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QUERY 1

A. Regarding the RNA integrity assay by CGE: Please explain how the (b) (4) (b) (4) If available, provide the work instructions for CGE (b) (4) or commit to generating these instructions.

RESPONSE 1

Pfizer Kalamazoo uses (b) (4) As Pfizer Kalamazoo does not have work instructions for (b) (4) (b) (4), we commit to formalizing these instructions by 30 September 2021.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 2

B. Regarding lot release of the 7 EUA lots:

1. Please send samples (20 vials) of each lot to the address noted below as soon as possible. We can receive them any day and prefer that they be received NO LATER THAN Wednesday 18 August 2021. Please contact Mr. Quander at Joseph.Quander@fda.hhs.gov for specific shipping instructions and to notify him of shipments.

   Shipments should be sent to:

   Food and Drug Administration
   Center for Biologics Evaluation and Research
   Sample Custodian
   10903 New Hampshire Avenue
   WO75-G707
   Silver Spring, MD 20993-0002

2. Please confirm your intent to accept all our instructions for the Lot Release Protocol template in the section below. Please request a telecon for clarification if needed. Please note that because we have expedited the review process, we may request changes to the protocol in the future.

3. Although we cannot commit to a 48-hour turnaround time for lot release as you have requested, we are committed to completing the required review and testing expeditiously.

RESPONSE 2

1. 20 vials of each of the identified EUA lots will be shipped to the provided address for receipt no later than Wednesday 18 August 2021.

2. Pfizer accepts all instructions included in this IR for the Lot Release Protocol template for the initial identified EUA lots. Pfizer respectfully requests the opportunity to propose changes to the Lot Release Protocol template for future lots.

3. Pfizer acknowledges that CBER cannot commit to a 48-hour turnaround time for lot release but will complete the review and testing expeditiously.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None

QUERY 3

C. Comments on lot release protocol (LRP) template submitted to BLA 125742/0.40

NOTE: Page numbers referenced below are from Adobe page numbering (not the page numbers on the footer).

It has been determined that lot release protocols will be submitted electronically. Due to that the following is requested regarding pages 1 and 2.

i. Throughout document

Renumber the entire document with the Electronic Protocol Signature Page as Page 1

ii. Page 2 of 12

Please remove the reason for submission as that is now on page 1 of 12.

Please replace the Fill Information with the table of Fill Information form Page 3 of 12.

iii. Page 3 of 12

Please remove the Reason for Submission.

Please remove the following:

All lot release tests conducted on this lot, as per the product license are reported and pass specifications as required.

Prepared By: Approved By:

iv. Page 6 of 12:

RNA encapsulation and content test

Sponsor question: What is required for R2 for standard A and B?

CBER Response: Regarding your RNA encapsulation and content test: The test described in TM#100010402 requires the coefficient of determination (R2) for (b) (4) to be (b) (4) Please provide the R2 values for standards A (standard in (b) (4)) and B (standard in (b) (4)) for each test performed. We note that you have not incorporated all requested information for this test in the LRP. Please include Encapsulated RNA and Total RNA results in mg/mL units, as requested previously.

v. Page 8 of 12

In Vitro Expression Assay

Sponsor Question: What is required for Average Number of Cells Counted for sample and % cell viability?

CBER Response: Regarding your in vitro expression assay: The SOPs for this assay (SOP#113198 and TM# 100010380) include assay acceptance criteria for number of cells counted (b) (4) cells) and cell viability (b) (4) Please provide the % cell viability and the average number of cells counted for the test sample (the average number of (b) (4) (b) (4) as described in the Data Analysis section of the test method).

vi. Page 10 of 12

Please replace the Limulus Amebocyte Lysate Test template with the template in Attachment 1 of this information request.

RESPONSE 3

The requested changes have been made to the Lot Release Protocol (LRP).

On Saturday 14 August 2020 provided an updated Lot Release Protocol to CBER via email with the following introduction:

> Pfizer has modified the Lot Release Protocol template to comply with each of CBER's requests, except that we believe there is a typo in the template provided by CBER for page 10, where units of "IU/mL" were prescribed, but these should actually be "EU/mL". If there is some other reason for this difference, we commit to aligning with CBER on the correct units to be used.
>
> Please notify us as soon as CBER has confirmed that this template is acceptable. We will then use the agreed template to begin to populate data from the first lots that will be sent for CBER release under the lot release program. Alternatively if there are any questions or issues, please contact me by phone at the mobile number below to resolve them.

CBER subsequently confirmed that the correct units on page 10 were EU/mL and that the template provided was acceptable.

The LRP provided as a part of this response is identical to the one provided to CBER via email on 14 August 2021.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

Lot Release Protocol, replaced

Previously submitted supporting documentation

None

QUERY 4

We have the following questions to your response (dated 08/11/21) to our IR (dated 08/06/21), regarding submission of diagrams (b) (4) with the Lot Release Protocols (LRP):

i. Regarding the Lipids assay (TM100010322): Your assay requires visual inspection of (b) (4) (SOP # TM100010322 section 15.2, which states "For identity testing the (b) (4) Hence, please attach the (b) (4) as requested. These can be attached as a separate page at the end of your LRP if the (b) (4) cannot be inserted into the template itself. In addition, please provide the following information in Table format: Retention times (RT) for each lipid component of the standard and the sample and the (b) (4) Please include a statement at the top or bottom of the table to indicate the assay has a (b) (4) limit as acceptance criterion and indicate if the assay results meet the criterion.

ii. Regarding the RNA integrity assay (TM100010392):

The SOP does not provide instructions on how the (b) (4) In addition, the (b) (4) provided suggest the (b) (4) could be subjective. Hence, please provide the (b) (4) in your LRPs as requested in our previous information request. These can be submitted as PDFs that are attached at the end of your LRP if they cannot be incorporated into the report automatically.

RESPONSE 4

i. Pfizer commits to providing (b) (4) for the Lipids assay as attachments at the end of the Lot Release Protocol. A table will be included which contains the retention times for each lipid component of the standard and sample and (b) (4) A statement at the top of the table will specify the assay acceptance criterion of (b) (4) and will indicate if the assay results meet the criterion.

ii. Pfizer commits to providing (b) (4) for the RNA integrity assay as attachments at the end of the Lot Release Protocol.

Literature References

None

SUPPORTING DOCUMENTATION

New or Replaced Supporting Documentation

None

Previously submitted supporting documentation

None