The review team has the below comments on the lot release protocol (LRP) template that was submitted to BLA 125742/0.14 on July 20, 2021.

QUERY 1

Throughout document

- Please correct the cc: line to STN 125742-0/2229/FC

Page 1 of 6

- Please replace with the attached example (Attachment 1 – Electronic Protocol Page 1)
- Please make sure that the electronic Protocol Number at the bottom of Page 1 matches the number on the eLRP Signature letter.
- Information after the Date of Manufacturing line and before the Storage Temperature is optional.
- Note: When submitting LRPs electronically, please use a letter formatted per Attachment 2 – eLRP Signature letter. Place this letter before the electronic protocol.

Page 2 of 6

Components table

- Please add component description for the LNP

Page 3 of 6

RNA Encapsulation and RNA content

- Please use the RNA content template (Attachment 3) to report the results

Lipid analysis

- Please provide full (b) (4) of the lipid components for the sample, (b) (4). Insert the (b) (4) for the reference standard above the sample lines and label all the (b) (4). The page on which the (b) (4) are provided should include a table with test date, specifications and results for each lipid content and identity.

Page 4 of 6

Table 1 (Continued) Filled Vaccine Quality Control Tests

- Please remove the abbreviations for (b) (4) (b) (4). These tests are not performed for the filled vaccine.

Identity of encoded RNA sequence

- Please use the identity test template (Attachment 4) to report the drug product test results

In vitro expression

- Please use the in vitro expression test template (Attachment 5) to report the drug product test results

RNA integrity

- Please provide (b) (4) that are (b) (4) RNA (b) (4) (b) (4) for each sample replicate and insert the reference standard (b) (4) above this line so that the sample lines are not obscured. Please include clear labels for product and (b) (4) (b) (4) that were included in the analysis of each (b) (4) Include the name of the test method, the specification, date of test and the result on the same page as the (b) (4) .

Bacterial endotoxin

- Please use the Limulus Amebocyte Lysate Test template (Attachment 6) to report the drug product endotoxin results.

Sterility

- Method: Please add (b) (4) Method to (b) (4) .
- Container: Please change 20 mL to (b) (4)

RESPONSE 1

- Pfizer/BioNTech agree to correct the cc: line to STN 125742-0/2229/FC throughout the document.

- Pfizer/BioNTech agree to the following requests of the LRP template. Attachment 1 was added to the LRP template.

    - Replacement of the provided example (Attachment 1-Electronic Protocol Page 1)

    - The electronic Protocol Number at the bottom of Page 1 will match the number on the eLRP Signature letter

    - It is noted that information after the Date of Manufacturing line and before the Storage Temperature is optional

    - It is noted when submitting LRPs electronically, to use a letter formatted per Attachment 2 – eLRP Signature letter. This letter is placed before the electronic protocol

- Pfizer/BioNTech agree to add the component description for the Lipid Nano Particle (LNP) to the Components table.

- Pfizer/BioNTech agree to use the RNA content template (Attachment 3) to report the results for RNA Encapsulation and RNA content. Some minor clarifications were made to the table to align with the testing performed. Pfizer/BioNTech requests clarification on what is required for R^2 for Standard A and R^2 for Standard B?

- Pfizer/BioNTech acknowledge the request to provide full (b) (4) for Lipid analysis. Providing (b) (4) cannot be achieved through a digital system. In addition, the resolution of the (b) (4) is such that the data would not provide additional value. Pfizer/BioNTech requests whether specific data from the (b) (4) could be provided in data format in lieu of the (b) (4)?

- Pfizer/BioNTech agree to remove the abbreviations for (b) (4) (b) (4) on the Filled Vaccine Quality Control Tests table. These tests are not performed for the filled vaccine.

- Pfizer/BioNTech agree to use the Identity test template (Attachment 4) to report the drug product test results for the Identity of encoded RNA sequence.

- Pfizer/BioNTech agree to use the In vitro expression test template (Attachment 5) to report the drug product test results for the In vitro expression assay. Pfizer/BioNTech request clarification on what is required for Average Number of Cells Counted for Sample and % cell viability.

- Pfizer/BioNTech acknowledge the request for (b) (4) for RNA Integrity. Providing (b) (4) cannot be achieved through a digital system. In addition, the resolution of the (b) (4) is such that the data would not provide additional value. As a result, Pfizer/BioNTech request whether specific data from the (b) (4) could be provided in data format in lieu of these (b) (4)?

- Pfizer/BioNTech agree to use the Limulus Amebocyte Lysate Test template (Attachment 6) to report the drug product endotoxin results. As per section 3.2.P.5.3.1 Verification of Bacterial Endotoxins (Pfizer Global Supply, Puurs, PGS-Puurs), the (b) (4) system may be used as an alternative endotoxin test for the (b) (4) assay. This method will impact the data available as per Attachment 6. Pfizer/BioNTech will provide all available/alternative data in line with Attachment 6 when this method is used.

- Pfizer/BioNTech agree to the add the (b) (4) Method to the (b) (4) (b) (4) method. Additionally, Pfizer/BioNtech will change 20 mL to (b) (4) for the container.

Pfizer/BioNTech are currently working on a (b) (4) for compiling the LRP. While every effort will be made to maintain the current formatting, there may be cases where the format of the LRP may need to change to support this enhancement. No data will be removed from the agreed template without consultation with CBER in advance. Under the

current lot release process CBER performs a 48-hour review. Pfizer/BioNTech respectfully request a continuation of the 48-hour timeframe to enable rapid release of doses.

An updated LRP Template is provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

Lot Release Protocol (LRP) Template, replaced

Previously submitted supporting documentation

None