Evidence Summary on Janssen Ad26.COV2.S (COVID-19) Vaccine for the prevention of COVID-19

Service Line	Evidence Summary
Publication Date	30 April 2021
Summary Length	78 Pages
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Background

The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has led to more than three million deaths worldwide, global economic and social disruption, and unprecedented challenges in the health system. As the world continues to face these challenges, several efforts, such as developing and implementing different health technologies that will ultimately lead us to our exit strategy from the crisis, were undertaken. Among these health technologies are vaccines against COVID-19 which are currently in different phases of trials around the world. Similar to other countries, the Philippine government has been exploring all means to access these vaccines and to ensure continuous supply of vaccines.

On April 19, 2021, the Philippine Food and Drug Administration (FDA) released the Emergency Use Authorization (EUA) for *Janssen Ad26.COV2.S (COVID-19) Vaccine*.

To date, at least 38 countries (e.g., the US, Canada, Germany, Italy, South Africa, the Philippines) have issued an emergency use authorization (EUA) for this product in their respective jurisdictions. Vaccine implementation of *Janssen Ad26.COV2.S (COVID-19) Vaccine* has already started in the US, Belgium, the Netherlands and South Africa. The US Food and Drug Administration (FDA) issued an EUA for the vaccine on 27 February 2021, while the European Medicines Agency issued a conditional marketing authorization for the product across the European Union on 11 March 2021. The vaccine was also included in the WHO emergency use listing on 12 March 2021. In the Philippines, our FDA has recently issued its EUA on 19 April 2021.

Basic information on *Janssen Ad26.COV2.S (COVID-19) Vaccine* is provided below:

Table 1.1 Characteristics of *Janssen Ad26.COV2.S (COVID-19) Vaccine*

Trade name	Janssen COVID-19 Vaccine
Other name	Ad26.CoV2.S
Manufacturer/s	Janssen Biotech Inc.
Vaccine platform	Replication-incompetent viral vector vaccine
Dose strength and administration	Consists of 1 dose of 0.5 mL per dose containing $5x10^{10}$ vp of Ad26.COV2.S
Route of administration	Suspension for injection, Intramuscular (IM)

Drug delivery system	Colorless to slightly yellow, clear to very opalescent sterile suspension. Each vial must contain 0.5 mL per dose containing $5x10^{10}$ vp of Ad26.COV2.S
Storage condition	2-8°C; shelf life: 3 months
Mechanism of action	The vaccine consists of a replication-incompetent recombinant adenovirus type 26 (Ad26) vector expressing the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike (S) protein in a stabilized conformation.
PHL EUA status	Released on 19 April 2021 *https://www.fda.gov.ph/wp-content/uploads/2021/04/EUA-Janssen-Website.pdf*
PHL FDA EUA indication	For active immunization to prevent COVID-19 caused by SARS-CoV-2 in individuals 18 years of age and older
WHO EUL status	Granted as of 12 March 2021 Reference: https://www.who.int/news/item/12-03-2021-who-adds-janssen-vaccine-to-list-of-safe-and-effective-emergency-tools-against-covid-19

The package insert is available via:
https://www.janssenlabels.com/emergency-use-authorization/Janssen+COVID-19+Vaccine-HCP-fact-sheet.pdf

Pursuant to the role of the Health Technology Assessment Council (HTAC) to develop coverage recommendations particularly in the selection and financing of COVID-19 vaccines using the Evaluation Framework set by the HTAC, this report presents all currently available evidence considered in the assessment of *Janssen Ad26.COV2.S (COVID-19) Vaccine*. This assessment follows the HTAC evaluation framework to assess COVID-19 vaccines using the following criteria: (1) responsiveness to magnitude and severity; (2) clinical efficacy and safety; (3) affordability and viability; (4) household financial impact; (5) social impact; and (6) responsiveness to equity.

Policy Question

The HTAC aims to answer the policy question:

Should ***Janssen Ad26.COV2.S (COVID-19) Vaccine*** be recommended for emergency use to reduce COVID-19 cases, severe infection, and deaths?

Recommendation *(as of 29 April 2021)*

The HTAC **recommends the emergency use of *Janssen Ad26.COV2.S (COVID-19) Vaccine*** to reduce the burden of COVID-19 among the population 18 years of age and older.

The HTAC considered the following criteria in formulating its recommendation for the vaccine:

Criteria	HTAC Judgment
Can *Janssen Ad26.COV2.S (COVID-19) Vaccine* significantly reduce the magnitude and severity of COVID-19?	**Yes.** *Janssen Ad26.COV2.S (COVID-19) Vaccine* has the potential to reduce the disease burden by averting a significant number of symptomatic infections, moderate to severe/critical infection, severe/critical infection, and hospitalization due to COVID-19 assuming sufficient vaccine coverage.
Is *Janssen Ad26.COV2.S (COVID-19) Vaccine* efficacious and safe?	Based on interim results of published peer-reviewed Phase III trial on *Janssen Ad26.COV2.S (COVID-19) Vaccine [cut-off analysis: date: 22 January 2021)]* (Sadoff et al., 2021a): **Yes**, it is efficacious for preventing: - symptomatic *(high certainty of evidence)* - moderate to severe/ critical COVID-19 cases *(high certainty of evidence)* - hospitalization due to COVID-19 *(moderate certainty of evidence)* - severe/critical cases *(moderate certainty of evidence)* The duration of protection cannot be assessed given the current data. **Yes**, it is safe in the known short-term safety outcomes, based on high certainty of evidence. Meanwhile, its long term safety outcomes cannot be determined given the short duration of observation at the time of the reports. Although vaccination appears to be associated with an extremely rare but potentially fatal thrombosis with

	thrombocytopenia syndrome (TTS), the HTAC deems the benefits far outweigh the risks. Pending stronger evidence of the association and consensus from stringent regulatory agencies, the HTAC finds no reason at this time not to recommend the use of the vaccine as approved by the FDA Philippines. However, measures against TTS must be included in all protocols for addressing adverse effects. The WHO interim recommendations for the use of this vaccine noted that a history of anaphylaxis to any component of the vaccine is a contraindication to vaccination.
Is *Janssen Ad26.COV2.S (COVID-19) Vaccine* affordable and feasible to use in a national immunization program (viability)?	**Yes.** It is affordable as the share of the population to be vaccinated using the said vaccine is highly commensurate to the share of the cost of the *Janssen Ad26.COV2.S (COVID-19) Vaccine* to the total vaccine budget. The share of the cost to implement vaccination using *Janssen Ad26.COV2.S (COVID-19) Vaccine* will constitute 4.74% of the total allocated budget for vaccination and will cover 8.57% of the 70 million target vaccinees for 2021. **Yes**, it is feasible as there are no significant barriers to vaccine implementation using *Janssen Ad26.COV2.S (COVID-19) Vaccine* in terms of storage, transport, and handling. Its one-dose requirement facilitates the completion of the vaccination schedule especially for those experiencing difficulty in returning for a second dose thereby improving compliance. In addition, the price per dose as well as the logistical and operational costs allow it to be utilized widely which can provide an opportunity to improve equitable access to COVID-19 vaccines. The non-stringent logistic requirements (i.e., 2 to 8 degrees Celsius) allows it to be utilized widely. However, we recommend that the DOH devise an efficient supply chain management that would take into account the three-month shelf life of the vaccine especially in ensuring the stability of the vaccines, from distribution up to administration to all target areas especially geographically isolated and disadvantaged areas (GIDA). Further, there is still a need for training of vaccinators to ensure product integrity across the entire supply chain and close monitoring of adverse events.
Does *Janssen Ad26.COV2.S (COVID-19)*	**Yes.** Based on interim results from the clinical trials, *Janssen Ad26.COV2.S (COVID-19) Vaccine* reduces the risk

Vaccine reduce out-of-pocket (OOP) expenses of households due to COVID-19?	for any symptomatic COVID-19, moderate to severe/critical COVID-19, hospitalization due to COVID-19, and severe/critical COVID-19. Further, its 1-dose requirement also reduces possible productivity loss and other non-medical costs related to having to go back for a second dose. Thus, *Janssen Ad26.COV2.S (COVID-19) Vaccine* has the potential to reduce out-of-pocket expenses of Filipino households due to averted costs of isolation, treatment and hospitalization due to COVID-19.
Does *Janssen Ad26.COV2.S (COVID-19) Vaccine* possess the characteristics desired by key stakeholders? (Social Impact)	**Yes.** Based on short term outcomes, *Janssen Ad26.COV2.S (COVID-19) Vaccine* possesses most of the characteristics desired by key stakeholders.
Does *Janssen Ad26.COV2.S (COVID-19) Vaccine* reduce or not further add to existing inequities in the health system?	**Yes**. The non-stringent logistic requirements (ie., 2-8 degrees Celsius) allows it to be utilized widely. However, we recommend that the DOH devise an efficient supply chain management that would take into account the three-month shelf life of the vaccine especially in ensuring the stability of the vaccines, from distribution up to administration to all target areas especially geographically isolated and disadvantaged areas (GIDA).

In the development of this recommendation, the HTA Council has appraised peer-reviewed interim results of a Phase III clinical trial on *Janssen Ad26.COV2.S (COVID-19) Vaccine* (Sadoff et al., 2021a).

The HTA Council also noted the results of Phase I/II trials conducted in the US and Belgium for populations 18-55 years old and 65 years old and above.

The HTA Council further emphasizes the need to enforce strict conditions for the emergency use of health products to safeguard against eventualities:

- Transparency and accountability in the processes of allowing emergency use of health products, especially for the public health response;
- Continuous collection of safety and effectiveness data in the context of clinical trials and actual use in the real world;

- Close monitoring of recipients and safeguards for expected and unexpected adverse events that may arise from the use of health products under an EUA;
- National coordination of the emergency use under the Philippine FDA and the DOH;
- Cascading of complete information to vaccinees and healthcare providers on potential risks and benefits, and securing of informed consent with regard to receiving the intervention; and
- Just compensation mechanisms and provisions for medical management of adverse events for patients and vaccinees assured by the national government

Finally, the HTAC recommends the conduct of research to address the current gaps in evidence with regard to the use of the *Janssen Ad26.COV2.S (COVID-19) Vaccine*:

- Real-world effectiveness in the Philippine context particularly focused on the following knowledge gaps:
    - Effectiveness in reducing COVID-19 cases, hospitalizations and deaths, and preventing outbreaks and transmission of disease across the population
    - Effectiveness in reducing asymptomatic infection
    - Duration of protection
    - Impact of the timing and number of doses received
    - Probable need for booster dosing
    - Differences in the effectiveness of the vaccine among special populations (i.e., elderly, individuals with comorbidities, pregnant and lactating women, immunocompromised patients)
    - Effectiveness of the vaccine against emerging SARS-CoV-2 viral strains
- Continuous safety surveillance and monitoring of all adverse events especially severe allergic reactions, Bell's palsy, serious adverse events such as thrombosis-thrombocytopenia syndrome (TTS) and adverse events of special interest (AESI) following vaccination
    - Across the general population
    - In special populations: elderly, patients with comorbidities, pregnant and lactating women, immunocompromised individuals
- Randomized controlled trials should also be done among populations not currently included in clinical trials: children below 18 years of age

- Best practices, challenges, and barriers in implementation across different localities
- Monitoring of unexpected or additional costs associated with vaccine implementation.

Current Evidence on *Janssen Ad26.COV2.S (COVID-19) Vaccine*

The table below summarizes the appraisal of available evidence on *Janssen Ad26.COV2.S (COVID-19) Vaccine* based on the HTAC evaluation framework.

In addition, the following appendices are provided for further details:

- Appendix 1. Evidence on evaluation criterion 2 - Clinical Efficacy and Safety
- Appendix 2. Evidence on evaluation criterion 3 - Affordability and Viability
- Appendix 3. References
- Appendix 4. Acknowledgment

Table 1.2 Key Findings in the Current Evidence Considered for the HTAC Evaluation of **Janssen Ad26.COV2.S (COVID-19) Vaccine**

Evaluation Criteria	Question	Current Evidence	HTAC specification
1. Responsiveness to magnitude and severity	*Can the Janssen Ad26.COV2.S (COVID-19) Vaccine significantly reduce the magnitude and severity of COVID-19?*	As of 29 April 2021, the total number of cases has exceeded more than 149 million cases and breached the 3 million mark in terms of the total number of deaths globally. In the Philippines, the cumulative number of laboratory-confirmed COVID-19 cases has already exceeded 1,028,738 cases with total deaths reported at 17,145 as of 29 April 2021. Based on the latest DOH-Epidemiology Bureau data (as of 18 March 2021), the young and productive age groups (20-49 years old) have the most exposure and highest prevalence of the disease. However, the most vulnerable are the senior citizens (>60 years) who have the highest case fatality rate (CFR) at 10.2% and comprise around 63% of COVID-19 deaths. In addition, individuals with existing comorbidities such as chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), other pulmonary, cardiovascular and blood diseases are also vulnerable with CFR reported at around 64 to 91%. COVID-19 has led to significant disruptions not only in the delivery of other priority health services (e.g., immunization, maternal and child health, noncommunicable diseases) but also in the social and economic life of the nation by arresting the growth of the economy, displacing migrant and local workers, loss of jobs, and food insecurity (NEDA, 2020; PSA 2020; TESDA, 2020). Social safety nets for the poorest and other vulnerable sectors have not been enough to compensate for these losses (TESDA, 2020). The lockdowns and community quarantines have also been shown to have an impact on the mental health of Filipinos and have affected how common Filipino households adjust under the new normal, unable to visit and freely	The vaccine can potentially reduce the COVID-19 disease burden (health, social and economic impact).

		enjoy quality time with members of their families, as captured in some focus group discussions conducted by the HTAC and the HTA Unit. Locally-contextualized modelling studies are needed for more accurate projections of the potential impact of vaccination along with other interventions, under different scenarios. These can better inform decision-making. **HTAC Judgment**: *Janssen Ad26.COV2.S (COVID-19) Vaccine* has the potential to reduce the disease burden by averting a significant number of symptomatic infections assuming sufficient vaccine coverage.	

2. Clinical efficacy and safety	*What is the efficacy of the Janssen Ad26.COV2.S (COVID-19) Vaccine in terms of reducing the incidence and/or severity of COVID-19 in the general and vulnerable populations?*	There are six ongoing trials and three future studies with *Janssen Ad26.COV2.S (COVID-19) Vaccine*: *On-going trials:* ● COV1001: a phase 1/2 trial in 1,045 healthy adults ages 18 to 55 in the United States and Belgium (1-dose and 2-dose regimens, with booster in 1 cohort); ● COV1002: a phase 1 safety and immunogenicity study in 250 healthy adults ages 20-55, and ≥65 years of age and above in good health in Japan (2-dose regimen at 56-day interval); ● COV2001: an ongoing, randomized, double-blind, placebo-controlled Phase 2a study, conducted in Germany, Spain, and the Netherlands in 550 healthy adults ≥18 to ≤55 years of age, and adults in good or stable health ≥65 years of age and 660 adolescents aged 12-17 years (1-dose and 2-dose regimens) (Note: enrolment of adolescents has not yet started); ● **COV3001:** an ongoing, multicentre, randomized, double-blind, placebo-controlled phase 3 study on efficacy and safety among 40,000 adults (1-dose regimen) (enrolment complete); ● COV3009: a phase 3 efficacy and safety trial in 30,000 adults (2-dose regimen) (enrolment ongoing); ● COV3012: an ongoing open-label, single-arm Phase 3B Implementation study among health care workers in South Africa *Future studies:* ● HORIZON 1: an open-label phase 2 trial to evaluate the safety, reactogenicity, and immunogenicity of Ad26.COV2.S in healthy pregnant participants (planned to begin late March/early April 2021) ● A study on immunocompromised individuals planned to begin	The vaccine achieves the following efficacy parameters: **Preferred VE: ≥70% reduction** in the risk of symptomatic infection with vaccination versus no vaccination **Minimum acceptable VE: 50% reduction** in the risk of symptomatic infection with vaccination versus no vaccination The following factors were taken into consideration upon setting the minimum acceptability of 50% efficacy: pandemic situation, no standard COVID-19 vaccine, limited production from each manufacturer, and the need for multiple sources of vaccines in the Philippines.

		Q3 2021 (details not specified) ● Post-authorization observational studies including pregnancy exposure registry Of these trials, study COV3001 was the main evidence source used for appraising the efficacy and safety in terms of clinical outcomes. Data for the said primary clinical evidence source are initially published in the assessment reports of US FDA, EMA and WHO, and recently in its manuscript version (Sadoff, et al., 2021a). All of these published reports refer to the same data set of the first interim results of their Phase III trial COV3001 (data analysis cut-off as of 22 January 2021). Meanwhile, study COV1001 was considered in the review of Phase I/IIa trials, with the results published as manuscripts ((Sadoff et al. (2021b) and Stephenson et al. (2021)). The details of Phase I/IIa trials are provided in Appendix 1. ***Phase III trial, N=44,325 (Sadoff et al., 2021a)*** The trial is a multi-center, randomized, double-blind, placebo-controlled Phase III trial among adults ≥18 years of age. Of the 44,325 randomized participants, 43,783 received a single intramuscular injection of *Janssen Ad26.COV2.S (COVID-19) Vaccine* containing $5x10^{10}$ viral particles or placebo containing 0.9% saline. Participants included in the safety and efficacy analyses were observed for a median follow-up duration of 58 days or 8 weeks after vaccination. Due to the phased enrollment of specific cohorts, there were slight differences in the median follow-up duration for the population ≥60 years of age (52 days), population ≥60 years of age without comorbidities (54 days), and population ≥60 years of age with	Adapted from WHO, US FDA, other stringent regulatory authorities

		comorbidities (50 days). Analysis of vaccine efficacy against symptomatic COVID-19 only included centrally confirmed cases i.e. cases that were subsequently confirmed in a central laboratory using m-2000 SARS-CoV-2 real-time RT-PCR. Meanwhile, vaccine efficacy against the following subgroups included both centrally confirmed and non centrally confirmed cases i.e., RT-PCR–positive cases from all sources regardless whether confirmed in a central laboratory or not: ● Moderate to severe/critical COVID-19 ● Severe/critical COVID-19 ● COVID-19 requiring hospitalization ● Death due to COVID-19 ● Asymptomatic COVID-19 Further, the study also performed a subgroup analysis on vaccine efficacy in South Africa (where 94.5% of 91 sequenced samples were identified as B.1.351 variant) and Brazil (where 69.4% of 124 sequenced samples were identified as coming from P.2 lineage). Regarding its efficacy in preventing asymptomatic COVID-19, the US FDA noted that given the available serology data from a small subset of participants in the study, with infrequent evaluations of serological and virological measurements, there is limitation in assessing the effect of the vaccine in preventing asymptomatic infection. Below are the key findings on its efficacy and the rating of evidence: **<u>Critical efficacy outcomes:</u>** ● Using *Janssen Ad26.COV2.S (COVID-19) Vaccine,* compared to placebo, **<u>reduces the risk for</u>:** ○ **Symptomatic COVID-19** (centrally confirmed cases only) - at least 14 days after vaccination by **66.9% (95% CI:**	

		59.1 to 73.4), based on high certainty of evidence - at least 28 days after vaccination by **66.5% (95% CI: 55.5 to 75.1)**, based on high certainty of evidence ○ **Moderate to severe/critical COVID-19** (centrally confirmed cases only) - at least 14 days after vaccination by **66.9% (95% CI: 59.0 to 73.4)**, based on high certainty of evidence - at least 28 days after vaccination by **66.1% (95% CI: 55.0 to 74.8)**, based on high certainty of evidence ○ **Moderate to severe/critical COVID-19** (including centrally and non-centrally confirmed cases), **regardless of baseline SARS-CoV-2 status** - at least 14 days after vaccination by **66.1% (95%CI: 59.7 to 71.6)**, based on high certainty of evidence - at least 28 days after vaccination by **65.5% (95%CI: 57.2 to 72.4)**, based on high certainty of evidence ○ **COVID-19 requiring hospitalization** (with onset of at least 14 days after vaccination, including both centrally and non-centrally confirmed cases) by **93.1% (95% CI: 72.7 to 99.2)**, based on moderate certainty of evidence. For its efficacy against COVID-19 requiring hospitalization at least 28 days after vaccination, there were no events in 19,306 participants in the intervention group versus 16 events in 19,178 participants in the control group. ○ **Severe/critical COVID-19** (including centrally and non-centrally confirmed cases) - at least 14 days after vaccination by **76.3% (95% CI: 57.9 to 87.5)**, based on moderate certainty of evidence - at least 28 days after vaccination by **83.5% (95% CI: 54.2 to 96.9)**, based on moderate certainty of evidence	

		<u>Important efficacy outcomes:</u> ● Using *Janssen Ad26.COV2.S (COVID-19) Vaccine,* compared to placebo, **<u>reduces the risk for:</u>** *<u>MODERATE TO SEVERE/CRITICAL</u> (including centrally and non-centrally confirmed cases)* *At least 14 days after vaccination:* ○ **For older adults <u>≥</u>65 years** (20.4% of trial population) by **76.5% (95% CI: 59.1 to 87.3)**, based on high certainty of evidence ○ For **population with comorbidities** (39.9% of trial population) by **64.2% (95% CI: 52.7 to 73.1)**, based on high certainty of evidence ○ For **population with comorbidities aged 18-59 years** (23.8% of trial population) by **63.9% (95% CI: 49.4 to 74.7)**, based on high certainty of evidence ○ For **population with comorbidities aged 60 years old and above** (17.01% of trial population) by **64.9% (95% CI: 42.2 to 79.4)**, based on high certainty of evidence ○ For **population with negative baseline** SARS-CoV-2 serostatus (87.5% of trial population) by **66.3% (95%CI: 59.9 to 71.8)** based on high certainty of evidence *At least 28 days after vaccination:* ○ For **older adults <u>≥</u>65 years** (20.4% of trial population) by **68.6% (95%CI: 38.6 to 85.1)**, based on high certainty of evidence ○ For **population with comorbidities** (39.9% of trial population) by **58.6 (95% CI: 40.6 to 71.6),** based on high certainty of evidence ○ For **population with comorbidities** aged 18-59 years (23.8% of trial population) by **64.0% (95% CI: 44.3 to 77.3)**, based on high certainty of evidence	

		○ For **population with negative baseline** SARS-CoV-2 serostatus (87.5% of trial population) by **65.5% (95%CI: 57.2 to 72.4)** based on high certainty of evidence *<u>SEVERE/CRITICAL COVID-19</u> (including centrally and non-centrally confirmed cases)* *At least 14 days after vaccination:* ○ For **population 18-59 years of age** (65.4% of the trial population) by **76.9% (95%CI: 56.2 to 88.8)**, based on moderate certainty of evidence ○ For **population 60 years and above** (34.6% of the trial population) by **75.1% (95%CI: 41.7 to 90.8)**, based on moderate certainty of evidence *At least 28 days after vaccination:* ○ For **population 18-59 years of age** (65.4% of the trial population) by **85.0% (95%CI: 61.2 to 95.4)**, based on moderate certainty of evidence ○ For **population 60 years and above** (34.6% of the trial population) by **80.2% (95%CI: 30.0 to 96.3)**, based on moderate certainty of evidence ● Meanwhile, *Janssen Ad26.COV2.S (COVID-19) Vaccine*, compared to placebo, shows **<u>inconclusive</u>** VE against moderate to severe/critical COVID-19 for the following specific groups: ○ **Asian population** (3.5% of the trial population) ■ at least 14 days after vaccination [VE: 54.4% (95% CI: -31.1 to 86.0)], based on low certainty of evidence ■ Asian population at least 28 days after vaccination [VE: 74.0% (95% CI: -36.5 to 97.4)], based on low certainty of evidence ○ **Population with positive baseline SARS-CoV-2**	

		serostatus (9.6% of trial population) ■ at least 14 days after vaccination [VE: 28.5% (95%CI: -322.8 to 89.5)], based on low certainty of evidence ■ at least 28 days after vaccination: There was 1 event in 2,118 participants in the intervention group versus 2 events in 2,021 participants in the control group. ● As for its **efficacy against new variants**, it cannot be evaluated at this time due to the limited number of sequenced samples in the subgroup analysis based on country participants. ● As for its **efficacy against asymptomatic COVID-19,** the available data are insufficient to assess the effect of the vaccine due to the infrequent serological and virological measurements in the trial. ● As for its **efficacy against death due to COVID-19**, there were zero events in 19,514 participants in the intervention group versus 7 events in 19,544 participants in the control group as early as 15 days after vaccination. All 7 deaths were in study sites in South Africa and had one or more comorbidities which placed them at higher risk for severe COVID-19. One death was in a participant PCR positive at baseline, who had onset of illness 10 days after vaccination. Vaccine efficacy for reducing deaths due to COVID-19 remains to be demonstrated. **HTAC Judgment**: *Janssen Ad26.COV2.S (COVID-19) Vaccine* passed the preferred VE threshold against symptomatic COVID-19. The vaccine has also demonstrated efficacy for reducing risk of moderate to severe/critical	

		COVID-19, severe/critical COVID-19 and hospitalization due to COVID-19.	
	What is the duration of protection of the Janssen Ad26.COV2.S (COVID-19) Vaccine in terms of reducing the incidence and/or severity of COVID-19?	The current interim evidence shows protection against laboratory-confirmed symptomatic COVID-19 infection based on a minimum median follow up period of two months after receiving one dose. Data on the duration of protection will be assessed as more evidence becomes available. **HTAC Judgment:** Cannot be assessed based on current data	**Minimum acceptable duration of protection:** confers at least 6 months protection **Preferred:** ≥1-year protective immunity *Reference: WHO Target Product Profile for COVID-19 Vaccines, 2020*

	What are the safety issues and incidence of adverse events caused by the Janssen Ad26.COV2.S (COVID-19) Vaccine?	Both trial and real world data were reviewed in assessing the safety of the vaccine. For the evidence from trial, study COV3001 was the main evidence source which is a multi-center, randomized, double-blind, placebo-controlled phase III trial among adults ≥18 years of age. Of the 44,325 randomized participants, 43,783 were included in the full analysis set (including for all-cause deaths and serious adverse events). Meanwhile, a safety subset of 6,736 were included for systemic reactogenicity, local reactogenicity and adverse events up to 28 days after vaccination. ***EVIDENCE FROM TRIALS*** **Phase III trial, N=44,325 (Sadoff et al., 2021a)** **Short-term outcomes:** Based on the computed risk ratio, *Janssen Ad26.COV2.S (COVID-19) Vaccine* shows higher risk of systemic and local reactogenicity when compared to placebo: ● **Systemic reactogenicity [RR: 1.57 (95% CI: 1.49 to 1.66)]**, based on high certainty of evidence ● **Local reactogenicity [RR: 2.58 (95% CI: 2.39 to 2.79)]**, based on high certainty of evidence Meanwhile, *Janssen Ad26.COV2.S (COVID-19) Vaccine* shows inconclusive safety data on the risk for any unsolicited adverse events up to 28 days after vaccination when compared to placebo **[RR: 1.09 (95% CI: 0.96 to 1.24)]**, based on moderate certainty of evidence. **Long-term outcomes:** ● In terms of **all-cause mortality**, *Janssen Ad26.COV2.S (COVID-19) Vaccine* shows lower risk vs placebo **[RR: 0.25 (95% CI: 0.09 to 0.67)]**, based on moderate certainty of evidence. There were a total of 25 all-cause deaths - 5 in the vaccine group and 20 in the	Local and systemic reactions are tolerable, self-limiting and do not require hospitalization. No serious adverse events were caused by the vaccine. **Short term outcomes** (e.g., reactogenicity and allergic reactions): at least 2 months **Long term outcomes** (e.g., serious AEs): at least 1 year

		placebo group. Seven of the 20 deaths in the placebo group were COVID-19 related deaths which were described in the efficacy analysis section. ● In terms of **non-fatal serious adverse events (SAEs),** there is inconclusive risk on the use of *Janssen Ad26.COV2.S (COVID-19) Vaccine* arm vs placebo **[RR: 0.86 (95% CI: 0.64 to 1.16)]**, based on low certainty of evidence. Further, the rates of non-fatal SAEs were observed to be balanced between the vaccine arm and placebo arm. There were 10 non-fatal SAEs which were assessed by the investigator to be related to the study vaccination, with 7 occurring in the vaccine group and 3 in the placebo group. Of the 7 events in the vaccine group, only 3 non-fatal SAEs were assessed by the US FDA to be likely related to the vaccine, which includes radiculitis brachial, post-vaccination syndrome (asthenia), and vaccination site hypersensitivity. *Non-fatal SAEs under the vaccine group (n = 7):* ○ *Radiculitis brachial (n=1), post-vaccination syndrome (asthenia) (n=1):* deemed to be likely related to the vaccine by the US FDA ○ *Pericarditis (n=1):* the possibility that the vaccine could have contributed to this event could not be excluded. However, upon further review of the safety profiles of other Ad26-based vaccines, no other additional reports of pericarditis were noted. ○ *Facial paralysis (n=2) and Guillain-Barré syndrome (n=1):* identified to be unlikely related to *Janssen Ad26.COV2.S (COVID-19) Vaccine* but a causal relationship could not be definitively excluded, according to US FDA (2021). ○ *Hypersensitivity (n=1):* The EMA and WHO noted one case of anaphylaxis in an open-label trial in South Africa that met the Brighton Collaboration criteria; however, none occurred	

		during the COV3001 clinical trial. Meanwhile, the US FDA noted one serious adverse event of hypersensitivity (not classified as anaphylaxis) beginning 2 days following vaccination in COV3001 trial and was deemed likely related to receipt of the vaccine. *Non-fatal SAEs under the placebo group (n= 3):* ○ *Deep vein thrombosis (n=1):* The Sponsor identified that the relationship between occurrence of deep vein thrombosis and administration of placebo was indeterminate. ○ *Epstein-Barr infection (n=1)*: The Sponsor identified that it was not related to administration of placebo. ○ *Atrial flutter (n=1)*: The Sponsor identified that it was not related to administration of placebo. ● In terms of *thromboembolic events (n=25): A* slight numerical imbalance between treatment arms was observed with reported thromboembolic events, with 15 events in the vaccine group and 10 events in the placebo group, based on the reports of EMA and the US FDA. While this may be a small imbalance, the possibility of the vaccine being a contributor to the event could not be excluded according to the US FDA. One event of transverse sinus thrombosis was reported. However upon investigation, a clear explanation to the event was not identified. On 14 April 2021, this case was reviewed together with 6 cases of thrombosis with thrombocytopenia syndrome (TTS) that occurred during the rollout of the *Janssen Ad26.COV2.S (COVID-19) Vaccine*.	

		REAL WORLD DATA ● **United States** (as of 23 April 2021) - 15 cases of TTS, a rare and severe type of blood clot, were reported after receiving the vaccine. All cases occurred in women under the age of 60 , 6 to 15 days after vaccination. One of the cases led to death. The ACIP COVID-19 vaccines workgroup convened to review the cases of thrombocytopenic thrombosis and included the one case of CSVT reported in the Phase III clinical trial. Upon thorough review by the US CDC and US FDA, the two agencies have determined that the benefits of vaccination outweigh the potential risk of TTS and recommended to resume the implementation of the vaccine after a temporary pause. The EUA and vaccine fact sheets were amended to include information about the rare adverse event and the signs and symptoms of TTS that healthcare professionals and individuals should monitor. (US FDA, US CDC, 2021) ● **South Africa** (as of 17 April 2021) - No reports of blood clots after administration of 289,787 doses were noted. The rollout was paused on 13 April 2021 for the South Africa Health Products Authority to make a thorough risk assessment. SAHPRA recommended to continue vaccination on 17 April 2021. (SAHPRA, 2021) ● **European Union** (as of 20 April 2021) - The EMA conducted a separate review on the data on embolic and thrombotic events collected from vaccination campaigns outside the EU and concluded that the overall benefits of the vaccine outweigh the risk of side effects. The regulatory authority recommended that a warning regarding the blood clots with thrombocytopenia adverse events should be added so that recipients of the vaccine are aware of the symptoms of the rare adverse event and can get prompt medical treatment. (EMA, 2021)	

		• **Overall** (as of 31 March 2021) - More than 20 million doses of the vaccine have been distributed and a total of 2,887 adverse events were recorded from the United States (including its US regions), Belgium, and the Netherlands. (Source: sponsor submission) **HTAC Judgment:** Short-term safety of *Janssen Ad26.COV2.S (COVID-19) Vaccine* is acceptable. However, further follow-up data is needed to establish longer-term safety. Although vaccination appears to be associated with an extremely rare but potentially fatal TTS, the HTAC deems the benefits far outweigh the risks. Pending stronger evidence of the association and consensus from stringent regulatory agencies, the HTAC finds no reason at this time not to recommend the use of the vaccine as approved by the FDA Philippines. Mitigation measures against TTS from detection, treatment and management of this rare but severe reaction must, however, be included in all protocols for addressing adverse effects. Information on TTS as a rare but serious adverse event should be included in the informed consent form of the vaccinees. The health system should be prepared to manage this rare though serious adverse reaction.	

	Does the Janssen Ad26.COV2.S (COVID-19) Vaccine provide a highly favorable benefit/risk profile in the context of observed vaccine efficacy?	The current evidence shows that likely clinical benefits in terms of decreased occurrence of: - **symptomatic COVID-19 infection** - **moderate to severe/critical COVID-19** - **hospitalization due to COVID-19** - **severe/critical COVID-19** outweigh the known short-term risks based on data available at the time of evaluation. Likewise, the clinical benefits in terms of vaccine efficacy against **moderate to severe/critical** COVID-19 infection outweigh the known short-term risks based on data available at the time of evaluation for the following sub-populations: - **older adults (65 years and above)** *(20.4% of the trial population)* - **among population with comorbidities** *(39.9% of the trial population)* - **among population with negative baseline SARS-CoV-2 serostatus** *(87.5% of trial population)* The VEs against moderate to severe/critical COVID-19 infection in the Asian population *(3.5% of trial population),* population with comorbidities aged 60 years old and above at least 28 days after vaccination *(17.01% of trial population),* population with positive baseline SARS-CoV-2 serostatus *(9.6% of trial population),* population with asymptomatic infections, and efficacy against new variants are **inconclusive**. Thus, the benefit/risk profile specifically for these subgroups cannot be determined. As for **severe/critical COVID-19 infection**, the clinical benefits in terms of **vaccine efficacy against severe/critical COVID-19 infection**	Favorable benefit/risk profile The benefit of preventing morbidity of at least 50% far outweighs the reported risk of adverse events

		outweigh the known short-term risks based on data available at the time of evaluation for the following sub-populations: - **population 18-59 years of age** *(65.4% of the trial population)* - **population 60 years old and above** *(34.6% of the trial population)* In terms of safety, there was one case of transverse sinus thrombosis that occurred in a 25-year old male trial participant who received the vaccine. The event was initially regarded as not related to vaccination but was further reviewed when multiple cases of TTS were reported after the vaccine rollout had commenced. **HTAC Judgment:** PASSED Although vaccination appears to be associated with an extremely rare but potentially fatal TTS, the HTAC deems the benefits far outweigh the risks. Pending stronger evidence of the association and consensus from stringent regulatory agencies, the HTAC finds no reason at this time not to recommend the use of the vaccine as approved by the FDA Philippines. Mitigation measures against TTS from detection, treatment and management of this rare but severe reaction must, however, be included in all protocols for addressing adverse effects.	

3. Affordability and viability	*Is Janssen Ad26.COV2.S (COVID-19) Vaccine affordable?*	Based on the projected calculations, the total cost of rolling out vaccination with *Janssen Ad26.COV2.S (COVID-19) Vaccine* for **6M Filipinos in 2021** (i.e., target vaccinees for this vaccine profile identified in the vaccination roll out plan) will amount to **Php 3,908,301,680.** According to the Department of Finance, the price of *Janssen Ad26.COV2.S (COVID-19) Vaccine* offered to the Philippine government is equal to or better than the price offered in other Southeast Asian countries. **HTAC Judgment:** The vaccine is affordable since the budget for the purchase and use of *Janssen Ad26.COV2.S (COVID-19) Vaccine* for the target number of vaccinees has been allocated.	Affordability will be measured using the sufficiency of the allocated amount to achieve vaccination targets. **The vaccine unit cost is comparable with those in other ASEAN countries.*

	What are the budget implications of using the Janssen Ad26.COV2.S (COVID-19) Vaccine?	The total cost of vaccination per individual, which accounts for other costs such as consumables, hauling and storage, and operations, was computed to be **Php 651.38**. The potential budget impact of the use of *Janssen Ad26.COV2.S (COVID-19) Vaccine* to the national government to cover 6 million Filipinos was calculated at about Php 3.91B. With 6M Filipinos to be vaccinated, it is estimated that **4.74%** of the total allocated budget for vaccination will go to **8.57%** of the 70 million target vaccinees for 2021. **HTAC Judgment:** The share of the population to be vaccinated using the said vaccine is highly commensurate to the share of the cost of the *Janssen Ad26.COV2.S (COVID-19) Vaccine* to the total vaccine budget.	The share of the cost to implement the COVID-19 vaccine within the total vaccination budget is not too disproportionate to the share of the population to be vaccinated using the said vaccine in the total population to be vaccinated.

	Does the Janssen Ad26.COV2.S (COVID-19) Vaccine represent good value for money in terms of: *a. preventing COVID-19 mortality* *b. lowering hospitalization (moderate, severe and critical cases)* *c. lowering incidence of symptomatic (mild) and asymptomatic cases (RT-PCR confirmed cases)*	*Janssen Ad26.COV2.S (COVID-19) Vaccine* represents good value for money in terms of lowering any symptomatic COVID-19, lowering moderate to severe/critical COVID-19 (among the elderly population, individuals with comorbidities, and population with negative baseline serostatus), lowering hospitalization due to COVID-19, and lowering severe/critical COVID-19 (among 18 years old and above). Whether *Janssen Ad26.COV2.S (COVID-19) Vaccine* represents good value for money in terms of moderate to severe/critical COVID-19 (among Asian population and among population with positive baseline serostatus), COVID-19 caused by new variants, death due to COVID-19, and asymptomatic cases (RT-PCR confirmed cases) cannot be fully assessed at the moment. Rough estimates of the vaccination cost per case averted are high. However, HTAC has bases to conclude that these will be offset by averted healthcare costs (i.e., total COVID-19-related PhilHealth claims, out of pocket expenditures), economic gains (i.e., in terms of recovery in GDP), and social gains. **HTAC Judgment:** The HTAC deems that the health, economic, and social benefits of using *Janssen Ad26.COV2.S (COVID-19) Vaccine* mitigates the negative impacts of COVID-19, such as deaths, medical costs, loss of productivity, social disruption and unprecedented challenges in the health system.	The health, economic, and social benefits of the vaccination program outweigh the costs. The vaccine is likely cost-effective. *Note: A full-blown cost-effectiveness analysis is currently not done for rapid reviews under a pandemic situation due to its emergency nature. A full-blown cost-effectiveness analysis that takes on a societal perspective (i.e., including the economic and social impacts) will be performed once sufficient evidence is available and when full market authorization has been granted.*

	Are there significant barriers to vaccine implementation in terms of vaccine storage and transport, handling; adequacy, skills and training of vaccinators; and access of the target population to the health care facility? Are there plans to overcome significant barriers?	The vaccine can be readily stored in a refrigerator at 2 to 8 degrees Celsius. Given this, it is expected that the *Janssen Ad26.COV2.S (COVID-19) Vaccine* can be widely distributed to facilities with the said equipment. However, with the three-month shelf life of the vaccine, the DOH should devise an efficient supply chain management to ensure the stability of the vaccines, from distribution up to administration to all target areas especially geographically isolated and disadvantaged areas (GIDA). Further, this vaccine requires only one dose, in comparison to all other COVID-19 vaccines which require 2 doses; hence, alleviating administrative burdens and resources to implement two doses several weeks apart. Moreover, the vaccine does not require dilution at the vaccination site which may simplify implementation of the vaccine especially in community settings. Like any vaccine implementation, there is still a need for training on vaccine storage and handling to ensure product integrity across the entire supply chain. Trained personnel in handling unreported or rare adverse reactions that could occur following vaccination should also be in place. **HTAC Judgment:** The HTAC notes that there are no significant barriers in vaccine implementation using *Janssen Ad26.COV2.S (COVID-19) Vaccine* in terms of storage, transport, and handling. It is recommended that the DOH should ensure an efficient supply chain management that would take into account the three-month shelf life of the vaccine. Further similar to other vaccines, there is still a need for training to: ensure product integrity across the entire supply chain; and, close monitoring of adverse events.	There are no significant barriers and if there are, the plans to address the barriers are clearly reflected in the vaccine roadmap and other relevant documents.

4. Household Financial Impact	*Will the Janssen Ad26.COV2.S (COVID-19) Vaccine reduce or not add further to the out-of-pocket expenses of Filipino households?*	**<u>For mild COVID-19 pneumonia:</u>** ● PhilHealth has issued the following packages and case rates related to mild COVID-19: - Isolation Package (C19CI): Php 22,499.00 - Mild COVID-19 pneumonia for elderly and with comorbidities (C19IP1): Php 43,997.00 ● Looking at the actual PhilHealth claims as of January 2021, the isolation package amounted to a median cost of **Php 22,499,** while claims for mild COVID-19 pneumonia for elderly and those with comorbidities amounted to a median cost of **Php 43,997.** ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients for isolation is at **Php 22,499** while mild cases among elderly and those with comorbidities is at **Php 60,020.25.** ● From the same dataset, the calculated median out-of-pocket spending for patients with mild COVID-19 pneumonia is at **Php 16,023.25.** Meanwhile, the median out-of-pocket reported for patients availing of an isolation package is 0. **<u>For moderate COVID-19 pneumonia:</u>** ● PhilHealth has issued a benefit package C19IP2 for moderate COVID-19 pneumonia with a case rate of Php 143, 267. ● Looking at the actual PhilHealth claims for moderate COVID-19 pneumonia as of January 2021, they amounted to a median of **Php 143, 267.00**. ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients with moderate COVID-19 is at **Php 234, 925.13**. ● From the same dataset, the calculated median out-of-pocket spending for patients with moderate COVID-19 pneumonia is at **Php 63,371.30**.	The adoption of the vaccine can reduce out-of-pocket spending of individuals and families due to averted COVID-19 disease and/or hospitalization.

		<u>For severe COVID-19 pneumonia:</u> ● PhilHealth has issued a benefit package C19IP3 for severe COVID-19 pneumonia with a case rate of Php 333,519. ● Looking at the actual PhilHealth claims for severe COVID-19 pneumonia as of January 2021, they amounted to a median of **Php 333,519.00**. ● Reviewing the hospital bills data collected by PhilHealth as of January 2021, the median amount spent by patients with severe COVID-19 pneumonia is at **Php 388,904.20**. ● From the same dataset, the calculated median out-of-pocket spending for patients with severe COVID-19 pneumonia is at **Php 388,903.20**. **HTAC Judgment**: Based on current evidence, *Janssen Ad26.COV2.S (COVID-19) Vaccine* has the potential to reduce out-of-pocket expenses of Filipino households due to averted costs of isolation, treatment and hospitalization due to COVID-19, and savings on indirect and direct non-medical costs related to the vaccination.	
5. Social Impact	*Does the Janssen Ad26.COV2.S (COVID-19) Vaccine possess the characteristics desired by key stakeholders (i.e., policy- and decision makers, health workers, program managers and/or*	Based on the results of the focus group discussions conducted by the HTAC among *healthcare workers, patient groups, civil society organizations and community leaders* from low- and high-prevalence areas, the results from the deliberations in congressional inquiries on the COVID-19 vaccination roadmap, public hearings, and consultations with government decision-makers and implementers, the following are the **important and desirable attributes of COVID-19 vaccines** and the corresponding evidences for the *Janssen Ad26.COV2.S (COVID-19) Vaccine*: 1) **Safe and efficacious** for the general population (18 years old and	The vaccine possesses all or most of the characteristics desired by key stakeholders Qualitative responses will contextualize the Filipino experience and may impact on implementation strategy

	implementers, patient groups, CSOs, communities, general public)? ● *Safety* ● *Efficacy* ● *Transparency in the regulatory/approval process and information on the vaccines* ● *Availability* ● *Potential for high and equitable coverage* ● *Ease in logistical and implementation requirements* ● *Cost-efficiency to the government* ● *Public acceptability* ● *Availability of mechanisms to compensate vaccine recipients for any untoward*	older) and for some vulnerable groups like the older population and individuals with comorbidities. - Evidence: Interim results from the clinical trial shows acceptable safety profile for known short-term risks and efficacy to reduce risk for symptomatic COVID-19, moderate to severe/critical COVID-19, hospitalization due to COVID-19, and severe/critical COVID-19**.** There are currently no data on the safety and efficacy of the vaccine in special populations such as children below 18 years old, pregnant and lactating women, and immunocompromised individuals. Trials are forthcoming to provide more conclusive evidence on the efficacy and safety for the special populations namely immunocompromised, pregnant women and children. Nevertheless, the WHO has recommended that individuals in these special populations who are recommended for vaccination may receive the vaccine. Currently, the EUA issued by the FDA Philippines has recommended its use among individuals aged 18 years and older. 2) Underwent a **transparent regulatory process** of being evaluated and approved by health authorities - Evidence: The *Janssen Ad26.COV2.S (COVID-19) Vaccine* underwent the usual regulatory process of the FDA Philippines. As of 27 February 2021, the US FDA issued an EUA for *Janssen Ad26.COV2.S (COVID-19) Vaccine* while the EMA issued a conditional marketing authorization for the product across the European Union on 11 March 2021. The vaccine was included in the WHO emergency use listing on 12 March 2021. 3) **Potential for high and equitable coverage across the population** - Evidence: The one-dose vaccination requirement with *Janssen Ad26.COV2.S (COVID-19) Vaccine* can facilitate utility in a	

	event following vaccination ● *Appropriateness of the vaccine to special at-risk groups and patients with comorbidities*	wider setting especially for those experiencing difficulty with completing their second dose required in other vaccines, thereby improving compliance. In addition, this can be made more available since vaccine handling and storage are within the capacity of the RHUs. 4) **Ease in logistics and administration** - Evidence: *Janssen Ad26.COV2.S (COVID-19) Vaccine* can be stored for 3 months at 2-8 degrees Celsius in a refrigerator which is present in most RHUs. The vaccine also does not require dilution at the vaccination site which may simplify implementation of the vaccine especially in community settings. 5) **Cost-effective** - Evidence: The health, economic, and social benefits of using *Janssen Ad26.COV2.S (COVID-19) Vaccine* mitigates the negative impact of COVID-19, such as deaths, medical costs, loss of productivity, social disruption and unprecedented challenges in the health system. 6) **Public acceptability** - Evidence: No brand-specific study has been conducted to provide evidence for this characteristic. Further, no study compared the public's preference between 1-dose and 2-dose vaccines. Based on COVID-19 Vaccine Sectoral surveys conducted by the DOH- Health Promotion Bureau: - 70.54% of participants from the Philippine National Police responded that they are willing to get COVID-19 vaccine (February 5-14, 2021). This is an increase from the 56.94% acceptance rate in a similar survey conducted last 29 December 2020 to 8 January 2021.	

		- 68.62% of participants from the Civil Service Commision (excluding DOH, PNP and AFP employees) responded that they are willing to get COVID-19 vaccine (6 February to 3 March 2021). This is an increase from the 44.85% acceptance rate in a similar survey conducted previously (Duration of survey not reported). - The certainty of the evidence provided by published and real world data that support the favorable recommendation, if appropriately communicated, will increase public acceptability of vaccines. **7) Availability of mechanisms to manage any untoward serious adverse reactions following vaccination** - Evidence: The Republic Act 11525 or the COVID-19 Vaccination Program Act of 2021 establishes the COVID-19 National Vaccine Indemnity Fund to provide funds and authorize PhilHealth to pay compensation to any person inoculated through the vaccination program, in the case of death and permanent disability. - According to the Philippine College of Hematology and Transfusion Medicine (PCHTM), the potential therapeutic strategies of TTS include: ● high-dose intravenous immune globulin (IVIG) (0.5 to 1g per kg daily for 2 days) ● high-dose glucocorticoids (methylprednisolone (1mg/kg) ● non-heparin anticoagulants (apixaban, rivaroxaban, argatroban, bivalirudin, danaparoid, fondaparinux) ● therapeutic plasma exchange if platelet remains below 30,000 despite IVIG and steroids - TTS treatments currently listed in the PNF include IVIG,	

		fondaparinux, and methylprednisolone. - The DOH has indicated its plan to prepare the system for detecting and managing the adverse events including rare serious adverse reactions. **8) Appropriateness of the vaccine to special at-risk groups and patients with comorbidities** - Evidence: The interim results from the Phase III clinical trial enrolled individuals 18 years and above. The current evidence for special populations allow it to be used in special at-risk groups such as the older population and patients with comorbidities. Currently, there is limited data from the trial on the use of the vaccine for pregnant and lactating women, children below 18 years old, persons living with HIV, immunocompromised individuals, and persons who have previously received antibody therapy for the treatment of COVID-19. The vaccine efficacy and safety for the older population and patients with comorbidities are detailed below. *<u>For older populations (36.4% of the trial population)</u>:* - According to the WHO interim guidance on the use of this vaccine, the efficacy and safety of the vaccine based on the interim phase III RCT are comparable across all age groups (above the age of 18), hence it is recommended for older persons. *<u>For populations with comorbidities (39.9 % of the trial population)</u>:* - According to the WHO interim guidance on the use of this vaccine, the vaccine has similar safety and efficacy profiles in persons with various underlying medical conditions, including those that place them at increased	

		risk for severe COVID-19, based on the results of the interim phase III RCT. The trial included the following comorbidities: hypertension, chronic lung disease, significant cardiac disease, obesity, diabetes, and human immunodeficiency virus (HIV) infection. Hence, the WHO recommends it for persons with such comorbidities that have been identified as increasing the risk of severe COVID-19. Further, the WHO interim recommendations (17 March 2021) for the use of *Janssen Ad26.COV2 (COVID-19) vaccine* in the following special populations noted the following for the other special groups of interest: <u>*For pregnant women*</u> - Evidence for efficacy and safety are insufficient to assess vaccine-associated risks in pregnancy. - No safety issues were noted from the 1,600 pregnant women who received vaccines with the same platform as *Janssen Ad26.COV2(COVID-19) vaccine*. Further studies which include pregnant women are forthcoming. - The WHO interim recommendation for pregnant women to receive the vaccine remains on the condition that the benefit of protection from COVID-19 outweigh the potential vaccine risks (i.e., pregnant woman is a frontline healthcare worker, with known comorbidities that increase their risk for severe COVID-19.) <u>*For lactating women*</u> - Vaccine efficacy in lactating women is expected to be similar to other adults.	

		- Currently, it is unknown whether Ad26.COV2.S is excreted in human milk. However, since this is a non-replicating vaccine, Ad26.COV2.S is unlikely to pose a risk to the breastfeeding child. - With the current evidence available, the WHO interim recommendations (17 March 2021) for the use of *Janssen Ad26.COV2 (COVID-19) vaccine* state that lactating women who are part of a group recommended for vaccination (e.g., health workers) should be offered vaccination on an equivalent basis. Further, discontinuing breastfeeding after vaccination is not recommended. *For children and adolescents below the age of 18 years* - Currently, no efficacy or safety data for children and adolescents below the age of 18 years are available. Hence, vaccination of individuals aged below 18 years is not yet considered at the moment. *For persons living with HIV* - Based on the current available evidence, no safety concerns were observed in persons with well-controlled HIV who were included in the trials. However, the current data is insufficient to allow assessment of vaccine efficacy for persons living with HIV. - In the interim, as the vaccine is nonreplicating, the WHO interim recommendations for the use of *Janssen Ad26.COV2 (COVID-19) vaccine* noted that persons with living HIV belonging to a group known to be recommended for vaccination may be given the vaccine. Further, counselling and information should	

		be provided to inform individual benefit-risk assessment. The recommendations also state that testing for HIV infection before vaccination is not necessary. *For immunocompromised persons* - Currently, the available data is insufficient to assess vaccine efficacy or vaccine-associated risks in severely immunocompromised persons, including those receiving immunosuppressant therapy. - Meanwhile, as the vaccine is nonreplicating, the WHO interim recommendations for the use of *Janssen Ad26.COV2 (COVID-19) vaccine* state that immunocompromised persons identified to be in the recommended group for vaccination may be administered with the vaccine. Further, counselling and information should be provided to inform individual benefit-risk assessment. *For persons who have previously had SARS-CoV-2 infection* - Vaccination should be offered regardless of personal history of SARS-CoV-2 infection. Hence, testing (i.e., viral or serological) for prior infection may not be necessary for decision making regarding vaccination. - Data from pooled analyses indicate that *Janssen Ad26.COV2 (COVID-19) vaccine* is safe in those with evidence of prior SARS-CoV-2 infection. - Given that symptomatic reinfection within 6 months after an initial natural infection is uncommon, it is advised to delay vaccination for persons with PCR-confirmed COVID infection in the last 6 months until the end of the period.	

		- However, given emerging evidence that symptomatic reinfection may occur in settings where there are circulating variants with evidence of immune escape, earlier immunization may be advisable. *For persons with current acute COVID-19* - Individuals with acute PCR-confirmed COVID-19 infection should not be vaccinated until after full recovery from the acute illness and meeting the criteria for discontinuation of isolation. - The optimal interval between a natural infection and vaccination is not yet known. *For persons who previously received passive antibody therapy for COVID-19* - Currently, there are no data on the safety or efficacy of vaccination in individuals who have received monoclonal antibodies or convalescent plasma as treatment for COVID-19. - Vaccination should be deferred for at least 90 days to avoid interference of the antibody therapy with the immune response elicited by vaccination. **HTAC Judgment:** Based on short-term outcomes, *Janssen Ad26.COV2.S (COVID-19) Vaccine* possesses most of the characteristics desired by key stakeholders.	
6. Responsiveness to equity	*How will the Janssen*	*Janssen Ad26.COV2 (COVID-19) vaccine* has been shown to have an efficacy against symptomatic COVID-19, moderate to severe/critical	Ideally, health interventions can be

	Ad26.COV2.S (COVID-19) Vaccine and its use impact pre-COVID and COVID-generated health and socioeconomic inequities? *Which groups might be unfairly disadvantaged in relation to the COVID-19 disease burden and delivery of the Janssen Ad26.COV2.S (COVID-19) Vaccine?*	COVID-19, hospitalization due to COVID-19, and severe/critical COVID-19, based on the interim results of its Phase III RCT. Vaccine efficacy against moderate to severe/critical COVID-19 among ≥65 years and population with comorbidities, and vaccine efficacy against severe/critical COVID-19 among ≥ 60 years were also noted to provide benefit. Meanwhile, vaccine efficacy against moderate to severe/critical COVID-19 in Asians was inconclusive. *Janssen Ad26.COV2.S (COVID-19) Vaccine* can be stored at normal cold storage conditions (2 to 8 degrees Celsius) for 3 months and protected from light. This will make vaccine distribution more logistically feasible which in turn does not aggravate inequities for patients living in geographically isolated and disadvantaged areas. Compared to other new vaccines, *Janssen Ad26.COV2.S (COVID-19) Vaccine* only has a one-dose vaccination requirement. The US Advisory Community on Immunization Practices (ACIP) noted that the single-dose regimen of *Janssen Ad26.COV2.S (COVID-19) Vaccine* can facilitate completion of vaccination schedule especially for those experiencing difficulty in returning for a second dose thereby improving compliance. In addition, the price per dose and the logistical and operational costs of *Janssen Ad26.COV2.S (COVID-19) Vaccine* allow it to be utilized widely which can provide an opportunity to improve equitable access to safe and effective COVID-19 vaccine. **HTAC Judgment:** The non-stringent logistic requirements (i.e., 2 to 8 degrees Celsius) allows it to be utilized widely. However, we recommend that the DOH devise an efficient supply chain management that would take into account the three-month shelf life of the vaccine especially in ensuring the stability of the vaccines, from distribution up to administration to all target areas	fairly adopted and distributed/ implemented for eligible populations without aggravating existing health inequities especially for vulnerable sectors of our society.

		especially geographically isolated and disadvantaged areas (GIDA). The trial excluded or has limited to no data on pregnant and breastfeeding women, and persons who were immunocompromised (WHO SAGE Background Document, 2021; EMA Public Assessment Report, 2021). Nevertheless, the WHO currently recommends vaccinating these special populations on the condition that they are included in the group recommended for vaccination (e.g., health workers, high risk for COVID). Likewise, the EMA also allows vaccination of these special populations given that considerations will be on a case by case basis.	

Appendix 1. Evidence for criterion 2 - Clinical Efficacy and Safety

Evidence from trials from Phase I to III were reviewed on the efficacy. Meanwhile for the assessment of safety, evidence from both trials and available real world data were reviewed.

EVIDENCE FROM TRIALS

As with evidence from trials, there are currently three published manuscripts reporting their trials. Two of these were published Phase I/II trials: the Sadoff et al. (2021b) trial, and Stephenson et al. (2021) which is a subtrial of the Sadoff et al. (2021b). The last publication is the published interim results of their ongoing Phase III randomized clinical trial which was conducted in the US (Sadoff et al., 2021a).

PHASE I/II TRIALS

Study characteristics

The Sadoff et al. (2021b) trial was a Phase I/IIa conducted in Belgium and the US with participants aged 18 years old and above (i.e., cohorts 1a, 2, 3). On the other hand, Stephenson et al. (2021) is a subtrial under the Sadoff et al. (2021b) Phase I/IIa trial which focused on participants aged 18 to 55 years old in the US (i.e., cohort 1b). It is an exploratory cohort for an in-depth analysis of immunogenicity. Table 1.1 characterizes these trials.

Table 1.1. Phase I/IIa trial characteristics of Sadoff et al. (2021b) and Stephenson et al. (2021).

Cohort	N	Age Group (y/o)	Intervention	Control	Remarks
1					
1a *published in Sadoff et al. (2021b)*	380	18 to 55	**Subgroup 1:** High-dose/high-dose **Subgroup 2:** High-dose/placebo **Subgroup 3:** Low-dose/low-dose **Subgroup 4:** Low-dose/placebo	**Subgroup 5:** Placebo/placebo	Single-dose regimens (subgroups 2 and 4) OR two-dose schedule, 56 days apart (subgroups 1 and 3)
1b *published in Stephenson et al. (2021)*	25	18 to 55	**Subgroup 1:** High-dose/high-dose **Subgroup 2:** High-dose/placebo **Subgroup 3:** Low-dose/low-dose **Subgroup 4:** Low-dose/placebo	**Subgroup 5:** Placebo/placebo	Added in-depth analysis of immunogenicity Single-dose regimens (subgroups 2 and 4) OR

					two-dose schedule, 56 days apart (subgroups 1 and 3)
2	*Longer-term data are needed hence the authors did not report yet the results in the interim publication of Sadoff et al. (2021b)*				Single-dose versus two- dose
3 *published in Sadoff et al. (2021b)*	405	≥ 65	**Subgroup 1:** High-dose/high-dose **Subgroup 2:** High-dose/placebo **Subgroup 3:** Low-dose/low-dose **Subgroup 4:** Low-dose/placebo	**Subgroup 5:** Placebo/placebo	Single-dose regimens (subgroups 2 and 4) OR two-dose schedule, 56 days apart (subgroups 1 and 3)

Note: ***Low-dose*** *= Janssen Ad26.COV2.S (COVID-19) Vaccine at* $5x10^{10}$ *viral particles per mL |* ***High-dose*** *= Janssen Ad26.COV2.S (COVID-19) Vaccine at* $1x10^{11}$ *viral particles per mL |* ***Placebo =*** *0.9% NaCl*

Primary endpoints of the study were the safety, and reactogenicity of each dosing schedule. These were evaluated at follow-up visits scheduled 7 days (solicited adverse events), 29 days (unsolicited adverse events) and 71 days after vaccination. The secondary endpoint was humoral and cellular immunogenicity. A separate cohort, cohort 2 was also included to assess long-term data of a one-dose regimen vs a two-dose regimen. As of publishing this evidence summary, the results and details of cohort 2 of this Phase I - IIa trial have yet to be published.

On the other hand, Stephenson et al., (2021) looked into immunogenicity endpoints, which included enzyme-linked immunosorbent assays (ELISA), pseudovirus neutralization assays, interferon (IFN)-γ, and IL-4 enzyme-linked immunospot (ELISPOT) assays to measure cellular immune responses, and intracellular cytokine staining (ICS) assays to measure CD4+ and CD8+ T-cell responses. Exploratory immunogenicity endpoints included Ad26 neutralization assays, systems serology assays, and electrochemiluminescence assays (ECLA). Adverse events (solicited, unsolicited, serious, not serious) were also collected. Results for the adverse events for cohort 1b are reported in Sadoff et al. (2021b).

Key Findings

Immunogenicity data from cohorts 1a & 3 (Sadoff et al. (2021b)

For the Phase I/IIa trial, 593 participants were screened for enrollment in cohort 1. A total of 405 participants were actually enrolled in the trial and 402 participants received either Ad26.COV2.S at a dose of $5x10^{10}$ viral particles (low dose) or $1x10^{11}$ viral particles (high dose) per mL or placebo. For cohort 3 of the trial, a total of 660 participants were screened, of which 405 were enrolled and 403 received

Ad26.COV2.S at a dose of $5x10^{10}$ viral particles (low dose) or $1x10^{11}$ viral particles (high dose) per mL or placebo.

The analysis results of the humoral immunogenicity data from the Phase I/IIa clinical trial suggest that a single dose of either the low dose or high dose *Janssen Ad26.COV2.S (COVID-19) Vaccine* can elicit a strong immune response in both age groups. In the younger cohort (i.e., cohort 1a), seroconversion rates are maintained at 100% even until day 71. Immunogenicity results of the Phase I/IIa clinical trial for cohort 1a (18 to 55 years age group) and cohort 3 (≥65 years age group) are found in Table 1.2 and Table 1.3, respectively.

Table 1.2. Phase I/IIa data on seroconversion rates of binding-antibodies measured against a stabilized SARS-CoV-2 full-length spike protein and neutralizing antibody titers at days 1, 29, 57, 71 on healthy adults, aged 18 to 55 years old (Cohort 1a, N=380)

Days after vaccination	High Dose/High Dose (subgroup 1, 2-dose)		High Dose/Placebo (subgroup 2, single dose)		Low Dose/Low Dose (subgroup 3, 2-dose)		Low Dose/Placebo (subgroup 4, single dose)		Placebo/Placebo (subgroup 5, single dose)	
	% Seroconversion rate	Geometric Mean Concentration (95% CI)	% Seroconversion rate	Geometric Mean Concentration (95% CI)	% Seroconversion rate	Geometric Mean Concentration (95% CI)	% Seroconversion rate	Geometric Mean Concentration (95% CI)	% Seroconversion rate	Geometric Mean Concentration (95% CI
Binding-Antibody Geometric Mean Concentrations										
Day 1	Baseline GMC below lower limit of quantitation (LLOQ)									
Day 29	100%	788 (628 to 988)	99%	625 (505 to 773)	99%	586 (445 to 771)	99%	478 (379 to 603)	1%	Below LLOQ
Day 57	100%	1100 (908 to 1332)	97%	873 (701 to 1087)	100%	754 (592 to 961)	100%	660 (513 to 849)	1%	
Day 71	100%	2292 (1846 to 2845)	100%	951 (696 to 1300)	100%	1677 (1334 to 2109)	100%	600 (443 to 814)	1%	
Day 85	100%	2465 (2063 to 2946)	97%	965 (772 to 1205)	99%	1994 (1674 to 2375)	99%	658 (502 to 862)	6%	
SARS-CoV-2 Neutralizing Antibody Titers										
Day 1	Baseline GMT below lower limit of quantitation (LLOQ)									
Day 29	92%	354 (220 to 571)	96%	215 (169 to 273)	88%	224 (168 to 298)	99%	224 (158 to 318)	0	Below LLOQ
Day 57	96%	488 (334 to	96%	370 (268 to	96%	288 (221 to	100%	310 (228 to	0	

		714)		511)		376)		422)		
Day 71	100%	1266 (746 to 2169)	100%	388 (290 to 509)	100%	827 (508 to 1183)	100%	321 (227 to 438)	0	
Day 85	100%	1229 (886 to 1706)	100%	377 (283 to 503)	100%	849 (664 to 1086)	100%	338 (230 to 496)	5%	

*LLOQ - lower limit of quantitation
Note: Values for Day 85 were obtained from European Medicines Agency *Assessment Report on COVID-19 Vaccine Janssen*

Table 1.3. Phase I/IIa data on seroconversion rates of binding-antibodies measured against a stabilized SARS-CoV-2 full-length spike protein and neutralizing antibody titers at days 1, 29, 57, 71 on healthy adults, ≥65 years old after first dose (Cohort 3, N=405)

Cohort 3: ≥65 years (N=405)						
Days after vaccination	**High Dose (subgroup 1 [2-dose] and subgroup 2 [single dose])**		**Low Dose (subgroup 3 [2-dose] and subgroup 4 [single dose])**		**Placebo (subgroup 5, [single dose])**	
	%Seroconversion Rate	**Geometric Mean Concentration (95% CI)**	**%Seroconversion Rate**	**Geometric Mean Concentration (95% CI)**	**%Seroconversion Rate**	**Geometric Mean Concentration (95% CI)**
Binding-Antibody Geometric Mean Concentrations						
Day 1	Baseline GMC below lower limit of quantitation (LLOQ)					
Day 15	77%	141 (114 to 175)	75%	122 (97 to 152)	2%	Below LLOQ (<53)
Day 29	96%	350 (281 to 429)	96%	312 (246 to 396)	0%	
SARS-CoV-2 Neutralizing Antibody Titers						
	%Seroconversion Rate	**Geometric Mean Titers(95% CI)**	**%Seroconversion Rate**	**Geometric Mean Titers (95% CI)**	**%Seroconversion Rate**	**Geometric Mean Titers (95% CI)**
Day 1	Baseline GMT below lower limit of quantitation (LLOQ)					
Day 15	84%	172 (119 to 269)	91%	212 (137 to 284)	0	Below LLOQ (<58)
Day 29	88%	212 (163 to 266)	96%	277 (193 to 307)	0	

*LLOQ - lower limit of quantitation

Cellular responses were also noted through S-specific CD4+ and CD8+ T-cells after the first dose. In cohort 1a, higher responses to S peptide (for both CD4+ and CD8+) were detected in the high dose group compared to the low dose

group. Meanwhile, in cohort 3, the low dose group showed higher responses to S peptide in terms of CD8+ vs high dose group. Vaccine-elicited responses in S-specific CD4+ and CD8+ T-cells are presented in Table 1.4.

Table 1.4. Phase I/IIa data on S-specific T-Cell Responses after first dose

T-cells	**Cohort 1a** (18 to 55 years old) **(%, 95% CI)**		**Cohort 3** (≥65 years old) **(%, 95% CI)**	
	Low dose (subgroup 3 [2-dose] and subgroup 4 [single dose])	**High dose (subgroup 1, [2-dose] and subgroup 2, [single dose])**	**Low dose (subgroup 3 [2-dose] and subgroup 4 [single dose])**	**High dose (subgroup 1, [2-dose] and subgroup 2, [single dose])**
CD4+	76 (65 to 86)	83 (73 to 91)	60 (46 to 74)	67 (53 to 79)
CD8+	51 (39 to 63)	64 (52 to 75)	36 (23 to 51)	24 (13 to 37)

Immunogenicity data from cohort 1b (Stephenson et al., 2021)

Additional immunogenicity outcomes were explored for Cohort 1b participants. In comparison to the humoral immunogenicity outcomes explored in Cohort 1a, Cohort 1b observed binding antibody response against the full-length S protein and the S receptor binding domain, as well as virus neutralizing antibodies. By day 15 (14 days after first dose vaccination), binding antibodies against full-length S protein and against S receptor binding domain were observed in all participants administered with a vaccine. By day 57 (day of second dose vaccination), virus neutralizing antibodies were also observed in all participants in addition to the binding antibodies. The participants with detected binding and neutralizing antibodies are found in Table 1.5.

Table 1.5. Phase I/IIa Cohort 1b participants with detected binding and neutralizing antibody response (Cohort 1b, N=20)

Days after vaccination	**Participants with binding antibodies against full-length S protein, n(%)**	**Participants with binding antibodies against S receptor binding domain (RBD), n(%)**	**Participants with virus neutralizing antibodies, n(%)**
Day 8	13 (65)	18 (90)	5 (25)

Day 15	20 (100)	20 (100)	17 (85)
Day 57	20 (100)	20 (100)	20 (100)
Day 71	20 (100)	20 (100)	20 (100)

In Day 8 of cohort 1b, the study only reported the binding antibody GMTs of all participants who received at least one dose of the vaccine - regardless if high or low dose - and compared it with Day 1. It was observed that the binding antibodies GMT for both S-specific and RBD-specific were both statistically significant compared to Day 1 (p=.02, p=.003, respectively). It was only in Day 71 that the study reported the individual GMT for each subgroup. High dose-high dose subgroup had the highest GMT on Day 71, followed by the low dose-placebo subgroup (for S-specific binding antibody) or high dose-placebo (for RBD-specific binding antibody and neutralizing antibody). The immunogenicity data on binding and neutralizing antibodies are found in Table 1.6.

Table 1.6. Phase I/IIa Cohort Ib immunogenicity data at days 1, 8, 15, and 71 on healthy adults, aged 18 to 55 years old (n=25)

Days after vaccination	**High Dose/High Dose** (subgroup 1, [2-dose])	**High Dose/Placebo** (subgroup 2, [single dose])	**Low Dose/Low Dose** (subgroup 3 [2-dose])	**Low Dose/Placebo** (subgroup 4, [single dose])	**Placebo/Placebo** (subgroup 5, [single dose])
	Geometric Mean Titer	**Geometric Mean Titer**	**Geometric Mean Titer**	**Geometric Mean Titer**	**Geometric Mean Titer**
S- specific Binding-Antibody Geometric Mean Titer (GMT)					
Day 1	Undetectable geometric mean titer				Not reported
Day 8	GMT = 41, (p=.02 compared to Day 1)				Not reported
Day 15	Not reported				Not reported
Day 71	5729	2852	2432	3249	20
RBD-specific binding antibody Geometric Mean Titer (GMT)					
Day 1	Undetectable geometric mean titer				Not reported
Day 8	GMT = 41(p=.003 compared to Day 1)				Not reported
Day 15	Not reported				Not reported
Day 71	3666	2372	1018	2023	21

Virus Neutralizing Antibody Titers (expressed in GMT)					
Day 1	Undetectable geometric mean titer				Not reported
Day 8	Not reported				Not reported
Day 57	Not reported				Not reported
Day 71	449	387	242	375	13

GMT: Geometric Mean Titer
Note: For Days 1, 8, and 57, the study did not report on the GMT per subgroup.

The study also analysed the diversity and specificity of the antibody responses elicited by the vaccine. Assessment of the binding and functional profiles of the antibodies found on day 29 by systems serology showed that the vaccine induced S- and RBD specific IgA1, IgA2, IgG1, IgG3, IgG4 and IgM subclasses; FcγR2a, FcγR2b, FcγR3a, and FcγR3b binding; and antibody dependent complement deposition, antibody-dependent neutrophil phagocytosis, antibody-dependent cellular phagocytosis, and antibody-dependent NK cell activation functional antiviral responses. S-specific cellular immune responses were also assessed using IFN-γ and IL4 ELISPOT assays. By day 15, IFN-γ ELISPOT responses were observed in 65% (13 of 20) of participants; by day 71, IFN-γ ELISPOT responses were observed in 84% (16 of 19) of the participants. No clear differences among groups were observed. Meanwhile, IL-4 responses were not observed. IFN-γ ELISPOT responses correlated with different antibody responses are the following: S-specific binding antibody titers (R = 0.55, p=.005), RBD specific binding antibody titers (R = 0.54, P = .006), and neutralizing antibody titers (R = 0.57, p=003) on day 29.

Safety analysis (Sadoff et al., 2021b)

The safety analysis for the Phase I/IIa trial after the administration of the first dose included data for 402 participants in cohort 1 and 403 participants in cohort 3.

Solicited local adverse events

- For both cohorts, the observed solicited local adverse events were mostly grade 1 or 2, with the most frequent event being injection site pain.

- For cohort 1, solicited local adverse events were observed in 103 of 162 low-dose recipients (64%), 123 of 158 high-dose recipients (78%) and 7 of 82 placebo recipients (9%).
- Meanwhile for cohort 3, solicited local adverse events were observed in 66 of 161 low-dose recipients (41%), 68 of 161 high-dose recipients (42%), and 11 of 81 placebo recipients (14%).

Solicited systemic adverse events

- For both cohorts, most solicited systemic adverse events were grade 1 or 2, with the most frequently reported events being fatigue, headache, and myalgia.
- In cohort 1, solicited systemic adverse events were observed in 105 low-dose recipients (65%), 133 high-dose recipients (84%), and 21 placebo recipients (26%).
- Meanwhile in cohort 3, solicited systemic adverse events were observed in 74 low-dose recipients (46%), 88 high-dose recipients (55%), and 19 placebo recipients (23%).

Solicited grade 3 systemic adverse events

- For cohort 1, solicited grade 3 systemic adverse events were observed in 15 low-dose recipients (9%) and 32 high-dose recipients (20%). No solicited grade 3 systemic adverse events were seen in placebo recipients from cohort 1.

Unsolicited adverse events

- For cohort 1, unsolicited adverse events were reported in 34 low-dose recipients (21%), 56 high-dose recipients (35%), and 14 placebo recipients (17%). While in cohort 3, unsolicited adverse events were observed in 27 low-dose recipients (17%), 38 high-dose recipients (24%), and 13 placebo recipients (16%). No grade 4 adverse events, whether solicited or unsolicited, were reported for both cohorts.

Table 1.7. Adverse events after dose 1 in cohort 1 and cohort 3 based on Sadoff et al. (2021b)

Outcomes	Cohort 1			Cohort 3		
	Low dose (n=162)	High dose (n=158)	Placebo (n=82)	Low dose (n=161)	High dose (n=161)	Placebo (n=81)
Solicited Local Adverse Events	103 (64%)	123 (78%)	7 (9%)	66 (41%)	68 (42%)	11 (14%)

Solicited Systemic Adverse Events	105 (65%)	133 (84%)	21 (26%)	74 (46%)	88 (55%)	19 (23%)
Solicited Systemic Grade 3 Adverse Events	15 (9%)	32 (20%)	0 (0%)	1 (1%)	4 (2%)	0 (0%)
Unsolicited Adverse Events	34 (21%)	56 (35%)	14 (17%)	27 (17%)	38 (24%)	13 (16%)

With regard to safety data after the administration of the second dose of the vaccine, the reported data was available for cohort 1a only (n=363).

Solicited adverse events

- One or more solicited adverse events were reported in 77% and 80% of participants in the low-dose and high-dose groups respectively, compared with the 34% and 31% of those who received placebo as a second dose after a first dose of vaccine and 22% of those who received placebo for both doses.

Solicited grade 3 systemic adverse events

- Solicited adverse events of grade 3 or higher were seen in 1% of low-dose recipients and in 7% of high-dose recipients, for those in the placebo group who received a first dose of the vaccine, the corresponding percentages were 1% and 2% respectively, and no solicited adverse events of grade 3 or higher were seen in participants who received placebo for both doses. No grade 3 fevers were reported in any group after a second dose of the vaccine.

Serious adverse events

- Five serious adverse events occurred for this trial, which were hypotension, bilateral nephrolithiasis, legionella pneumonia, and worsening of multiple sclerosis, however all of these were determined to be unrelated to the vaccine. One case of fever that resulted in hospitalization due to suspicion of COVID-19 was observed, however this case recovered within 12 hours and the fever was subsequently deemed to be related to the vaccine.

Table 1.8. Adverse events after dose 2 in cohort 1a based on Sadoff et al., (2021b)

Outcomes	**Cohort 1a (n=363)**				
	High dose/ High dose (n=not	**High dose/ Placebo (n=not specified)**	**Low dose/Low dose (n=not**	**Low dose/ Placebo (n=not specified)**	**Placebo/Placebo (n=not specified)** (subgroup 5, [single

	specified) (subgroup 1, [2-dose])	(subgroup 2, [single dose])	specified) (subgroup 3 [2-dose])	(subgroup 4, [single dose])	dose
Solicited adverse events	80%	31%	77%	34%	22%
Solicited grade 3 systemic adverse events	7%	2%	1%	1%	0%
Serious adverse events	The authors did not specify in which subgroup the five serious adverse events had occurred.				

PHASE III TRIAL *(adults aged 18 years old and above, N=44, 325)*

The trial is a multi-center, randomized, double-blind, placebo-controlled phase III trial among adults ≥18 years of age. Of the 44,325 randomized participants, 43,783 received a single intramuscular injection of *Janssen Ad26.COV2.S (COVID-19) Vaccine* containing $5x10^{10}$ viral particles or placebo containing 0.9% saline. Participants included in the safety and efficacy analyses were observed for a median follow-up duration of 58 days or 8 weeks after vaccination. Due to the phased enrollment of specific cohorts, there were slight differences in the median follow-up duration for the population ≥60 years of age (52 days), population ≥60 years of age without comorbidities (54 days), and population ≥60 years of age with comorbidities (50 days).

Methodology of Evidence Appraisal

The HTAC's clinical research question elements are as follows:

Population: General and vulnerable population

Intervention: Janssen Ad26.COV2.S (COVID-19) Vaccine

Comparator: Placebo (Saline) OR Active Control

Outcomes: Vaccine efficacy (VE) and safety (see table below for details)

Table 1.9 Definitions and rating of importance of efficacy outcomes of interest

Name of outcome	Definition	HTAC rating of outcome importance
Vaccine efficacy (VE) against symptomatic COVID-19 after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2: • Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status • Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**CRITICAL** to decision making Subgroup analyses: **IMPORTANT** but not critical to decision-making

VE against Hospitalization due to COVID-19	Hospital admission for the management of COVID-19	**CRITICAL** to decision making
VE against Severe COVID-19 Occurrence after at least dose 1	Symptomatic COVID-19 after dose 1 with the addition of the following clinical manifestations: pneumonia, severe acute respiratory syndrome, multi-organ failure, and death *Reference: US FDA*	**CRITICAL** to decision making
VE against Severe COVID-19 Occurrence after dose 2	Symptomatic COVID-19 after dose 2 with the addition of the following clinical manifestations: pneumonia, severe acute respiratory syndrome, multi-organ failure, and death *Reference: US FDA*	**CRITICAL** to decision making
VE against symptomatic COVID-19 after at least Dose 1	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 1: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against symptomatic COVID-19 among older adults after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in older adults as defined in the trials: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against symptomatic COVID-19 among population with comorbidities after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in population with comorbidities: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against symptomatic COVID-19 among Asians, after dose 2	Positive Nucleic Acid Amplification Test (NAAT) and the following symptoms after dose 2 in Asian population: ● Acute onset of any of three or more signs and symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status ● Anosmia (loss of smell), ageusia (loss of taste) in the absence of any other identified cause *Reference: WHO COVID-19 case definitions*	**IMPORTANT** but not critical to decision-making
VE against asymptomatic COVID-19	Absence of COVID-19 symptoms but with positive NAAT results	**IMPORTANT** but not critical to decision-making

Table 1.2 Definitions and rating of importance of safety outcomes of interest

Name of outcome	Definition	HTAC rating of outcome importance
Serious adverse events	An adverse event is any undesirable experience associated with the use of a vaccine. The event is serious when the patient outcome is: ● Death ● Life threatening ● Hospitalization (initial or prolonged) ● Disability of permanent damage ● Congenital anomaly/ birth defect ● Required intervention to prevent permanent impairment of damage ● Other serious events which may jeopardize the patient and may require medical or surgical intervention to prevent one of the other outcomes *Reference: US FDA*	**CRITICAL** to decision making
Death (All-cause mortality)	Reported deaths regardless of cause	**CRITICAL** to decision making
Systemic reactogenicity (Dose 1)	General systemic reactions to injectable products such as vaccines include nausea/vomiting, diarrhea, headache, fatigue, and myalgia *Reference: US FDA*	**CRITICAL** to decision making
Systemic reactogenicity (Dose 2)		
Local reactogenicity (Dose 1)	Local reaction to injectable products such as vaccines include pain, tenderness, erythema/redness, and induration/ swelling *Reference: US FDA*	**IMPORTANT** but not critical to decision-making
Local reactogenicity (Dose 2)		
Adverse Events, Unsolicited	Any untoward medical occurrence associated with the use of a vaccine in humans, whether or not considered vaccine- related. *Reference: US FDA*	**IMPORTANT** but not critical to decision-making

The risk of bias for each outcome was assessed through Version 1 of the Cochrane risk-of-bias tool for randomized trials (RoB1 tool). Two reviewers independently appraised the risk of bias. Any disagreements between reviewers were resolved through consensus. Quality of evidence was then appraised by two reviewers through the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) Approach.

Efficacy and Safety from the Interim Results of Phase III trial

Table 1.9. HTAC outcomes of interest and the corresponding outcomes reported by Sadoff et al., 2021a

HTAC outcome of interest	Matching reported outcome from the ***Janssen Ad26.COV2.S (COVID-19) Vaccine*** **trial** (Sadoff et al., 2021a)	Definition of outcome from the ***Janssen Ad26.COV2.S (COVID-19) Vaccine*** **trial** (Sadoff et al., 2021a)

Efficacy outcomes		
VE against symptomatic COVID-19 after dose 1	VE against centrally confirmed symptomatic COVID, at least 14 days after vaccination *(PP)*	• A SARS-CoV-2 positive RT-PCR or molecular test result from any available respiratory tract sample (e.g., nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample; and • Any COVID-19 symptom: fever or chills, cough, shortness of breath or difficulty breathing, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, congestion or runny nose, nausea or vomiting, diarrhea.
	VE against centrally confirmed symptomatic COVID, at least 28 days after vaccination *(PP)*	
VE against hospitalization due to COVID-19	Vaccine efficacy of first occurrence COVID-19 requiring hospitalization, with onset at least 14 or at least 28 days after vaccination (*PP)*	Defined as inpatient stay for longer than 24 hours or overnight stay
VE against severe COVID-19	VE against adjudicated severe/critical COVID-19 (*PP)*	A RT-PCR or molecular test result from samples described above **and** any one of the following at any time during the course of observation • Clinical signs at rest indicative of severe systemic illness (respiratory rate ≥30 breaths/minute, heart rate ≥125 beats/minute, oxygen saturation (SpO2) ≤93% on room air at sea level, or partial pressure of oxygen/fraction of inspired oxygen (PaO2/FiO2) <300 mmHg) • Respiratory failure (defined as needing high-flow oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation [ECMO]) • Evidence of shock (defined as systolic blood pressure <90 mmHg, diastolic blood pressure <60 mmHg, or requiring vasopressors) • Significant acute renal, hepatic, or neurologic dysfunction • Admission to the ICU • Death
VE against moderate COVID-19 after dose 1	VE against centrally confirmed moderate to severe/critical COVID-19 with onset at least 14 and at least 28 days after vaccination *(PP)*	A SARS-CoV-2 positive reverse-transcriptase polymerase chain reaction (RT-PCR) or molecular test result from any available respiratory tract sample (eg, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample. Any 1 of the following new or worsening signs or symptoms: • Respiratory rate ≥20 breaths/minute • Abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level* • Clinical or radiologic evidence of pneumonia • Radiologic evidence of deep vein thrombosis (DVT) • Shortness of breath or difficulty breathing Any 2 of the following new or worsening signs or symptoms: • Fever (≥38.0°C or ≥100.4°F) • Heart rate ≥90 beats/minute • Shaking chills or rigor
	VE of first occurrence of moderate to severe/Critical COVID-19, including non-centrally confirmed cases, with onset at least 14 or at least 28 days after vaccination, by demographic characteristics *(PP)*	

		● Sore throat ● Cough ● Malaise as evidenced by one or more of the following**: ○ Loss of appetite ○ Generally unwell ○ Fatigue ○ Physical weakness ● Headache ● Muscle pain (myalgia) ● Gastrointestinal symptoms (diarrhea, vomiting, nausea, abdominal pain)** ● New or changing olfactory or taste disorders ● Red or bruised looking feet or toes
VE against symptomatic COVID-19 after dose 1 in older adults	Vaccine Efficacy of First Occurence of moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, with onset at least 14 days after vaccination in ≥65 yo, (PP)	A SARS-CoV-2 positive reverse-transcriptase polymerase chain reaction (RT-PCR) or molecular test result from any available respiratory tract sample (eg, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample. Any 1 of the following new or worsening signs or symptoms: ● Respiratory rate ≥20 breaths/minute ● Abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level* ● Clinical or radiologic evidence of pneumonia ● Radiologic evidence of deep vein thrombosis (DVT) ● Shortness of breath or difficulty breathing Any 2 of the following new or worsening signs or symptoms: ● Fever (≥38.0°C or ≥100.4°F) ● Heart rate ≥90 beats/minute • Shaking chills or rigor ● Sore throat ● Cough ● Malaise as evidenced by one or more of the following**: ○ Loss of appetite ○ Generally unwell ○ Fatigue ○ Physical weakness ● Headache ● Muscle pain (myalgia) ● Gastrointestinal symptoms (diarrhea, vomiting, nausea, abdominal pain)** ● New or changing olfactory or taste disorders ● Red or bruised looking feet or toes
	Vaccine Efficacy of First Occurence of moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases ,with onset at least 28 days after vaccination in ≥65 yo, *(PP)*	
VE against symptomatic COVID-19 after dose 1 in population with	VE of first occurrence of moderate to severe/Critical COVID-19, including non-centrally confirmed cases, with onset at least 14 or at least 28 days after vaccination, by presence of comorbidity *(PP)*	A SARS-CoV-2 positive reverse-transcriptase polymerase chain reaction (RT-PCR) or molecular test result from any available respiratory tract sample (eg, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample. Any 1 of the following new or worsening signs or symptoms: ● Respiratory rate ≥20 breaths/minute ● Abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level* ● Clinical or radiologic evidence of pneumonia

comorbidities	VE of first occurrence of moderate to severe/Critical COVID-19, including non-centrally confirmed cases, with onset at least 14 or at least 28 days after vaccination, presence of comorbidity, 18 to 59 years *(PP)* VE of first occurrence of moderate to severe/Critical COVID-19, including non-centrally confirmed cases, with onset at least 14 or at least 28 days after vaccination, presence of comorbidity, ≥60 years *(PP)*	● Radiologic evidence of deep vein thrombosis (DVT) ● Shortness of breath or difficulty breathing Any 2 of the following new or worsening signs or symptoms: ● Fever (≥38.0°C or ≥100.4°F) ● Heart rate ≥90 beats/minute • Shaking chills or rigor ● Sore throat ● Cough ● Malaise as evidenced by one or more of the following**: ○ Loss of appetite ○ Generally unwell ○ Fatigue ○ Physical weakness ● Headache ● Muscle pain (myalgia) ● Gastrointestinal symptoms (diarrhea, vomiting, nausea, abdominal pain)** ● New or changing olfactory or taste disorders ● Red or bruised looking feet or toes
VE against COVID-19 infection in Asians	VE of first occurrence of moderate to severe/Critical COVID-19, including non-centrally confirmed cases, with onset at least 14 or at least 28 days after, Asians *(PP)*	A SARS-CoV-2 positive reverse-transcriptase polymerase chain reaction (RT-PCR) or molecular test result from any available respiratory tract sample (eg, nasal swab sample, sputum sample, throat swab sample, saliva sample) or other sample. Any 1 of the following new or worsening signs or symptoms: ● Respiratory rate ≥20 breaths/minute ● Abnormal saturation of oxygen (SpO2) but still >93% on room air at sea level* ● Clinical or radiologic evidence of pneumonia ● Radiologic evidence of deep vein thrombosis (DVT) ● Shortness of breath or difficulty breathing Any 2 of the following new or worsening signs or symptoms: ● Fever (≥38.0°C or ≥100.4°F) ● Heart rate ≥90 beats/minute • Shaking chills or rigor ● Sore throat ● Cough ● Malaise as evidenced by one or more of the following**: ○ Loss of appetite ○ Generally unwell ○ Fatigue ○ Physical weakness ● Headache ● Muscle pain (myalgia) ● Gastrointestinal symptoms (diarrhea, vomiting, nausea, abdominal pain)** ● New or changing olfactory or taste disorders ● Red or bruised looking feet or toes
VE against asymptomatic COVID-19	VE against asymptomatic SARS-CoV-2 infection, Day 1-29 *(FAS)*	Participant who does not fulfill the criteria for suspected COVID-19 based on signs and symptoms (further specified as no symptoms on the day preceding, the day of, or any time after the positive PCR test) AND has a SARS-CoV-2 positive RT-PCR test result OR develops a positive serology based on a SARS-CoV-2 N-specific immunoglobulin assay within Day 1 (pre-vaccination) and Day 29

		(28 days post- vaccination)
	VE against asymptomatic SARS-CoV-2 infection, after day 29 *(PP)*	Participant who does not fulfill the criteria for suspected COVID-19 based on signs and symptoms (further specified as no symptoms on the day preceding, the day of, or any time after the positive PCR test) AND has a SARS-CoV-2 positive RT-PCR test result OR develops a positive serology based on a SARS-CoV-2 N-specific immunoglobulin assay after Day 29 (28 days post- vaccination).
Safety outcomes		
Serious adverse events	Serious adverse events *(FAS)*	Suspected transmission of an infectious agent by a medicinal product will be reported as an SAE. Any event requiring hospitalization (or prolongation of hospitalization) that occurs during participation in the study must be reported as an SAE, except hospitalizations for the following: ● Hospitalizations not intended to treat an acute illness or AE (eg, social reasons such as pending placement in long-term care facility) ● Surgery or procedure planned before entry into the study (must be documented in the eCRF). Note: Hospitalizations that were planned before the signing of the ICF, and where the underlying condition for which the hospitalization was planned has not worsened, will not be considered SAEs. Any AE that results in a prolongation of the originally planned hospitalization is to be reported as a new SAE. The cause of death of a participant in a study, whether or not the event is expected or associated with the study vaccine, is considered a SAE.
Death (all-cause mortality)	Effect on all-cause mortality *(FAS)*	Deaths due to all causes
Systemic reactogenicity	Frequency of solicited systemic adverse reactions within 7 days following vaccination *(SS)*	Vomiting, nausea, diarrhea, headache, fatigue, myalgia
Local reactogenicity	Frequency of solicited local adverse reactions within 7 days following vaccination *(SS)*	Pain/tenderness, erythema, swelling
Adverse events	Unsolicited adverse events occurring in ≥1% of vaccine group participants within 28 days following vaccination, by MedDRA primary system organ class and preferred term *(SS)*	Unsolicited AEs are all AEs for which the participant is not specifically questioned.

Below are the details of the analysis sets used in the Phase III interim analysis as reported in the US FDA report (2021).

Table 1.10 Analysis Set definitions used in the report by US FDA, 2021

Analysis Set	Population
Randomized	All participants who are randomized, regardless of the treatment status during the study.
Full analysis set (FAS)	All randomized participants with a documented study vaccine administration. The FAS was used for all analyses of safety except solicited adverse reactions.
Per-protocol (PP) set	All participants in the FAS who had no immunologic or virologic evidence of prior COVID-19 at the time of vaccination and no major protocol deviations that were judged to possibly impact the efficacy of the vaccine.
Safety subset (SS)	Subset of the full analysis set for the analysis of solicited and unsolicited AEs

Janssen Ad26.COV2.S (COVID-19) Vaccine demonstrated vaccine efficacy of 66.9% (95% CI 59.1 to 73.4) for the prevention of symptomatic COVID-19 at least 14 days after vaccination, based on high certainty of evidence. Meanwhile, for VE against symptomatic COVID-19 at least 28 days after vaccination the vaccine has shown 66.5% (95% CI 55.5 to 75.1) efficacy, based on high certainty of evidence. In terms of VE against moderate to severe/critical disease, the vaccine has shown 66.9% (95% CI 59.0 to 73.5) efficacy, based on high certainty of evidence. A VE of 76.3% (95% CI 57.9, 87.5) was seen for preventing severe/critical COVID-19, beginning at 14 days after vaccination, at a median follow up of two months (58 days), based on moderate certainty of evidence. Subgroup analysis showed that *Janssen Ad26.COV2.S (COVID-19) Vaccine* provides adequate protection against moderate to severe COVID-19 infection to older adults aged ≥65 years old and to those with at least one comorbidity for both at least 14 days and after 28 days of vaccination, based on high certainty of evidence. Cumulative incidence of moderate to severe/critical COVID-19 diverge following Day 14 with more cases accumulating in the placebo group rather than the vaccine group. Vaccine efficacy against specific SARS-CoV-2 variants is planned in the study. However, as sequencing of all cases was still incomplete at the time of the report, the investigators deemed the vaccine efficacy against specific SARS-CoV-2 variants was not evaluable. Nonetheless, their findings were included in this review.

Starting at 14 days after vaccination, *Janssen Ad26.COV2.S (COVID-19) Vaccine* showed high protection against hospitalization [VE: 93.1%, (95%CI: 72.7 to 99.2)], based on moderate certainty of evidence. The two hospitalizations in the *Janssen*

Ad26.COV2.S (COVID-19) Vaccine group were in participants who were ≥60 years of age with comorbidities. As for its efficacy against asymptomatic infection, the available data are insufficient to assess the effect of the vaccine due to the infrequent evaluation of serological and virological measurements in the trial. As of February 5, 2021, no COVID-related deaths were reported in the vaccination group compared with seven in the placebo group. Vaccine efficacy for reducing deaths due to COVID-19 remains to be demonstrated.

Overall, rates of unsolicited adverse events, medically attended adverse events, serious adverse events, and deaths were balanced between treatment arms. Ten serious adverse events, 7 occurring in the vaccine group and 3 in the placebo group, were assessed to be related to the study product. However, upon investigation, the US FDA deemed that only 3 were likely related to the vaccine, namely, radiculitis brachial, post-vaccination syndrome (asthenia), and vaccination site hypersensitivity. For pericarditis, the US FDA could not exclude the possibility that the vaccine could have contributed to the event. However, further review of the safety database including other Ad26-based vaccines did not report other additional reports of pericarditis. In terms of the US FDA assessment on facial paralysis (Bell's palsy) and Guillain Barré Syndrome, these events were identified to be unlikely related to the study vaccine but a causal relationship could not be definitively excluded. Both Bell's palsy and Guillain Barré Syndrome were included in the list of adverse events of special interest to be taken during routine monitoring and pharmacovigilance. Additionally, though no specific risk has been identified, a causal relationship between chronic pulmonary disorders exacerbation could not be confirmed nor ruled out by the EMA.

As for hypersensitivity, the WHO and EMA also noted that in an open-label trial in South Africa, one case of anaphylaxis that met the Brighton Collaboration criteria occurred although none were noted during the COV3001 clinical trial. Overall, there were 77 cases of hypersensitivity in the vaccine group and 65 cases in the placebo group reported in the Phase 3 clinical trial. However, the US FDA noted one serious adverse event of hypersensitivity (not classified as anaphylaxis) beginning two days following vaccination in COV3001 trial and was deemed likely related to receipt of the vaccine.

The US FDA and EMA both noted the slight numerical imbalance between treatment arms in the reported thromboembolic events including deep vein thrombosis, pulmonary embolism, transverse sinus thrombosis, thrombosed hemorrhoid, cerebrovascular arterial events, and cardiovascular arterial events. There were 15 events from 14 participants in the vaccine group and 10 events from 10 participants in the placebo group. While the imbalance is small, the US FDA could not exclude the vaccine as a possible contributor to the event. One notable event was of a transverse sinus thrombosis, similar to the rare blood clots that have been reported during the rollout of the vaccine in the United States. The event occurred in a 25-year old male with no past medical history or concurrent medications, 21 days after vaccination. It was initially thought to be related to the study vaccine and caused a study pause. Upon investigation, a clear explanation to the event was not identified but the study was resumed after revisions to the informed consent form and brochure. During the deliberation after the pause of the implementation of *Janssen Ad26.COV2.S (COVID-19) Vaccine,* this case was also reviewed together with the 6 cases of thrombocytopenic thrombosis that occurred during the vaccine rollout.

Other notable numerical imbalances in the reported events were tinnitus, which had 6 events in the vaccine group and none in the placebo group; urticaria, which had 8 events in the vaccine group and 5 events in the placebo group; arthralgia, which had 92 events in the vaccine group and 62 events in the placebo group; and muscular weakness, which had 31 events in the vaccine group and 18 events in the placebo group. At the time of the report, there was insufficient information to establish the causality for tinnitus but the other three adverse events were considered to represent vaccine reactogenicity.

Table 1.11 Summary of findings for efficacy outcomes

EFFICACY OUTCOMES										
OUTCOME	Quality Assessment					Summary of Findings			Certainty	Importance
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ad26.COV2.S n/N (%risk)	Placebo n/N (%risk)	Effect Size (95% CI)		
1. SYMPTOMATIC COVID-19										
1A. VE against Centrally Confirmed symptomatic COVID-19 *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not Serious	None	117/19514 (0.6%)	351/19544 (1.8%)	**VE: 66.9** (59.1 to 73.4)	⨁⨁⨁⨁ **HIGH**	CRITICAL
1B. VE against Centrally Confirmed symptomatic COVID-19 *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	66/19306 (0.3%)	195/19178 (1.0%)	**VE:66.5** (55.1 to 75.1)	⨁⨁⨁⨁ **HIGH**	CRITICAL
2. MODERATE TO SEVERE/CRITICAL										
2A. Centrally confirmed cases only										
at least 14 days after vaccination										
2A.1 VE against Centrally Confirmed Moderate to Severe/Critical COVID-19 *(at least **14 days** after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	116/19514 (0.6%)	348/19544 (1.8%)	**VE: 66.9** (59.0 to 73.4)	⨁⨁⨁⨁ **HIGH**	CRITICAL
at least 28 days after vaccination										
2A.2.VE against Centrally Confirmed Moderate to Severe/Critical COVID-19 *(at least **28 days** after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	66/19306 (0.3%)	193/19178 (1.0%)	**VE:66.1** (55.0 to 74.8)	⨁⨁⨁⨁ **HIGH**	CRITICAL

2B. Including centrally and non-centrally confirmed cases										
2B.1. *at least 14 days after vaccination*										
2B.1.1. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>older adults ≥ 65 years old</u> (at least 14 days after vaccination, per protocol set)	Not serious	NA	Not serious	Not Serious	None	16/3970 (0.4%)	68/3992 (1.7%)	**VE: 76.5** (59.1 to 87.3)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.1.2 VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>Asians</u> *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (Asians not well-represented)	Serious (Wide CI, crosses null value)	None	6/714 (0.8%)	12/649 (1.8%)	**VE: 54.4** (-31.1 to 86.0)	⨁⨁◯◯ **LOW**	IMPORTANT
2B.1.3. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>population with comorbidity</u> *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	70/7777 (0.1%)	194/7798 (2.5%)	**VE: 64.2** (52.7 to 73.1)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.1.4. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>population with comorbidity aged 18-59 years old</u> *(at least 14 days after vaccination, per protocol set)*	Not Serious	NA	Not serious	Not Serious	None	48/4404 (1.1%)	131/4371 (3.0%)	**VE:63.9** (49.4 to 74.7)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.1.5. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>population with comorbidity aged 60 years old and above</u> *(at least 14 days after vaccination, per protocol set)*	Not Serious	NA	Not serious	Not Serious	None	22/3373 (0.6%)	63/3427 (1.8%)	**VE: 64.9** (42.2 to 79.4)	⨁⨁⨁⨁ **HIGH**	IMPORTANT

2.B.1.6. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, regardless of baseline SARS-CoV-2 Status *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	176/21636 (0.8%)	513/21574 (2.4%)	**VE: 66.1** (59.7 to 71.6)	⨁⨁⨁⨁ **HIGH**	CRITICAL
2.B.1.7. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, positive baseline SARS-CoV-2 serostatus *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Very Serious (wide CI, crosses null value)	None	3/2122 (0.1%)	4/2030 (0.2%)	**VE: 28.5** (-322.8 to 89.5)	⨁⨁◯◯ **LOW**	IMPORTANT
2.B.1.8. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, negative baseline SARS-CoV-2 serostatus *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	173/19514 (0.9%)	509/19544 (2.6%)	**VE: 66.3** (59.9 to 71.8)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2.B.1.9. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in South Africa *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	43/2473 (1.7%)	90/2496 (3.6%)	**VE: 52.0** (30.3 to 67.4)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2.B.1.10. VE against moderate to severe/critical COVID- 19, including centrally and non-centrally confirmed cases in Brazil *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	39/3370 (1.2%)	114/3355 (3.4%)	**VE: 66.2** (51.0 to 77.1)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.2. ***at least 28 days after vaccination***										

2B.2.1. VE against moderate to severe/critical COVID-19 COVID-19, including centrally and non-centrally confirmed cases in <u>older adults ≥ 65 years old</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not Serious	None	12/3928 (0.3%)	38/3925 (1.0%)	**VE: 68.6** (38.6 to 85.1)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.2.2. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>Asians</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious (Asians not well-represented)	Serious (Wide CI, crosses null value)	None	2/689 (0.2%)	7/626 (1.1%)	**VE: 74.0** (-36.5 to 97.4)	⨁⨁◯◯ **LOW**	IMPORTANT
2B.2.3.VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>population with comorbidity</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	44/7684 (0.6%)	105/7626 (1.4%)	**VE: 58.6** (40.6 to 71.6)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.2.4 VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in <u>population with comorbidity aged 18-59 years old</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	29/4350 (0.7%)	79/4273 (1.8%)	**VE: 64.0** (44.3 to 77.3)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2B.2.5. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in population with <u>comorbidity aged 60 years old and above</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Serious (wide CI, crosses null value)	None	15/3334 (0.4%)	26/3353 (0.8%)	**VE: 42.3** (-13.1 to 71.6)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
2.B.2.6. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, <u>Regardless of baseline SARS-CoV-2 Status</u> *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	114/21424 (0.5%)	326/21199 (1.5%)	**VE: 65.5** (57.2 to 72.4)	⨁⨁⨁⨁ **HIGH**	CRITICAL

2.B.2.7. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, positive baseline SARS-CoV-2 serostatus *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not assessed	None	1/2118 (<0.1%)	2/2021 (0.1%)A	**Not evaluable**	**N/A**	IMPORTANT
2.B.2.8. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases, negative baseline SARS-CoV-2 serostatus *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	113/19306 (0.6%)	324/19178 (1.7%)	**VE: 65.5** (57.2 to 72.4)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2.B.2.9. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in South Africa *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	23/2449 (0.9%)	64/2463 (2.6%)	**VE: 64.0** (41.2 to 78.7)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
2.B.2.10. VE against moderate to severe/critical COVID-19, including centrally and non-centrally confirmed cases in Brazil *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Not serious	Not serious	None	24/3354 (0.7%)	74/3312 (2.2%)	**VE: 68.1** (48.8 to 80.7)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
3. COVID-19 REQUIRING HOSPITALIZATION										
3A. VE against COVID-19 requiring hospitalization *(with onset at least 14 days after vaccination including centrally and non-centrally confirmed cases, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Not serious	None	2/19514 (<0.1%)	29/19544 (0.1%)	**VE: 93.1** (72.7 to 99.2)	⨁⨁⨁◯ **MODERATE**	CRITICAL
3B. VE against COVID-19 requiring hospitalization *(with onset at least 28 days after vaccination including centrally and non-centrally confirmed cases, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Serious (wide CI)	None	0/19306 (0.0%)	16/19178 (<0.1%)	**VE: 100** (Not estimable)	⨁⨁◯◯ **LOW**	CRITICAL
4. SEVERE/ CRITICAL COVID-19 (including centrally and non-centrally confirmed cases)										

4A. ***at least 14 days after vaccination***										
4A.1. VE against Severe/Critical COVID- 19 (including centrally and non-centrally confirmed cases) *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (Needs longer follow up period)	Not serious	None	19/19514 (<0.1%)	80/19544 (0.4%)	**VE: 76.3** (57.9 to 87.5)	⨁⨁⨁◯ **MODERATE**	CRITICAL
4A.2. VE against Severe/Critical COVID- 19 (including centrally and non-centrally confirmed cases), 18-59 yo *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (Needs longer follow up period)	Not serious	None	12/12750 (0.1%)	52/12782 (0.4%)	**VE: 76.9** (56.2 to 88.8)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4A.3. VE against Severe/Critical COVID- 19 (including centrally and non-centrally confirmed cases), ≥60 yo *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (Needs longer follow up period)	Not serious	None	7/6764 (0.1%)	28/6762 (0.4%)	**VE: 75.1** (41.7 to 90.8)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4A.4. VE against severe/critical COVID- 19, including centrally and non-centrally confirmed cases in South Africa *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Not serious	None	8/2473 (0.3%)	30/2496 (1.2%)	**VE: 73.1** (40.0 to 89.4)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4A.5. VE against severe/critical COVID- 19 COVID-19 infection, including centrally and non-centrally confirmed cases in Brazil *(at least 14 days after vaccination, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Serious (Wide CI, breaches threshold)	None	2/3370 (<0.1%)	11/3355 (0.3%)	**VE: 81.9** (17.0 to 98.1)	⨁⨁◯◯ **LOW**	IMPORTANT
4B.*at least 28 days after vaccination*										
4B.1. VE against Severe/Critical COVID-19 (including centrally and non-centrally confirmed cases) *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious	Not serious	None	8/19306 (<0.1%)	48/19178 (0.3%)	**VE: 83.5** (54.2 to 96.9)	⨁⨁⨁◯ **MODERATE**	CRITICAL

4B.2. VE against Severe/Critical COVID- 19 (including centrally and non-centrally confirmed cases), 18-59 yo *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious (Needs longer follow up period)	Not serious	None	5/12617 (<0.1%)	33/12527 (0.3%)	**VE: 85.0** (61.2 to 95.4)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4B.3. VE against Severe/Critical COVID- 19 (including centrally and non-centrally confirmed cases), ≥60 yo *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious (Needs longer follow up period)	Not serious	None	3/6689 (<0.1%)	15/6651 (0.2%)	**VE: 80.2** (30.0 to 96.3)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4B.4. VE against severe/critical COVID- 19, including centrally and non-centrally confirmed cases in South Africa *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Not serious	None	4/2449 (0.2%)	22/2463 (0.9%)	**VE: 81.7** (46.2 to 95.4)	⨁⨁⨁◯ **MODERATE**	IMPORTANT
4B.5. VE against severe/critical COVID- 19 COVID-19 infection, including centrally and non-centrally confirmed cases in Brazil *(at least 28 days after vaccination, per protocol set)*	Not serious	NA	Serious (needs longer follow up period)	Serious (Wide CI, breaches threshold)	None	1/3354 (<0.1%)	8/3312 (0.2%)	**VE: 87.6** (7.8 to 99.7)	⨁⨁◯◯ **LOW**	IMPORTANT
5. DEATH DUE TO COVID-19										
5A. VE against death due to COVID-19 *(as early as 15 days after vaccination)*	Not serious	NA	Serious (needs longer follow up period)	Serious (wide CI)	None	0/19514 (0.0%)	7/19544 (<0.1%)	**VE: 100** (not estimable)	⨁⨁◯◯ **LOW**	IMPORTANT
6. ASYMPTOMATIC SARS-COV2 INFECTION										
6A. +PCR and/or serology without previous symptoms, Day 1-29 VE against asymptomatic SARS-CoV-2 infection *(+ PCR and/or serology without previous symptoms, Day 1-29, full analysis set)*	Very Serious (infrequent available data from a small subset with infrequent evaluations of	NA	Not serious	Serious (Wide CI; crosses null value)	None	87/19739 (0.4%)	109/19809 (0.6%)	**VE: 20.0** (-7.0 to 40.4)	⨁◯◯◯ **VERY LOW**	IMPORTANT

	serological and virological measurements)									
6B. +PCR and/or serology without previous symptoms, after Day 29 **VE against asymptomatic SARS-CoV-2 infection** *(+ PCR and/or serology without previous symptoms, After Day 29, per protocol set)*	Very Serious (infrequent available data from a small subset with infrequent evaluations of serological and virological measurements)	NA	Not serious	Not serious	None	10/19301 (<0.1%)	38/19162 (0.2%)	**VE: 74.0** (46.8 to 88.4)	⨁⨁◯◯ **LOW**	IMPORTANT

Table 1.12. Summary of findings for safety outcomes

OUTCOME	Quality Assessment *Note: The study design and number of studies column were collapsed since the input for these columns are the same across all outcomes*					Summary of Findings			Certainty	Importance
	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ad26.COV2.S n/N (%risk)	Placebo n/N (% risk)	Relative Risk *(Computed)*		
1. Serious adverse events	Not serious	NA	Serious (needs longer follow up period)	Serious (wide CI, crosses null value)	None	83/21895 (0.4%)	96/21888 (0.4%)	**0.86** (0.64 to 1.16)	⨁⨁◯◯ **LOW**	CRITICAL
2. Death (All-cause mortality)	Not serious	NA	Serious (needs longer follow up period)	Not serious	None	5/21895 (<0.1%)	20/21888 (<0.1%)	**0.25** (0.09 to 0.67)	⨁⨁⨁◯ **MODERATE**	CRITICAL
3. Systemic adverse reactions	Not serious	NA	Not serious	Not serious	None	1850/3356 (55.1%)	1185/3380 (35.1%)	**1.57** (1.49 to 1.66)	⨁⨁⨁⨁ **HIGH**	CRITICAL
4. Local adverse reactions	Not serious	NA	Not serious	Not serious	None	1685/3356 (50.2%)	657/3380 (19.4%)	**2.58** (2.39 to 2.79)	⨁⨁⨁⨁ **HIGH**	IMPORTANT
5. Any unsolicited adverse event up to 28 days after vaccination	Not serious	NA	Not serious	Serious (Wide CI, crosses null value)	None	440/3356 (13.1%)	407/3380 (12.0%)	**1.09** (0.96 to 1.24)	⨁⨁⨁◯ **MODERATE**	IMPORTANT

Notes:
NA- not applicable, cannot be assessed at the moment

REAL WORLD DATA

As of this writing, among the countries that have initiated the rollout of *Janssen Ad26.COV2.S (COVID-19) Vaccine,* the following reports were noted from selected countries/agencies:

- As of 23 April 2021, 7.98 million doses of *Janssen Ad26.COV2.S (COVID-19) Vaccine* have been administered. The US Vaccine Adverse Event Reporting System has collected 15 reports of a rare and serious type of blood clot called thrombosis with thrombocytopenia syndrome (TTS). All 15 cases occurred among women between the ages of 18 and 59 , and symptoms occurred 6 to 15 days after vaccination. One of the cases led to death. In addition to the 15 cases that occurred during the vaccine rollout, one case of CVST that occurred in a 25-year old male study participant was also reviewed. In light of these reports, the US CDC and the US FDA conducted a safety review and have determined that the known and potential benefits of the vaccine outweigh the potential risks and recommended to lift the pause of the vaccine rollout. The EUA, the fact sheet for vaccine providers, and the fact sheet for recipients have been amended to include information about the risk of TTS and the signs and symptoms of TTS that healthcare professionals and individuals should monitor.
- As of 17 April 2021, a total of 289,787 doses of the *Janssen Ad26.COV2.S (COVID-19) Vaccine* have been administered with no reports of the blood clot serious adverse events. South Africa Health Products Regulatory Authority (SAHPRA, 2021) recommended to pause the vaccine rollout of *Janssen Ad26.COV2.S (COVID-19) Vaccine* in light of the cases of the blood clot adverse events but was recommended to continue on 17 April 2021 after thorough assessment. The South African government is currently in partnership with Johnson and Johnson in a real world implementation study to monitor vaccine effectiveness in preventing severe COVID-19, hospitalizations and deaths among healthcare workers in South Africa.
- On 20 April 2021, the European Medicines Agency conducted a separate review on the data on embolic and thrombotic events collected from vaccination campaigns outside the EU and concluded that the overall benefits of the vaccine outweigh the risk of side effects. A possible explanation given by the EMA for the occurrence of blood clots in combination with thrombocytopenia is that the vaccine may trigger an immune response similar to heparin-induced thrombocytopenia. However, risk

factors for the rare adverse event have not yet been identified as the pathophysiology is still unknown. The regulatory authority recommended that a warning regarding the blood clots with thrombocytopenia adverse events should be added so that recipients of the vaccine are aware of the symptoms of the rare adverse event and can get prompt medical treatment.

- Based on the monthly safety report (sponsor submission), more than 20 million doses of the vaccine have been distributed as of 31 March 2021. A total of 2,887 adverse events were reported from the period 25 February 2021 to 31 March 2021 from the United States (including US regions), Belgium, and Netherlands.

Appendix 2. Evidence for Criteria 3 - Affordability and viability

Cost of Implementing *Janssen Ad26.COV2.S (COVID-19) Vaccine*

The following cost items were identified in calculating for the total resource requirement in implementing *Janssen Ad26.COV2.S (COVID-19) Vaccine* to the Philippine government: the *Janssen Ad26.COV2.S (COVID-19) Vaccine* and vaccine consumables; logistics (hauling and storage); and operations (recruitment and training of vaccinators). The source of these costs was derived from the DOH - Disease Prevention and Control Bureau's (DPCB) overall vaccine budget plan. Overall, the projected cost of vaccine and consumables, logistics and operations based on the data ranges from Php 1,195,856,420.00 to Php 3,908,301,680.00. The paragraphs below will detail the costing calculation for cost components.

Vaccine and Consumables

The total cost of vaccines and consumables for 6 million Filipinos will amount to Php 3,199,355,142.86. This amount takes into account 5% estimated wastage of vaccines and cost of one dose of *Janssen Ad26.COV2.S (COVID-19) Vaccine*. Vaccine consumables include personal protective equipment (PPE) of the vaccination team and injection devices.

Logistics

Included under logistics are hauling and storage costs. Hauling cost includes the procurement of transport boxes that can contain 1,000 vials each box. Given a weight of 31.4 kg per box, the total cost for hauling *Janssen Ad26.COV2.S (COVID-19) Vaccine* is estimated at Php 79,919,280. This cost range also includes a 1% valuation cost. For storage, the transport boxes are assumed to be stored in warehouses with storage capacity of 100 boxes per warehouse which will be used as temporary location before distribution to vaccination sites. The storage of the vaccines is assumed to last for a month at most, and is estimated to cost Php 2,800 per warehouse occupied, resulting in a storage cost at Php 176,400 per month. The overall cost for logistics is estimated to be Php 80,095,680.

Operations

Operations cost includes mobilization, hiring costs, as well as training for vaccine implementation. Since it is projected that at most 6,000,000 Filipino will receive

Janssen Ad26.COV2.S (COVID-19) Vaccine, it is assumed that 42,857 vaccinators will be needed for the rollout. Further, the number of supervisors needed is estimated at 14,286, with the assumption that one supervisor is needed per three vaccinators. The duration of the activity provided by DPCB was seven (7) days. With a salary of Php 500 per day for 7 days, the cost of mobilization of these individuals is estimated to be Php 200,000,000. For the training of the vaccinators and supervisors, two days are allotted to train them with a cost of Php 1,200 per head per day. We note that in the training costing, DPCB included an input quantity of 121,545 on top of the total number of trainees (i.e., 57,143) multiplied by the cost (in peso) of training per day. This input value is currently being validated with DPCB. In total, the operations cost is computed at Php 628,850,857.14. Excluded in the operations cost are the cost of conducting routine RT-PCR tests among vaccination teams, as well as their transportation or any other costs necessary for mobilization and service delivery.

Table 2.1 presents the resource requirement costs and assumptions in the roll-out of the *Janssen Ad26.COV2.S (COVID-19) Vaccine* for 6 million Filipinos in 2021.

Table 2.1 Resource requirement costs in the roll-out of *Janssen Ad26.COV2.S (COVID-19) Vaccine* in the Philippines in 2021 (for 6M Filipinos)

Description	Cost	Assumptions/Notes	Source
Vaccine and Vaccine Consumables	**Php 3,199,355,142.86**	For a single dose, with 5% wastage; consumables include syringes, personal protective equipment, hand rub, cotton *(estimated costs for vaccinating 6,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB
Logistics	**Php 80,095,680.00**	For 2°C to 8°C vaccine storage temperature only. This includes hauling and storage costs. *(estimated costs for vaccinating 6,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB

Operations	**Php 628,850,857.14**	This does not include yet cost of their testing, transportation of vaccinators, or any other costs necessary for mobilization and service delivery. Note that the duration of activity provided by DPCB was 7 days. *(estimated costs for vaccinating 6,000,000 Filipinos based on identified target vaccinees for this brand)*	DPCB
TOTAL COST	**Php 3,908,301,680.00**		
TOTAL VACCINATION COST PER INDIVIDUAL	**Php 651.38**		

Acronym: **DPCB:** Disease Prevention and Control Bureau

Based on the projected calculations, the total cost of rolling out vaccination with *Janssen Ad26.COV2.S (COVID-19) Vaccine* for 6,000,000 Filipinos would amount to Php 3,908,301,680.00 (which translates to Php 651.38 per individual). This would entail utilization of 4.74% of the total allocated budget for vaccination while the roll out using *Janssen Ad26.COV2.S (COVID-19) Vaccine* will cover 8.57% of the target vaccinees for 2021.

Deployment and Feasibility

The COVID-19 Vaccine Deployment Plan outlines the prioritization of eligible populations in receiving the COVID-19 vaccine which includes *Janssen Ad26.COV2.S (COVID-19) Vaccine*. For Stage 1 of the Vaccine Deployment Plan of COVID-19 vaccines, 22.8% (24,668,128) of the Philippine population is targeted to receive the vaccine under Priority Eligible Population A. This group includes frontline health workers (1.6% or 1,762,994), indigent senior citizens (3.5% or 3,789,874), senior citizens (5.3% or 5,678,544), indigent populations (12.0% or 12,911,193), and uniformed personnel (0.5% or 525,523). On the other hand, Stage 2 of the Vaccine Deployment Plan will increase coverage to 32.95% of the population that will include teachers and social workers (0.95% or 1,179,097), other government workers (1.66% or 1,728,641), other essential workers (1.63% or 1,690,206), other socio-demographic groups with a significantly higher risk (1.72% or 1,785,000), overseas Filipino workers or OFWs (1.66% or 1,728,641), and other remaining members of the workforce (1.25%

or 1,298,729) will be inoculated with the vaccine. Finally, in Stage 3 of the Vaccine Deployment Plan, the remaining Filipinos (67.05% or 73,888,198) will be vaccinated. In terms of the priority areas for the deployment of the COVID-19 vaccine, regions determined to have a higher prevalence would be prioritized for the vaccine rollout (i.e., NCR and Region III – Central Luzon).

In the rollout of the vaccine deployment plan, the logistics involved must be taken into consideration. The required storage temperature for the *Janssen Ad26.COV2.S (COVID-19) Vaccine* is at 2 to 8 degrees Celsius protected from light. This temperature requirement can be addressed by use of refrigerators. It is expected that the *Janssen Ad26.COV2.S (COVID-19) Vaccine* can be widely distributed to facilities with the said equipment; examples of which include tertiary hospitals, Rural Health Units, Municipal Health Offices, and City Health Offices. *Janssen Ad26.COV2.S (COVID-19) Vaccine* can be accessible at the rural level.

Even though there is anticipated easier and wider distribution brought about by the storage temperature requirements, there is still a need for training on vaccine storage and handling to ensure product integrity across the entire supply chain, and a need to ensure the availability of trained personnel in handling unreported or rare adverse reactions that could occur following vaccination.

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Appendix 4. Acknowledgement

The Health Technology Assessment Unit recognizes the contribution of the following institutions in the completion of this assessment:

- DOH- Disease Prevention and Control Bureau (DPCB)
- DOH- Epidemiology Bureau (EB)
- DOH-Health Promotion Bureau (HPB)
- DOH- Supply Chain Management Office (SCMO)
- Department of Foreign Affairs (DFA)
- Department of Finance (DOF)
- Philippine COVID-19 Living CPG Group - Institute of Clinical Epidemiology, National Institutes of Health, University of the Philippines Manila
- Philippine Insurance Corporation (PhilHealth)