Interim recommendations for use of the CanSinoBIO Ad5-nCoV-S [recombinant] vaccine (Convidecia™) against COVID-19

Interim guidance

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World Health Organization

Background

This interim guidance[1] has been developed on the basis of the advice issued by the Strategic Advisory Group of Experts (SAGE) on Immunization at its plenary meeting on 5 April 2022.

Declarations of interests were collected from all external contributors and assessed for any conflicts of interest. Summaries of the reported interests can be found on the SAGE meeting website and SAGE Working Group website.

This interim recommendation pertains to the COVID-19 vaccine, Ad5-nCoV-S recombinant (Ad5-nCoV), developed by CanSino Biologics Inc., Tianjin, China. The most commonly used trade name is Convidecia™. The guidance is based on the initial evidence summarized in the Background document and the Annexes which include GRADE and evidence-to-recommendations (ETR) tables.

All referenced documents are available on the SAGE COVID-19 webpage: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/covid-19-materials.

Methods

SAGE applies the principles of evidence-based medicine and has set in place a thorough methodological process for issuing and updating recommendations *(1)*. A detailed description of the methodological processes as they apply to COVID-19 vaccines may be found in the SAGE evidence framework for COVID-19 vaccines *(2)*. This framework contains guidance on considering data emerging from clinical trials and post-introduction effectiveness and safety monitoring.

[1] The recommendations contained in this publication are based on the advice of independent experts who have considered the best available evidence, a risk–benefit analysis, and other factors, as appropriate. This publication may include recommendations on the use of medicinal products for an indication, in a dosage form, dose regimen, population or other use parameters that are not included in the approved labelling. Relevant stakeholders should familiarize themselves with applicable national, legal, and ethical requirements. WHO does not accept any liability for the procurement, distribution and/or administration of any product for any use.

General goal and strategy for the use of the Ad5-nCoV vaccine against COVID-19

The COVID-19 pandemic has caused significant morbidity and mortality throughout the world, as well as major social, educational and economic disruptions. There remains an urgent global need to make COVID-19 vaccines available and deploy them at scale and equitably across all countries. Countries are recommended to use the WHO Prioritization Roadmap *(3)* and the WHO Values Framework *(4)* as guidance for their prioritization of target groups. The WHO Prioritization Roadmap recommends that priority of vaccine use be given to the highest priority-use groups (health workers, older persons, persons with moderate to severe immunocompromising conditions), and high priority-use groups (persons with comorbidities, teachers, pregnant women etc). Within the capacity of programmes and vaccine availability, additional priority-use groups should be vaccinated as outlined in the WHO Prioritization Roadmap *(4)*, taking into account national epidemiological data and other relevant considerations.

Vaccine performance

A double-blind, randomized, international, placebo-controlled phase 3, clinical trial (NCT04526990) in adults aged 18 years and older was conducted in Argentina, Chile, Mexico, Pakistan, and Russia. The study involved 18 363 vaccinated and 18 354 unvaccinated participants and took place from September 2020; the endpoint of 150 COVID-19 cases was reached in January 2021, i.e. before the emergence of Delta and Omicron variants. The multi-country phase 3 study efficacy cohort included approximately 70% male participants. About 21% of the participants were aged 45–59 years and about 8% were aged 60 years or older *(5)*. The predetermined primary measure of efficacy of this one-dose vaccine was from 28 days or more after vaccination. At the time of analysis, 21 250 participants had been followed for 28 days or more with 105 cases of PCR-confirmed COVID-19 reported in the placebo group and 45 cases in the vaccine group (vaccine efficacy (VE): 58% [95% CI: 40–70%]). The median follow-up time was 45 days [interquartile range (IQR): 36–58]. There were 12 severe cases in the placebo group and 1 severe case in the vaccine group (VE: 92% [95% CI: 36–99%]). A difference in disease incidence between those in the vaccine group and the placebo group was apparent from about 14 days after vaccination. Measured from 14 days after vaccination, overall VE against symptomatic disease was 64% (95% CI: 53–72%) and among those aged 60 years or older 53% (95% CI: 1–78%). Efficacy against symptomatic disease 14 or more days after vaccination in persons with comorbidities was 60% (95% CI: 36–76%); efficacy against symptomatic disease 28 days or more after vaccination was 49% (95% CI 0, 74). The most common comorbidities included in the trial were hypertension, diabetes and obesity. No significant differences in efficacy were found by age, race, sex and body mass index.

In the primary safety analysis undertaken at the time of the efficacy analysis (36 717 participants), there was no significant difference between the Ad5-nCoV group and the placebo group in the incidence of serious adverse events (14 [0.1%] of 18 363 Ad5-nCoV recipients; and 10 [0.1%] of 18 354 placebo recipients, p=0.54), or medically attended adverse events (442 [2%] of 18 363 Ad5-nCoV recipients; and 411 [2%] of 18 354 placebo recipients, p=0.30), or any serious adverse events considered related to the study product (none in either Ad5-nCoV or placebo recipients). In the extended safety cohort, 1004 (63.5%) of 1582 Ad5-nCoV recipients; and 729 (46.4%) of 1572 placebo recipients reported a solicited systemic adverse event (p<0.0001), of which headache was the most common (699 [44.2%] of Ad5-nCoV recipients; and 481 [30.6%] of placebo recipients; p<0.0001). A total of 971 (61.3%) of 1584 Ad5-nCoV recipients and 314 (20.0%) of 1573 placebo recipients reported an injection-site adverse event (p<0.0001), of which pain at the injection site was the most frequent (939 [59.3%] of Ad5-nCoV recipients and 303 [19.3%] of placebo recipients *(6)*).

Children: a phase 2b trial (NCT04566770) was completed in children aged 6–17 years, with a two-dose regimen, 0.3 ml each dose, administered 56 days apart. The age indication for children for this vaccine has not yet received WHO Emergency Use Listing.

Persistence of immune response and booster doses:

Immuno-persistence and booster effects of Ad5-nCoV were studied (NCT04568811), which showed that neutralizing antibody was maintained at 70% of the peak level at 6 months after the first dose. Boosted at 6 months, the neutralizing antibody titres increased more than 7 times compared with the peak level following the first dose.

A heterologous versus homologous booster study was conducted (randomized, observer-blinded, parallel-controlled phase 4 trial; NCT04892459). In the study, adults who had received two doses of the inactivated vaccine CoronaVac (Sinovac) during the past 3–6 months were subsequently vaccinated with Ad5-nCoV (n=96) or CoronaVac (n=102). Heterologous boosting with Ad5-nCoV elicited significantly increased geometric mean titres (GMTs) of neutralizing antibody against SARS-CoV-2 when compared to homologous boosting with CoronaVac. These data suggest that heterologous boosting with Ad5-nCoV following initial vaccination with CoronaVac is safe and more immunogenic than homologous boosting *(7)*.

The phase 3 clinical trial (NCT04526990) vaccinated 44 247 participants with Ad5-nCoV or placebo. To keep the blinded status of the trial and meet the immunization request of trial participants, the protocol was updated to version 2.0 where participants were enrolled in a relative efficacy trial with two doses vs one dose immunization at 6-8 months after the primary immunization. At present, approximately 21 000 participants have received either their second dose or their first dose of vaccine. The safety and efficacy data of the booster immunization will be available towards the end of 2022.

Safety:

As of 31 December 2021, about 58 million doses of Ad5-nCoV have been distributed worldwide, of which around 13.8 million doses were administered in mainland China and the remaining in countries such as Argentina, Chile, Indonesia, Malaysia and Mexico. Data on adverse events were obtained from regulatory authorities (National Medical Products Association (NMPA), WHO-Uppsala Monitoring Centre (UMC) and regulatory authorities of other countries) and safety surveillance from the American Region, Chile, China and Mexico (data from UMC). Among those 58 million doses, 47 cases of thrombosis with thrombocytopenia syndrome (TTS) were reported (0.081 cases per 100 000 vaccinees) as of 31 December 2021. In comparison, the cumulative incidence of TTS following vaccination with other non-replicative adenovirus vector-based vaccines ranges from 0.5 to 6.8 cases per 100 000 vaccinees *(9)*. Of the 47 cases of TTS, 27 were males and 20 females; 25 cases were aged 18–59 years; 12 cases were aged 60 years and above, and for 10 cases, information on age was not available. Of the 47 cases, 33 occurred within 30 days following vaccination; 1 case occurred more than 30 days after vaccination; for the remainder no data are available. Among the 58 million vaccinees, 28 cases with Guillain-Barre Syndrome were reported, corresponding to an incidence rate of 0.05 per 100 000, which is below or similar to the background rate. A total of 39 reports of anaphylaxis were received, with a reported incidence of 0.07 per 100 000 vaccinees. According to literature reports, the incidence of anaphylaxis for other COVID-19 vaccinees is 0.25–2.47 per 100 000.

Due to limited global safety data available, it is recommended to monitor the safety of Ad5-nCoV vaccine closely as the use increases.

Intended use

Persons aged 18 years and above (for prioritization of subpopulations by age and other considerations, see the WHO Prioritization Roadmap *(3)*).

Administration

The recommended schedule is a single dose (0.5 ml) given intramuscularly into the deltoid muscle.

Booster doses

In accordance with the WHO Prioritization Roadmap, a booster dose is recommended for the highest and high priority-use groups (i.e. older adults, health workers, persons with comorbidities), administered 4–6 months after completion of the primary series. Countries with moderate-to-high rates of primary series coverage in higher priority-use groups should usually prioritize available resources to first achieve high booster dose coverage in higher priority-use groups before offering vaccine doses to lower priority-use groups.[2] If more than 6 months have elapsed since completion of the primary series, the booster dose should be given at the earliest opportunity.

Heterologous booster doses

The Ad5-nCoV booster dose following a primary series with the inactivated COVID-19 vaccine developed by Sinovac (CoronaVac) was associated with higher vaccine effectiveness compared to a homologous CoronaVac booster *(7)*. Ad5-nCoV vaccine may be used as a booster dose following a completed primary series using any other EUL COVID-19 vaccine.

Heterologous boosters should take into account current vaccine supply, vaccine supply projections, and other access considerations, alongside the potential benefits and risks of the specific products being used.

Co-administration with other vaccines

For adults, based on several co-administration studies of COVID-19 vaccines and inferred from co-administration studies of other adult vaccines, COVID-19 vaccines may be given concomitantly, or any time before or after, other adult vaccines including live attenuated, inactivated, adjuvanted, or non-adjuvanted vaccines *(8)*. When administered concomitantly, the vaccines should be injected in separate sites, preferably different extremities. Continued pharmacovigilance monitoring is recommended.

Contraindications

A history of anaphylaxis to any component of the vaccine is a contraindication to vaccination. People who have an anaphylactic reaction following the first dose of the Ad5-nCoV vaccine should not receive any further doses of the same vaccine. People who have had TTS following the first dose of this vaccine should not receive a second dose of the same vaccine.

[2] In some circumstances, there may be a relatively close trade-off in optimizing the impact of vaccine use between offering booster doses to older adults to avert more hospitalizations and deaths versus offering primary series doses to the remaining adults, adolescents, and children, that depend on country conditions, including supply and rollout timelines, past epidemic dynamics and infection-induced immunity, vaccine product, vaccine effectiveness, and waning of protection.

Precautions

A history of anaphylaxis to any other vaccine or injectable therapy (i.e. intramuscular, intravenous, or subcutaneous vaccines or therapies) is not a contraindication to vaccination. For such persons, a risk assessment should be conducted by a health professional. It is uncertain if there is an increased risk of anaphylaxis, but counselling should be given about the potential risk of anaphylaxis and the risks should be weighed against the benefits of vaccination. Such persons should be observed for 30 minutes after vaccination in health-care settings where anaphylaxis can be immediately treated.

In general, persons with an immediate non-anaphylactic allergic reaction to the first dose (i.e. urticaria, angioedema without respiratory signs or symptoms that occur within 4 hours of administration) should not receive additional doses, unless recommended after review by a health professional with specialist expertise. Subject to individual risk–benefit assessment, Ad5-nCoV could be provided under close medical supervision if it is the only available vaccine for persons at high risk of severe COVID-19. If a booster dose is offered, the patient should be observed closely for 30 minutes after vaccination in a health-care setting where severe allergic reactions can be immediately treated.

No severe allergic reactions or anaphylaxis caused by Ad5-nCoV have been recorded in the context of clinical trials, but rare cases have been reported following use in national vaccination programmes. As for all vaccines, Ad5-nCoV should be given under health-care supervision, with the appropriate medical treatment available in case of allergic reactions. As for any other vaccine, an observation period of 15 minutes after vaccination should be ensured.

Thrombosis with thrombocytopenia syndrome (TTS), a very rare syndrome of blood clotting combined with low platelet counts *(11)*, has been reported around 3–30 days following vaccination with Ad5-nCoV. A causal relationship between the vaccine and TTS is considered plausible although the biological mechanism for this syndrome is still being investigated. From the experience of TTS with other adenoviral-vectored COVID-19 vaccines, there is considerable geographical variation in the reported incidence, with very few cases reported from non-European countries, despite extensive use of the vaccine in these countries. An estimation of the risk needs further data collection and analysis.

In countries with ongoing SARS-CoV-2 transmission, the benefit of vaccination in protecting against COVID-19 far outweighs the risks of TTS. However, benefit–risk assessments may differ from country to country, and countries should consider their epidemiological situation, individual and population-level risks, availability of other vaccines, and alternate options for risk mitigation. The benefit–risk ratio is greatest in older age groups as the risk of severe COVID-19 disease outcomes including COVID-19-related thromboembolic events increases with age.

Vaccination of specific populations

Persons aged 65 years and over

The risk of severe COVID-19 and death increases steeply with age. WHO recommends the vaccine for use in all older persons without an upper age limit.

Persons with comorbidities

Certain comorbidities and health states such as diabetes mellitus, cardiovascular and respiratory disease, neurodegenerative disease and obesity have been identified as increasing the risk of severe COVID-19 and death. WHO recommends vaccination of persons with comorbidities.

Children and adolescents below the age of 18 years

There are limited data on efficacy or safety for persons below the age of 18 years for the Ad5-nCoV vaccine, and this age indication has not yet received Emergency Use Listing. Until EUL has been granted, vaccination of individuals below 18 years of age with this vaccine is not routinely recommended.

Pregnant persons

Pregnant women with COVID-19 are at higher risk of developing severe disease, with increased risk of intensive care unit admission and invasive ventilation, compared to non-pregnant women of reproductive age. COVID-19 in pregnancy is associated with an increased risk of preterm birth and of neonates requiring neonatal intensive care, and it may also be associated with an increased risk of maternal mortality *(9, 10)*. Pregnant women who are aged 35 years and older, or have a high body mass index, or have an existing comorbidity such as diabetes or hypertension, are at particular risk of serious outcomes from COVID-19.

Developmental and reproductive toxicology (DART) studies have not shown harmful effects of the vaccine in pregnant women and their foetuses. Available data from clinical trials are insufficient to assess vaccine safety or efficacy of Ad5-nCoV in pregnancy. Based on previous experience with other vaccines during pregnancy, the effectiveness of Ad5-nCoV in pregnant women is expected to be comparable to that observed for non-pregnant women in similar age groups. Compared with non-pregnant women, pregnancy is associated with higher rates of thrombosis, thrombocytopenia, and haemorrhage. However, current evidence does not suggest that pregnant women are at any greater risk of TTS than non-pregnant women. As data become available, recommendations on vaccination with Ad5-nCoV will be updated accordingly.

WHO has identified pregnant women as a priority-use group for COVID-19 vaccination, given their increased risk of severe outcomes. WHO recommends the use of Ad5-nCoV in pregnant women when the benefits of vaccination to the pregnant woman outweigh the potential risks. To help pregnant women make this assessment, they should be provided with information about the risks of COVID-19 in pregnancy, the likely benefits of vaccination in the local epidemiological context, and the current limitations of the safety data in pregnant women. WHO does not recommend pregnancy testing prior to vaccination. WHO does not recommend delaying pregnancy or terminating pregnancy because of vaccination.

Breastfeeding persons

WHO recommends the same use of Ad5-nCoV vaccine in breastfeeding and non-breastfeeding women. This is based on the following considerations: breastfeeding offers substantial health benefits to breastfeeding women and their breastfed children; and vaccine effectiveness is expected to be similar in breastfeeding women as in non-breastfeeding individuals. Data are not available on the potential benefits or risks of the vaccine to breastfed children. However, as Ad5-nCoV vaccine is not a live virus vaccine, it is biologically and clinically unlikely to pose a risk to the breastfeeding child. WHO does not recommend discontinuing breastfeeding because of vaccination.

Moderately and severely immunocompromised persons, including persons living with HIV with CD4 cell count of <200 cells/µl

Moderately and severely immunocompromised persons (ICPs) are at higher risk of severe COVID-19, regardless of age, although increasing age remains an important co-factor. For purposes of this interim recommendation, moderately and severely immunocompromised persons include those with active cancer, transplant recipients, immunodeficiency, and

active treatment with immunosuppressives. It also includes people living with HIV with a current CD4 cell count of <200 cells/µl, evidence of an opportunistic infection, not on HIV treatment, and/or with a detectable viral load (i.e. advanced HIV disease).[3] For more details, see the WHO Interim recommendations for an extended primary vaccination series in immunocompromised persons *(11)*.

Available data for WHO EUL COVID-19 vaccine products suggest that vaccine effectiveness and immunogenicity are lower in ICPs compared to persons without immunocompromising conditions *(11)*. The emerging evidence suggests that an additional dose included in an extended primary series enhances immune responses in some ICPs *(12)*.

WHO recommends an extended primary series including an additional (i.e. second dose) for ICPs. Although there are no data for the Ad5-nCoV vaccine in ICP populations, available evidence from other COVID-19 vaccines *(11)* suggests that an additional (second) dose should be given 1–3 months after the first dose in the standard primary series in order to increase protection as quickly as possible in ICPs. The most appropriate timing for the additional dose may vary depending on the epidemiological setting and the extent and timing of immune suppressive therapy and course of the disease, and should be discussed with the treating physician.

Information and, where possible, counselling about the limitations around the data on administration of an additional dose to ICPs should be provided to inform individual benefit–risk assessment.

Given that protection may remain inadequate in a portion of immunocompromised persons even after the administration of an additional dose, WHO further recommends that close contacts (in particular caregivers) of such individuals should be vaccinated if eligible (according to the product-specific vaccines that have received EUL). Additional public health and social measures at household level to protect immunocompromised persons are also warranted depending on the local epidemic circumstances.

Persons living with HIV (PLWH) who are stable on antiretroviral therapy

Available data on administration of the Ad5-nCoV vaccine are currently insufficient to allow assessment of vaccine efficacy or safety for PLWH. In the interim, given that the vaccine is not a live virus, PLWH may be vaccinated. Information and, where possible, counselling about vaccine safety and efficacy profiles in immunocompromised persons should be provided to inform individual benefit–risk assessment. It is not necessary to test for HIV infection prior to vaccine administration.

Persons who have previously had SARS-CoV-2 infection

Vaccination should be offered regardless of a person's history of symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serological testing for prior infection is not recommended for the purpose of decision-making about vaccination. Data from the pooled analyses indicate that the vaccine is safe in people with evidence of prior SARS-CoV-2 infection. With the emergence of Omicron, reinfections after natural infection are common. Hybrid immunity induced by exposure to a vaccine and to natural infection is superior to immunity induced by vaccine or infection alone *(13)*. The optimal

[3] **Active cancer:** Active immunosuppressive treatment for solid tumour or hematologic malignancy (including leukaemia, lymphoma, and myeloma), or within 12 months of ending such treatment. **Transplant recipients**: Receipt of solid organ transplant and taking immunosuppressive therapy; receipt of stem cell transplant (within 2 years of transplantation, or taking immunosuppressive therapy). **Immunodeficiency:** Severe primary immunodeficiency; chronic dialysis. **HIV** with a current CD4 count of <200 cells/µl and/or lacking viral suppression. **Immunosuppressives:** Active treatment causing significant immunosuppression (including high-dose corticosteroids), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents, tumor-necrosis factor (TNF) blockers, and other drugs that are significantly immunosuppressive or have received in the previous 6 months immunosuppressive chemotherapy or radiotherapy

time interval between a natural infection and vaccination is not yet known. Persons with PCR-confirmed SARS-CoV-2 before the administration of the primary series may choose to delay vaccination for 3 months following the infection. When more data on duration of immunity after natural infection become available, the length of this time period may be revised as well as the number of doses needed.

Persons with current acute COVID-19

Persons with acute PCR-confirmed COVID-19, including persons who are in-between doses, should not be vaccinated until after they have recovered from acute illness and the criteria for discontinuation of isolation have been met as per government advice. The optimal minimum interval between a natural infection and vaccination is not yet known. A minimum interval of 3 months could be considered.

Persons who previously received passive antibody therapy for COVID-19

In people who have previously received monoclonal antibodies or convalescent plasma as part of COVID-19 treatment, vaccination does not need to be delayed. Although some reduction in vaccine-induced antibody titres has been observed in people who previously received antibody products, the clinical significance of this reduction is unknown, and the balance of benefits versus risks favours proceeding with vaccination even considering the possibility of diminished vaccine effectiveness in this situation.

Special settings

Persons in settings such as refugee and detention camps, prisons, slums, and other settings with high population densities, where physical distancing is not implementable, should be prioritized for vaccination as outlined in the WHO Prioritization Roadmap *(14),* taking into account national epidemiological data, vaccine supply and other relevant considerations.

As noted in the WHO Prioritization Roadmap, national programmes should give special consideration to groups that are disproportionately affected by COVID-19 or that face health inequities as a result of social or structural inequities. Such groups should be identified, barriers to vaccination should be addressed, and programmes should be developed to enable equitable access to vaccines.

Populations with high HIV incidence

There is some concern that an Ad5-vectored vaccine could potentially increase the risk of HIV acquisition. Two placebo-controlled phase 2b trials in different populations that evaluated an Ad5-vectored HIV-1 vaccine found an increased risk of HIV acquisition among those vaccinated. In the first trial – the STEP study – the increased risk was observed in a subpopulation of uncircumcised mostly bisexual men who had pre-existing Ad5 immunity, and in the second trial – the Phambili study – the increased risk was observed in heterosexual men *(18–20)*. However in the Phambili trial seropositivity for Ad5 and circumcision were not associated with increased susceptibility to HIV infection. No increased risk of HIV acquisition was observed in a third trial using a different Ad5-vectored HIV vaccine *(20–22)*. In a non-human primate challenge study of Ad5-infected rhesus macaques, vaccination with a replication-incompetent Simian Immunodeficiency Virus (SIV) Ad5-vaccine increased the risk of SIV acquisition from low-dose SIV penile challenge *(23)*, replicating the results observed in human trials. In a case–control study, Ad5-seropositive rhesus macaques vaccinated with the empty Ad5 vector were not more susceptible to the SIV challenge, in contrast to those who received the Ad5-SIV vaccines, suggesting that the vector alone is not responsible for the heightened risk of HIV acquisition observed in some human studies.

The current data compatible with the increased HIV risk are confined to a specific Ad5 vectored HIV vaccine. Not all Ad5 platforms are the same. Among approximately 58 million persons vaccinated with Ad5-nCoV, no safety signal was identified in terms of HIV acquisition; however, surveillance was not set up to detect HIV infections and countries involved and the vaccine was mostly used in countries without high HIV transmission. A possible association between Ad5 vectored COVID-19 vaccines and increased susceptibility to HIV acquisition is currently of a theoretical nature only and is unproven. Further research and nested surveillance studies are encouraged. Data from an extended follow-up from the CanSinoBIO phase 3 trial investigating seroconversion in trial participants will become available towards the end of 2022. Given the uncertainties until more data are available, countries with a high risk of HIV transmission might consider using alternative vaccines, if available.

Other considerations

SARS-CoV-2 tests

Prior receipt of the Ad5-nCoV vaccine will not affect the results of SARS-CoV-2 nucleic acid amplification or antigen tests for diagnosis of acute/current SARS-CoV-2 infection. However, it is important to note that currently available antibody tests for SARS-CoV-2 assess levels of IgM and/or IgG to the spike or the nucleocapsid protein. The Ad5-nCoV vaccine contains the spike protein; thus, a positive test for spike protein IgM or IgG could indicate either prior infection or prior vaccination. To evaluate for evidence of prior infection in an individual who has received the vaccine, a test that specifically evaluates IgM or IgG to the nucleocapsid protein should be used. A positive nucleocapsid protein-based assay indicates prior infection, while a negative nucleocapsid protein-based assay is expected after vaccination (unless a natural infection has occurred). Antibody testing at an individual level is currently not recommended to assess immunity to COVID-19 following Ad5-nCoV vaccination.

Other preventive measures

As recent data suggest limited effect of the vaccine on transmission, particularly against Omicron, it is advisable that public health and social measures to reduce SARS-CoV-2 transmission should be considered, including use of face masks, physical distancing, handwashing, appropriate ventilation and other measures as appropriate in particular settings, depending on the COVID-19 epidemiology and potential risks of emerging variants. Each country is facing a different situation in the pandemic depending on several factors including the intensity of SARS-CoV-2 circulation, amount of population level immunity, capacities to respond, and agility to adjust measures. As the pandemic continues and the virus evolves, policy adjustments related to SARS-CoV-2 public health and social measures, will be needed. Government advice on public health and social measures should continue to be followed by vaccinated individuals, as well as those who have not yet been vaccinated.

Countries' strategies related to COVID-19 control should be designed to facilitate the participation of children in education and other aspects of social life, regardless of vaccination *(15)*.

Community engagement, and effective communication

Community engagement and effective communication (including risk communication) are essential to the success of COVID-19 vaccination programmes. Prioritization decisions should be made through transparent processes that are based on shared values, the best available scientific evidence, and appropriate representation and input by affected parties. Furthermore, communication needs to be strengthened about the mechanism of action of vector-based vaccines, efficacy and safety data derived from clinical trials and post-marketing studies, as well as background mortality,

maternal and neonatal outcomes, and rates of adverse events of special interest (AESIs) in groups prioritized for vaccination. Strategies should include: (i) culturally-acceptable and linguistically-accessible communications regarding COVID-19 vaccination made freely available; (ii) active community engagement and involvement of community opinion leaders and trusted voices to improve awareness and understanding of such communications; and (iii) inclusion of diverse and affected stakeholder opinions in decision-making. Such efforts are especially important in subpopulations who may be unfamiliar with or distrustful of health-care systems and immunization.

Vaccination logistics

The Ad5-nCoV vaccine is presented as a single dose vial or 3-dose vial with stopper (elastomeric with aluminium overseal), packaged in 40 vials per pack (total 40 doses per pack or 120 doses per pack). Unopened multidose vials should be stored in a refrigerator (2 °C to 8 °C) and should not be frozen. Once a vial has been opened (first needle puncture), it should be handled according to the WHO policy on opened multidose vaccines and be discarded at the end of the vaccination session or within six hours of opening, whichever comes first. The open vaccine vials should also be kept at cooled temperatures between 2 °C to 8 °C during the in-use period.

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded in patient records.

When scheduling vaccination for occupational groups, e.g. health workers, consideration should be given to the reactogenicity profile of Ad5-nCoV vaccine observed in clinical trials, which may occasionally lead to time off work in the 24–48 hours following vaccination.

In considering the programme implications of implementing these recommendations, particular attention should be given to equity, including the feasibility, acceptability, and effectiveness of the programme in resource-constrained settings.

Recommendations on addressing current knowledge gaps through further research

WHO recommends the following post-authorization monitoring activities and research.

- Safety surveillance and monitoring:
  - serious adverse events such as TTS *(16)*, anaphylaxis and other serious allergic reactions;
  - cases of multisystem inflammatory syndrome following vaccination;
  - cases of COVID-19 following vaccination that result in hospitalization or death;
  - background rates of AESIs (including thromboembolic events, cerebral venous sinus thrombosis, and TTS), maternal and neonatal outcomes, and mortality in groups prioritized for vaccination;
  - incidence by WHO region, age and sex, and pathophysiology of TTS;
  - background rates of Ad5 immunity
  - research and nested surveillance on HIV incidence in vaccinated versus non-vaccinated persons stratified by Ad5 seropositivity.

- Vaccine effectiveness:
  - correlates of initial protection (seronegative and seropositive persons) and correlates of durability of protection;
  - vaccine effectiveness in relation to current and future variants of concern;
  - vaccine effectiveness over time and whether protection can be prolonged by booster doses;
  - second doses and booster studies with heterologous vaccines;
  - studies to investigate whether this vaccine reduces SARS-CoV-2 transmission and viral shedding;
  - assessment and reporting of breakthrough infections and virus sequence information;
  - head-to-head studies with other vaccines on extent and duration of immunity using standardized neutralization, T-cell and mucosal immunity assays;
  - impact against transmission and indirect protection of unvaccinated populations; and
  - vaccine effectiveness against post-COVID-19 conditions (post-acute sequelae of SARS-COV-2 infection) including cardiovascular and pulmonary complications, cognitive impairment, mental health disorders, etc.

- Subpopulations:
  - studies on safety in pregnant and breastfeeding women;
  - immunogenicity and safety studies in persons below the age of 18 years; and
  - safety data on vaccination in immunocompromised persons, including persons living with HIV and persons with autoimmune disease.

- Vaccination logistics
  - immunogenicity and safety studies of co-administration with other vaccines, including influenza and pneumococcal vaccines

- Virus variants
  - global surveillance of virus evolution and the impact of virus variants on vaccine effectiveness to support possible update of vaccines;
  - modelling to determine the trade-offs for the use of vaccines with reduced effectiveness against emergent variants; and
  - booster studies with original and updated vaccine formulations.

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WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication.

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