LRP TEMPLATE FOR STN 125742/0:

QUERY 1:

Please submit a lot release protocol template for COVID-19 mRNA Vaccine for CBER review by COB Friday, July 9, 2021. Please include the assays performed and acceptance criteria for the drug product.

RESPONSE 1

The Lot release protocol that included the assays performed and acceptance criteria was previously provided with the initial submission. The same Lot Release Documentation Package is attached here for easy of reference.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

Lot Release Documentation Package

The requested samples and reagents were shipped to the following address in four shipments as detailed below:

Emnet Yitbarek
Food and Drug Administration
Center for Biologics Evaluation and Research
Division of Biological Standards and Quality Control
10903 New Hampshire Avenue
WO75, G-650
Silver Spring, MD 20993

- Three drug substance batches, shipped on July 8, 2021

- Three drug product lots, shipped on July 8, 2021

- Drug substance, drug product and lipid reference materials/controls and (b) (4), shipped on July 8, 2021

- Materials for In vitro expression, RT-PCR and ddPCR, shipped on July 7, 2021

SAMPLE AND REAGENT IR FOR 125742/0: DRUG SUBSTANCE (DS)

QUERY 2

Please provide 50 aliquots (200 µL aliquots preferred) of DS from three different lots and the following reagents in sufficient quantity to perform 50 independent tests for the following DS assays:

RESPONSE 2

The Sponsor is providing 1 X 35 ml bottle of DS each from lots 21Y513C2301, 21Y513C2401 and 21Y513C2501. The Certificate of Analysis for each lot is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

21Y513C2301 Certificate of Analysis

21Y513C2401 Certificate of Analysis

21Y513C2501 Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 3

5' – Cap assay

i. The current assay control (PF-07305885 DS reference material or equivalent as stated in TM100010578)

(b) (4)

RESPONSE 3

The Sponsor is providing 50 vials of drug substance reference material lot # (b) (4), which is adequate to perform 50 tests. As stated on the Certificate of Analysis, this material may be stored up to (b) (4) days at (b) (4) °C if sampled aseptically.

The Certificate of Analysis for drug substance reference material lot # (b) (4) is also provided.

The Sponsor is also providing 6 vials of (b) (4), which is sufficient volume to perform the requested number of independent tests. The concentration of the (b) (4) (b) (4)

Batch and Reference numbers are printed on the vials.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

(b) (4) Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 4

Poly(A) Tail

i. The current internal control as stated in TM100010379

(b) (4)

RESPONSE 4

The Sponsor is providing 50 vials of drug substance reference material lot # (b) (4) for use as internal control, which is adequate to perform 50 tests. As stated on the Certificate of Analysis, this material may be stored up to (b) (4) days at (b) (4) °C if sampled aseptically.

The Certificate of Analysis for drug substance reference material lot # (b) (4) is also provided.

The sponsor is providing the following reagents inclusive of all materials required to perform the analytical procedure: Refer to Table 1.

Table 1. List of Reagents

Reagent Name	(b) (4) Lot Number	Vendor Catalog, Lot Number	Expiry Date	Concentration	Quantity (vial)	Vial Volume (µL)	Storage Temp (ºC)
(b) (4)							

Table 1. List of Reagents

Reagent Name	(b) (4) Lot Number	Vendor Catalog, Lot Number	Expiry Date	Concentration	Quantity (vial)	Vial Volume (µL)	Storage Temp (°C)
(b) (4)							

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

(b) (4)

Previously submitted supporting documentation

None

Drug Product (DP)

QUERY 5

Please provide 170 vials of DP per lot from three different DP lots and the following reagents for the following DP release assays:

RESPONSE 5

The Sponsor is providing 170 vials of the drug product lots FC3181, FC3184 and FD0809. The Certificate of Analysis for each lot is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

FC3181 Certificate of Analysis

FC3184 Certificate of Analysis

FD0809 Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 6

LNP Size

i. Current assay control - an amount (in 3 aliquots) adequate to perform 10 independent tests

RESPONSE 6

The Sponsor is providing 10 vials of assay control lot # PF-07302048-DP-RM, which is adequate to perform 10 independent tests. Each vial is suitable for a single use and the remaining material should be discarded.

The Certificate of Analysis for PF-07302048-DP-RM is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

PF-07302048-DP-RM Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 7

RNA Encapsulation and RNA Content

i. Reference Standards A and B - 50 vials of each standard or enough to perform 50 tests

RESPONSE 7

The Sponsor is providing 50 vials of drug substance reference material lot # (b) (4) which is adequate to perform 50 tests. One aliquot is suitable to prepare both the (b) (4) for determination of RNA content and RNA encapsulation. As stated on the Certificate of Analysis, the drug substance reference material may be stored up to (b) (4) days at (b) (4) °C if maintained aseptically.

The Certificate of Analysis for drug substance reference material lot # (b) (4) is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

(b) (4) Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 8

Lipid identities

i. Reference PF-07302048 - 20 vials

ii. Four (4) lipid standards - 5 grams of each

RESPONSE 8

The Sponsor is providing 5 single-use aliquots of cholesterol, DSPC and ALC-0159, and (b) (4) (b) (4) of ALC-0315 in a multi-use bottle that may undergo 5 freeze/thaw cycles. These materials may be used to prepare up to (b) (4) stock standard solutions with each preparation having a shelf-life of (b) (4) and enough volume for approximately (b) (4) assays. In total, these lipid materials are sufficient to perform approximately (b) (4) assays.

The Certificate of Analysis for cholesterol lot # 677100P-1G-A-010, DSPC lot # 677365-1G-A-010, ALC-0315 lot # 67735O-1G-010 and ALC-0159 lot 677159P-1G-A-010 are also provided.

The Sponsor is providing 20 vials of drug product lot # PF-07302048-DP-RM, which is adequate to perform 20 independent tests. Each vial is suitable for a single use and the remaining material should be discarded.

The Certificate of Analysis for PF-07302048-DP-RM is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

PF-07302048-DP-RM Certificate of Analysis

677100P-1G-A-010 Certificate of Analysis

677365-1G-A-010 Certificate of Analysis

67735O-1G-010 Certificate of Analysis

677159P-1G-A-010 Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 9

Identity of encoded RNA sequence

50 vials of each reagent OR enough to perform 50 tests

i. Positive PCR Control: PF-07305885 DS or equivalent as stated in TM100010407

ii. Positive (b) (4) Control: PF-07302048 DP or equivalent as stated in TM100010407

(b) (4)

RESPONSE 9

The Sponsor is providing 50 vials of drug substance reference material lot # (b) (4), which is adequate to perform 50 tests. As stated on the Certificate of Analysis, this material may be stored up to (b) (4) days at (b) (4) °C if sampled aseptically.

The Certificate of Analysis for drug substance reference material lot # (b) (4) is also provided.

The Sponsor is also providing 50 vials of positive (b) (4) control lot # DP-CONT-EL8983, which is adequate to perform 50 independent tests. As stated on the Certificate of Analysis, this material may be stored up to (b) (4) days at (b) (4) °C if sampled aseptically.

The Certificate of Analysis for DP-CONT-EL8983 is also provided.

Finally, the sponsor is providing the following reagents:

Reagent Name	Lab Notebook Reference	Manufacturer Catalogue and Lot Numbers	Expiry date	Sample Concentration (µM)	Quantity (vial)	Volume (µL)	Storage Temp (ºC)
(b) (4)							

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

DP-CONT-EL8983 Certificate of Analysis

(b) (4) Certificate of Analysis

Previously submitted supporting documentation

None

QUERY 10

In Vitro Expression Potency assay

i. (b) (4)

ii. Reference Standards, Qualified (b) (4) - 50 vials of each or enough of each to perform 50 tests

RESPONSE 10

The Sponsor is providing the following materials requested to perform the in vitro expression potency assay.

Reagent Name	Reagent Lot #	Quantity	Expiry	Concentration	Storage Condition (°C)
(b) (4)					

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 11

RNA Integrity

i. (b) (4) Reference Material - 50 vials of each reagent OR enough to perform 50 tests

RESPONSE 11

The Sponsor is providing 50 vials of drug substance reference material lot # (b) (4) which is adequate to perform 50 tests. As stated on the Certificate of Analysis, the drug substance reference material may be stored up to (b) (4) days at (b) (4) °C if maintained aseptically.

The Certificate of Analysis for drug substance reference material lot # (b) (4) is also provided.

The Sponsor is also providing 50 vials of drug product lot # DP-CONT-EL8983, which is adequate to perform 50 independent tests.

The Certificate of Analysis for DP-CONT-EL8983 is also provided.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

DP-CONT-EL8983 COA

Previously submitted supporting documentation

None

DOCUMENTATION

QUERY 12

1. Please provide Certificates of Analysis for all reagents

2. Please provide results of the assays listed for the DS lots and DP lots submitted to CBER

Response 12

1. Certificate of analysis for all reagents are provided. Reference responses supporting documentation sections.

2. The results of the assays listed for the DS lots and DP lots submitted to CBER are provided in the attached Certificate of analysis. Reference supporting documentation sections.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

Supporting Documentation	
(b) (4) Certificate of Analysis	DS reference material
FC3181 Certificate of Analysis	DP Lot COA
FC3184 Certificate of Analysis	DP Lot COA
FD0809 Certificate of Analysis	DP Lot COA
PF-07302048-DP-RM Certificate of Analysis	DP reference material
677100P-1G-A-010 Certificate of Analysis	Cholesterol Lot COA
677365-1G-A-010 Certificate of Analysis	DSPC lot COA
677315O-1G-A-010 Certificate of Analysis	ALC-0315 Lot COA
677159P-1G-A-010 Certificate of Analysis	ALC-0159 Lot COA
DP-CONT_EL8983 Certificate of Analysis	Positive (b) (4) control
Lot 21Y513C2301 Certificate of Analysis	DS COA
Lot 21Y513C2401 Certificate of Analysis	DS COA
Lot 21Y513C2401 Certificate of Analysis	DS COA

Previously submitted supporting documentation

None