**From:** Agnihothram, Sudhakar
**To:** Lorenzo, Anthony; Levis, Robin; Echeozo, Obinna; Renshaw, Carolyn; Amin, Pankaj (Pete)
**Cc:** Eltermann, John; McVittie, Loris; Weir, Jerry P.; Gagneten, Sara; Dabrazhynetskaya, Alena; Peden, Keith; Resnick, Josephine; Kulinski, Joseph; Pandey, Rakesh; Fritz, Timothy
**Subject:** COMMUNICATED TO MODERNA _ STN125752 Late Component Submission _
**Date:** Monday, September 27, 2021 5:44:02 PM
**Attachments:** image002.png
image008.png
image010.png
image012.png
image013.png
image014.png
image015.png
image016.png
CBER RESPONSE EXTERNAL RE STN 125752 SPIKEVAX BLA Advice # 2.msg

---

Dear all,

As a follow up to the discussion below, the attached email has been sent to Moderna.

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)
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Email: Sudhakar.Agnihothram@fda.hhs.gov



---

**From:** Agnihothram, Sudhakar
**Sent:** Monday, September 27, 2021 8:51 AM
**To:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: UPDATE FROM MODERNA _ STN125752 Late Component Submission _

Thanks, Tony. Appreciate the response. Moderna will submit the nonproprietary Catalent information to BLA by October 15, 2021, and if the information is proprietary, it will be submitted to Catalent DMF and cross referenced appropriately.

My understanding is DVP is fine with DMPQ's approach as well and will wait to hear the final word before I communicate to Moderna.

Thanks again to all.

Sudhakar Agnihothram

**Sudhakar Agnihothram, B.Pharm., Ph.D**
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202-870-6949 (Cell)
Fax: 301-827-3532
Email: Sudhakar.Agnihothram@fda.hhs.gov

---

**From:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>
**Sent:** Monday, September 27, 2021 8:44 AM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: UPDATE FROM MODERNA _ STN125752 Late Component Submission _

Sudhakar,

Information submitted by Moderna on October 15 containing supportive data to the listed protocols is acceptable to DMPQ. We will review that. We did not want to waste time reviewing protocols with no supportive data.

Thanks
Tony

Anthony Lorenzo
Branch Chief
FDA/CBER/OCBQ/DMPQ/MRB2
Office 240-402-9706
Cell (b) (6)

---

**From:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
**Sent:** Saturday, September 25, 2021 12:43 PM
**To:** Levis, Robin <Robin.Levis@fda.hhs.gov>; Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** UPDATE FROM MODERNA _ STN125752 Late Component Submission _

Dear all,

I am writing to provide an update on this issue being discussed below.

Moderna responded and clarified. Attached are my communications with Moderna. Please refer to the yesterday's 9:47 PM EST email from Moderna in the attached trail.

As usual, they were unclear in their September 21, 2021, email to us in terms of what was submitted and what will come in by October 15, 2021.

**Apparently they have submitted the comparability protocols for the following changes in Section 3.2 R.**

**Moderna plans on submitting the actual supportive data for these changes to the BLA by October 15, 2021.**

**Regarding the below two items**

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

If the information for these items are not proprietary to Catalent, Moderna plans on submitting the information to STN 125752, the BLA. I have asked Moderna on their plans for submission if the information is Properitary to Catalent. I will provide an update as soon as I hear from them.

My understanding from the below email yellow highlight, is that if it were actual data (and not the comparability protocols) DMPQ and DVP were fine with reviewing that under the BLA to avoid repetitive review work.

If everyone agrees, I can let Moderna know that they can go ahead and submit the data for all the proposed changes to BLA.

Please let me know.

Thanks,
Sudhakar Agnihothram

**Sudhakar Agnihothram, B.Pharm., Ph.D**
*Biologist (Primary Reviewer)*
**Center for Biologics Evaluation and Research**

**Office of Vaccines Research and Review**
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Email: Sudhakar.Agnihothram@fda.hhs.gov



---

**From:** Agnihothram, Sudhakar
**Sent:** Friday, September 24, 2021 8:16 PM
**To:** Levis, Robin <Robin.Levis@fda.hhs.gov>; Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** CBER Comments Communicated: STN125752 Late Component Submission _DMPQ UPDATE

Dear all,

The attached communication outlining our advice has been sent to Moderna.

Thanks,
Sudhakar

**Sudhakar Agnihothram, B.Pharm., Ph.D**
*Biologist (Primary Reviewer)*
**Center for Biologics Evaluation and Research**
**Office of Vaccines Research and Review**
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---

**From:** Levis, Robin <Robin.Levis@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 7:47 PM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** Re: REQUESTING DMPQ INPUT: STN125752 Late Component Submission _DMPQ UPDATE

Dear All:

DVP will defer to DMPQ and we agree with what you have suggested as a path forward.

Thanks much,
Robin

Get Outlook for iOS

---

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

**Sent:** Friday, September 24, 2021 6:46:36 PM
**To:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission _DMPQ UPDATE

Thanks, Tony and Obinna.

The message is very clear that know that if it is comparability protocol for a proposed CMC change, Moderna should wait and submit it as PAS. If the proposed change is supported by the data, Moderna could submit it to the BLA.
For AIM, Moderna needs to submit the information to BLA and not DMF.
I will wait to hear from DVP as well on whether they concur with this.

Thanks,
Sudhakar Agnihothram

**Sudhakar Agnihothram, B.Pharm., Ph.D**
*Biologist (Primary Reviewer)*
**Center for Biologics Evaluation and Research**
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202-870-6949 (Cell)
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---

**From:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 5:56 PM
**To:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission _DMPQ UPDATE

Dear Sudhakar,

Please refer to the table in Obinna's email below:

- The following items in yellow, if only protocols will be submitted by Moderna, DMPQ would prefer not to review them. These should be submitted after BLA approval as individual CBE-30s with the data to support approval.
- The items in green were according to Paul Davidochyzk going to be submitted with data for the BLA. That is acceptable.
- The item in red is our recommendation that the automated visual inspection machine (AIM) be submitted in the BLA and not referenced in the DMF. The firm could submit the AIM IOQ in the DMF if they have other IND submissions referring to it.

Thanks
Tony

Anthony Lorenzo
Branch Chief
FDA/CBER/OCBQ/DMPQ/MRB2
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---

**From:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 5:18 PM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis,

Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission _DMPQ UPDATE

Dear Sudhakar,

Please inform Moderna that the information submitted in the Table below under DMPQ's purview could be submitted post-approval as CBE-30 (including the protocols). The protocols should not be submitted under section 3.2.R of the current BLA submission as we might not have adequate time to review them. Also, we recommend submitting the information as separate CBE-30 submissions, if possible (to minimize potential approval delays).

Please reiterate that all information for the Catalent Automated Visual Inspection Machine (AIM) should be submitted to the BLA. If Catalent wants to submit the information **additionally** to their DMF that's fine but we should have the information in the Moderna BLA submission.

| | DMPQ Comments | Description | Protocol in BLA 125752 SN002 |
|---|---|---|---|
| 1. | | (b) (4) PPQ Lonza | |
| 2. | | (b) (4) Mixers PPQ | PV-VAL-PRO-0056 |
| 3. | | (b) (4) PPQ | PV-VAL-PRO-0050 |
| 4. | | LSS Change | PV-VAL-PRO-0052 |
| 5. | | (b) (4) | PV-VAL-PRO-0015 and PV-VAL-PRO-0016 |
| 6. | Product Office (not reviewed by DMPQ) | Direct Injection Purity and Product-related Impurity Analytical Method | QC-MVP-0025 |
| 7. | | (b) (4) | Refer to Section 3.2.S.7.1 {CX-024414} or Section 3.2.S.7.1 {mRNA-1273 LNP} |
| 8. | | Catalent Vial Line (b) (4) PPQ for 6.3 mL Fill | |
| 9. | Product Office (not reviewed by DMPQ) | Catalent Label/Pack Serialization | PQ summary reports to be included in Catalent DMF # 024888 upon completion. |
| 10. | Submit in BLA. DMF not acceptable. | Catalent (b) (4) Automated Visual Inspection Machine (AIM) | IOQ to be included in Catalent DMF # 024888 upon completion. |

Thanks,
Obinna

---

**From:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 4:36 PM
**To:** Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission

Thanks, Carolyn. Just following up to see if there are any updates post DMPQ's internal meeting.

Thanks,
Sudhakar Agnihothram

**Sudhakar Agnihothram, B.Pharm., Ph.D**
*Biologist (Primary Reviewer)*
**Center for Biologics Evaluation and Research**
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FDA U.S. FOOD & DRUG ADMINISTRATION

**From:** Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 9:09 AM
**To:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission

I think we need to meet to discuss as the heading states that these are studies for changes to be implemented after approval and these protocols are in the Regional section which is where CPs are supposed to be included. I will set up a meeting for DMPQ only to discuss this.

Thanks
Carolyn

---

**From:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 8:57 AM
**To:** Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission

Hi Carolyn,

From my understanding of Sudhakar's email, it appears the items in the Table below will all be submitted on October 15th (though the heading states "… changes to be implemented post-approval…").

For the PPQ data, two DP volumes are filled on Vial Line (b) (4) at Catalent: 6.3mL and 8.0mL. Currently, the firm submitted the PPQ protocol and final PPQ report for the 8.0mL fill volume. They've only submitted the PPQ protocol for the 6.3mL fill volume but will submit the final PPQ report to the BLA on October 15th (per Sudhakar's email). Note, this information (for the final PPQ report) has already been submitted to the IND.

Thanks,
Obinna

---

**From:** Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>
**Sent:** Friday, September 24, 2021 8:11 AM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** RE: REQUESTING DMPQ INPUT: STN125752 Late Component Submission

Hi,

It sounds like these are comparability protocols that are/will be (by Oct. 15th) submitted to the Regional section of the BLA with a proposal to have the data submissions come in as CBE-30s after approval. This is probably reasonable although shouldn't we assess the CPs first before agreeing to the downgrade to CBE30 at this time? Another question is the PPQ data. Is that for a change to be implemented after approval as a CBE30? I am not clear about the PPQ data and if that data should be in the BLA for the BLA approval. Regarding Catalent information, yes, if it is not proprietary, we would prefer the information be submitted to the application. They are welcome to submit it to both the DMF and the application.

DMPQ – let me know if you want to meet briefly this morning to discuss.

Thanks
Carolyn

---

**From:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
**Sent:** Thursday, September 23, 2021 9:16 PM
**To:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>; Amin, Pankaj (Pete) <Pete.Amin@fda.hhs.gov>
**Cc:** Lorenzo, Anthony <Anthony.Lorenzo@fda.hhs.gov>; Eltermann, John <John.Eltermann@fda.hhs.gov>; Renshaw, Carolyn <Carolyn.Renshaw@fda.hhs.gov>; McVittie, Loris <Loris.McVittie@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Gagneten, Sara <Sara.Gagneten@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>; Pandey, Rakesh <Rakesh.Pandey@fda.hhs.gov>; Fritz, Timothy <Timothy.Fritz@fda.hhs.gov>
**Subject:** REQUESTING DMPQ INPUT: STN125752 Late Component Submission
**Importance:** High

**Dear DMPQ,**

I am circling back with you on the email trail below (from September 21, 2021, @ 10:42 AM EST) to seek reconfirmation from DMPQ on the following so that all of us are on the same page on the following issue prior to the upcoming filing meeting on Sep 28, 2021 -

Please note that Moderna will be submitting the items in the below table (from the document submitted in 3.2.R Regional Information in STN 125752) to **STN 125752 on October 15, 2021**(email attached). Please confirm whether DMPQ is fine reviewing this information.
If not Properitary to Catalent, we can ask Moderna to submit the information that they plan on submitting to Catalent DMF to the STN 125752 instead.
Please let us know DMPQ's concurrence by tomorrow. DVP is fine reviewing this information to come in in October 15, 2021. Of note, Moderna did not clearly specify these 9 items as 'late components' during the Pre BLA meeting.
If any one needs to access the CMC/Regulatory PreBLA responses communicated under IND 19745, they are attached herewith.

## 3.2.R.6 SUMMARY OF STUDIES INTENDED TO BE CONDUCTED

The following protocols are included as manufacturing changes that are to be implemented post-approval with a proposed {CBE-30} reporting:

| Description | Protocol |
|---|---|
| (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 |
| (b) (4) 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. |

Thanks,
Sudhakar Agnihothram

**Sudhakar Agnihothram, B.Pharm., Ph.D**
*Biologist (Primary Reviewer)*
**Center for Biologics Evaluation and Research**
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Fax: 301-827-3532
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**From:** Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>
**Sent:** Wednesday, September 22, 2021 7:01 AM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
**Subject:** RE: STN125752 RNA Purity method SOP1142 & validation

Hi Sudhakar,

The late components (i.e., manufacturing changes that are to be implemented post-approval) under DMPQ purview appear agreeable. However, it would be best to have all information within the BLA rather than the DMF (Catalent).

Thanks,
Obinna

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**From:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>
**Sent:** Tuesday, September 21, 2021 10:42 AM
**To:** Yitbarek, Emnet <Emnet.Yitbarek@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith <Keith.Peden@fda.hhs.gov>; Sheng Fowler, Li <Li.ShengFowler@fda.hhs.gov>; Echeozo, Obinna <Obinna.Echeozo@fda.hhs.gov>
**Cc:** Pan, Tao <Tao.Pan@fda.hhs.gov>; Francis, Kori <Kori.Francis@fda.hhs.gov>; Eichelberger, Maryna <Maryna.Eichelberger@fda.hhs.gov>; Levis, Robin <Robin.Levis@fda.hhs.gov>; Weir, Jerry P. <Jerry.Weir@fda.hhs.gov>; Resnick, Josephine <Josephine.Resnick@fda.hhs.gov>; Kulinski, Joseph <Joseph.Kulinski@fda.hhs.gov>
**Subject:** RE: STN125752 RNA Purity method SOP1142 & validation

Hi Emnet,

Thanks for the note. I have looked through this and clarified things. Hence is the delay in response. Validation for SOP 1142 has been completed and bridging between the two SOPs is ongoing and we will get the SOP 1142 **in two weeks**.

Apparently the table presented in Page 4 of the last document in 3.2R

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are the late components that we will be receiving and the SOP 1142 is one among them.

Please let me know if alleviates your concern.

**Alena, Keith and Obinna**,

please also look through the table and please make sure whether the **late components listed in the table are agreeable**. In the PDF document they refer to these 9 items as CBE 30 submission post approval. However, as per Moderna, they will be coming in October. It will be better if we look through this prior to filing meeting to address any concerns.

Please note that during our CMC/Reg PreBLA responses we sent them (attached) Moderna only specified the PPQ for (b) (4) formulation as a late component
-

Thanks,
Sudhakar

**Sudhakar Agnihothram, B.Pharm., Ph.D**
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**From:** Yitbarek, Emnet <Emnet.Yitbarek@fda.hhs.gov>
**Sent:** Wednesday, September 15, 2021 2:47 PM
**To:** Agnihothram, Sudhakar <Sudhakar.Agnihothram@fda.hhs.gov>; Dabrazhynetskaya, Alena <Alena.Dabrazhynetskaya@fda.hhs.gov>; Peden, Keith

<Keith.Peden@fda.hhs.gov>; Sheng Fowler, Li <Li.ShengFowler@fda.hhs.gov>
**Cc:** Pan, Tao <Tao.Pan@fda.hhs.gov>; Francis, Kori <Kori.Francis@fda.hhs.gov>; Eichelberger, Maryna <Maryna.Eichelberger@fda.hhs.gov>
**Subject:** STN125752 RNA Purity method SOP1142 & validation

Hi Sudhakar and CMC reviewers,
I need your help locating the SOP and validation docs for the updated IP-RP-HPLC method (SOP 1142) which is used for purity/impurity determination of DS/DP. The final document submitted in the BLA is the old SOP996 which has deficiencies resolving impurities from the product peak. The sponsor recently stated (in a pre-BLA briefing, ) the old SOP996 was improved and replaced by SOP1142 but I didn't find the updated document in the BLA; also, the specification (DS & DP) references SOP996 not SOP1142. Please refer to page 12 of the attached PRE-BLA briefing document regarding the method update/change. The link to the DS and DP specifications in BLA125752 are provided below for your convenience. Thanks and look forward to hearing from you.

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\\cber-fs3\m\eCTD_Submissions\bla125752\0002\m3\32-body-data\32s-drug-sub\cx-024414-all\32s4-contr-drug-sub\32s41-spec\specification.pdf

Thanks

Emnet

***Emnet Yitbarek, PhD***

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