 trials, 22 are in phase 1-2, 3 are in phase 2, 4 in phase 2-3 and 13 in phase 3 trials.

Q.3 Which Covid vaccines are likely to be available in India?

Ans. The vaccines to be made available in India are presently, Covishield of Oxford-Astra-SII and Covaxin of Bharat Biotech and at a later time, Sputnik V of Gamelaya Institute Russia and ZyCov-D of Zydus Vaxxicare.

Q.4 Are healthcare workers (HCWs) at increased risk of infection by Covid-19?

Ans. Healthcare workers (HCWs) are at increased risk of acquiring Covid-19 infection in the workplace. In a study done in USA and UK, compared with the general community, front-line health-care workers were at increased risk for

reporting a positive COVID-19 test (adjusted HR 11·61, 95% CI 10·93–12·33). Probable reasons include a shortage of personal protective equipment (PPE), long-time exposure to large numbers of infected patients, inadequate training in infection prevention and control, and exposure to unrecognized Covid-19 patients. Infection in HCWs may also occur due to contact in non-clinical settings. In a study from Oman, 35% of hospital-acquired infections were a result of contact with another infected colleague, particularly during 'break' times, as the HCWs were not compliant with social distancing and universal masking when eating. Among 2,633,585 U.S. COVID-19 cases reported individually to CDC during February 12–July 16, 18% were identified as HCW, 8% were hospitalized and 5% were treated in an ICU. Underlying comorbid conditions were found in 44%.

In a study done in China, the authors found that 13% of virologically-confirmed cases had asymptomatic infection, a rate that almost certainly understates the true rate of asymptomatic infection, since many asymptomatic children are unlikely to be tested.

As of October 29, 2020, 9% of all cases of COVID-19 reported to the Centers for Disease Control and Prevention (CDC) were among children. Children were 1-3.4% of total reported hospitalizations (25 states and NYC reported), and between 0.6-6.4% of all child COVID-19 cases resulted in hospitalization.

Therefore, despite the low Covid-19 incidence and severity in children, the pediatricians should not lower his/her guard against the disease.

Q.5 What is Emergency Use Authorization (EUA) and which are the vaccines that have been granted EUA in India?

Ans. In an emergency situation, like the current Covid-19 pandemic, mechanisms have been developed to grant interim approval to a vaccine, if there is evidence of reasonable efficacy and safety. This is known as Emergency Use Authorization (EUA). For an EUA to be issued for a vaccine, for which there is adequate manufacturing information to ensure quality and consistency, the National Regulatory Authority (NRA) must determine that the known and potential benefits outweigh the known and potential risks of the vaccine.

Marketing approval is granted only after completion of the trials and analysis of full data. EUA permits governmental bodies to use the vaccine for the public before market authorization. In India, two vaccines have received EUA. They are Oxford-Astra-SII vaccine (Covishield) and Covaxin, which is the inactivated vaccine by Bharat Biotec.

Q.6 What is the efficacy and safety profile of viral vectored vaccines?

Ans. Adenoviruses are excellent vectors for delivering genes or vaccine antigens to the target host tissues and are being tested in several vaccine and gene therapy studies for cancers. The advantages of Adenovirus-based vectors include broad range of tissue tropism, well-characterized genome, ease of genetic manipulation including acceptance of large transgene DNA insertions, inherent adjuvant properties, ability to induce robust transgene-specific T cell and antibody responses, non-replicative nature in host, and ease of production at large scale. Most adenoviruses cause mild diseases in immunocompetent human adults and by deletion of crucial regions of the viral genome the vectors can be rendered replication-defective, which increases their predictability and reduces unwanted side effects.

The major disadvantage could be the pre-existing immunity to the viral vector, in humans. This may blunt the response to the vaccine. This is usually overcome by adjusting the dose of the viral vector, using a prime-boost combination with different vectors or by using non-human adenovirus vectors.

Human adenovirus-based drugs have been in use for more than 50 years. An anti-cancer drug was approved for use among the civilian population in China, and has already been given to more than 30,000 patients. Adenovectors are being tested in vaccines against HIV, Malaria, Ebola, Zika, Hepatitis C and many other diseases. No major safety issues have been observed.

Q.7 What is the safety profile of mRNA vaccines?

Ans. mRNA vaccine are being investigated in vaccines against HIV, Rabies, Influenza, Zika and other infective agents. mRNA exerts its effects in the cytoplasm and does not enter the nucleus. Thus, there is no risk for integration into the host genome. Except for an increased local and systemic reactogenicity, no major safety issues have been described with mRNA vaccines. In the recent clinical studies, the occurrence of neurological problems (Bell's palsy, Transverse myelitis) has not been causally related to the mRNA vaccine.

Q.8 What are the results of the Phase 3 studies of ChAdOx1 nCoV-19 vaccine (AZD1222) of Astra Zeneca-Sii (Covishield)?

In symptomatic Covid-19 participants with NAAT +ve test, the overall VE was 70·4% (54·8 to 80·6). In those who received the low-dose (LD) followed by the standard dose (SD), LD/SD, the VE was 90.0% (67.4-97), while it was 60.3% (28.0-78.2) in the

SD/SD group. There were no hospitalizations in the vaccine group vs 10 in the control group. The VE was better with a 6 weeks interval between doses.

The vaccine had a good safety profile with serious adverse events and adverse events of special interest balanced across the study arms. One case of transverse myelitis, 14 days after the 2nd dose of vaccine, was possibly unrelated to the vaccine. 2 cases of transverse myelitis were observed one each in vaccine and control groups. This was determined to be unrelated by the Independent Safety and Data Monitoring Board (ISDMB).

Q.9 What are the results of the Phase 3 studies of the Russian Gameleya institute vaccine (Sputnik V)?

Ans. This vaccine is an Adeno-based (rAd26-S+rAd5-S) vaccine utilizing the prime-boost principle.

In a small phase 2 study, with 76 subjects, the vaccine demonstrated high anti RBD-IgG titres and a good T-cell response. Most adverse events were mild and no serious adverse events were detected.

The Russian government granted EUA and subsequently based on the analysis of data on volunteers (n = 18,794) who received both the first and second doses, a VE of 91.4% has been claimed. In India a Phase 2 trial with, 100 subjects has been completed and a phase 3 with 1500 subjects is ongoing.

Q.10 What is the data about Covaxin, the vaccine by Bharat Biotech?

Ans. This vaccine is a whole-virion inactivated SARS-CoV-2 vaccine formulated with a TLR 7/8 agonist molecule adsorbed to alum (Algel-IMDG). In a phase 1 study, the vaccine elicited high IgG antibodies against the S1 protein, RBD and the

Nucleoprotein. Pain at the injection site was the most common local adverse event in the Algel-IMDG groups. The distribution of local and systemic AEs was equal among the vaccine treatment groups when compared to the control arm.

In the phase 2 study, in 380 participants, the vaccine was found to be safe with no serious adverse events. Humoral and cell-mediated responses reported in this study is expected to persist until at least 6-12 months after the second vaccination dose

A phase 3 study with 25800 subjects is in the final stages.

This vaccine has been granted EUA.

Q.11 What is the data about ZyCov-D, the vaccine by Zydus Vaxxicare?

Ans. This vaccine is a plasmid-DNA vaccine. This vaccine is administered intradermally, 3 doses at 0-28-56 days. Phase 1 trial has been completed. The vaccine was found to be safe and immunogenic. Phase 2 study was initiated in August 2020, in 1085 subjects in 9 centers and the results are being analyzed. Approval has been granted for the phase 3 study.

Q.12 What is the schedule of the Covid-19 vaccines?

Generally, most Covid-19 vaccines are administered in two-dose schedule, 21-28 days apart. The exact schedule depends upon the manufacturer.

Astra-Zeneca: 2 doses IM at 0-28d

Pfizer: 2 doses IM at 0-21d

Moderna: 2 doses IM at 0-28d

Gamelaya: 2 doses IM at 0-21d

Covaxin (BBIL): 2 doses IM at 0-28d

Q.13 What are the storage requirements for Covid vaccines?

The University of Oxford/AstraZeneca/SII vaccine and Covaxin of Bharat Biotech, can be stored, transported and handled at $+2^0$ C to $+8^0$ C.

- BioNTech/Fosun Pharma/Pfizer vaccine has a recommended temperature condition of -70^0 C and can be stored for five days at $+2^0$ C to $+8^0$ C.
- The Moderna/NIAID vaccine remains stable at -20^0 C for up to six months and remains stable at $+2^0$ C to $+8^0$ C, for 30 days
- The freeze -dried formulation of the Gamaleya institute, Sputnik-V vaccine can be stored at $+2^0$ C to $+8^0$ C.

Q.14 What is the efficacy of the vaccines against severe Covid-19 and hospitalization due to Covid-19?

Ans. The remarkable finding is that all the three vaccines, which have published phase 3 trials, have shown almost 100% efficacy against severe Covid-19 and hospitalization due to Covid-19.

Q.15 How long after vaccination does protection begin?

Significant protection is observed at least 14 days after the last dose of the vaccine.

Q.16 How long will the vaccine induced protection last?

These are new vaccines with limited follow up period of 2-3 months. Only follow up of the vaccinees will provide information about the longevity of the immune response. While antibody titers may wane rather rapidly, memory B-cell and memory T-cell responses are expected to provide longer term protection. Generally, protection is expected to last for 6-12 months.

Q.17 Which Covid-19 vaccines are contraindicated in the immunocompromised?

All the live attenuated vaccines and replicating viral vector vaccines are contraindicated in this group.

Q.18 Can these vaccines be administered in pregnancy?

Ans. The vaccine has not been studied in pregnant women. Pregnancy is not a contraindication for the inactivated Covid vaccines. Pregnant high-risk individuals should be offered the vaccine after a one-to-one discussion.

Q.19 Can these vaccines be offered during lactation?

Ans. These vaccines can be offered to breast feeding mothers.

Q.20 Will the currently available vaccines be effective against mutated variant of covid-19?

Ans. Mutations are not uncommon with SARS-COV-2. Researchers have not found any major changes in neutralization by the N501Y mutation, which is the main mutation in UK variant. This mutation makes the receptor binding stronger and allow the virus to spread better. Similar is the case with other variants too. Some concerns exist about the effectiveness of current vaccines against the South African variant virus. Follow up studies would be able to throw more light on this aspect.

Q.21 Are the vaccines interchangeable?

Ans. There is no data available to support interchangeability of doses between vaccines. Therefore, it's always advisable to complete the vaccination schedule with same brand of vaccine.

Q.22 Which vaccine should I take?

Ans. It is preferable to take any vaccine that is offered first.

Q.23 How will the government of India (GOI) prioritize the groups for vaccination?

Ans. Based on the potential availability of vaccines, the Government of India has selected the priority groups who will be vaccinated on priority as they are at higher risk. The first group includes healthcare and frontline workers. The second group to receive Covid-19 vaccine will be persons over 50 years of age and persons under 50 years with comorbid conditions. The reason for including more than 50 years of age group for vaccination is that it will be able to cover 78% of persons having co-morbidities and thereby reduce mortality on account of Covid- 19.

Q.24 Why have children not been prioritized for vaccination with Covid-19 vaccine?

A. As of now, studies have shown that Covid-19 is relatively uncommon in children and when infected, typically have milder symptoms and the rate of complications are lower. The role of children in transmission of the disease is uncertain. While contact tracing studies have shown that children are rarely the index case in family outbreaks of Covid-19 have been reported in schools and school camps.
Thus, children are not high in the priority list for vaccination against Covid-19. So far, none of the Covid vaccines in phase 3 trials have included young children.

Q.25 Is it mandatory to take the vaccine?

Ans. Vaccination for Covid-19 is voluntary. However, it is advisable to receive the complete schedule of Covid-19 vaccine for protecting one-self against this disease

and also to limit the spread of this disease to the close contacts including family members, friends, relatives and co-workers.

Q.26 Can a person presently having Covid-19 (confirmed or suspected) infection be vaccinated?

Ans. Since this group can transmit the infection at the vaccination sites, vaccination is to be deferred for 14 days after resolution of symptoms.

Q.27 Is it necessary for a Covid-19 recovered person to take the vaccine?

Ans. Yes. A person who has recovered from Covid should take the full course of the vaccine, as protective antibody titers after disease, tend to wane rapidly.

Q.28 What is CoWin?

The central government has introduced an application named CoWin (Covid Vaccine Intelligence Work). It is a digitized platform for the roll-out of the vaccine in the country.

It has the data of over 75 lakhs health officials who will be first in line to get the vaccination. The app will have four modules — User administrator module, beneficiary registration, vaccination and beneficiary acknowledgment, and status updation.

Q.29 Do I have to register my name for vaccination?

Ans. Unless you are registered with your local health authority, you will not be eligible for vaccination. Even if unregistered till now, you still have an opportunity to register now with your local health authority. Registration of beneficiary is mandatory for vaccination for Covid-19.

Q.30 How will I know my vaccination date, timings and location for vaccination?

Ans. The eligible beneficiaries will be informed through their registered mobile number regarding the Health Facility where the vaccination will be provided and the scheduled time for the same. This will be done to avoid any inconvenience in registration and vaccination of beneficiaries.

Q.31 Will the private sector be involved in the Covid vaccination program?

Ans. Presently, private practitioners may volunteer as vaccinators in the government program. Covid-19 vaccines have not received market authorization and are unlikely to be available to private practitioners for professional use.

Finally, it is essential that we should not lower our guard. We should continue observing the preventive measures commonly known as SMS (Social Distancing, Mask, Sanitation) to decrease the transmission of the disease.

This document has been compiled by the members of the ACVIP 2020-21.

SG Kasi, Convener, ACVIP

Piyush Gupta, Chairperson ACVIP, National President IAP 2021

GV Basavaraja, HSG IAP 2020-2021