Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Manufacturing and Product Quality

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Applicant: BioNTech Manufacturing GmbH in partnership with Pfizer, Inc.

Product: COVID-19 Vaccine (BNT162b2; PF-07302048) COMIRNATY

Indication: Prevention of COVID-19 in adults ≥16 years of age

Subject: Inspection Waiver for Pre-License Inspections (PLI) of manufacturing and testing facilities listed herein for Biologics License Application (BLA) STN 125742/0

Due Date: 16 January 2022

The following information provides justification to support the waiver recommendations:

Inspection history:

Location	Activity	Most Recent Inspection
Pfizer Inc. 875 Chesterfield Parkway West Chesterfield, MO 63017 (referred to as Pfizer, Chesterfield) FEI#: 1940118	Manufacturing of (b) (4) , drug substance release and stability testing, drug product release and stability testing	Surveillance ORA August 2019 NAI
Pharmacia & Upjohn Company LLC[a] 7000 Portage Road Kalamazoo, MI 49001	LNP production, bulk drug product formulation, fill and finish, primary packaging, secondary packaging, drug product release and stability testing	Surveillance ORA/OBPO May 2021 VAI

Location	Activity	Most Recent Inspection
(referred to as Pfizer, Kalamazoo) FEI#: 1810189		
Pfizer Ireland Pharmaceuticals Grange Castle Business Park Clondalkin, Dublin 22 Ireland (referred to as Pfizer, Grange Castle) FEI#: 3004145594	Drug product release and stability testing	Surveillance ORA/OBPO November 2019 VAI
Hospira Zagreb Ltd[b] Prudnička cesta 60 10291 Prigorje Brdovečko Croatia FEI#: 3010630287	Drug product release testing (sterility)	PAI CDER November 2019 VAI
SGS Lab Simon SA Vieux Chemin du Poète 10 Wavre, 1301 Belgium FEI#: 3004186644	Drug product release testing (sterility)	Surveillance ORA September 2017 VAI

[a] Pharmacia & Upjohn Company LLC is a wholly owned subsidiary of Pfizer Inc.

[b] Hospira is a wholly owned subsidiary of Pfizer Inc.

NAI = No Action Indicated
VAI = Voluntary Action Indicated
CDER = Center for Drug Evaluation and Research
ORA = Office of Regulatory Affairs
OBPO = Office of Biological Products Operations

For the subject BLA, the following manufacturing facilities are proposed for an inspection waiver.

Pfizer, Chesterfield:

The Pfizer, Chesterfield facility will be used to manufacture the (b) (4) and for drug substance and drug product release and stability testing. In August 2019, ORA performed the most recent inspection, which covered the quality system, facilities, and equipment operations and was classified as NAI.

Since the last inspection, changes were made to the facility, which included updates and commitments to update the (b) (4) manufacturing area as part of the investigational new drug application and Emergency Use Authorization (EUA) request for the same BNT162b2 product as the subject BLA. For instance, the (b) (4) manufacturing area classification was updated to a “controlled, not classified” area and improvements were made to provide better facility, equipment, and quality control.

For the (b) (4) manufactured at the facility, there are production and process controls that mitigate risk to the product, such as the performance of all open manufacturing operations in a (b) (4) at the establishment and the (b) (4). Regarding the release and stability testing of BNT162b2 drug substance and drug product performed in the Pfizer (b) (4) (b) (4) at Pfizer, Chesterfield, the establishment has been registered as an analytical testing facility and laboratory system controls include environmentally monitored stability chambers and qualified, maintained, and calibrated instruments and equipment.

Pfizer, Kalamazoo:

The Pfizer, Kalamazoo site will be used for lipid nanoparticle production (LNP), bulk drug product formulation, drug product filling and finish, primary and secondary packaging, and drug product release and stability testing. The site is currently used to manufacture the same BNT162b2 product under an EUA dated December 11, 2020.

The BNT162b2 manufacturing operations occur in the same facility and under the same quality systems as other FDA-regulated products, including non-biological finished drug products (sterile injectables, liquids & semi-solids), active pharmaceutical ingredients, medical devices, and three licensed biological products. Specifically:

- The BNT162b2 bulk drug product formulation occurs in the (b) (4) manufacturing area (Building (b) (4)), which is where two FDA licensed biological products were previously manufactured.
- The BNT162b2 drug product is filled on existing Lines (b) (4), which have been previously used to fill other FDA-regulated products and are now primarily dedicated to BNT162b2.
- Automated visual inspection of the vialed BNT162b2 can be conducted on Line (b) (4) AVI machine, (b) (4) of which can accommodate other FDA-regulated product flows filled in vials or ampoules.

In May 2021, ORA/OBPO performed the most recent inspection, which was a Level I surveillance inspection with comprehensive focus on the BNT162b2 drug production operations that covered the quality system, production system, facilities & equipment system, packaging and labeling system, and cursory coverage of the laboratory system. Throughout the inspection, the inspectors reviewed and observed the following critical activities: receipt operations for the mRNA (b) (4), LNP (b) (4) operations, specific formulation operations, (b) (4) sterile filtration, aseptic filling, automated visual inspection, capping, labeling and packaging into vial boxes, loading / unloading of ultralow temperature freezers, and packaging of the packed vial boxes into styrofoam boxes for distribution. Additionally, for filling Lines (b) (4), the inspectors reviewed the routine media fills and the three specific BNT162b2 media fills, which passed specifications with no concerns noted. The inspectors noted (b) (4) and (b) (4) BNT162b2 vaccine lots were filled on Lines (b) (4), respectively, and there were no reported

recalls for any of the licensed biological products since the previous ORA/OBPO surveillance inspection conducted in October 2017. Furthermore, the inspectors followed up on six complaints related to BNT162b2 and determined there were no concerns with the associated investigations or conclusions. Regarding the release and stability testing of the drug product, coverage of the laboratory system included observation of sterility operations, review of bioburden testing, incubations of environmental monitoring plates, plate counting operations, and a walk-through of endotoxin testing with no deficiencies identified. At the conclusion of the inspection, an FDA Form 483 was issued to the firm, and the inspection was classified as VAI based on the adequacy of the firm's response to the FDA Form 483.

Pfizer, Grange Castle:
The Pfizer, Grange Castle facility will be used for drug product release and stability testing for BNT162b2. This site has an acceptable compliance history with the last four US FDA inspections classified as VAI. In November 2019, ORA/OBPO performed the most recent inspection, which covered vaccine products and laboratory controls. The observations from the most recent inspection do not indicate concerns regarding the laboratory or drug product testing.

Hospira Zagreb Ltd.:
The Hospira Zagreb Ltd. facility will be used for sterility release testing of the finished BNT162b2 drug product. This site has an acceptable compliance history with the last two US FDA inspections classified as VAI. In November 2019, CDER performed the most recent inspection, which included the laboratory controls. The observations from the most recent inspection do not indicate concerns regarding sterility testing in the microbiology laboratory of the facility.

SGS Lab Simon SA:
The SGS Lab Simon SA facility will be used for sterility release testing of the finished BNT162b2 drug product. This site has an acceptable compliance history with the last inspection conducted in 2017 by US FDA. The 2017 inspection, which covered sterility testing, was classified as VAI based on the adequacy of the firm's response to an FDA Form 483 issued to the firm.

Recommendation: Waive PLIs of aforementioned facilities.

Concurrence signatures:

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