1.11.1 Quality Information Amendment

ModernaTX, Inc. (Moderna) is filing this quality information amendment to provide the additional information referenced in Section 3.2.R.4 of BLA 125752 Sequence Number (SN) 002 dated August 16, 2021.

As clarified in the Response to Information Request #3 received 23 September 2021 (BLA 125752 SN 011 dated October 08, 2021, the intent is to continue testing the purity of the mRNA-1273 Drug Product, CX-024414 mRNA and mRNA-1273 LNP in accordance with SOP-0996 until the BLA is approved. Once the BLA is approved, the transition of the purity testing of the mRNA-1273 Drug Product, CX-024414 mRNA and mRNA-1273 LNP from SOP-0996 to SOP-1142 will independently occur within 60 days for the initiation of manufacturing. The Sponsor will provide a formal notification to the BLA when the transition has been completed concerning lot impact.

The summary of revised Module 3 CTD sections that are being submitted with this quality information amendment are described in the following table.

Table 1: Summary of Revised Module 2.3 and Module 3 CTD Sections

CTD Section		Changes
2.3.S	Quality Overall Summary Drug Substance-CX-024414	• Added Lonza Portsmouth (Lonza PO) (b) (4) PPQ lots manufacturing information (Table 18, Table 21Table 27, • Update Table 26 to include reference to replacement Purity method, SOP-1142 with revised acceptance criteria. Updated abbreviations in the table. • Updated batch release tables for Lonza PO (b) (4) (b) (4) PPQ lots (Table 28 – Table 30) • Update Table 35 to include reference to the justification summary for the new Purity method, SOP-1142. Updated acceptance criteria • Added Lonza PO to stability protocol for (b) (4) registration lots at-20°C ± 5°C and 5°C ± 3°C storage conditions. (Section 2.3.S.7.1) • Revised Section 2.3.S.7.2 to align with current Section 3.2.S.7.2 • Added stability protocol and reference for representative studies/reports in (b) (4) 20°C ± 5°C and 5°C ± 3°C
	Quality Overall Summary Drug Substance-mRNA-1273 LNP	• Provided updated process flow diagram for mRNA-1273 LNP (Figure 1) • Revised in-process hold time table description for (b) (4) forward process operation Table 4) • Revised abbreviation list for Table 4 • Added Process (b) (4) PPQ lots manufacturing information (Table 18, Table 20, Table 24) • Updated batch release tables for Process (b) (4) PPQ lots (Table 25 – Table 28) • Added Lot 5007421578 stability protocol and reference for -60°C to -90°C and 5°C ± 3°C storage conditions. (Section 2.3.S.7.1 and Section 2.3.S.7.3) • Revised Section 2.3.S.7.2 to align with current Section 3.2.S.7.2 • Revised Proven Acceptable Range (PAR) for mRNA-1273 LNP to a percentage (Table 47)

CTD Section		Changes
		• Added manufacturing information for PPQ lots for (b) (4) mixer and (b) (4) (Table 50, Table 51, Table 53and Table 57) • Update Table 56 to include reference to the new Purity method, SOP-1142. Updated acceptance criteria • Added release data for (b) (4) Mixer and (b) (4) PPQ lots (Table 58 – Table 63) • Update Table 70 to include reference to the justification summary for the new Purity method, SOP-1142. Updated acceptance criteria. • Added Lot 5008921001 to mRNA-1273 LNP registration stability program Table 78. • Added new table for mRNA-1273 LNP lots 5007521296 and 5007521308 that support CX-024414 (b) (4) change supporting stability lots (Table 79). • Added Lot 500892001stability protocol for -60°C to -90°C (Table 82) and 5°C ± 3°C (Table 84) storage conditions. • Revised Section 2.3.S.7.2 to align with current Section 3.2.S.7.2 • Provided reference to development stability study data (DHM-50837) to support storage of mRNA-1273 LNP in (b) (4) in introduction section. • Added Lot 5008921001 to mRNA-1273 LNP registration stability Table 88 • Added new table for mRNA-1273 LNP lots 5007521296 and 5007521308 that support CX-024414 (b) (4) change supporting stability lots (Table 89).
2.3.P	Quality Overall Summary Drug Product	• Table 6, Table 8 Addition of Catalent Vial Line (b) (4) 6.3 mL PPQ lot (b) (4) genealogy • Table 17 Administrative correction of typographical error from (b) (4) vials for Catalent 8 mL presentation • Table 49 Administrative correction of typographical error from SM102 HPLC-CAD to SM-102 HPLC-CAD
3.2.S.2.2 {CX-024414}	Description of Manufacturing Process and Process Controls	• Addition of reference to Lonza Portsmouth refiltration protocol (Section 3.2.S.2.2.2.11). • Minor clarification updates to Sections 3.2.S.2.2.2.1, 3.2.S.2.2.2.3, 3.2.S.2.2.2.5, and 3.2.S.2.2.2.7 to align process steps between Lonza Portsmouth and ModernaTX. • Added (b) (4) volume target range and requirement for (b) (4) process scales (Table 15).
3.2.S.2.5 {CX-024414}	Process Validation and/or Evaluation	• Throughout section, inclusion of (b) (4) scale CX-024414 data and results for Lonza Portsmouth. • Removal of Purity, Product Related Impurities, %Tailed,%Tailless, DNA Residual and %Cap1 from CPV Plan (Table 22). • Added ribogreen method as a test used for column cleaning (Section 3.2.S.2.5.5.1.5) • Addition of (b) (4) PPQ protocol and qualification summary report (EXT-3630 and PV-VAL-RPT-0072)
3.2.S.2.6 {CX-024414 Manufacturing History}	Manufacturing Process Development	• Update of manufacturing history for three (3) (b) (4) (b) (4) CX-024414 registration/PPQ/comparability lots (4007921027, 4007921028 and 4007921029). Refer to Table 4.
3.2.S.2.6 {Comparability from Scale A to Scale B}{CX-024414 }	Manufacturing Process Development	• Added (b) (4) lots data for Lonza Portsmouth (Table 1, Table 3, Section 3.2.S.2.6.3.3.6) • Included updated control charts

CTD Section		Changes
3.2.S.4.1 {CX-024414}	Specifications	• Update Table 1 to include reference to replacement Purity method, SOP-1142 with revised acceptance criteria. • Revised method for %5'Capped from RP-IP-UPLC to RP-IP-HPLC (administrative - to align) • Updated abbreviations list below Table 1
3.2.S.4.2 {CX-024414}	Analytical Procedures	• Update Table 1 to include reference to new Purity method, SOP-1142. • Revised method for %5'Capped from RP-IP-UPLC to RP-IP-HPLC (administrative - to align) • Updated abbreviations list below Table 1
3.2.S.4.2 {CX-024414- Direct Injection}	Analytical Procedures	• New CTD section for purity method, SOP-1142
3.2.S.4.3 {CX-024414}	Validation of Analytical Procedures	• Update Table 1 to include reference to the validation summary for the new Purity method, SOP-1142. • Revised method for %5'Capped from RP-IP-UPLC to RP-IP-HPLC (administrative - to align) • Updated abbreviations list below Table 1
3.2.S.4.4 {CX-024414}	Batch Analyses	• Update section (Table 1- Table 4) to include manufacturing and release data for lots 4007921027, 4007921028 and 4007921029 • Added Certificate of Analysis for lots 4007921027, 4007921028 and 4007921029
3.2.S.4.5 {CX-024414}	Justification of Specifications	• Update Table 2 to include reference to the justification summary for the new Purity method, SOP-1142. Updated acceptance criteria. • Added new section for mRNA Purity by SOP-1142 justification of specification (Section 3.2.S.4.5.3.6)
3.2.S.7.1 {CX-024414}	Stability Summary and Conclusions	• Added Lonza PO to stability protocol for (b) (4) registration lots at-20°C ± 5°C (Table 7) and 5°C ± 3°C (Table 10) storage conditions. • Added stability protocol and reference for representative studies in (b) (4) 20°C ± 5°C (Table 4 and Table 8) and 5°C ± 3°C (Table 4 and Table 11)
3.2.S.7.3 {CX-024414}	Stability Data	• Added reference to representative stabilities studies for CX-024414 in (b) (4) (Table 3) • Included stability reports for the supporting data in (b) (4) 4007421005, 4007421006, 4007421008 and 4007421009

(b) (4)

CTD Section	Changes
(b) (4)	
3.2.S.2.2 {mRNA-1273 LNP}	Description of Manufacturing Process and Process Controls	• In Table 2, revised Bioburden and Endotoxin Dilution (Pre-filtration) In-Process Control from (b) (4) (b) (4) respectively. -administrative error. • Added abbreviation "NMT" for Table 3. • Included use of (b) (4) filter prior to mixing of (b) (4), use of new (b) (4) mixer and its dimensions, and updated process parameters, (Section 3.2.S.2.2.2.2, Table 4, Table 5) • Updated abbreviations list for Table 5 ("NMT" and "PSIG") • Revised process flow diagram (Figure 1) to reflect use of new mixer. • Included process parameter requirement for use of new mixer (Table 6, Table 7) • Addition of reference to Lonza Portsmouth refiltration protocol (Section 3.2.S.2.2.2.7). • Added new part number, (b) (4), for mRNA-1273 LNP product manufactured using the new mixer
3.2.S.2.4 {mRNA-1273 LNP}	Controls of Critical Steps and Intermediates	• Revised mixing critical process parameter proven acceptable range to a percentage (Table 2) • Revised abbreviations list for Table 3, "psi" to "PSIG"
3.2.S..2.5 {mRNA-1273 LNP}	Process Validation and/or Evaluation	• Throughout section provided manufacturing and qualification data and results for (b) (4) Mixer (5008921001, 5008921002 and 5008921005) and Freeze/Thaw (5007521557, 5007521569, 5007521576) PPQ lots. • Provided (b) (4) Mixer PPQ report, PV-VAL-RPT-0071

CTD Section		Changes
3.2.S.2.6 {mRNA-1273 LNP Manufacturing History}	Manufacturing Process Development	• Updated mRNA-1273 LNP batch genealogy (Table 2) • Added (b) (4) Mixer PPQ lots (5008921001, 5008921002 and 5008921005) and (b) (4) PPQ lots (5007521557, 5007521569, 5007521576) to registration lot manufacturing history Scale B (Table 4) • Updated comparison of manufacturing changes for initial Scale B and Scale B (ModernaTX) to include use of (b) (4) mix skid and (b) (4) Mixer in Scale B manufacturing process
3.2.S.2.6 {Comparability from Scale A to Scale B} {mRNA-1273 LNP }	Manufacturing Process Development	• Added lots data/results for (b) (4) Mixer and (b) (4) PPQ lots (Table 3, Section 3.2.S.2.6.3.3.3) • Revised manufacturing change summary table (Table 4) • Revised summary of analytical procedure revisions (Table 6) • Included updated control charts
3.2.S.2.6 {mRNA-1273 LNP Process Characterization}	Manufacturing Process Development	• Revised proven acceptable range for mRNA-1273 LNP critical process parameters to percentage (Table 2) • Revised proven acceptable range for mRNA-1273 LNP mixing flow rate study to percentage (Table 8) • Revised proven acceptable range for mRNA-1273 LNP neutralization operation study to percentage (Table 10) • Revised proven acceptable range for mRNA-1273 LNP PEG2000-DMG addition operation study to percentage (Table 11) • Added new section for characterization of lots using (b) (4) filter (Section 3.2.S.2.6.1.3.1) • Revised Scale B target from (b) (4) for mRNA (b) (4) during mRNA dilution preparation unit operation to (b) (4) • Provided (b) (4) filtration of (b) (4) parameter, scale target and scale down model target information (Section 3.2.S.2.6.1.6, Table 19, and Section 3.2.S.2.6.1.9)
3.2.S.4.1 {mRNA-1273 LNP}	Specifications	• Update Table 1 to include reference to replacement Purity method, SOP-1142 with revised acceptance criteria.
3.2.S.4.2 {mRNA-1273 LNP}	Analytical Procedures	• Update Table 1 to include reference to new Purity method, SOP-1142.
3.2.S.4.2 {mRNA-1273 LNP - Direct Injection}	Analytical Procedures	• New CTD section for purity method, SOP-1142
3.2.S.4.3 {mRNA-1273}	Validation of Analytical Procedures	• Update Table 1 to include reference to the validation summary for the new Purity method, SOP-1142.
3.2.S.4.3 {mRNA-1273- Particle Size and Polydispersity}	Validation of Analytical Procedures	• Revised section to include validation summary for particle size and PDI for mRNA-1273 sample matrix
3.2.S.4.4 {mRNA-1273}	Batch Analyses	• Update section (Table 1- Table 7) to include manufacturing and release data for lots 5008921001, 5008921002, 5008921005, 5007521557, 5007521569, and 5007521576 • Added Certificate of Analysis for lots 5008921001, 5008921002, 5008921005, 5007521557, 5007521569, and 5007521576
3.2.S.4.5 {mRNA-1273}}	Justification of Specifications	• Update Table 2 to include reference to the justification summary for the new Purity method, SOP-1142. Updated acceptance criteria. • Added new section for mRNA Purity by SOP-1142 justification of specification (Section 3.2.S.4.5.3.5)
3.2.S.7.1 {mRNA-1273}	Stability Summary and Conclusions	• Added Lot 5008921001 to mRNA-1273 LNP registration stability program Table 3. • Added new table for mRNA-1273 LNP lots 5007521296 and 5007521308 that support CX-024414 (b) (4) change supporting stability lots (Table 4).

CTD Section		Changes
		• Added Lot 500892001stability protocol for -60°C to -90°C (Table 7) and 5°C ± 3°C (Table 9) storage conditions. • Added protocols for mRNA-1273 LNP lots placed on stability to support changes to the CX-024414 (b) (4) process (Section 3.2.S.7.1.3). • Provided report (b) (4) to support justification of using (b) (4) for bulk frozen and storage of mRNA-1273 LNP
3.2.S.7.3 {mRNA-1273}	Stability Data	• Provided reference to development stability study data (DHM-50837) to support storage of mRNA-1273 LNP in (b) (4) in introduction section. • Added Lot 5008921001 to mRNA-1273 LNP registration stability Table 2 • Added new table for mRNA-1273 LNP lots 5007521296 and 5007521308 that support CX-024414 (b) (4) change supporting stability lots (Table 3). • Provided DHM-50837 Stability Report
3.2.P.2.3 {Manufacturing History}	Manufacturing Process Development	• Table 2, Table 4 Addition of Catalent Vial Line (b) (4) 6.3 mL PPQ lot 023F21 genealogy
3.2.P.2.3 {Comparability}	Manufacturing Process Development	• Table 1, Table 2, Table 4 administrative correction of nominal batch size for the 8.0 mL presentation from (b) (4) to up to (b) (4) align across eCTD sections • Table 3 Addition of Catalent Vial Line (b) (4) 6.3 mL PPQ lot 023F21 • Addition of Section 3.2.P.2.3.3.7 Phase 3 -Scale B Catalent, Vial Line (b) (4) 6.3 mL Fill • Figure 1 through Figure 22 revised to include Vial line (b) (4) 6.3 mL PPQ lot 023F21 (Moderna reference for UDP lot 6010721002)
3.2.P.3.5 {Catalent}	Process Validation and/or Evaluation	• Table 2 changed the validation status of the Vial Line (b) (4) 6.3 mL fill volume from “Ongoing” to “Qualified” • Table 3, Table 5 - Table 8, Table 10, Table 12 - Table 14, Table 23 - Table 25 added PPQ CPP data for Catalent vial line (b) (4) PPQ Lot 023F21 • Section 3.2.P.2.3.5.8 added reference to second AIM (b) (4) and associated IOQ and PQ summary reports • Clarified that each vial type is validated on each AIM independently, PQ summary reports are kept on file at Catalent, and that AIM is only enabled for each vial type on each machine after successful IOPQ of that vial type on that machine • Added Attachment VPPQ-256-100-00010-S-ADD01, mRNA-1273 DP Primary PPQ Vial Line (b) (4) for 6.3 mL Fill volume Qualification Addendum Final Summary report
3.2.P.5.1	Specifications	• Replaced Purity and Product-Related Impurities SOP-0996 with SOP-1142 • Removed IG2 (PolyA Tail Variants) as a product related impurity from release and end of shelf life acceptance criteria • Administrative change for Container content acceptance criteria to replace “Maximum 11 dose (0.5 mL Per Dose)” and “Maximum 15 dose (0.5 mL per Dose)” descriptions with “5.5 mL Presentation” and “7.5 mL presentation” respectively
3.2.P.5.2	Analytical Procedures	• Addition of reference for Section 3.2.P.5.2 {Purity and Product-related impurities -Direct Injection}
3.2.P.5.2 {Purity and Product-Related Impurities- Direct Injection}	Analytical Procedures	• Added New Section • Added Attachment SOP-1142

CTD Section		Changes
3.2.P.5.3	Validation of Analytical Procedures	• Addition of reference for Section 3.2.P.5.3 {Purity and Product-related impurities -Direct Injection}
3.2.P.5.3 {Purity and Product-Related Impurities- Direct Injection}	Validation of Analytical Procedures	• Added New Section • Added Attachment QC-MVR-0025
3.2.P.5.3 {Particle Size and Polydispersity}	Validation of Analytical Procedures	• Revised attachment QC-MVR-0011 to include repeat validation of mRNA-1273 LNP test sample
3.2.P.5.4	Batch Analyses	• Table 1 – Table 7 Addition of Comparability, PPQ lot 023F21 batch analysis data • Addition of Attachment CoA-2267 for Catalent lot 023F21
3.2.P.5.6	Justification of Specifications	• Table 2 removed Purity and Product-related impurities acceptance criteria for PolyA tail variants and revised section reference from Section 3.2.P.5.6.2.4 to Section 3.2.P.5.6.2.5 • Added Section 3.2.P.5.6.2.5 for mRNA Purity by Reverse Phase Ion-Paired High-Performance Liquid Chromatography SOP-1142 • Added Attachment QC-OTH-0801 SOP-0996 and SOP-1142 Method Bridging Report
3.2.A.1 {ModernaTX, Inc.}	Facilities and Equipment	• Provided equipment qualification protocol and report for (b) (4) mixer . Reference included in Table 15. • Added a statement regarding the use of the Laminar Flow Hood (Section 3.2.A.1.4.3) • Removed “T-mix/T-mixing” and replaced with “mixing”. T-mixer was utilized in earlier/clinical scale. (Sections 3.2.A.1.4.5, 3.2.A.1.4.6, 3.2.A.1.4.7.6, Table 14 • Updated cleaning process/procedure for mixer (Section 3.2.A.1.4.5) • Updated cleaning process/procedure for mixer (Section 3.2.A.1.4.6) • Included 2.5 (b) (4) mixer in Section 3.2.A.1.4.7.6 • Reflected current contact time for disinfecting/sanitizing agent for transport to CNC area (Table 20) • Revised environmental monitoring section (Section 3.2.A.1.7.4) to reflect current practice for operations that occur in Laminar Flow Hood/Biosafety Cabinets • Revised viable monitoring alert and action levels (Table 25)
3.2.A.1 {Catalent}	Facilities and Equipment	• Section 3.2.A.1.1 Administrative correction to (b) (4) square footage from approximately (b) (4) to approximately (b) (4) and Table 1 Total facility approximate square footage from (b) (4) to (b) (4) • Table 6 Administrative correction to add °C to all temperatures and to add (%) to Relative Humidity column header • Section 3.2.A.1.4.2 Administrative correction from A-VAL-01-01-3552 to A-VAL-01-01-3135 • Added Section 3.2.A.1.4.5.2 Automated Inspection Machine (b) (4) and Automated Tray Loader System (b) (4) to describe a second AIM • Section 3.2.A.1.4.7 Addition of reference to Serialization Performance Qualification document VPQ-256-100-00032-S-VL-062AUG21 • Section 3.2.A.1.4.9 Addition of reference to IOQ document for (b) (4), A-VIOQ-0032s-S-VL-044DEC20