UGANDA NATIONAL ACADEMY OF SCIENCES

Recommendation Report: The Use of the Inactivated SARS-CoV-2 BBIBP-CORV-CorV Sinopharm Vaccine

Ratified Addendum Recommendation to COVID- 19 Vaccine selection (April 2021) Report submitted in June 2021

By

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Executive Summary

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the virus responsible for the coronavirus disease of 2019 (COVID-19). First identified in Wuhan (Hubei, China) in December of 2019,it has since been declared a pandemic by the World Health Organization in March of 2020. (WHO, 2020).

According to a Ministry of Health press release dated 27th May 2021, Uganda was experiencing a second wave of the infection with 44,594 cumulative infections reported, 194 on hospital admissions,and 361 cumulative deaths due to COVID-19. (https://www.health.go.ug/cause/update-on-the- response-to-covid-19-pandemic/). Also of concern, is the increasing reports of cases of Variants of Concern in Uganda, including the Indian, UK, Nigeria and South African variants.

On 3rd November 2020, the Uganda Ministry of Health (MoH) made a request to the Uganda National Immunisation Technical Advisory Group (UNITAG) for advice on COVID-19 vaccine selection in the event that more than one vaccine is prequalified and approved for use by WHO (Annex1). As of 10th May 2021, five COVID-19 vaccines have been authorized for use through WHO Emergency Use Listing. These include: Vaxzevria formerly Astrazeneca, Pfizer/BioNTech, Moderna, Janssen and most recently, Sinopharm vaccine. UNITAG has reviewed the first four vaccines and made recommendations for Vaxzevria formerly Astrazeneca, and Janssen vaccine.

In light of the approval of the BBIBP-CorV Vaccine (Sinopharm) by WHO/SAGE on 7th May 2021, UNITAG has reviewed evidence related to the BBIBP-CorV vaccine to further update guidance offered to the Ministry of Health regarding COVID-19 vaccine selection.
Below is a summary of evidence that pertains to the BBIBP-CorV Vaccine and draft conclusions and recommendations;

The evidence considered:

1. **Vaccine characteristics**
   i. **Safety:** BBIBP-CorV has an acceptable and comparable safety profile as the other WHO EUL approved COVID-19 vaccines. Adverse events following immunization are mostly mild and transient, including injection site pain, headache, and fever.

   ii. **Efficacy considerations:** Two doses of COVID-19 vaccine BIBP administered at an interval of 21 days demonstrated efficacy against non-severe COVID-19 disease in the younger adult population and vaccine efficacy against hospitalization both of which reported a value of 79%. Efficacy among older persons, those with comorbidities, severe disease and duration of protection were not established in the BBIBP-CorV vaccine trials.

2. **Economic considerations**
   i. The cost of BBIBP-CorV vaccine ranges from $5 to $19 through bilateral agreements and $29.8 to $32.5 through private markets. Uganda earmarked UGX 500 billion (USD 13.3 Million) for purchase of COVID-19 vaccines in the 2021/22 national budget. The target is to vaccinate 49.6% of the population (21.9 million people).
   ii. BBIBP-CorV vaccine is not yet on the COVAX facility but African Union is in negotiations to secure the vaccine through the Africa Vaccine Acquisition Trust.

3. Health policy and programmatic aspects

a. The BBIBP-CorV Vaccine can be easily used in Uganda given it be distributed and stored using existing cold-chain infrastructure of 2-8^{o}C and has a shelf life of 24 months.
b. The BBIBP-CorV Vaccine obtained WHO Emergency Use Listing on 7th May 2021.
c. Uganda has a functional AEFI system that can ably detect and handle any severe adverseevents following immunization with Sinopharm vaccine.
d. The vaccine comes in one dose vials or syringes, with a VVM monitor.

Conclusions

Based on the available evidence examined, the UNITAG COVAX Working Group made the following conclusions;

i. The Sinopharm (BBIBP-CorV) vaccine, which received WHO/SAGE approval for EmergencyUse Listing, meets the minimum efficacy requirement of 50%, and is safe for use among the Uganda population aged 18 years and above.
ii. The BBIBP-CorV vaccine cold chain requirements are suited to the existing cold chain infrastructure in Uganda. The single dose prefilled syringes with VVM are easy to use in mass vaccination exercises, although they take up more storage space than single/multidose vials.
iii. The BBIBP-CorV is relatively more affordable than the mRNA vaccines, and has a comparable cost to Vaxzevria formerly AstraZeneca, and Janssen vaccines.

Recommendations

Based on the aforementioned evidence and informed conclusions, the UNITAG working group madethe following **recommendations**:

a) BBIBP-CorV vaccine (Sinopharm) is recommended for use in Uganda for persons aged 18 years and above, since it meets the minimum use requirements of efficacy, safety, affordability andprogrammatic fit.
b) The Immunisation program should weigh the benefits of ease of use of the prefilled syringes against the additional cold-chain space requirements compared to the single dose vials before choosing the packaging option to go for.
c) Ministry of Health together with the Ministry of Finance and Economic Development should work together on issues related to vaccine cost and procurement. Preference is given to use of trusted channels such as UNICEF and African Union.

1. Introduction

On 3rd November 2020, the Uganda Ministry of Health made a request to the Uganda National Immunisation Technical Advisory Group for advice on a) allocation framework and criteria to be used to prioritize COVID-19 vaccine recipients in the initial phase of vaccine scarce supply; b) vaccine selection in the event that more than one vaccine is prequalified and approved for use byWHO; c) what steps should be taken to mitigate vaccine hesitancy to COVID-19 vaccines especiallyamong high priority groups and most appropriate methods for communication.

This interim recommendation report is an update of the COVID-19 Vaccines Selection report submitted to the Ministry of Health in April 2021 and provides information on BBIBP-CorV Vaccine(Sinopharm) that was given Emergency Use Listing by WHO on 7th May 2021.

2. General Information on COVID-19

i. Update on COVID-19 disease situation

The WHO weekly epidemiological update dated 18th May 2021 (https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19---18-may-2021) showed that the number of new COVID-19 cases and deaths globally continued todecrease, although overall counts for both remained high with just over 4.8 million new cases andnearly 86, 000 new deaths reported in the past week. All regions reported a decline in new casesexcept for the Western Pacific where the number of new cases did not increase ordecrease. The highest numbers of new cases were reported from India (2,387,663 new cases; 13%decrease), Brazil (437,076 new cases; 3% increase), the United States of America (235, 638 newcases; 21% decrease), Argentina (151,332 new cases; 8% increase), and Colombia (115,834 newcases).

The African Region reported over 40, 000 new cases and over 900 new deaths in the week of 18thMay 2021. The highest numbers of new cases were reported from South Africa (16,326 new cases); 27.5 new cases per 100 000 population), Botswana (3,745 new cases; 159.3 new cases per 100 000 and Ethiopia (3,615 new cases; 3.1 new cases per 100 000). Cases in South Africa comprised 41% of cases reported in the region. The highest numbers of new deaths were reported from South Africa (459 new deaths; 0.8 new deaths per 100 000 population), Kenya (118 new deaths; 0.2 new deaths per 100 000), and Ethiopia (105 new deaths; 0.1 new deaths per 100 000).

According to a Uganda Ministry of Health press release dated 27th May 2021, Uganda was experiencing a second wave of the infection with 44,594 cumulative infections reported, 194 on hospital admissions, and 361 cumulative deaths due to COVID-19. (https://www.health.go.ug/cause/update-on-the-response-to-covid-19-pandemic/). Also of concern, is the increasing reports of cases of Variants of Concern in Uganda, including the Indian,UK, Nigeria, and South African variants (See Figures 1 and 2).

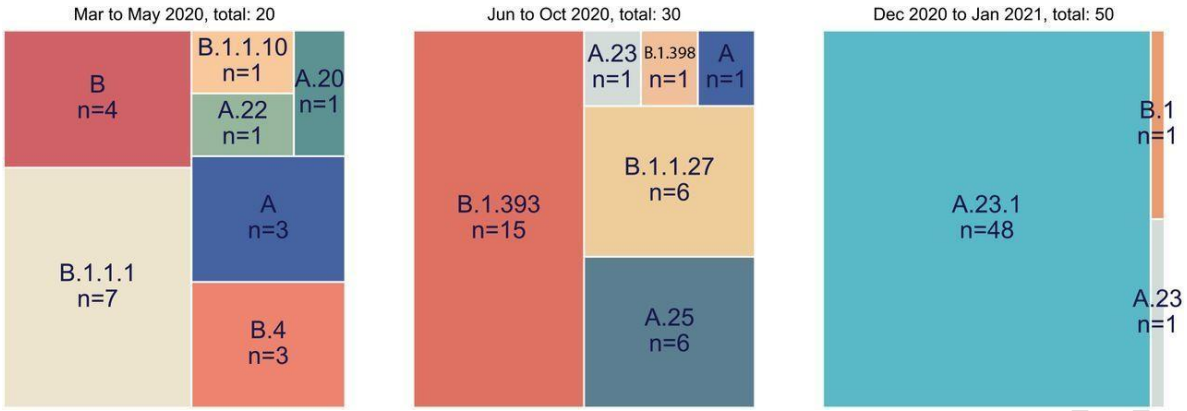

Figure 1: Covid-19 Variants in Uganda Mar 2020 – Jan 2021. Source: Bugembe et al 2021.https://www.medrxiv.org/content/10.1101/2021.02.08.21251393v1.full

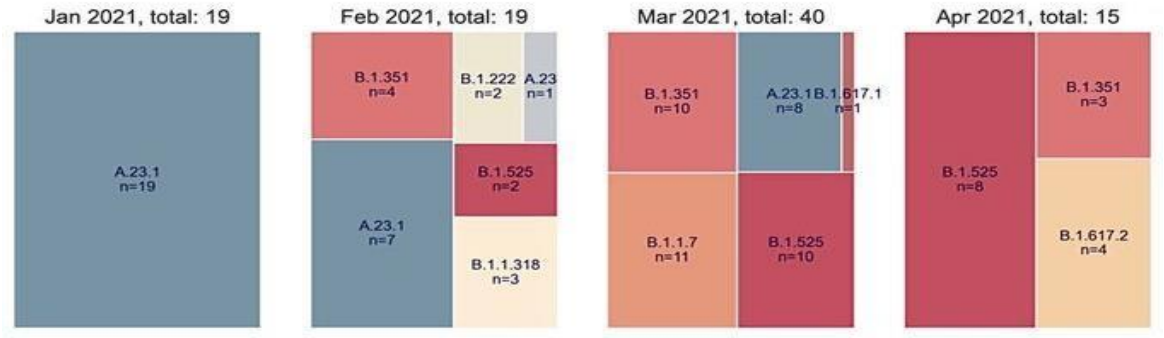

Figure 2: COVID-19 variants in Uganda Jan 2021 – April 2021. Source: Matthew Cotton (MRC/UVRI)(unpublished) https://twitter.com/mlcotten13/status/1399267387615109120

ii. COVID-19 Vaccines

As at 20th May 2021, five COVID-19 vaccines had received WHO Emergency Use Listing. These include: Vaxzevria fmr. Astrazeneca (ChAdOx1-nCoV-19), Pfizer/BioNTech (BNT 1626), Moderna (mRNA 1273), Janssen (Ad26.COV2-S [recombinant]), and Sinopharm vaccine (BBIBP-CorV). Uganda received 964,000 doses of Vaxzevria fmr. AstraZeneca Vaccine on 5th March 2021. 864,000 doses were from the COVAX facility, and 100,000 doses were a donation from Serum Institute of India. Vaccine rollout started on 10th March 2021.

As of 25th May 2021, the number of people that had received the vaccine was 541,569 (63.9%) and segregation by the target population groups is shown in Table 1.

However, due to delays in supply from the Serum Institute of Inia attributed to the increaseddemand from within India following an upsurge of cases, COVAX Facility notified its beneficiariesthat it anticipated delays in shipments of additional doses of Vaxzevria fmr AstraZeneca Vaccines.(https://www.who.int/news/item/25-03-2021-covax-updates-participants-on-delivery-delays- for-vaccines-from-serum-institute-of-india-(sii)-and-astrazeneca).

This has further prompted the drive to consider use of other WHO listed COVID-19 vaccines in thecountry.

Table 1: Number vaccinated by target population groups as of 25th May 2021

Priority groups (Individual)	Target	No. Vaccinated with 1st Dose	Performance(% Coverage)
Health workers (Ind)	150,000	49,897	33.3%
Security (Agg+Ind)	250,000	101,885	40.8%
Teachers (Ind)	550,000	68,780	12.5%
Elderly (>=50yrs)	3,348,500	56,071	1.7%
People with Co-morbidities (Ind)	500,000	12,467	2.5%
Others (Ind)	201,500	35,291	17.5%
Total	5,000,000	324,391	6%

Source: (UNEPI COVID-19 Vaccination Performance Update, 26 May 2021, Unpublished)

3. Presentation of Evidence on BIBBP-CorV (Sinopharm Vaccine)

a) Vaccine Immunization characteristics

Ref. WHO/SAGE Background document:
https://apps.who.int/iris/bitstream/handle/10665/341252/WHO-2019-nCoV-vaccines-SAGE-recommendation-BIBP-background-2021.1-eng.pdf?sequence=1&isAllowed=y

COVID-19 vaccine BIBP is a Vero cell-based, aluminium hydroxide-adjuvanted, β-propiolactone inactivated vaccine based on the 19nCOV-CDC-TAN-HB02 strain (HB02 strain) (3). The original Vero cell line was obtained from WHO, and the original cell bank, master cell bank, and working cell bankwere established by BIBP. The cells used for vaccine manufacture are the working Vero cell bank, which is of the 142nd generation.

i. Vaccine presentation and Use

The dosage form of the vaccine is injectable liquid. The product is a semi-transparent suspension, slightly white in color (after shaking), in a single-dose vial or non-auto disable prefilled syringe. The BBIBP-CorV vaccine is thermo-stable when stored and transported at 2-8^{0}C.

ii. Formulation of the Vaccine

The final vaccine product in each 0.5 ml dose is composed of 6.5 U (4 µg) of inactivated SARS-CoV-2 antigens and aluminium hydroxide adjuvant in phosphate-buffered saline (PBS). PBS is composed of disodium hydrogen phosphate dodecahydrate, sodium dihydrogen phosphate, and sodium chloride. None of the excipients are of animal or human origin.

iii. Dosage and route of administration

The recommended schedule is two doses(0.5ml) given intramuscularly into the deltoid muscle at an interval of 3 weeks. WHO recommends the use interval of 3–4 weeks. If the second dose is administered less than 3 weeks after the first, the dose does not need to be repeated. If administration of the second dose is delayed beyond 4 weeks, it should be given at the earliest possible opportunity.

iv. Co-administration with other vaccines

There should be a minimum interval of 14 days between administration of this vaccine and any othervaccine against other conditions.

v. Contraindications

A history of anaphylaxis to any component of the vaccine is a contradiction to vaccination. People whohave an anaphylactic reaction following the first dose of this vaccine should not receive a second doseof the same vaccine.

b) Vaccine Safety and Efficacy

i. Safety

Article: Zhang et. al. Lancet.2021 February:21(2):181-192. https://doi.org/10.1016/S1473-3099(20)30843-4

Method: Randomized double-blind placebo-controlled phase 1/2 trial among healthy adults aged 18-59 years in China.

***Finding*:** Study found that most adverse reactions were mild in severity and participants recovered within 48 hours.

Article: Xia et. al. Lancet. 2021 January; 21(1):39-51. https://doi.org/10.1016/S1473-3099(20)30831-8

Method: Randomized double-blind placebo-controlled phase 1/2 trial among healthy adults in China

Finding: Study findings show all adverse reactions were mild and moderate in severity. No serious adverse event was reported within 28 days after vaccination. One adverse event was reported within the first 28 days post vaccination and the most common systematic adverse reaction was fever.

Article: WHO. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BIBP-background-2021.1

Method: Review of clinical trial data

Finding: Study showed that the most common reported adverse reactions were pain and fever.

ii. Efficacy and Effectiveness

Article: Xia et. al. Lancet. 2021 January; 21(1):39-51. https://doi.org/10.1016/S1473-3099(20)30831-8

Method: Randomized double-blind placebo-controlled phase 1/2 trial among healthy adults in China

Finding: Study found that humoral responses against SARS-CoV-2 were induced in all vaccine recipients on day 42. Two-dose immunisation with 4 μg vaccine on days 0 and 21 or days 0 and 28 achieved higher neutralising antibody titres than the single 8 μg dose or 4 μg dose on days 0 and 14.

Article: WHO. 2021. https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccines-SAGE_recommendation-BIBP-background-2021.1

Method: Review of clinical trial data

Finding: Clinical trial data showed that two doses of COVID-19 vaccine BIBP demonstrated efficacyagainst non-severe COVID-19 disease in the younger adult population. Data are currently unavailable on protection against severe disease and in older adults ≥60 years of age. Phase 3 trial data has shown that 2 doses, administered at an interval of 21 days, have an efficacy of 79% against symptomatic SARS-CoV-2 infection 14 or more days after the second dose. Vaccine efficacyagainst hospitalization was 79%. The median duration of follow-up available at the time of evidence review was 112 days. The seroconversion rate of neutralizing antibody in the COVID-19 vaccine BIBP group was 99.5% in those aged 18–59 years and 100.0% in those ≥60 years

Efficacy among adults aged 60 and above

Clinical efficacy among adults aged 60 and above has not been established.

Ref https://apps.who.int/iris/bitstream/handle/10665/341252/WHO-2019-nCoV-vaccines-SAGE-recommendation-BIBP-background-2021.1-eng.pdf?sequence=1&isAllowed=y

Interim data from a multicentre, randomized, double-blind, placebo-controlled, phase 3 clinical trial to evaluate the efficacy, safety and immunogenicity of COVID-19 vaccine BIBP and COVID-19 vaccine WIBP in healthy people aged 18 years and above being conducted in Bahrain, Egypt, Jordan and the United Arab Emirates, involving 41,301 participants, showed that theseroconversion rate of neutralizing antibody in the COVID-19 vaccine BIBP group was 99.5% in those aged 18–59 years and 100.0% in those ≥60 years. However, Geometric Mean Titres (GMT) in younger adults 18-59 years of age were 156.2 (95%CI 149.8, 163.0) compared with 109.7 (95%CI97.4, 123.4). Thus, across both phase 1 and phase 3 studies, neutralizing antibody GMTs were lower in the older adult age group despite high rates of seroconversion.

Efficacy against severe disease

Vaccine efficacy against severe disease has not been demonstrated as only two cases of severe disease were registered in the control group during the phase 3 trial.

Efficacy among persons with co-morbidities

Vaccine efficacy among persons with co-morbidities was not established as only healthy adults were included in the BBIBP-CorV vaccine trial.

iii. Duration of Duration

There is currently no available data on the duration of protection of the BBIBP-CorV vaccine. The median duration of follow-up available at the time of evidence review was 112 days.

c) Economic Considerations

i. Vaccine related costs and resource use

The current prices paid range $5 to $19 through bilateral agreements and $29.8 to $32.5 on the private market (UNICEF COVID 19 market dashboard. https://www.unicef.org/supply/covid-19-vaccine-market-dashboard).

ii. Vaccine affordability

Uganda earmarked UGX 500 billion (USD 13.3 Million) for purchase of COVID-19 vaccines in the2021/22 national budget. The target is to vaccinate 49.6% of the population (21.9 million

people). (https://www.monitor.co.ug/uganda/news/national/budget-revised-to-shs44-trillion-3376690)

Uganda is part of the COVAX facility platform that is offering vaccines for about 20% of the country's population. BBIBP-CorV vaccine is not yet on the COVAX facility platform but African Union is in negotiations to secure the Sinopharm vaccine through the Africa vaccine acquisition trust. (http://www.chinadaily.com.cn/a/202104/23/WS6082d601a31024ad0bab9fd1.html).

d) Feasibility

i. Cold chain Requirements (temperature and space)

The product should be stored and transported refrigerated (2–8 °C) and protected from light. It should not be frozen. The proposed shelf-life on the label is 24 months. The Uganda vaccine logistics and delivery infrastructurein Uganda is suited to the 2-8^{o}C temperature range.

The cold-chain space requirements for BIBBP-CorV are 43.0 X 31.0 X 23.5 cm for a box with a total of 400 vials (400 doses) or 43.0 X 33.0 X 24.5 cm for a box with a total of 300 syringes (300 doses) giving a per dose space requirement of 61.8 cm^3 or 94.9 cm^3 respectively.

ii. Ability to Evaluate

Uganda has a functional AEFI surveillance system in place down to the district level, that has effectively responded to safety events related to immunization campaigns as demonstrated inthe 2019 MR campaign. (https://reliefweb.int/report/uganda/statement-uganda-s-minister- health-national-measles-rubella-and-polio-immunisation). AEFI reporting is part of the weekly Ministry of Health COVID-19 Vaccination updates delivered to the National Coordination Committee. (UNEPI 2021, Unpublished Reports).

iii. Regional and International Considerations

The BIBP Vaccine obtained WHO Emergency Use Listing on 7th May 2021. https://www.who.int/news/item/07-05-2021-who-lists-additional-covid-19-vaccine-for-emergency-use-and-issues-interim-policy-recommendations.

Four African countries have rolled out the BBIBP-CorV vaccine namely; Nigeria, Egypt, Algeria and Zimbabwe. (https://www.businessinsider.co.za/the-sinopharm-covid-19-vaccine-is-now-being-rapidly-rolled-out-in-several-other-african-countries-2021-2)

iv. Equity

Both the SAGE Values framework and roadmap and Uganda specific COVID-19 Values framework offer guidance on the fair allocation of COVID-19 vaccines based on core ethical principles. If distributed fairly, COVID-19 vaccines may have considerable impact on reducing health inequities.

v. Acceptability

Uganda received 964,000 doses of AstraZeneca vaccine and rolled out vaccination on 10th March 2021. As of 23rd May, 537,440 doses had been administered pointing to low vaccine uptake.

A survey of medical students showed that 62.7% were not willing to be vaccinated against

COVID-19 and 38% were willing to be vaccinated with any brand of approved vaccine (Kanyike et. al, 2021. https://tropmedhealth.biomedcentral.com/articles/10.1186/s41182-021-0)

4. Conclusions and Recommendations

Conclusions

Based on the available evidence examined, the UNITAG COVAX Working Group made the following conclusions;

a) The Sinopharm (BBIBP-CorV) vaccine, which received WHO/SAGE approval for Emergency Use Listing, meets the minimum efficacy requirement of 50%, and is safe for use among the Uganda population aged 18 years and above.

b) The BBIBP-CorV vaccine cold chain requirements are suited to the existing cold chain infrastructure in Uganda. The single dose prefilled syringes with VVM are easy to use in mass vaccination exercises, although they take up more storage space than single/multidose vials.

c) The BBIBP-CorV is relatively more affordable than the mRNA vaccines, and has a comparable cost to Vaxzevria formerly AstraZeneca, and Janssen vaccines.

Recommendations

Based on the aforementioned evidence and informed conclusions, the UNITAG working group made the following recommendations:

a) BBIBP-CorV vaccine (Sinopharm) is recommended for use in Uganda for persons aged 18 years and above, since it meets the minimum use requirements of efficacy, safety, affordability and programmatic fit.

b) The Immunisation program should to weigh the benefits of ease of use of the prefilled syringes against the additional cold-chain space requirements compared to the single dose vials before choosing the packaging option to go for.

c) Ministry of Health together with the Ministry of Finance and Economic Development should work together on issues related to vaccine cost and procurement. Preference is given to use of trusted channels such as UNICEF and African Union

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