2.3. INTRODUCTION

Pfizer and BioNTech have developed a vaccine intended to prevent Coronavirus Disease 2019 (COVID-19) caused by the virus SARS-CoV-2. The vaccine is based on SARS CoV-2 spike (S) glycoprotein antigen encoded in RNA and formulated in lipid nanoparticles (LNPs), referred to as COVID-19 Vaccine (BioNTech code number BNT162b2, Pfizer code number PF 07302048).

The purpose of this submission is to provide a response to:
1. Specific Obligation #3 (SO3) : In order to confirm the consistency of the finished product manufacturing process, the MAH should provide additional validation data. The following data are requested to be provided in order to ensure batch to batch consistency and to complete the information on process validation of the finished product manufacturing process.

a) Full commercial scale finished product PPQ-batches will be manufactured at the commercial facility Pfizer Puurs, Belgium. The applicant should provide the summary report on the completed commercial scale process validation activities. Due date: March 2021.

b) The applicant should perform testing of future process validation-batches of finished product according to the extended comparability testing protocol and the results should be provided for assessment. Due date: March 2021.

2. Recommendation #15 (REC15): Data on verification of in-process test methods should be provided.

The Applicant is submitting the requested information as a grouping of variations to fulfill SO3 and REC15:

- A Type II variation (C.I.11.b), Introduction of, or change(s) to, the obligations and conditions of a marketing authorization, including the risk management plan, Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment by the competent authority is required.

- A Type IB variation (B.II.b.5.z), Change to in-process tests or limits applied during the manufacture of the finished product.

2.3.1. Overview of the Submission

In 2021, Pfizer and BioNTech completed full scale finished product PPQ batches at Pfizer Puurs, Belgium, Polymun, and mibe and are now providing summary reports of the completed commercial scale process validation batches. This information is included in

3.2.P.3.5 Process validation and/or Evaluation Puurs PPQ Summary Report, 3.2.P.3.5 Process Validation and/or Evaluation-Network PPQ Summary Report and 3.2.P.3.5 Process Validation and/or Evaluation-Polymun/mibe/Puurs PPQ Summary Report. In addition, testing was performed on process validation batches of finished product according to an extended comparability testing protocol. The results of the comparability assessment are provided in 3.2.P.2.3 Comparability Summary Report.

Data on verification of the analytical procedures used for in-process control (IPTC) are provided in section 3.2.P.3.5 Process Validation and or Evaluation - Verification of In-Process Test Methods (Puurs).

Table 2.3-1 summarizes the documents that have been updated to reflect the proposed changes identified as part of this submission.

Table 2.3-1. Overview of the Submission

Module 3 CTD Sections	Documents	Rationale
3.2.P.2.3	Comparability summary report	Comparability report and the results of the assessment
3.2.P.3.5	3.2.P.3.5 Process validation and/or Evaluation Puurs PPQ Summary Report	Summary report combined from two process validation activities and results from Pfizer Puurs.
3.2.P.3.5	3.2.P.3.5 Process Validation and/or Evaluation-Network PPQ Summary Report	Summary report of process validation activities and results from Pfizer Puurs, Pfizer Kalamazoo, mibe and Polymun.
3.2.P.3.5	3.2.P.3.5 Process Validation and/or Evaluation-Polymun/mibe/Puurs PPQ Summary Report	Summary report of process validation activities and results from mibe and Polymun
3.2.P.3.5	3.2.P.3.5 Process Validation and/or Evaluation- Verification of In-Process Test Methods (Puurs)	Description of validation of analytical procedures for in-process controls at Pfizer Puurs.

2.3.2. Information to Fulfil Specific Obligation #3

There are three EU supply nodes registered for COVID-19 Vaccine drug product:

- LNP Production and Bulk Drug Product Formulation, Filling, Inspection, packaging and freezing at Pfizer Puurs
- LNP Production and Bulk Drug Product Formulation by Polymun, transport to Pfizer Puurs, sterile filtration, Filling, Inspection, packaging and freezing.

- LNP Production and Bulk Drug Product Formulation by mibe (Dermapharm, also abbreviated as DER), transport to Pfizer Puurs, sterile filtration, Filling, Inspection, packaging and freezing.

In addition there is an ex-EU supply node(s) which was included in the Network PPQ strategy for COVID-19 Vaccine:

- LNP Production and Bulk Drug Product Formulation, Filling, Inspection, packaging and freezing at Pfizer Kalamazoo.

To fulfil SO3, additional validation data to confirm the consistency of the finished product manufacturing processes across the 4 supply nodes is provided in 3.2.P.3.5 Process Validation and/or Evaluation-Network PPQ Report. One (1) lot was manufactured per each EU supply node and two (lots) at the ex-EU supply node.

Subsequently, full scale commercial scale finished product PPQ-batches were manufactured at the commercial facility Pfizer Puurs with three (3) batches at 139 L and three (3) batches at 278L batch sizes. The results are provided in 3.2.P.3.5 Process validation and/or Evaluation Puurs PPQ Summary Report. In addition, validation activities utilizing the Polymun site and mibe site for the LNP production steps and Pfizer Puurs for the aseptic fill and finish of the drug product, were completed. Three (3) PPQ lots were manufactured at Polymun/ Puurs and three (3) batches were manufactured at mibe/Puurs. The summary report is provided in 3.2.P.3.5 Process Validation and/or Evaluation-Polymun/mibe/Puurs PPQ Summary Report. Lastly, testing was performed on process validation batches of finished product according to an extended comparability testing protocol. The results of the comparability are provided in 3.2.P.2.3 Comparability Report.

2.3.3. Information to Fulfil Recommendation #15

To fulfil REC15, the description and data of the verification of the analytical procedures used for in-process control test, including pH, RNA Content and Bioburden, is provided in section 3.2.P.3.5 Process Validation and or Evaluation - Verification of In-Process Test Methods (Puurs). Endotoxin, which was previously inadvertently stated as an IPT-C, is an IPT-M and method verification is not provided. A summary of the method validation for in-process testing for RNA content was previously provided and detailed in Section 3.2.P.5.3 Fluorescence Assay.

Closing Submission

The Applicant plans to submit a grouping of variations at a later stage to update all needed leaflets with the information included in the reports supporting the fulfillment of SO#3.

2.3.4. Conclusion

Full commercial scale batches were manufactured and process validation activities/PPQ were successfully completed at Pfizer Puurs. Also, PPQ activities utilizing the Polymun site and

mibe site for the LNP production steps and Pfizer Puurs for the aseptic fill and finish of the drug product were successfully completed. The results of all validation activities at Pfizer Puurs, Polymun and mibe demonstrate that the processes at all the sites are consistent and result in drug product that meets all quality attributes. In addition, results of the testing of finished product according to the extended comparability testing protocol demonstrated batch to batch consistency of the manufacturing processes across the different sites. Based on the successful completion of the process validation activities and batch consistency across the different sites, the process is now deemed validated and the information provided fulfils SO#3.

Summary data that supports the verification of in-process test methods at Pfizer Puurs demonstrate that the methods are effective. Therefore, the analytical procedures are considered verified for intended use and the information provided fulfils REC15.