JANSSEN BIOTECH, INC.
(A PHARMACEUTICAL COMPANY OF JOHNSON & JOHNSON)

COVID-19 Vaccine Ad26.COV2.S

VAC31518 (JNJ-78436735)

SPONSOR BRIEFING DOCUMENT ADDENDUM

VACCINES AND RELATED BIOLOGICAL PRODUCTS ADVISORY COMMITTEE

MEETING DATE: 26 FEBRUARY 2021

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
CI	confidence interval
COVID-19	coronavirus disease-2019
EUA	Emergency Use Authorization
FAS	Full Analysis Set
FDA	Food and Drug Administration
Ig	immunoglobulin
MRU	Medical resource utilization
PCR	polymerase chain reaction
PP	Per-protocol (efficacy)
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV(-2)	severe acute respiratory syndrome coronavirus(-2)
SN	seronegative
US	United States
VE	vaccine efficacy
VRBPAC	Vaccines and Related Biological Products Advisory Committee

1 VACCINE IMPACT ON ASYMPTOMATIC SARS-COV-2 INFECTIONS AS INFERRED THROUGH SEROCONVERSION

At the time of submission of the EUA application (4 February 2021), the Sponsor included the analysis on asymptomatic SARS-CoV-2 infections based on 965 Day 71 serology results. In this addendum, the Sponsor highlights the impact of an updated analysis on asymptomatic SARS-CoV-2 infections based on 2,892 Day 71 serology results. This updated analysis has been submitted as an EUA supplement on 12 February 2021. Both the initial and updated analysis are based on the database cutoff for the primary analysis (22 January 2021). Note that this is still an interim analysis of the Day 71 serology results.

Below is a copy of the impacted paragraphs of Section 7.1.6.6 of the Sponsor Briefing Document, with updates marked in bold and underlined.

> In a preliminary analysis of asymptomatic or undetected **SARS-CoV-2** infection based on an assessment of (SARS-CoV-2 N IgG) seroconversion in **2,650** individuals with Day 71 results available, **50** asymptomatic or undetected cases occurred in the placebo group versus **18** cases in the Ad26.COV2.S group resulting in VE of **65.5%** (95% CI: **39.91; 81.08**).
>
> When a sensitivity analysis was done removing all participants with symptoms at any time since screening prior to the SARS-CoV-2 N IgG positive result (i.e., removing the undetected cases with symptoms), **10** and **37** seroconversions occurred in the Ad26.COV2.S and placebo group, respectively (VE [95% CI]: **74.2%** [**47.13; 88.57**]). Based on 50 cases and 1,304 participants in the serology at risk set in the placebo group, the seroconversion attack rate equals 3.8%.

Since these analyses are based on a larger number of N serology results, they supersede the results and conclusions on VE against asymptomatic or undetected SARS-CoV-2 infections that were presented in the Sponsor Briefing Document.

2 EFFICACY IN REGIONS WITH NEWLY EMERGING SARS-COV-2 STRAINS

At the time of submission of the EUA application (4 February 2021), the Sponsor included available data on whole genome sequencing of SARS-CoV-2 in molecularly confirmed COVID-19 cases from study COV3001. At that time, S gene sequences were available for 337 of 714 (47.2%) molecularly confirmed cases. In this addendum, the Sponsor includes an update based on sequencing results of 512 out of 714 (71.7%) cases. This updated information has been submitted as an EUA supplement on 12 February 2021. Both the initial and updated sequencing data were based on confirmed cases accrued up to database cutoff for the primary analysis (22 January 2021).

This Addendum presents an update to Table 2 (on p17) and Section 7.1.7.4 of the Sponsor Briefing Document. Updates to the sequence analysis results are marked in bold and underlined.

> In South Africa, efficacy was observed against severe/critical COVID-19 and robust VE was observed for moderate to severe/critical COVID-19. This is especially important since preliminary sequence data confirm that approximately **94.5%** (**86/91** sequenced samples) of the COVID-19 cases that occurred in the study in South Africa were due to the SARS-CoV-2 variant 20H/501Y.V2 (belonging to the B.1.351 lineage), implying that Ad26.COV2.S is efficacious against this newly emerging and rapidly spreading strain. Vaccine efficacy (95% CI) against severe/critical COVID-19 was 73.1% (40.03; 89.36) at least 14 days after vaccination and increased to 81.7% (46.18; 95.42) at least 28 days after vaccination. An effect was also seen on mortality, since all COVID-19-associated deaths in the study, all in the placebo group, occurred in participants from South Africa. Vaccine efficacy (95% CI) against moderate to severe/critical COVID-19 was 52.0% (30.26; 67.44) at least 14 days and 64.0% (41.19; 78.66) at least 28 days after vaccination.
>
> In Brazil, VE estimates were higher than those in South Africa and similar to those in the US. Preliminary sequence data confirm that approximately **69.4%** (**86/124** sequenced samples) of the COVID-19 cases in the study that occurred in Brazil appeared to be due to a variant from the P.2 lineage. This implies that efficacy in Brazil is not impacted by the high prevalence of the variant of the P.2 lineage as it is quite similar to the VE observed in the US, where D614G is highly prevalent (see Table 1).

Table 1: SARS-CoV-2 Variant Prevalence in Molecularly Confirmed COVID-19 Cases in COV3001 in the US, South Africa, Brazil

Country	Molecularly Confirmed Cases	Molecularly Confirmed Cases with Sequence data (%)	Variant SARS-CoV-2 Distribution Over Sequenced Cases
US	268	**197** (**73.5**%)	**190** with D614G (**96.4**%) **5** with CAL.20C (**2.5**%) **2** with variant of P.2 lineage (**1.0**%)
South Africa	136	**91** (**66.9**%)	**86** with 20H/501Y.V2 (**94.5**%) **3** with D614G (**3.3**%) **2** with variant of P.2 lineage (**2.2**%)
Brazil	179	**124** (**69.3**%)	**86** with variant of P.2 lineage (**69.4**%) **38** with D614G (**30.6**%)

Updates to Table 2 from the Sponsor Briefing Document are shown in bold and underlined.

3 PREVENTION OF COVID-19 RELATED HOSPITALIZATION

At the request of FDA, an additional vaccine efficacy analysis has been performed to assess the impact of the vaccine on all COVID-19 related hospitalizations, combining information from all sources (e.g., MRU forms and SAE forms). The requested analysis is based on cases accrued up to the database cutoff of the primary analysis (22 January 2021) and has been submitted to the FDA on 12 February 2021.

To evaluate the onset for this analysis, the earliest of either the onset of the AE linked to COVID-19 or the onset of the COVID-19 episode as determined in the SAP algorithm was used.

In total, 52 COVID-19 related hospitalizations (PCR+ from any source) were identified using the algorithm above. Four cases had a PCR+ result on Day 1. For the remaining 48 cases with an onset at least 1 day after vaccination the following results were observed (Table 2):

- In the per-protocol analysis set, as of 28 days after vaccination, 0 versus 16 COVID-19 related hospitalizations (VE: 100% with 95% CI [74.26; 100.00)]) were observed in the Ad26.COV2.S group compared to placebo (PCR+ from any source).
- In the per-protocol analysis set, as of 14 days after vaccination, 2 versus 29 COVID-19 related hospitalizations (VE: 93.1% with 95% CI [72.74; 99.20]) were observed in the Ad26.COV2.S group compared to placebo (PCR+ from any source).
- In baseline-seronegative participants of the full analysis set, 6 versus 42 COVID-19 related hospitalizations (VE: 85.7% with 95% CI [66.13; 95.02]) were observed in the Ad26.COV2.S group compared to placebo (PCR+ from any source).

The differences in case numbers between the analyses with and without confirmation by the central laboratory can be explained by operational reasons: operational time from local sampling to PCR confirmation in the central laboratory was estimated to be an average of 14 days, with a longer confirmation time in some countries in the Latin America region and South Africa. Therefore, central confirmation may be pending for COVID-19 related hospitalizations that occurred close to the database cutoff (22 January 2021).

These data support a substantial effect of Ad26.COV2.S in the prevention of COVID-19 related hospitalizations.

Table 2: COVID-19 Related Hospitalizations

	Ad26.COV2.S Cases, n	Placebo Cases, n	VE (95% CI)
At least 1 day after vaccination[a], FAS-SN			
PCR+ by central laboratory[b]	6	18	66.6% (12.06; 89.13)
PCR+ from any source[c]	6	42	85.7% (66.13; 95.02)
At least 14 days after vaccination[a], PP			
PCR+ by central laboratory[b]	2	11	81.8% (16.69; 98.04)
PCR+ from any source[c]	2	29	93.1% (72.74; 99.20)
At least 28 days after vaccination[a], PP			
PCR+ by central laboratory[b]	0	6	100.0% (15.67; 100.00)
PCR+ from any source[c]	0	16	100.0% (74.26; 100.00)

[a] Onset for this analysis, the earliest of either the onset of the AE linked to COVID-19 or the onset of the COVID-19 episode as determined in the SAP algorithm.
[b] Analysis based on a data set of centrally confirmed COVID-19 cases.
[c] Analysis based on a data set including all COVID-19 cases with a positive PCR from any source, regardless of central confirmation.