

2.4 NONCLINICAL OVERVIEW

Justification for the Absence of an Update to the Nonclinical Overview

April 2023

LIST OF ABBREVIATIONS

Abbreviation	Term
CMC	Chemistry Manufacturing and Controls
MAH	Marketing Application Holder
NCO	Nonclinical Overview
PPQ	Process Performance Qualification
TFF	Tangential Flow Filtration

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1. INTRODUCTION

Reference is made to Pfizer/BioNTech's line extension application intended to be filed in April 2023 to seek marketing authorization of a new pharmaceutical form (dispersion for injection) for Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose multidose and single dose vials.

Rationale is provided in Section 2 below justifying why a nonclinical overview will not be submitted with the line extension application.

2. JUSTIFICATION FOR OMISSION OF THE NONCLINICAL OVERVIEW FROM THE LINE EXTENSION APPLICATION

The MAH believes that an updated nonclinical overview for Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) multidose and single dose vials is not required with this line extension application because the formulation and associated manufacturing process remains unchanged (See Section 2.1). There is no change in the clinical administration route (intramuscular) or posology. Therefore, there are no safety concerns specific to the formulation that would warrant additional measures compared to those already in place for the current registered product (concentrate for dispersion for injection pharmaceutical form). The benefit-risk profile of the vaccine remains favorable and unchanged. According to the Guideline on nonclinical local tolerance testing of medicinal products (EMA/CHMP/SWP/2145/2000 Rev. 1) "changes in formulation composition will not necessitate further testing unless the concentration of active substance increases beyond that previously tested or a major change of formulation has been introduced (eg, novel excipients)". Therefore, there were no new nonclinical studies conducted to support the change in concentration or dosing volume and thus the NCO has not been updated.

2.1. CMC/MANUFACTURING

The following modifications have been made to Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) multidose and single dose vials that differentiate it from the current registered product:

1. The concentration of the Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) multidose and single dose vials is 0.033 mg/mL RNA while the current registered product is 0.1 mg/mL RNA;
2. The new multidose vials for Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) product will contain 6 doses of 0.3 mL while the current registered product contains 10 doses of 0.2 mL after dilution;
3. The Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) drug product will have an injection volume of 0.3 mL while the current registered product has an injection volume of 0.2 mL;

4. The Comirnaty Original/Omicron BA.4-5 (5/5 micrograms)/dose (dispersion for injection) drug product will have either a royal blue (MDV) or light blue (SDV) cap while the current registered product has an orange cap.

The overall manufacturing process and equipment remain unchanged from 0.1 mg/mL presentations, with the exceptions that lot size has been optimized for the 0.033 mg/mL presentations and the buffer exchange and concentration (via TFF and final dilution) steps adjust the concentration of the drug product to 0.033 mg/mL RNA. Process validation was successfully completed and consisted of three PPQ lots demonstrating that the manufacturing process consistently produces drug product lots of acceptable quality for both multidose and single dose vials.

There are no changes to specifications with the exception of RNA content and lipid content, which are directly related to the change in the final concentration. The amount of RNA and amount of each lipid component per dose remain constant between the 0.1 mg/mL and 0.033 mg/mL presentations. Sucrose (31 mg/dose) and Tris buffer components (Tromethamine 0.06 mg/dose and Tris aminomethane hydrochloride 0.4 mg/dose) are dosed at higher levels in the 0.033 mg/mL formulations than in the 0.1 mg/mL formulation for pediatric 10 mcg (Sucrose 10.3 mg/dose, Tromethamine 0.02 mg/dose and Tris aminomethane hydrochloride 0.13 mg/dose), as the 0.033 mg/mL formulations are not diluted prior to use. These amounts do not exceed levels applied in presentations for adults (15/15 micrograms/dose). Both primary and PPQ stability studies are ongoing; however, available stability data for the 0.033 mg/mL at both long term and accelerated storage conditions indicate a similar stability profile to the approved 0.1 mg/mL presentation and support the proposed shelf life of 12 months for the 0.033 mg/mL presentation.

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