U.S. FOOD & DRUG ADMINISTRATION

LABELING REVIEW MEMORANDUM

To: The File

Date: September 1, 2021

STN: 125742/0

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

Product: COVID-19 Vaccine, mRNA (COMIRNATY)

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Summary:
This memorandum outlines the labeling review of the original BLA (STN 125742/0) from BioNTech Manufacturing GmbH (in partnership with Pfizer, Inc.) for COVID-19 Vaccine, mRNA (COMIRNATY) for active immunization to prevent coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in individuals 16 years of age and older. This BLA was a Rolling Submission and the labeling information was included in the second (last) roll (STN 125742/0.1) submitted and received on May 18, 2021.

The product labeling submitted in this original BLA included carton and container labels and a proposed Package Insert (PI) incorporating safety and efficacy data that support the licensure of COMIRNATY for use in individuals 16 years of age and older. Additionally, a Dear Health Care Provider (HCP) Letter was submitted as part of the labeling to be included with the packaging of lots considered by CBER to be BLA-compliant.

COMIRNATY is packaged at two sites: Pfizer Manufacturing Belgium NV (Puurs) and Pharmacia and Upjohn Company LLC (Kalamazoo). Separate carton and container labels for both Kalamazoo and Puurs were included in the submission. Labels for the following COMIRNATY cartons and containers were submitted:

- COMIRNATY Multiple Dose Vial Labels (Kalamazoo)
- COMIRNATY Multiple Dose Vial Labels (Puurs)
- COMIRNATY 25 Vial Carton Labels (Kalamazoo)
- COMIRNATY 25 Vial Carton Labels (Puurs)
- COMIRNATY 195 Vial Carton Labels (Kalamazoo)
- COMIRNATY 195 Vial Carton Labels (Puurs)

Vials of sterile 0.9% Sodium Chloride Injection, USP will also be provided but shipped separately for use as a diluent for COMIRNATY. The diluent is supplied by two manufacturers: Fresenius Kabi USA, LLC and Hospira, Inc. Separate carton and container labels for both Fresenius Kabi and Hospira were included in the submission. Labels for the following diluent cartons and containers were submitted:

- Diluent Vial Label (Fresenius Kabi) – 2 mL single dose vial
- Diluent Vial Label (Hospira) – 10 mL single dose vial
- Diluent Carton Labels (Fresenius Kabi) – 25 single-dose vials
- Diluent Carton Labels (Hospira) – 25 single-dose vials
- Diluent Supplemental Carton Stamp (Fresenius Kabi)
- Diluent Supplemental Carton Sticker (Hospira)

Revisions to the proposed labels for the cartons and containers, PI and Dear HCP Letter were communicated to Pfizer/BioNTech, as indicated below in Table 1, and the corresponding amendments that were received are described in Table 2. The principal reviewers of the PI were the Clinical Reviewers, the Pharmacovigilance Reviewer, the Biostatistics Reviewers, the Advertising and Promotional Labeling Branch Reviewer, the Committee Chair, the RPMs, and supervisors, with additional advice from DVP, DVRPA and OVRR Immediate Office of the Director.

Table 1. Labeling Review History

Date	Action	Labels		
		PI	Cartons & Containers	Dear HCP Letter
07/28/2021	First set of labeling comments regarding the PI were sent.	✓		
08/04/2021	Internal labeling meeting	✓		
08/05/2021	Internal labeling meeting	✓		
08/05/2021	Second set of labeling comments regarding the PI were sent.	✓		
08/05/2021	Four questions regarding the diluent were sent.	✓		
08/09/2021	Internal labeling meeting		✓	
08/09/2021	First set of labeling comments regarding the cartons and containers were sent.		✓	
08/11/2021	Internal labeling meeting	✓		
08/13/2021	Internal labeling meeting	✓		
08/13/2021	Third set of labeling comments regarding the PI were sent.	✓		
08/16/2021	Two internal labeling meetings: one carton and container discussion and one PI discussion	✓	✓	
08/16/2021	Second set of labeling comments regarding the cartons and containers were sent.		✓	
08/16/2021	Teleconference with Pfizer to discuss identification of BLA-compliant lots and a draft Dear HCP Letter			✓
08/17/2021	Two internal labeling meetings: one carton and container discussion and one PI discussion	✓	✓	

Date	Action	Labels		
		PI	Cartons & Containers	Dear HCP Letter
08/17/2021	Two separate set of comments were sent: Third set of carton and container comments and fourth set of PI comments.	✓	✓	
08/18/2021	A request was sent to submit to the BLA the information that was emailed to Mary Malarkey on 08/16/2021 regarding identification of BLA-compliant lots and a draft Dear HCP Letter.			✓
08/18/2021	Internal labeling meeting	✓		
08/18/2021	Fifth set of PI comments sent and a request to submit specific carton and container label versions together in a new amendment for ease of refencing in the Approval Letter was sent.	✓	✓	
08/19/2021	Internal labeling meeting	✓		
08/19/2021	Sixth set of labeling comments regarding the PI were sent.	✓		
08/20/2021	Two internal labeling meetings: one PI discussion and one Dear HCP Letter discussion	✓		✓
08/20/2021	Seventh set of labeling comments regarding the PI were sent.	✓		
08/20/201	First set of comments regarding identification of BLA lots/Dear HCP Letter were sent.			✓
08/21/2021	Internal meeting to discuss the PI, carton and container labels and Dear HCP Letter	✓	✓	✓
08/21/2021	The Applicant was notified that the carton and container labels submitted in Amendment 63 on August 19, 2021 are considered the Final Draft Labels.		✓	
08/21/2021	Eighth set of labeling comments regarding the PI sent	✓		
08/21/2021	Second set of comments regarding the Dear HCP Letter were sent.			✓
08/21/2021	The Applicant was notified that there are no additional comments on their Dear HCP Letter.			✓
08/22/2021	The Applicant was notified that the PI submitted in Amendment 74, dated August 21, 2021 is considered the Final Draft Label.	✓		

Table 2. Labeling Amendments

Date	Amendment	Summary	Labels		
			PI	Cartons & Containers	Dear HCP Letter
08/02/2021	125742/0.27	Response to July 28, 2021, first set of labeling comments regarding the PI.	✓		
08/09/2021	125742/0.36	Response to four questions regarding the diluent from dated August 5, 2021.	✓		

Date	Amendment	Summary	Labels		
			PI	Cartons & Containers	Dear HCP Letter
08/09/2021	125742/0.38	Response to August 5, 2021, second set of comments on the PI.	✓		
08/13/2021	125742/0.46	Response to August 9, 2021 first set of comments on the carton and container labels.		✓	
08/16/2021	125742/0.49	Response to August 13, 2021, third set of comments on the PI.	✓		
08/17/2021	125742/0.53	Response to August 16, 2021 second set of comments on the carton and container labels. This amendment also contains the full diluent carton labels and diluent vial labels that were not included in the original BLA submission.		✓	
08/18/2021	125742/0.58	Response to August 17, 2021, fourth set of comments on the PI.	✓		
08/19/2021	125742/0.63	Responses to August 18, 2021, third set of comment on the carton and container labels.		✓	
08/18/2021	125742/0.64	Response to August 18, 2021, comments regarding identification of BLA-compliant lots/Letter to HCP.			✓
08/19/2021	125742/0.66	Response to August 18, 2021, fifth set of comments on the PI.	✓		
08/20/2021	125742/0.68	Response to August 19, 2021, sixth set of comments on the PI.	✓		
08/20/2021	125742/0.71	Response to August 20, 2021, seventh set of comments on the PI.	✓		
08/20/2021	125742/0.73	Response to August 20, 2021, first set of comments regarding identification of BLA lots/Dear HCP Letter.			✓
08/21/2021	125742/0.74	Response to August 21, 2021, eighth set of comments on the PI.	✓		
08/21/2021	125742/0.76	Response to August 21, 2021, second set of comments regarding identification of BLA lots/Dear HCP Letter.			✓
08/23/2021	125742/0.77	Final PI	✓		
08/24/2021	125742/0.78	Final PI with license number included.	✓		

Regarding Pfizer/BioNTech's amendments containing revisions to the PI:
Pfizer/BioNTech submitted to CBER eight versions of the PI (as amendments to the BLA) in response to CBER's comments in the following amendments: 125742/0.27, 125742/0.38,

125742/0.49, 125742/0.58, 125742/0.66, 125742/0.68, 125742/0.71 and 125742/0.74. The clean copy Word version of the PI submitted on August 21, 2021 (Amendment 74) was considered the Final Draft PI for approval. Pfizer/BioNTech was notified on August 23, 2021, that CBER considered the clean version of the PI included in Amendment 74 as the Final Draft PI for approval.

Two additional versions of the PI were submitted to the BLA after the date of approval. A Final Version of the PI with an updated version number was submitted in Amendment 77 on August 23, 2021. Pfizer/BioNTech then submitted a revised Final Version of the PI in Amendment 78 on August 24, 2021 which included the license number that was inadvertently left off previous versions. Pfizer/BioNTech submitted each of these final versions of the PI in amendments to the BLA without being requested to do so by CBER.

Regarding Pfizer/BioNTech's amendments containing revisions to the carton and container labels:
Pfizer/BioNTech submitted to CBER three versions of the revised carton and container labels in response to CBER's comments in the following amendments: 125742/0.46, 125742/0.53 and 125742/0.63. Pfizer/BioNTech was notified on August 21, 2021, that the carton and container labels submitted in Amendment 63 on August 19, 2021 were considered the Final Draft Labels.

Regarding Pfizer/BioNTech's amendments containing revisions to the Dear HCP Letter:
In response to CBER's inquiry about BLA-compliant EUA-labeled lots that may be available for use upon licensure of COMIRNATY, Pfizer submitted information listing which lots they considered to be manufactured according to the BLA. To address the issue of these lots not bearing the vial label associated with BLA-approval, CBER worked with Pfizer to develop a Dear HCP letter to be included with lots considered by CBER to be BLA-compliant. This letter explained that some lots labeled for EUA use were also considered BLA-compliant and refers HCP to a website for additional information. CBER requested and Pfizer agreed that only EUA-labeled lots that had also undergone CBER lot release according to the BLA would be considered BLA-compliant and listed at the website included in the Dear HCP letter.

Pfizer/BioNTech submitted to CBER two versions of the revised Dear HCP Letter in response to CBER's comments in the following amendments: 125742/0.73 and 125742/0.76. Pfizer/BioNTech was notified on August 21, 2021, that CBER has no additional comments on the Dear HCP Letter provided in Amendment 76 on
August 21, 2021.

Review of National Drug Codes (NDCs):
A review of the NDCs on the COMIRNATY and diluent carton and container labels was conducted according to the Job Aid JA 900.08.

Table 3. NDC assignments for COMIRNATY and diluent carton and container labels

Label	NDC#
COMIRNATY Vial Label (Kalamazoo and Puurs)	0069-1000-01
COMIRNATY 25 Vial Carton Label (Kalamazoo and Puurs)	0069-1000-03
COMIRNATY 195 Vial Carton Label (Kalamazoo and Puurs)	0069-1000-02

Diluent Vial Label (Fresenius Kabi) – 2 mL single dose vial	63323-186-04
Diluent Carton Label (Fresenius Kabi) – 25 single-dose vials	63323-186-02
Diluent Vial Label (Hospira) – 10 mL single dose vial	0409-4888-02
Diluent Carton Label (Hospira) – 25 single-dose vials	0409-4888-10

The first segments (NDC labeler code) were verified using the NDC/NHRIC Labeler Code site. The first segments are correct and appropriately assigned.

Table 4. Search Results for NDC Labeler Codes

NDC Labeler Code	Firm Name
0069	Pfizer Laboratories Div Pfizer Inc
63323	Fresenius Kabi USA, LLC
0409	Hospira, Inc.

The second segments (the product code that identifies a specific strength, dosage form, and formulation) are different (unique) for COMIRNATY labels (-1000-) and diluent labels (-186- [Fresenius Kabi] and -4888- [Hospira]).

The third segments (the package code that identifies package sizes and types) are different (unique) for labels of cartons containing 25 (-03) and 195 (-02) vials of COMIRNATY and for the individual vials (-01) of COMIRNATY. Additionally, the third segments are also distinct for the two diluent cartons (-02 [Fresenius Kabi] and -10 [Hospira]) and the two diluent vials (-04 [Fresenius Kabi] and -02 [Hospira]).

2D Bar Code Review Under the Drug Supply Chain Security Act (DSCSA):
During the COVID-19 public health emergency, FDA interprets the exemption and exclusion from certain requirements of the DSCSA to cover the distribution of prescription drug products either (a) issued an emergency use authorization under section 564 of the FD&C Act (21 U.S.C. 360bbb-3) to combat COVID-1917 or (b) approved by FDA to diagnose, cure, mitigate, treat, or prevent COVID-19. Therefore, COMIRNATY is exempt from the product identifier requirements, including serialization.

Additional information can be found in the Guidance for Industry: *Exemption and Exclusion from Certain Requirements of the Drug Supply Chain Security Act During the COVID-19 Public Health Emergency* (April 2020).

Recommendation:
The discipline reviewers mentioned above have reviewed the relevant labeling documents and found them to be acceptable as Final Draft Labeling for approval. As the Regulatory Project Manager, I concur with their recommendation. The Final Draft PI will be provided to the Office of Communication, Outreach and Development as part of the approval package for web posting.