Table of Contents

List of Tables

List of Figures

2.3.S.1 GENERAL INFORMATION

Nomenclature

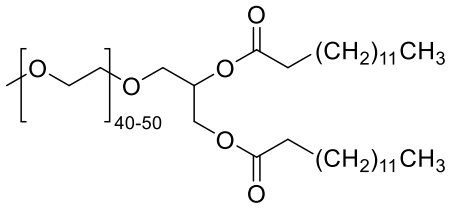
Table 1: Nomenclature

Category	Name
Proprietary Name	Not available
Recommended International Nonproprietary Name (INN)	Not available
Compendial Name	Not applicable
Chemical Name(s)	1. 1,2-dimyristoyl-rac-glycero-3-methoxypolyethylene glycol-2000 2. mPEG2000-DMG 3. 2,5,8,11,14,17,20,23,26,29,32,35,38,41,44,47,50,53,56,59,62,65,68,71,74,77,80,83,86,89,92,95,98,101,104,107,110,113,116,119,122,125,128,131,134,137,140,143,146-nonatetracontaoxanonatetracontahectane-148,149-diyl ditetradecanoate
Laboratory Codes	mPEG2000-DMG, PEG2000-DMG, LP-04-468
Chemical Abstract Index Name	Not available
Chemical Abstracts Service (CAS) Registry Number	160743-62-4
Unique Ingredient Identifier (UNII)	Not available

Structure

Empirical Formula: CH_3-$[OC_2H_4]_n$-O-$C_{31}H_{59}O_5$; n=40-50
Molecular Mass: 2287.5 - 2727.8 m/z (40 - 50 ethylene oxide units)
Molecular Weight: 2289 - 2719 g/mol (40 - 50 ethylene oxide units)
The structure of mPEG2000-DMG is shown below

Figure 1: Structure of PEG2000-DMG



General Properties

mPEG2000-DMG is a white to off-white non-hydroscopic solid with a melting point of 42 – 56°C.

2.3.S.2 MANUFACTURE

Manufacturer(s)

The name and address for the manufacturing and testing facilities are listed in the table below.

Table 2: Manufacturers

Company and Address	Responsibility
CCI [redacted]	• Manufacture • Packaging • Release and stability testing
	• Release and stability testing ([redacted] water content, residual solvents, elemental impurities, bacterial endotoxin, microbial quality)
	• Release and stability testing (identity by [redacted])
	• Release testing (residue on ignition)

Description of Manufacturing Process

The mPEG2000-DMG manufacturing process consists of one step performed under cGMPs.

Figure 2: PEG2000-DMG Synthetic Scheme, GMP Step

CCI [redacted]

Table 3: PEG2000-DMG Manufacturing Process Flow Diagram

Materials	Process Step	In-process Controls
CCI	[redacted]	
	↓	
	Filling into bags	
	↓	
	Release Testing	→ Section 2.3.S.4.1

CCI [redacted]

CCI [redacted]

CCI [redacted]

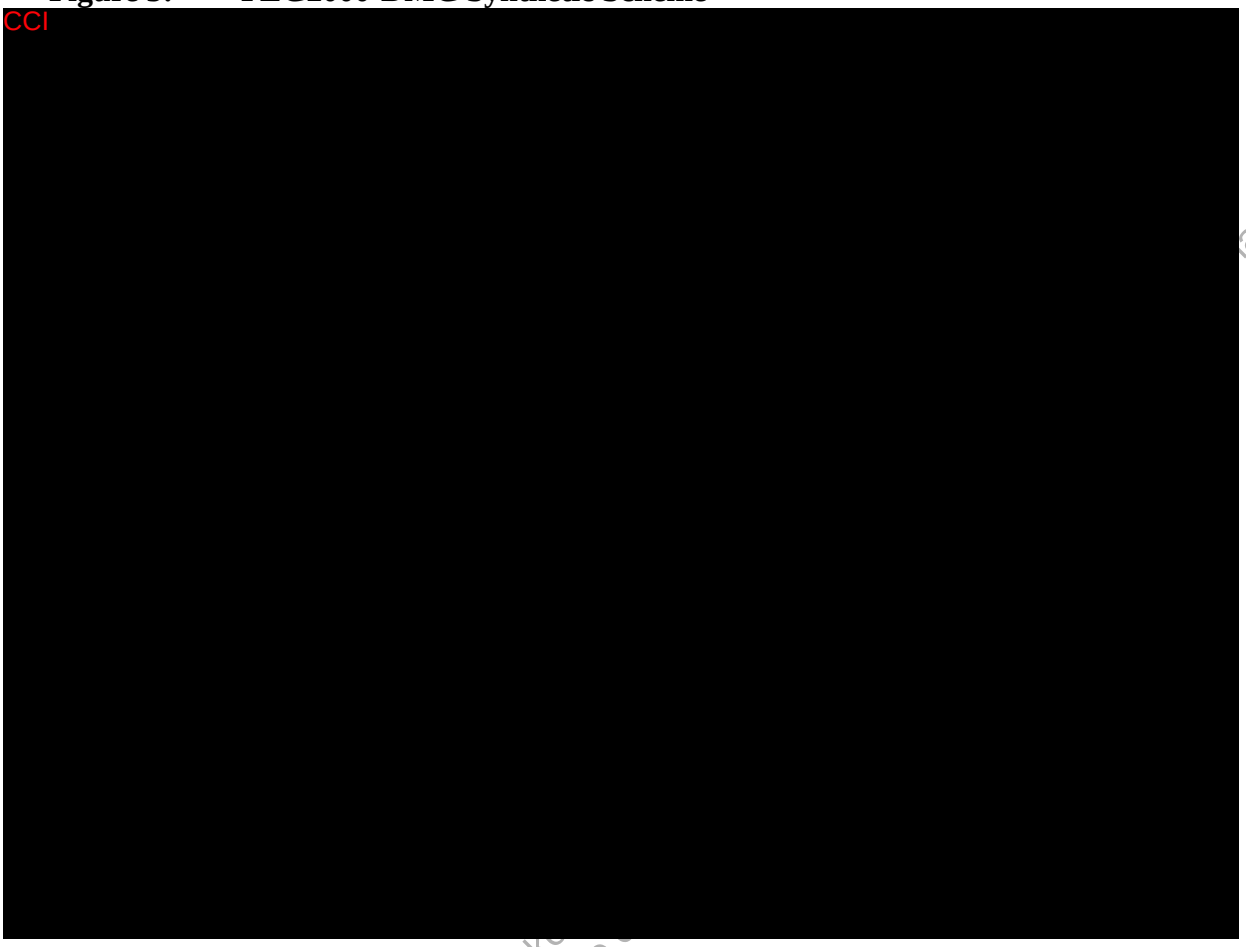
At ambient temperature, the mPEG2000-DMG material is sampled for release and stability testing then filled into polyethylene (PE) bags. The PE bag is purged with inert gas (argon or nitrogen) and sealed. The PE bags are then packaged into multilayer aluminum pouches lined with low-density polyethylene (LDPE) on the inner surface, flushed with inert gas (argon or nitrogen) and a desiccant is added prior to being heat-sealed.

Control of Materials

Starting Materials

The designated starting materials for the synthesis of mPEG2000-DMG are CCI [redacted]. The mPEG2000-DMG synthetic scheme is shown in the figure below with steps performed under GMPs denoted with a red box.

Figure 3: PEG2000-DMG Synthetic Scheme



Justification of Starting Materials

CCI have been established as starting materials containing the structural elements of the final mPEG2000-DMG target. These CC compounds can be manufactured with reproducible purity and consistent impurity profiles. CCI

CCI was established as a starting material for the manufacture of mPEG2000-DMG because it is a CCI which incorporates the major CCI of the structure of mPEG2000-DMG.

In Step 1 of the CCI that has a well-controlled low polydispersity. As expected, the downstream mPEG2000-DMG manufacturing process has no impact on polydispersity of the resultant polyethylene oxide structural element of mPEG2000-DMG.

There are CC significant impurities of the CCI starting material. The CCI are formed or introduced in Step 1 during the formation of CCI. These impurities are carried over to CCI starting material. The relative amount of these impurities in CCI are controlled by the manufacturing

process and in-process controls. The fate of these two impurities is well understood and effectively purged in downstream manufacture of mPEG2000-DMG.

CCI has also been established as a starting material of mPEG2000-DMG. This material is relatively active. The production of CCI is well-established and uses the commercially available raw material, CCI, in Step 3. CCI quality is consistent and well-controlled by the vendor. Control of incoming CCI quality enables consistent and reproducible quality of mPEG2000-DMG.

CCI

is manufactured by CCI.

The synthetic manufacturing route for CCI is provided in the figure below.

CCI

The in-process controls are as follows.

Table 4: CCI In-Process controls

Test	Method	Acceptance Criteria
Relative amount of product	CCI	
Dryness loss (solvents residue)		

CCI

is manufactured by CCI

Figure 5: CCI Synthetic Scheme

CCI

The in-process controls are as follows.

Table 5: CCI In-Process Controls

Test	Method	Acceptance Criteria
Purity	CCI	
DCU		
Drying loss (solvents residue)		
Water content		

Specifications for raw materials used in the mPEG2000-DMG manufacturing process are provided.

Controls of Critical Steps and Intermediates

The in-process controls testing of for manufacture of mPEG2000-DMG are summarized in the table below.

Table 6: In-Process Controls for PEG2000-DMG

Process Step	Method	Purpose	Target Range
CCI			

Process Validation and/or Evaluation

The mPEG2000-DMG manufacturing process will be evaluated for the consistent operation of each manufacturing step, through process capability studies, process development reports and scale-up reports, ensuring that each step of the manufacturing process is controlled to the extent necessary and meets established specifications.

Manufacturing Process Development

Process development investigations were conducted to establish a commercial manufacturing process. Scope of the optimization included design of experiments (DoE) for CCI steps up to and including the GMP Step 4 with focus on process efficiency, manufacturing safety, and especially mPEG2000-DMG product quality.
Information on changes in Step 1 and Step 4 have been provided.

2.3.S.3 CHARACTERIZATION

Elucidation of Structure and Other Characteristics

The structure of mPEG2000-DMG was elucidated using the following analytical procedures: CCI . CCI

Impurities

Product-related Impurities

Impurities are determined by CCI . Impurities are reported based on %w/w for assessing the compliance with the currently defined purity acceptance criteria. The list of potential product-related impurities in purified mPEG2000-DMG Lots is provided in the table below. Identification and characterization of individual impurities are in progress CCI . Limits for currently known/identified impurities are controlled in the specification. However, any new individual impurities will be identified and established as additional batch history becomes available.

Table 7: PEG2000-DMG Product-Related Impurities

Structure and Proposed Denomination	Data	Comments
CCI		• Impurity from Step 1
		• Impurity from Step 4
		• Impurity from Step 4
		• Impurity from Step 2 • Coelutes with mPEG2000 in purity method
		• Starting material for CCI synthesis from Step 3 and hydrolysis product formed during workup of Step 4
		• Starting material from Step 4
CCI		

Elemental Impurities

The elements are quantitatively analysed by CCI in mPEG2000-DMG are: CCI, for release are controlled within the established specification.

Residual Solvents

mPEG2000-DMG batches are tested using CCI for the levels of CCI.

Water Content

Testing for water content is performed using a Karl-Fisher USP <921> 1a method with a CCI acceptance criteria for release.

Inorganic Impurities

Testing for inorganic impurities is performed using a residue on ignition USP <281> method with a C CCI acceptance criteria for characterization.

2.3.S.4 CONTROL OF DRUG SUBSTANCE

Specification

Table 8: PEG2000-DMG Specification

Test	Method	Acceptance Criteria
Appearance	Visual	Solid
Color	Visual	White to off-white
Average molecular weight (Mn)	MALDI-TOF	CCI
Identity [a]	UPLC-CAD-RT	Retention time comparable to reference
	^{1}H-NMR	Conforms: Multiplicity and chemical shift of the ^{1}H-NMR signals are in accordance with the proposed structure of the test item
Purity	UPLC-CAD	CCI
Related impurities	UPLC-CAD	Report RRT and % w/w of all impurities CCI Identified Impurities CCI Unidentified Impurities Each unidentified impurity CCI
	UPLC-CAD qNMR Calculation	CCI Total related impurities
Water content	Karl Fischer (USP <921> 1a, EP 2.5.12)	CCI
Residual solvents		
CCI	HS-GC-FID	CCI
Elemental impurities		
CCI	ICP-MS	CCI
Bacterial endotoxin	USP <85>, EP 2.6.14	
Microbial quality		
TAMC TYMC	USP <61>, EP 2.6.12	CCI

Analytical Procedures

Summaries of analytical procedures specifically developed for mPEG2000-DMG are provided below.

Non-Compendial Analytical Procedures

Appearance and Color

Appearance and color tests are a qualitative visual inspection method. A sample is inspected under ambient working light conditions for inhomogeneity, discoloration, foreign matter and any unusual appearance.

Average Molecular Weight (Mn)

The average molecular weight of mPEG2000-DMG is obtained using MALDI-TOF technique. An aliquot of each sample CCI spotted, and dried with heat gun. CCI fragments are used to calibrate the instrument.

Identity by 1H-NMR

The method is a CCI technique in which the ^{1}H-NMR CCI of a sample at ~10mg/mL is compared against intrinsic compound functional group chemical shifts to confirm identity of the sample CCI .

Identity by UPLC-CAD

This CCI UPLC method reports the identification of mPEG2000-DMG by comparing the retention time of the sample against a well-characterized reference standard. The details of the UPLC-CAD method are listed in the next section.

Purity and Related Impurities by UPLC-CAD

This CCI UPLC method utilizes a CCI column with a gradient flow of mobile phases: CCI . Flow rate is set at CCI and the column temperature is CCI . Quantification is based on Charge Aerosol Detection (CAD), reporting as %w/w at a sample concentration of ~20mg/mL in CCI .

CCI by UPLC-CAD

This CCI UPLC method specifically quantitates residual CCI only. This method utilizes a CCI column with a gradient flow of mobile phases: CCI

Flow rate is set at CCI and the column temperature is CCI . Quantification is based on CAD, reporting as %w/w at a sample concentration of ~20mg/mL in CCI .

CCI by qNMR

This qNMR method specifically quantitates residual CCI by leveraging the spectrum of the sample against theoretically expected chemical shifts, reporting results as %w/w. A sample at ~10mg/mL in CCI is compared against intrinsic compound functional group chemical shifts to quantitate of the sample.

Total Impurities

This calculation is based on the sum of all impurities contained in this section, reported as %w/w. It is calculated as 100 %w/w – [Sum of impurities (%w/w from UPLC-CAD) – CCI (%w/w from UPLC-CAD) – CCI (%w/w from qNMR)].

Residual Solvents

The procedure uses a headspace Gas Chromatograph with Flame Ionization Detection (HS-GC-FID) to determine solvent levels by quantitation against solvent standards with results expressed as ppm. The section of solvents is based on the final process step and related purification steps. Sample concentration is ~40mg/mL in CCI for sample.

Elemental Impurities

The procedure uses inductively coupled mass spectrometry (ICP-MS) to determine each elemental impurity's content by quantitation against standards with results expressed as ppm. The USP <232> parenteral panel of elements namely Cd, Pb, As, Hg, Co, V, Ni, Li, Sb, Cu are quantitated against standard solutions. The sample is mineralised by microwave with strong inorganic acids and the digestion solution is diluted and directly measured.

Compendial Analytical Procedures

Water Content

The procedure uses a Karl-Fischer direct titration (Method 1a) to measure water content and run against water standards per USP <921> and EP 2.5.12 with results expressed as %w/w.

Endotoxin

This test follows the USP <85> and EP 2.6.14 compendial method and utilizes the gel-clot technique for endotoxin detection with results reported as EU/g.

Microbial Quality

This test follows the USP <61> and EP 2.6.12 procedures by membrane filtration with results reported as CFU/g.

Validation of Analytical Procedures

All non-compendial procedures will be validated, demonstrating each procedure is suitable for its intended use. Method validations are currently on-going. All compendial procedures will be verified, demonstrating each procedure is suitable for its intended use.

Batch Analysis Data

A summary of mPEG2000-DMG lots that have been manufactured to date and the respective batch analysis data are provided in the tables below.

Table 9: Batch Analyses Data for PEG2000-DMG Lots

PEG2000-DMG Lot Number			Lot CF0852		Lot CF0995	
Date of Manufacture			October 2020		November 2020	
Manufacturing Location			[redacted]			
Scale (kg)			[redacted]			
Batch Size (kg)						
Test	**Acceptance Criteria**		**Results**			
Appearance	Solid		solid		solid	
Color	White to off-white		white		white	
Average molecular weight (Mn)	[redacted]					
Polydispersity						
Identification [b] by UPLC-CAD and ^{1}H-NMR	Conforms	UPLC-CAD: Comparable (Retention time comparable to reference)	Conforms	Comparable	Conforms	Comparable
		^{1}H-NMR: Conforms (Multiplicity and chemical shift of the ^{1}H-NMR signals are in accordance with the proposed structure of the test item)		Conforms		Conforms
Purity by UPLC-CAD	[redacted]					
Related Impurities	Report RRT and % w/w of all impurities [redacted]					
	Identified Impurities by UPLC-CAD (% w/w)					
	[redacted]					
					ND	
					ND	
	Unidentified Impurities by UPLC-CAD (% w/w)					
	Each unidentified impurity [redacted]		RRT	% w/w	RRT	% w/w
			[redacted]			
	[redacted] by UPLC-CAD (% w/w)	[redacted]	[redacted]			
	[redacted] by qNMR (% w/w)		ND		ND	
	Total related impurities [redacted] (% w/w)		[redacted]			
Water content by Karl Fischer (USP <921> 1a, EP 2.5.12)	[redacted]					
Residual solvents by HS-GC-FID						
[redacted]	[redacted]					
Elemental impurities by ICP-MS						
[redacted]	[redacted]					
Bacterial endotoxin by USP <85>, EP 2.6.14						
Microbial quality by USP <61>, EP 2.6.12						
TAMC	[redacted]					
TYMC						

(a) The average molecular weight data were generated as characterization data while the method is being qualified for use.
(b) The method used for identity of mPEG2000-DMG is not prescribed per Moderna specification. Both UPLC-CAD-RT and ^{1}H-NMR methods are performed for Identity testing at [redacted]. The respective acceptance criterion are provided in the table above.

Justification of Specification

Table 10: PEG2000-DMG Justification of Specifications

Test Attribute	Acceptance Criteria		Justification
Appearance and Color	White to Off-white, Solid		CCI
Identification by UPLC-CAD and ^{1}H-NMR [(a)]	See criteria per test attribute below		
	Conforms	UPLC-CAD: Comparable (Retention time comparable to reference)	
		^{1}H-NMR: Conforms (Multiplicity and chemical shift of the ^{1}H-NMR signals are in accordance with the proposed structure of the test item)	
Average Molecular Weight by MALDI-TOF (Mn)	CCI		
Purity by UPLC-CAD			
Related Impurities	Report RRT and % w/w of all impurities CCI		
	Identified Impurities by UPLC-CAD (% w/w) CCI		
	Unidentified Impurities by UPLC-CAD (% w/w)		
	Each unidentified impurity CCI		
	CCI by UPLC-CAD (% w/w)		
	CCI by qNMR (% w/w)		
	Total related impurities (% w/w) (calculation)		
Water Content by Karl-Fischer	CCI		

2.3.S.5 REFERENCE STANDARDS OR MATERIALS

Development mPEG2000-DMG Lot rok-001-136, prepared and tested by CCI, and is the current interim reference standard for mPEG2000-DMG. The qualification of the primary reference standard is ongoing which is stored at -20°C ± 5°C , well characterized with a known purity and will be retested annually.

2.3.S.6 CONTAINER CLOSURE SYSTEM

The primary packaging for mPEG2000-DMG consists of FDA and EU food contact grade polyethylene bags (PE), compliant with USP <661>, USP <87>, USP <88>, and Commission Regulation (EU No. 10/2011).

Each PE bag is purged with inert gas (argon or nitrogen) and sealed. The PE bag is then placed into a multi-layered aluminium pouch lined with low-density polyethylene (LDPE) on the inner surface. The aluminium pouches are flushed with inert gas (argon or nitrogen) and a desiccant added prior to being heat-sealed.

Specifications for both components have been provided as well as Certificate of Conformance and Compliance Statements.

2.3.S.7 STABILITY

mPEG2000-DMG is stored at the intended condition of -20°C ± 5°C under inert gas. Development mPEG2000-DMG Lot RD-02254 was initially placed onto stability at the intended condition of -20°C ± 5°C under inert gas and at 5°C ± 3°C under inert gas. mPEG2000-DMG GMP Lot CF0852 is placed on stability at the recommended storage condition of -20°C ± 5°C, and at -75°C ± 5°C, 5°C ± 3°C and 25°C ± 2°C/60% ± 5% RH all under inert gas, in accordance with ICH Q1A (R2) guidelines. Development and GMP mPEG2000-DMG stability samples are stored in representative container closures.

An overview of the mPEG2000-DMG lots placed on stability with the site of manufacture, date of manufacture and batch size are presented in the table below.

Table 11: Summary of PEG2000-DMG Stability Lots

Batch Number	Manufacturer	Manufacturing Date	Batch Size	Data Available at Intended Storage Condition -20°C ± 5°C
RD-02554	CCI [redacted]	September 2020	11.0 kg	1 month
CF0852		October 2020	23.2 kg	Initial

Stability protocols for the development mPEG2000-DMG Lot RD-02554 and the GMP mPEG2000-DMG Lot CF0852 have been provided. The latter is shown below.

Table 12: GMP PEG2000-DMG Stability Protocol

Condition	Time Interval (Months)								
	0	1	3	6	9	12	18	24	36
CCI [redacted]	XY	X	X	X	X	X	X	X	X
		X	X	X	X	XY	X	XY	XY
		X	X	X	X	X	N/A	N/A	N/A
		X	X	X	X	X	N/A	N/A	N/A

X = Appearance, color, purity by UPLC-CAD, related impurities by UPLC-CAD, CCI [redacted] by UPLC-CAD, myristic anhydride by qNMR and water content
Y = Microbiological quality and bacterial endotoxins
N/A = Not Applicable, time point not required per stability protocol

One (1) month of stability data at CCI and at CCI are available for Development mPEG2000-DMG Lot RD-02554. All acceptance criteria were met.
There is currently no stability data are available for GMP mPEG2000-DMG Lot CF0852. This section will be updated as stability data becomes available.
Based on the current stability data available for mPEG2000-DMG, a shelf life of six (6) months is proposed.
Post-marketing stability protocol for GMP mPEG2000-DMG is shown below.

Table 13: Post-Marketing Stability Protocol for GMP PEG2000-DMG Lots

Condition	Time Interval (Months)								
	0	1	3	6	9	12	18	24	36
CCI	XY	X	X	X	X	X	X	X	X
		X	X	X	X	XY	X	XY	XY
		X	X	X	X	X	N/A	N/A	N/A
		X	X	X	X	X	N/A	N/A	N/A

X = Appearance, color, purity by UPLC-CAD, related impurities by UPLC-CAD, CCI by UPLC-CAD, CCI by qNMR and water content
Y = Microbiological quality and bacterial endotoxins
N/A = Not Applicable, time point not required per stability protocol

2.3.S.2.3 Control of Materials CCI

A comparability assessment of PEG2000-DMG from the two suppliers has been performed. PEG2000-DMG is commercially available but is not contained in any approved products. PEG2000-DMG (Option A) is manufactured under cGMPs by CCI and also by CCI (Option B). The product specifications are shown in the tables below.

Table 14 PEG2000-DMG (Option A, CCI)

Attribute	Acceptance Criteria
Vendor Specifications	
Appearance	White to off-white powder
Identification	Conforms structure
Average molecular weight	CCI
Purity GM-020 (%)	
Content of Monomyristoylglycerol-PEG2000 (%)	Report value
Content of other PEG derivatives (%)	Report value
Content of free fatty acid (%)	Report value
Content of unknown (%)	Report value
Moisture (%)	CCI
Residual solvent (ppm)	
CCI	
Endotoxin (EU/g)	
TAMC (CFU/g)	
TYMC (CFU/g)	
CCI	
CCI (CCI)	
CCI	

Abbreviations: BSE/TSE = bovine spongiform encephalopathy/transmissible spongiform encephalopathy; CFU = colony-forming unit(s); EU = endotoxin unit(s); TAMC = total aerobic microbial count; TYMC = total yeast and mold count

Table 15: PEG2000-DMG (Option B, CCI)

Attribute	Acceptance Criteria
Vendor Specifications	
Appearance	Solid, white to off-white
Identification	Conforms structure
Average molecular weight	CCI
Purity (% w/w)	
CCI	
Total impurities (% w/w)	
Moisture (%)	
Residual solvent (ppm)	
CCI	
Endotoxin (EU/g)	
TAMC (CFU/g)	
TYMC (CFU/g)	
CCI	
CCI)	
CCI	

Abbreviations: BSE/TSE = bovine spongiform encephalopathy/transmissible spongiform encephalopathy; CFU = colony-forming unit(s); EU = endotoxin unit(s); TAMC = total aerobic microbial count; TYMC = total yeast and mold count

CCI is the registered manufacturer of the critical raw material, PEG2000-DMG. In order to support the inventory demand of mRNA-1273 vaccine, an additional manufacturer has been qualified to supply PEG2000-DMG, for use in CCI mRNA-1273 LNP (as part of CCI). CCI , manufacturer of SM-102 lipid, is currently qualified as a supplier within the Moderna Quality Management System. CCI has performed process development and scale-up activities to produce PEG2000-DMG in sufficient quantities of commercially representative material to support the manufacture CCI mRNA-1273 LNP.

A comparability assessment between the CCI PEG2000-DMG and CCI PEG2000-DMG consisted of two elements. The first is a comparison of critical material attributes. The results of this comparison is presented in Table 30 and shows that the critical material attributes of CCI PEG2000-DMG are equivalent to CCI PEG2000-DMG. No additional toxicology assessment has been performed on the CCI arma PEG2000-DMG material as the chemical entity is the same as CCI PEG2000-DMG with equivalent impurity profiles.

Table 16: Comparability of Critical Material Attributes between PEG2000-DMG Manufacturers

Critical Material Attributes	Critical Material Attributes Reference Criteria	CCI Lot Pre-005-145-UK	CCI Lot 1902GM21	Assessment of Equivalence
Purity by UPLC-CAD	CCI			Equivalent
Average Molecular Weight (Mn) by MALDI-TOF				Equivalent
Identity	Conforms	Pass	Pass	Equivalent
Water Content by Karl Fischer	CCI			Equivalent
Residual Solvents by GC-FID	< ICH Q3C Option 1 limits for process solvents	None detected	1 ppm chloroform	Equivalent
Elemental Impurities by ICP-MS	CCI	< LOQ < LOQ < LOQ < LOQ	Pass	Equivalent

The second element of comparability assessment for the PEG2000-DMG material consisted of comparing small scale representative mRNA-1273 DP Lots each manufactured with PEG2000-DMG from CCI . mRNA1273 DP Lot DH-04708.1 was manufactured using CCI PEG2000-DMG and mRNA-1273 DP Lot DH-04708.2 was manufactured using CCI PEG2000-DMG. mRNA-1273 DP Lots DH-04708.1 and DH-04708.2 were compared for critical material attributes of mRNA-LNPs and over 14 day and 35 day time points at -20°C ± 5°C , 5°C ± 3°C and 25°C ± 3°C storage conditions. This study is on-going and will conclude after 3 month, 6 month, 9 month and 12 month time points. The comparison of data are provided in the tables below and support the comparability of CCI PEG2000-DMG to CCI PEG2000-DMG.

In conclusion, the critical material attributes of PEG2000-DMG produced by either CCI or CCI showed no significant difference and the materials are considered equivalent. Comparison of the critical material attributes of LNPs in the small-scale mRNA-1273 DP lots produced both manufacturers of PEG2000-DMG demonstrates that PEG2000-DMG produces equivalent material.

Based on these analyses, both manufacturers of PEG2000-DMG are equivalent and suitable for use with mRNA1273 Drug Product Production.

Table 17: Stability Assessment of mRNA-1273 DP manufactured with CCI [redacted] PEG2000-DMG Critical Raw Material

Test	Analytical Method	T = 0, -20°C ± 5°C		T = 14 days, 5°C ± 3°C		T = 14 days, 25°C ± 3°C	
		DH-04708.1	DH-04708.2	DH-04708.1	DH-04708.2	DH-04708.1	DH-04708.2
		CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]
Appearance	Visual	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.
Total RNA content	Anion Exchange HPLC	CCI [redacted]					
Purity	RP- HPLC						
Product-related impurities							
% RNA encapsulation	CCI [redacted]						
Mean particle size	Dynamic Light Scattering						
Polydispersity							
Lipid identification							
SM-102	UPLC-CAD	Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Cholesterol		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
DSPC		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
PEG2000-DMG		Conforms	Conforms	Conforms	Conforms	Conforms	Conforms
Lipid content							
SM-102	UPLC-CAD	CCI [redacted]					
Cholesterol							
DSPC							
PEG2000-DMG							
Lipid impurities	UPLC-CAD	No impurities detected	No impurities detected	CCI [redacted]			
pH	USP <791>	CCI [redacted]		NT	NT	NT	NT
Osmolality	USP <785>			NT	NT	NT	NT

Abbreviations: RT = retention time; RRT = relative retention time

Table 18: Stability Assessment of mRNA-1273 DP manufactured with CCI [redacted] and CCI [redacted] PEG2000-DMG Critical Raw Material

Test	Analytical Method	T = 35 days, -20°C ± 5°C		T = 35 days, 5°C ± 3°C		T = 35 days, 25°C ± 3°C	
		DH-04708.1	DH-04708.2	DH-04708.1	DH-04708.2	DH-04708.1	DH-04708.2
		CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]	CCI [redacted]
Appearance	Visual	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.	White to off-white dispersion. Essentially free of particulates.
Total RNA content	Anion Exchange HPLC	CCI [redacted]					
Purity	RP- HPLC						
Product-related impurities							
% RNA encapsulation	CCI [redacted]						
Mean particle size	Dynamic Light Scattering						
Polydispersity							
Lipid content							
SM-102	UPLC-CAD	CCI [redacted]					
Cholesterol							
DSPC							
PEG2000-DMG							
Lipid impurities	UPLC-CAD	No impurities detected	No impurities detected	CCI [redacted]			

Abbreviations: RT = retention time; RRT = relative retention time