From: Agnihothram, Sudhakar
To: Paul Dawidczyk
Cc: Carla Vinals; Michelle Olsen; Resnick, Josephine; Kulinski, Joseph
Subject: CBER RESPONSE [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**
Date: Monday, September 27, 2021 5:38:47 PM
Attachments: image001.png

Hi Paul/Michelle,

We have discussed the Moderna deliverables as outlined from Paul's email dated September 24, 2021 (9:47 PM EST). We agree with your plan to submit the following items to STN 125752 **no later than October 15, 2021**.

- (b) (4) PPQ Lonza (USPO-29627 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) Mixers PPQ (PV-VAL-PRO-0056 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) PPQ (PV-VAL-PRO-0050 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- LSS Change (PV-VAL-PRO-0052 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) (PV-VAL-PRO-0015 and PV-VAL-PRO-0016 protocols submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- Direct Injection Purity and Product-related Impurity Analytical Method (QC-MVP-0025 method validation submitted in BLA 125752 SN002, final executed analytical bridging data to be submitted on October 10, 2021 per RTQ received September 22, 2021)
- (b) (4) (Stability protocols provided in Section 3.2.S.7.1 {CX-024414} or Section 3.2.S.7.1 {mRNA-1273 LNP} in BLA 125752 SN002 and executed stability data to be provided on October 15, 2021)
- Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill (VPPQ-256-100-00010-P-ADD01 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)

For the following Catalent items, we agree with your proposal that if the information are proprietary to Catalent, then they be submitted to the Catalent DMF **no later than October 15, 2021**, and cross referenced as appropriate. If the information is not confidential, the information should be provided in BLA 125752 **no later than October 15, 2021**.

- Catalent Label/Pack Serialization
- Catalent Additional Automated Visual Inspection Machine (AIM)

From Paul's email dated September 21, 2021, 9:17 PM EST, we infer there will be **NO ADDITIONAL ITEMS** other than the bullet points listed above, that will be submitted to the STN 125752 during the review cycle.

Please acknowledge the receipt of this email.

Thanks,

Sudhakar Agnihothram

Sudhakar Agnihothram, B.Pharm., Ph.D
Biologist (Primary Reviewer)
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-348-3056 (Off)
202-870-6949 (Cell)
Fax: 301-827-3532
Email: Sudhakar.Agnihothram@fda.hhs.gov

From: Paul Dawidczyk (b) (6) @modernatx.com>
Sent: Saturday, September 25, 2021 5:03 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: RE: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

Hello Sudhakar:

Correct, if it is determined that there is confidential information, the information will be submitted to the DMF by October 15, 2021. For the second AIM, as with the first AIM, the protocols are referenced in 32A1 {Catalent} and were not/will not be submitted.

Regards,
Paul

From: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Sent: Saturday, September 25, 2021 12:27 PM
To: Paul Dawidczyk (b) (6) @modernatx.com>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: Re: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

EXTERNAL

Hi Paul,

In the event it is confidential, are the plans are to submit the information to DMF by October 15, 2021?

I need the information to discuss this internally with my team and management. By the way, for the Catalent AIM, no protocols have been submitted to 3.2 R and it will be a direct submission of data, correct?

Thanks,
Sudhakar Agnihothram

Get Outlook for iOS

From: Paul Dawidczyk (b) (6) @modernatx.com>
Sent: Saturday, September 25, 2021 12:21:14 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: RE: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Hello Sudhakar:

I am awaiting a response from Catalent on the two following items to see if they are company confidential. If this is not confidential, the information will be provided in BLA 125752 by October 15, 2021

- Catalent Label/Pack Serialization
- Catalent Additional Automated Visual Inspection Machine (AIM)

Regards,
Paul

From: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>

Sent: Saturday, September 25, 2021 11:55 AM
To: Paul Dawidczyk (b) (6) @modernatx.com>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: Re: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

EXTERNAL

Hi Paul,

Following up on my email below from last night (10:01 PMEST). Please let us know if there is update on the questions below regarding the content and the exact time line of Catalent submissions to the BLA and not DMF.

Please respond by today.

Thanks,
Sudhakar Agnihothram

Get Outlook for iOS

From: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Sent: Friday, September 24, 2021 10:01 PM
To: Paul Dawidczyk
Cc: Carla Vinals; Michelle Olsen; Resnick, Josephine; Kulinski, Joseph
Subject: RE: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

Hi Paul,

Does the Catalent-related activities include the following two items?

- Catalent Label/Pack Serialization
- Catalent Additional Automated Visual Inspection Machine (AIM)

When will you know from Catalent on whether the information can be submitted to the BLA? Is that information also expected to be submitted by October 15, 2021?

Thanks,
Sudhakar

Sudhakar Agnihothram, B.Pharm., Ph.D
Biologist (Primary Reviewer)
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration

Tel: 301-348-3056 (Off)
202-870-6949 (Cell)
Fax: 301-827-3532
Email: Sudhakar.Agnihothram@fda.hhs.gov

From: Paul Dawidczyk (b) (6) @modernatx.com>
Sent: Friday, September 24, 2021 9:47 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: RE: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

Hello Sudhakar:

The executed PPQ data/reports for the items in the list provided in my email dated September 21, 2021 were intended to be submitted to BLA 125752 on October 15, 2021. We can redirect the PQ data for Catalent related activities (assuming Catalent is in agreement and they are non-proprietary) to the BLA as well.
Specifically for Moderna deliverables:

- (b) (4) PPQ Lonza (USPO-29627 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) Mixers PPQ (PV-VAL-PRO-0056 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) PPQ (PV-VAL-PRO-0050 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- LSS Change (PV-VAL-PRO-0052 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)
- (b) (4) (PV-VAL-PRO-0015 and PV-VAL-PRO-0016 protocols submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15,

2021)
- Direct Injection Purity and Product-related Impurity Analytical Method (QC-MVP-0025 method validation submitted in BLA 125752 SN002, final executed analytical bridging data to be submitted on October 10, 2021 per RTQ received September 22, 2021)
- (b) (4) (Stability protocols provided in Section 3.2.S.7.1 {CX-024414} or Section 3.2.S.7.1 {mRNA-1273 LNP} in BLA 125752 SN002 and executed stability data to be provided on October 15, 2021)
- Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill (VPPQ-256-100-00010-P-ADD01 protocol submitted in BLA 125752 SN002, executed PPQ data to be provided on October 15, 2021)

Please let me know if any additional clarification is needed.

Regards,
Paul

From: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Sent: Friday, September 24, 2021 8:36 PM
To: Paul Dawidczyk (b) (6) @modernatx.com>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: RE: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

EXTERNAL

Thanks for the note, Paul.

It was unclear from your September 21, 2021 email on whether the comparability protocols were submitted in section 3.2 R for all the items listed in the table.

Please clarify if that is the case. Please clarify whether the plan is to submit supportive data for all the items listed in the table.

Sudhakar Agnihothram

Sudhakar Agnihothram, B.Pharm., Ph.D
Biologist (Primary Reviewer)
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-348-3056 (Off)
202-870-6949 (Cell)
Fax: 301-827-3532
Email: Sudhakar.Agnihothram@fda.hhs.gov

From: Paul Dawidczyk (b) (6) @modernatx.com>
Sent: Friday, September 24, 2021 8:28 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: [EXTERNAL] RE: **STN 125752 SPIKEVAX BLA_ Advice # 2**

Hello Sudhakar:

I acknowledge receipt of this email.

I would however like to quickly clarify. Moderna has already provided the protocols for the following changes in BLA 125752 and was intending to submit the final PPQ reports/data to the BLA on October 15, 2021. The protocols are located in Section 3.2.R. Please let me know if we can quickly discuss.

Regards,
Paul

Description	Protocol in BLA 125752 SN002
(b) (4) PPQ Lonza	USPO-29627
(b) (4) Mixers PPQ	PV-VAL-PRO-0056
(b) (4) PPQ	PV-VAL-PRO-0050
LSS Change	PV-VAL-PRO-0052
(b) (4)	PV-VAL-PRO-0015 and PV-VAL-PRO-0016
Direct Injection Purity and Product-related Impurity Analytical Method	QC-MVP-0025
(b) (4)	Refer to Section 3.2.S.7.1 {CX-024414} or Section 3.2.S.7.1 {mRNA-1273 LNP}

Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill	VPPQ-256-100-00010-P-ADD01

From: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Sent: Friday, September 24, 2021 8:14 PM
To: Paul Dawidczyk (b) (6) @modernatx.com>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
Subject: **STN 125752 SPIKEVAX BLA_ Advice # 2**

EXTERNAL

Dear Paul,

We have internally discussed regarding the submission of the items listed in the table from your September 21, 2021 (9:17 PM EST), email below.

Our understanding is as follows:

For the following items, we believe that Moderna plans on submitting (to STN 125752 BLA by October 15, 2021) the protocols and not the actual data supporting the proposed change:

- (b) (4) Mixers PPQ
- (b) (4) PPQ
- LSS Change
- (b) (4)
- Direct Injection Purity and Product-related Impurity Analytical Method
- (b) (4)
- Catalent Label/Pack Serialization
- Catalent Additional Automated Visual Inspection Machine (AIM)

We **do not agree** with the submission of the protocols pertaining to these items to the BLA STN 125752 by October 15, 2021. Instead, we recommend that these changes be submitted with the supportive data as Prior Approval Supplement (in the applicable CBE category) post regulatory action on STN 125752.

For the following items, we believe that Moderna plans on submitting the actual data (including PPQ data) supporting the proposed change, by October 15, 2021 to the BLA STN 125752:

- (b) (4) PPQ Lonza
- Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill

We **agree with** the submission of data for these proposed changes to the BLA.

Our recommendation is that all information for the Catalent Automated Visual Inspection Machine (AIM) should be submitted to the BLA STN 125752 and not cross-referenced in the DMF. Catalent may submit the AIM IOQ in the DMF if they have other IND submissions referring to it.

Please acknowledge receipt of this email.

Thanks,
Sudhakar Agnihothram

Sudhakar Agnihothram, B.Pharm., Ph.D
Biologist (Primary Reviewer)
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-348-3056 (Off)
202-870-6949 (Cell)
Fax: 301-827-3532
Email: Sudhakar.Agnihothram@fda.hhs.gov

From: Paul Dawidczyk (b) (6) @modernatx.com>
Sent: Tuesday, September 21, 2021 9:22 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>
Subject: [EXTERNAL] RE: BLA 125752, follow up

Hello Sudhakar:

One clarification. The items in the following list will be submitted no later than October 15, 2021. Please note that the initial submissions for the (b) (4) at Lonza Portsmouth and Vial Line (b) (4) Catalent 6.3 mL fill volume have been submitted to EUA 27073 and that the final PPQ reports are intended to be submitted to the BLA.

Regards,
Paul

From: Paul Dawidczyk
Sent: Tuesday, September 21, 2021 9:17 PM
To: Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
Cc: Carla Vinals (b) (6) @modernatx.com>; Michelle Olsen <Michelle.Olsen@modernatx.com>
Subject: BLA 125752, follow up

Hello Sudhakar:
As discussed today and as described in Section 3.2.R.4 in BLA 125752, Moderna proposed to submit the following items within 60-days of the submission of the BLA. Initial information was provided in BLA 125752 (PPQ protocols/method validation/stability protocol). This following list is complete and Moderna can confirm that no additional information will be submitted beyond the items in the list below. Please note that the last two items will be submitted to DMF 24888 by Catalent.

Description	Protocol in BLA 125752 SN002
(b) (4) PPQ Lonza	USPO-29627
(b) (4) Mixers PPQ	PV-VAL-PRO-0056
(b) (4) PPQ	PV-VAL-PRO-0050
LSS Change	PV-VAL-PRO-0052
(b) (4)	PV-VAL-PRO-0015 and PV-VAL-PRO-0016
Direct Injection Purity and Product-related Impurity Analytical Method	QC-MVP-0025
(b) (4)	Refer to Section 3.2.S.7.1 {CX-024414} or Section 3.2.S.7.1 {mRNA-1273 LNP}
Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill	VPPQ-256-100-00010-P-ADD01
Catalent Label/Pack Serialization	PQ summary reports to be included in Catalent DMF # 024888 upon completion.
Catalent Additional Automated Visual Inspection Machine (AIM)	IOQ to be included in Catalent DMF # 024888 upon completion.

Regards,
Paul

Paul Dawidczyk
VP, Regulatory Affairs CMC | Moderna
mobile (b) (6) | modernatx.com