

## RESPONSE TO FDA REQUEST FOR INFORMATION

### Introduction

Information requests were sent by FDA via email to Carla Vinals on November 20, 2020 (concerning comments and questions regarding IND 19745 SN0053).

This document provides the Sponsor's responses to CBER's requests (in **Bold**).

### **Request for Information for IND 19745 SN0053 Dated November 20, 2020**

#### **Item 1a from November 20, 2020:**

The following quality tests will be performed at Moderna or at alternative sites: DS bioburden (Moderna or Lonza), DS and DP endotoxin (Lonza or Associates of Cape Cod), DP sterility (Moderna or Catalent), (b) (4)

For the bioburden, endotoxin and sterility tests, please confirm that the testing at alternative sites will be performed according to the same SOPs or compendia as listed in the IND and provide verification or qualification information for the tests performed at those sites.

#### **Sponsor Response:**

Bioburden, endotoxin and sterility testing is completed per the associated compendial method as described in IND 19745. The following table outlines the test, testing site and location of the information in IND 19745.

Material	Test	Test Location	Analytical Method Description Location	Analytical Method Verification Description
CX-024414	Endotoxin	Lonza Biologics, Inc.	<a href="#">Section 3.2.S.4.2.9</a>	<a href="#">Section 3.2.S.4.3.2</a>
	Bioburden	Lonza Biologics, Inc.	<a href="#">Section 3.2.S.4.2.10</a>	<a href="#">Section 3.2.S.4.3.2</a>
(b) (4)				
mRNA-1273 LNP	Endotoxin	Associates of Cape Cod	<a href="#">Section 3.2.S.4.2.10</a>	<a href="#">Section 3.2.S.4.3.2</a>
	Bioburden	Lonza Biologics, Inc.	<a href="#">Section 3.2.S.4.2.11</a>	<a href="#">Section 3.2.S.4.3.2</a>
mRNA-1273 Drug Product	Endotoxin	Associates of Cape Cod	<a href="#">Section 3.2.P.5.2.13</a>	<a href="#">Section 3.2.P.5.3.2</a>
	Sterility	Catalent	<a href="#">Section 3.2.P.5.2.14</a>	<a href="#">Section 3.2.P.5.3.2</a>

As noted in the table above, LNP testing of endotoxin is only conducted at Associates of Cape Cod and that any material manufactured at a site is tested at that site. Revised sections for the analytical procedure for bioburden testing at Lonza for the (b) (4) and mRNA-1273 are provided in this submission ([Section 3.2.S.4.2 {SM-102 LNP}](#) and [Section 3.2.S.4.2 {mRNA-1273 LNP}](#)).

#### **Item 1b from November 20, 2020:**

Please confirm that DS and DP samples will be shipped from Lonza and Catalent to Moderna for the quality release and stability tests performed at Moderna.

#### **Sponsor Response:**

The Sponsor can confirm that DS and DP samples are shipped from Lonza and Catalent to ModernaTX, Inc. for the quality release and stability tests performed at ModernaTX, Inc.

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**Item 2 from November 20, 2020:**

**Please note that as per 21 CFR 610.14, before release each lot will need to be tested for identity after all labeling operations are completed (i.e., after filled vials are labeled and packaged). If possible, please also conduct this test for release of lots distributed under EUA. If this is not possible, please include a brief description of segregation, tracking and testing procedures at the Catalent site where the DP will be packaged and warehoused prior to release. Please note this test will need to be implemented prior to licensure.**

**Sponsor Response:**

At this time, filling and labelling/packaging activities are conducted as a continuous process. Samples for release testing are collected after visual inspection at Catalent. The samples are then sent to ModernaTX, Inc. Confirmation of the identity of the labeled product is conducted as part of the release testing for the mRNA-1273 Drug Product as specified in [Section 3.2.P.5.1](#) and as described in [Section 3.2.P.5.2.2](#).

The Sponsor is actively working with Catalent to streamline the filling and labelling/packaging procedures and acknowledges that if changes are required to the above-mentioned process that compliance to 21 CFR 610.14 will need to be implemented prior to licensure. Any procedural changes to the process prior to licensure for lots distributed under EUA will be submitted to Agency accordingly.

**Item 3a from November 20, 2020:**

**Regarding the quality testing of the pDNA template:**

**Please confirm that the pDNA template to be used for DS manufacture at Lonza will be produced and quality tested at Moderna as per the information in the IND. If this is not the case, please update the information in the IND.**

**Sponsor Response:**

As discussed in IND 19745 SN0077, submitted on November 24, 2020, all plasmid manufacturing steps and testing to source the linearized pDNA template for EUA/commercial manufacturing of CX-024414 has transitioned to Aldevron (Fargo, ND, USA), a GMP compliant facility with appropriate quality oversight. The transition to Aldevron will enable a significantly higher manufacturing capacity and pDNA template for CX-024414 will no longer sourced from Moderna's Norwood facility. It is anticipated that this information will be submitted to IND 19745 no later than December 11, 2020.

**Item 3b from November 20, 2020:**

**In section 3.2.S.2.1 Manufacturer(s) [CX-0244] [ModernaTX, Inc], please include the site(s) where the pDNA will be manufactured and tested.**

**Sponsor Response:**

The Sponsor will include the manufacture and testing sites for the linearized pDNA template in Section 3.2.S.2.1 in IND 19745 no later than December 11, 2020.

**Item 3c from November 20, 2020:**

**In 3.2.S.2.3 Control of Materials – Starting Materials, in the release testing section (3.2.S.2.3.2.5.2), please specify the reference sequence used to confirm plasmid identity by Sanger sequencing.**

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**Sponsor Response:**

(b) (4)



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**Item 4 from November 20, 2020:**

With regard to SOP-0999 (mRNA content by ion exchange chromatography with (b) (4) (b) (4) and SOP-0996 (mRNA purity by RP-HPLC) for release testing of mRNA-1273 LNP and mRNA-1273 DP, please describe the procedure for (b) (4) (b) (4) from the test samples. Please update SOP-0999 and SOP-0996 to include the (b) (4) procedure or include a reference to an SOP describing this step (e.g., similar to that described in SOP-1032 (mRNA sequence by RT-PCR/Sanger)).

**Sponsor Response:**

Sample preparation for SOP-0999 is described in [Section 8.2.3.1 in SOP-0999](#). A combination of (b) (4)

(b) (4) [Section 8.2.3.1 in SOP-0999](#) states (b) (4)

[Section 8.1.9 in SOP-0999](#).

Sample preparation for SOP-0996 is described in [Section 8.5.6 in SOP-0996](#). The method diluent of (b) (4)

(b) (4)  
(b) (4) [Section 8.5.6 in SOP-0996](#) states (b) (4)

(b) (4) is described in [Section 8.1.7 in SOP-0996](#).