2.3. INTRODUCTION TO THE QUALITY OVERALL SUMMARY

This document summarizes updates and changes to the Chemistry, Manufacturing and Controls (CMC) information for the COVID-19 vaccine for use under BLA 125742. Specifically, this CMC informational amendment covers the following changes.

- Introduction of additional stability data to support extending the shelf-life of the undiluted drug product vial from 6 months to 9 months when stored at -90 to -60 °C.
- Corrections made a typographical error in DSPC result for lot EJ0553 made in a stability data tables that occurred in a previous submission.
- Addition of inverted vial orientation data for various lots at the 5 °C and -20 °C long term and accelerated conditions.
- Addition of Figures illustrating stability data for LNP polydispersity, LNP size, RNA content, RNA encapsulation, lipid content, RNA integrity, and in vitro expression.

2.3.1. Description of the Amendment

2.3.1.1. Drug Product Shelf Life

To enhance global distribution of and broaden patient access to the Pfizer/BioNTech COVID-19 vaccine, the shelf-life of the undiluted drug product vial is extended from 6 months to 9 months when stored at -90 to -60 °C. The change in shelf-life is supported by drug product stability data.

2.3.1.1.1. Drug Product Stability and Shelf Life

Drug product stability data are updated in Section 3.2.P.8.1 Stability Summary and Conclusions, Section 3.2.P.8.3 Long Term, and Section 3.2.P.8.3 Accelerated for clinical lots, emergency supply and PPQ lots. Current available data at the long-term storage condition of -90 to -60 °C include up to 12 months of data from clinical trial material lots (stored at -70±10 °C), up to 9 months of data from emergency supply lots (stored at -90 to -60 °C) and up to 6 months of data from PPQ lots (stored at -90 to -60 °C).

Additionally, figures have been added in Section 3.2.P.8.3 Long Term, and Section 3.2.P.8.3 Accelerated illustrating stability data for LNP polydispersity, LNP size, RNA content, RNA encapsulation, lipid content, RNA integrity, and in vitro expression.

All data generated to date at -90 to -60 °C are within the specifications in place at the time of testing for drug product lots and overall, the data generated to date indicate that there have been no significant changes in terms of quality, purity, or strength for the drug product. The data provided supports a drug product expiry of 9 months when stored at the intended storage condition of -90 to -60 °C.

2.3.1.2. Drug Product Stability Protocol and Data Corrections

Corrections have been made for drug product lot EJ0553, in which a typographical error was corrected in DSPC result at 1 month at -90 to -60 °C from (b) (4). These changes have been updated in Section 3.2.P.8.3 Long Term. There is no impact to the data assessment based on these corrections.

Additionally, data tables for upright and inverted vial orientation results are now included for lots EK4242, EL1491, EL3248 and EL3249 at the 5 °C and -20 °C condition in Section 3.2.P.8.3 Long Term as well as in Section 3.2.P.8.3 Accelerated.

For drug product lot EL8723, revised initial time point results from T=0 testing results to batch release results, which are more appropriate initial data for this stability study. These changes for -60 to -30 °C condition have been updated in Section 3.2.P.8.3 Accelerated.

2.3.2. Submission Overview

In addition to updates to the Module 3, the corresponding 2.3.P.8 Stability section has been updated. Also, the Product Information is updated accordingly.

A summary of the updated CMC information is provided in Table 2.3-1.

Table 2.3-1. Submission Overview – Module 3 References

Module 3 CTD Sections	Documents	Modifications
modRNA Drug Product		
P.8.1	Stability Summary and Conclusions	Updated document to provide updated stability summary information, including additional lots, additional available data, and conclusions, including support of up to 9 months at -90 to -60 °C.
P.8.3	Stability Data – Long Term	Updated document to provide additional stability data from additional lots and additional time points. Added figures illustrating stability data for LNP polydispersity, LNP size, RNA content, RNA encapsulation, lipid content, RNA integrity, and in vitro expression. Both upright and inverted vial orientation results now included for lots EK4242, EL1491, EL3248 and EL3249 at the 5 °C and -20 °C condition. Corrected DSPC results at 1M result for lot EJ0553 (typographical error).

Table 2.3-1. Submission Overview – Module 3 References

Module 3 CTD Sections	Documents	Modifications
P.8.3	Stability Data – Accelerated	Updated document to provide additional stability data from additional lots, additional stability studies in additional storage conditions (inverted vials), and additional time points. Added figures illustrating stability data for LNP polydispersity, LNP size, RNA content, RNA encapsulation, lipid content, RNA integrity, and in vitro expression. Both upright and inverted vial orientation results now included for lots EK4242, EL1491, EL3248 and EL3249 at the 5 °C and -20 °C condition. Updated T=0 results for Lot EL8723 to batch release results. Minor editorial updates.

2.3.3. Conclusion

The shelf-life of the undiluted drug product vial is extended from 6 months to 9 months.

Cartons with an expiry date of August 2021 through January 2022 printed on the label may remain in use for three months beyond the printed date as long as the approved storage conditions have been maintained. Table 2.3-2 represents expiry dates for Drug Product lots that have already been dispositioned and their new expiry dates.

Table 2.3-2. Drug Product Expiry Extension for Dispositioned Batches

Printed Date	Updated Expiry Date
August 2021	November 2021
September 2021	December 2021
October 2021	January 2022
November 2021	February 2022
December 2021	March 2022
January 2022	April 2022