



MEMORANDUM

TO: Janssen COVID-19 Vaccine EUA 27205

FROM: Peter Marks, MD, PhD, Director, Center for Biologics Evaluation and Research (CBER)

CC: CBER Office of Vaccine Research (OVR) and CBER Office of Compliance and Biologics Quality (OCBQ)

DATE: June 11, 2021

RE: Assessment of certain Janssen COVID-19 Vaccine Batches

The purpose of this memorandum is to document the Food and Drug Administration's (FDA, the Agency, or we) determination regarding the disposition of certain Janssen's AD26.COV2.S drug substance (DS) batches and/or vaccine manufactured from these batches.

I. Background

Emergent BioSolutions Inc. (Emergent) is a proposed manufacturing facility¹ for the Janssen COVID-19 Vaccine emergency use authorization (EUA).² FDA has not authorized this facility to manufacture or distribute any of Janssen's COVID-19 Vaccine or components; and to date, no COVID-19 vaccine manufactured at this plant has been distributed for use in the United States. Since it is relevant for the following discussion, it should be noted that the EMOB facility was also a site for the manufacturing of the AstraZeneca (AZ) COVID-19 vaccine from August 2020 through April 2021.

A. Summary of relevant events at the EMOB facility

In August 2020, manufacturing of the AZ COVID-19 vaccine DS began in Area 3 of the EMOB facility. Subsequently, FDA conducted its first pre-EUA site visit for EUA 27205 from September 21 to 23, 2020. Conditions in the facility potentially affecting the manufacture of any

¹ Emergent's headquarters are located in Gaithersburg, Maryland. The EMOB Bayview facility, which is the facility discussed in this memorandum, is located in Baltimore, MD.

² On February 27, 2021, FDA issued a third EUA (EUA 27205) for a vaccine for the prevention of COVID-19 caused by SARS-CoV-2. The EUA allows the Janssen COVID-19 Vaccine to be distributed in the United States for use in individuals 18 years of age and older.



vaccine included: crowded manufacturing areas with equipment and supplies; inadequate quality assurance support; and several issues related to laboratory controls. Additionally, improvements were needed in the material and equipment flows.

In November 2020, manufacturing of the Janssen COVID-19 vaccine commenced in Area 2 of the EMOB facility. Initially, the weigh and dispense operations occurred in the Area 2 production suites and did not utilize the common weigh and dispense area. Subsequently, in December, production for Area 2 (Janssen) and Area 3 (AZ) began using the common weigh and dispense area. Full production, which was implemented in December, resulted in increased waste production in the latter part of December 2020.

To handle the increased waste production, Emergent implemented certain measures from January 2021 to February 8, 2021. This included adding daily removal of waste from Area 3 by operators who were also working in controlled spaces. Additionally, special medical waste was disposed of in provided totes along a specific pathway, including through the common weigh and dispense area. Beginning February 8, 2021, additional mitigating measures were implemented, which included adjustments to waste flow, changes in personnel movement, and the segregation of personnel functions.

FDA returned to EMOB for a second pre-EUA site visit from February 9 to 11, 2021. At that time, concerns regarding many personnel changes and new hires in Quality and Manufacturing were noted, as well as the need for better documentation and procedures, and consistency with established practices.

On March 26, 2021, Janssen notified FDA that they had detected AZ COVID-19 Vaccine virus in the Janssen COVID-19 Vaccine DS batch 21003600 (GMP8). This batch was produced during a period when Emergent implemented measures to handle increased waste production.

FDA subsequently engaged actively with Emergent and Janssen to facilitate the investigation of the root cause of this contamination event. It was concluded that most probable contributing root cause was that the bioreactor media prepared for use in the cell expansion process at that time was contaminated in the common weigh and dispense area through contact with the waste path for materials from Area 3 (AZ manufacturing area).³

The contamination event reported on March 26, 2021 ultimately triggered a for-cause inspection by the Office of Regulatory Affairs (ORA) from April 12 to 20, 2021 that resulted in the

³ See FDA's review entitled "CBER's assessment of the quality of JNJ Ad26.COV2.S Drug Substance batches GMP 5 through 9 manufactured in Area 2 at the EMOB facility," dated June 10, 2021 (FDA Review of GMP 5-9).



issuance of a notice of Inspectional Observations (Form 483). Several objectionable conditions were noted at that time, including, for example, the failure to conduct thorough investigations into unexplained discrepancies.⁴ These observations indicated that the facility had not been operating in a manner that was in compliance with current good manufacturing practice (cGMP) during the production of the Janssen COVID-19 vaccine. Emergent provided its initial response to the Form 483 on April 30, 2021. An Establishment Inspection Report (EIR) was subsequently drafted and dated May 14, 2021, but not issued.⁵ The unissued EIR documented the findings of the inspection and supports the issues noted in Form 483.

II. Discussion

On March 5, 2021, out of specification (OOS) test results were reported for GMP8. Following additional testing, Janssen confirmed the OOS test results and subsequently notified Emergent of product cross contamination of DS GMP8 with AZ's adenovirus vectored vaccine that was being manufactured in other parts of the EMOB facility. As noted above, it was concluded that the most probable contributing root cause was that the bioreactor media prepared for use in the cell expansion process at that time was contaminated in the common weigh and dispense area through contact with the waste path for materials from Area 3 (AZ manufacturing area).⁶

A. Disposition of certain of Janssen's AD26.COV2.S DS batches

Below is the Agency's assessment of the quality of certain batches manufactured in Area 2 of the EMOB facility, and the suitability of those batches for distribution in light of their production at this facility, which was not operating in compliance with cGMP.

- a. Ad26.COV2.S DS Area 2 batches 21003124 (GMP5), 21003530 (GMP6), 21003533 (GMP7), and 21003603 (GMP9)

Information provided to FDA and collected during the April inspection indicated that the manufacturing operations and waste flow procedures in place for the manufacture of Janssen DS batches GMP 5, 6, 7 and 9 were the same as for DS batch GMP8, i.e., there was a significant increase in production coupled with a lack of segregation of media preparation activities, waste flow, and personnel handling waste (see Figure 1 below). The quality of these batches is judged based on the manufacturing practices in place at the time of the media preparation. Therefore, in addition to GMP8, the quality of batches GMP 5, 6, 7 and 9 is questionable as these batches were

⁴ See generally FDA's Form 483 for Emergent Manufacturing Operations Baltimore, LLC, issued on April 20, 2021.

⁵ See generally the unissued ORA EMOB Establishment Inspection Report (EIR) dated May 14, 2021, which is incorporated by reference here.

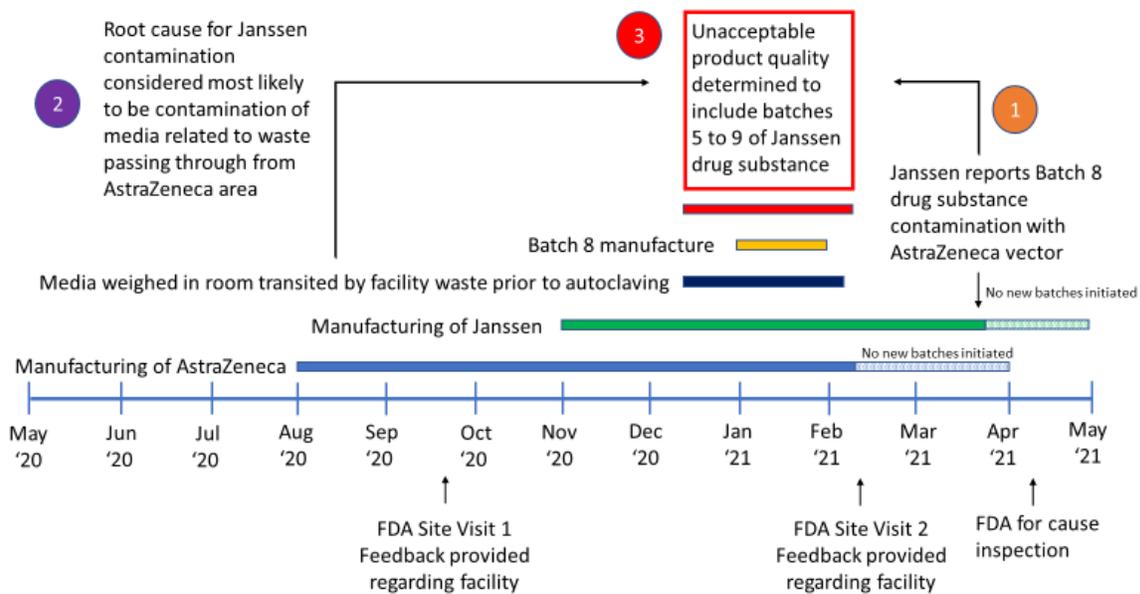
⁶ For more information regarding Batch 8, see FDA Review of GMP 5-9.



all made with media prepared when the same manufacturing practices were in place for GMP8. Additionally, Janssen cannot exclude the possibility of AZ vaccine virus contamination in batches GMP 5, 6, 7 and 9. There is no evidence that contamination of the vaccine, even at a low level of contamination, would have no impact on the safety and effectiveness of the vaccine.⁷

FDA has, therefore, determined that the EMOB facility was not operating in compliance with cGMP requirements during the time batches GMP 5 through 9 were manufactured and batches GMP 5, 6, 7 and 9 failed to meet the Agency’s expectations for quality. Consequently, batches GMP 5, 6, 7 and 9 are not suitable for use as the safety and effectiveness of these batches cannot be assured. Additionally, any batches made from a combination of other batches that include batches GMP 5 through 9 are not suitable for use. The Janssen COVID-19 vaccine EUA 27205 will not be amended to include these batches within the scope of the authorization. Given this determination, the Agency recommends discarding GMP 5, 6, 7 and 9.

Figure 1: Timeline Related to Batches GMP 5 through 9



b. Ad26.COVS.S DS Area 2 batches 21003042 (GMP2) and 21003117 (GMP4)

⁷ For more information regarding batches GMP5, GMP6, GMP7, and GMP9, see FDA Review of GMP 5-9.



With respect to Janssen’s AD26.COVID.S DS batches GMP2 and GMP4 specifically, CBER has conducted a thorough review of available information concerning the manufacturing conditions of the EMOB facility during the time period in which these batches were made and the testing of the DS batches produced.⁸

Based on the conditions present in the EMOB facility at the time that the GMP 2 and 4 batches were manufactured, as documented in the unissued EIR, FDA has determined that the EMOB facility was not operating in full compliance with cGMP requirements during the relevant time period. However, the quality of the product produced, as illustrated by a review of facility records and the results of the in process and release testing, support FDA’s determination that the product is suitable for use.

The Agency reviewed, among other things, information provided to FDA and collected during FDA’s inspections of the EMOB facility. This included information regarding manufacturing operations and waste flow procedures from Area 3 in place for the manufacture of Janssen DS batch GMP8, which was found to be cross-contaminated with AZ’s adenovirus vectored vaccine. Additionally, the Agency reviewed the in process and release testing results for batches GMP2 and GMP4. Based on its review of this information, the Agency concluded that the test results for batches GMP2 and GMP4 were within the defined quality specifications for these batches. Additionally, both GMP2 and GMP4 were made in the EMOB facility during a time period when there was low waste production, and the media preparation for these batches was separated from the waste path for materials from Area 3 through distance and timing. That is, GMP2 and GMP4 were produced prior to the overloading of the facility’s capacities and the transit of waste in the area that led to the cross contamination. Given all the above, FDA has determined that GMP batches 2 and 4 are suitable for use, considering the current COVID-19 public health emergency. Given this determination, batches 2 and 4 meet the EUA standard and will be added to the Janssen COVID-19 Vaccine EUA 27205 for distribution in the United States and potential export to other countries.⁹ Additionally, a condition on any export of these batches, or of vaccine manufactured from these batches, is that Janssen and Emergent must agree that FDA may share all relevant information about the manufacture of the batches with the regulatory authorities of the countries in which the vaccine may be used. This will provide the regulatory authorities in destination countries with the relevant information necessary for those authorities

⁸ See FDA’s review entitled “CBER assessment of the quality of JNJ Ad26.COVID.S DS batches GMP 2 and 4 manufactured at the EMOB facility (Area 2),” dated June 10, 2021.

⁹ The Agency notes it is only authorizing batches GMP 2 and 4 and/or vaccine manufactured from these batches and not a combination of other batches that include batches GMP 5 through 9 or any batches not authorized under the EUA.



who may wish to make their own judgment on the suitability of these two batches for use in their countries.¹⁰

¹⁰ We recognize that regulatory authorities in other countries may wish to make their own judgment on the suitability of these two batches for use in their countries, with full access to all available information regarding the manufacturing conditions at the EMOB facility during the relevant time period. FDA has asked Janssen and Emergent for permission to share confidential commercial information and trade secret information with foreign countries that express interest in importing DS batches GMP2 and GMP4, or product made from these batches. With this permission, FDA intends to share the FDA Form 483, the unissued EIR, and CBER's analysis of DS batches GMP2 and GMP4 to regulatory authorities in countries who have expressed interest in importing these batches. These countries would then have access to all of the information that was available to FDA regarding the EMOB manufacturing issues, and full transparency regarding FDA's determination that these batches were not made in compliance with cGMP requirements. With this information, these countries can make a fully informed decision regarding whether to import DS batches GMP2 and GMP4, or product made from these batches.