	Technical Summary	Date: 16DEC2020
100 Tech Drive Norwood, MA 02062 www.modernatx.com	Project: mRNA-1273 Drug Product UDP Lot: 6007320011 (Catalent Lot 038K20) LDP Lot: 7006520014 (Catalent Lot 038K20A) Event: REC 283121	Page 1 of 2

1. Triggering Event Summary

- 1.1. **Problem Statement:** During filling start-up activities for Lot 038K20 at Catalent, Bloomington, IN, the fill/finish facility for mRNA-1273 Drug Product, the operators noticed that product had begun to leak from the (b) (4). As the leak was (b) (4), the sterile boundary had been breached. The operators immediately clamped the tubing to stop the leak. No product had been filled at the time of detection. The product was stored in 2-8°C for ~8 hours. A second redundant sterile filtration pathway was setup and the batch was refiltered following process steps outlined in the batch record. Additional pages from the formulation section of the MBR were issued for Lot 038K20 to document the re-filtration.

2. Root Cause:

- 2.1. The most probable root cause of the aseptic leak was determined to be a material failure (connector fault).

3. CAPAs:


3.1. Immediate Actions

- 3.1.1. Re-filtration performed: Leaks are addressed per A-SOP-21-01-066, Drug Product Formulation and Filling Product Leaks Program, a leak (b) (4) is an overall medium risk to product SISPQ (minimal risk to bioburden due to (b) (4) environment and gowning, and assuming subsequent sterile filtration).
- 3.1.2. The operators immediately clamped the tubing to stop the leak. The product was stored in 2-8°C for ~8 hours.
- 3.1.3. Manufacturing Technology Specialist reviewed the (b) (4). The (b) (4) appeared to be fully engaged when they performed a visual review of the connection.
- 3.1.4. A second filtration pathway was setup. Bioburden and (b) (4) were resampled, and the batch was re-filtered (only (b) (4) of the batch was able to be filtered during the subsequent filtration).

3.2. Long Term Actions

- (b) (4) vendor investigation initiated by Catalent
- Conduct awareness communication of this issue per A-SOP-03-01-008 Event and Deviation Reporting to remind operators to handle (b) (4) with care and to inspect for damaged (b) (4) prior to making the Aseptic connection.

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	Technical Summary	Date: 16DEC2020
100 Tech Drive Norwood, MA 02062 www.modernatx.com	Project: mRNA-1273 Drug Product UDP Lot: 6007320011 (Catalent Lot 038K20) LDP Lot: 7006520014 (Catalent Lot 038K20A) Event: REC 283121	Page 2 of 2

4. Product Impact

4.1. In-process and release testing passed all specifications:

- The leak potentially impacted sterility of product as a result the leak. The product underwent re-filtration on 26NOV20. Additional bioburden and (b) (4) (b) (4) samples were collected from the re-filtration.
- Pre-filtration bioburden results from both the initial and re-filtration were within specification with counts of (b) (4)
- Final Product Sterility Testing, as well as supplemental B/M/E PPQ sterility testing, was found within specification.
- (b) (4) results pre- and post- the initiation sterile filtration were within specification (b) (4)
- All release testing is within specification (see attached CoA)

4.2. Impact of Refiltration: Development study data is available for mRNA 1273 diluted Drug product for undergoing multiple filtrations. Moderna document PD-MEM-0428 summarizes work performed to evaluate diluted bulk mRNA-1273 Drug Product sterile filtered for a total of (b) (4) Samples were collected after each of the (b) (4) filtrations and analyzed for particle diameter, encapsulation efficiency, polydispersity, subvisible particulate, RNA content and lipid content. The biophysical and content characteristics of the drug product from this study remained within acceptance criteria for all the materials generated from re-processing.

4.3. Leachables Assessment: Moderna Document PD-MEM-0429 summarizes that re-filtration of Lot 038K20 through (b) (4) sterilizing grade filters does not pose any additional safety risk due to leachables from these extra filters.

5. Disposition

5.1. Moderna release of this batch will be put on hold pending response from FDA.

Document Approvals
Approved Date: 16 Dec 2020

Task: Approval Task Verdict: Approve	Paul Dawidczyk, (b) (6) @modernatx.com) Regulatory Approval 16-Dec-2020 20:06:46 GMT+0000
Task: Approval Task Verdict: Approve	(b) (6) @modernatx.com) MS&T Approval 16-Dec-2020 20:10:23 GMT+0000
Task: QA Approval Task Verdict: Approve	Jennifer White, (b) (6) @modernatx.com) Quality Assurance Approval 16-Dec-2020 20:26:16 GMT+0000

CERTIFICATE OF ANALYSIS

Product Description:	mRNA-1273	Moderna Part #:	70065
Manufacturer Name:	Catalent	Container/Closure:	10R Ompi Glass Vial, 20 mm Stopper, 20 mm Cap
Manufacturer Lot:	038K20A		
Moderna Lot Number:	7006520014	Specification:	SPC-1128
Date of Manufacture:	25Nov2020	Expiry Date:	25Jun2021

Product Attribute	Method	Parameter	Specification	Result
Appearance	SOP-0278	Appearance - Color	White to off-white dispersion.	White to off-white dispersion
		Appearance - Particulates	May contain visible, white or translucent product-related particles	Essentially Free of Particulates
Concentration	SOP-0999	RNA Content	(b) (4) (Target: 0.20 mg/mL)	
Identity	SOP-1032	Identity	(b) (4)	
Purity	SOP-0996	Purity		
		% IG1		
		% IG2		
		% IG3		
% RNA Encapsulation	SOP-1000	% Encapsulation		
In vitro Translation	SOP-0937	Result		
pH	SOP-0288	pH		
Osmolality	SOP-0279	Osmolality		
Dynamic Light Scattering	SOP-0998	Particle Size		
		Polydispersity		
Lipid Identification	SOP-1001	SM102		
		Cholesterol		

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CERTIFICATE OF ANALYSIS

Product Description:	mRNA-1273	Moderna Part #:	70065
Manufacturer Name:	Catalent	Container/Closure:	10R Ompi Glass Vial, 20 mm Stopper, 20 mm Cap
Manufacturer Lot:	038K20A		
Moderna Lot Number:	7006520014	Specification:	SPC-1128
Date of Manufacture:	25Nov2020	Expiry Date:	25Jun2021

Product Attribute	Method	Parameter	Specification	Result
Lipid Content		DSPC	(b) (4)	
		PEG-DMG		
		SM102		
		Cholesterol		
Lipid Impurities		DSPC		
		PEG-DMG		
		% Area 1		
		% Area 2		
		% Area 3		
		% Area 4		
		% Area 5		
		RRT 1		
		RRT 2		
		RRT 3		
		RRT 4		
		RRT 5		
		% Total Impurities		
Particulate Matter	SOP-0509	10 µm particles per container		

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CERTIFICATE OF ANALYSIS

Product Description:	mRNA-1273	Moderna Part #:	70065
Manufacturer Name:	Catalent	Container/Closure:	10R Ompi Glass Vial, 20 mm Stopper, 20 mm Cap
Manufacturer Lot:	038K20A		
Moderna Lot Number:	7006520014	Specification:	SPC-1128
Date of Manufacture:	25Nov2020	Expiry Date:	25Jun2021

Product Attribute	Method	Parameter	Specification	Result
		25 µm particles per container	(b) (4)	
Container Content	SOP-0950	Container Content	>= 5.0 mL (>=10 doses of 0.5 mL from one vial)	(b) (4)
Bacterial Endotoxins	USP <85>	Bacterial Endotoxins	(b) (4)	
Sterility	USP <71>	Sterility		

This material meets specification: Yes

Revision History:

1.0 - Original

Unlabeled Drug Product Lot 6007320011

Drug Substance Manufacturer: Moderna, Norwood, MA

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Document Approvals
Approved Date: 15 Dec 2020

Approval Verdict: Approved	Steven Anderson, (b) (6) @modernatx.com) Quality Control Approval 15-Dec-2020 19:15:46 GMT+0000
QA Approval Verdict: Approved	(b) (6) (b) (6) @modernatx.com) Quality Assurance Approval 15-Dec-2020 21:21:43 GMT+0000

Site	State	Date Current State	Date Closed	Parent Record #
Bloomington, US	Closed - Done	16-Dec-2020	16-Dec-2020	N/A

General Information

Originator: (b) (6) **Date Opened:** 26-Nov-2020

Short Description: Leak at sterile connection and Overall Accountability Not in Range MBR 256-100-300P-101 Lot 038K20 WO# 4377814

Assigned To: (b) (6) **Date Due:** 26-Dec-2020

Description:

- Project: 256-10-300P
- Master Batch Record (MBR): 256-100-300P-101
- Lot: 038K20
- Item Number: N/A
- Room/Location: (b) (4)
- Date/Time of Occurrence: 0015 on 26NOV20
- Date/Time of Observation: 0015 on 26NOV20

During start-up activities for MBR 256-100-300P-101 Lot 038K20, Equipment Lead (b) (6) and Manufacturing Senior Associate (b) (6) noticed that product had begun to leak from the (b) (4). (b) (6) and (b) (6) immediately clamped of the tubing to stop the leak. Value Stream Supervisor (b) (6) and QA Representative (b) (6) were contacted and the issue was escalated. A rapid response was held with the client and Manufacturing Technology Senior Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Manufacturing Technology Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Value Stream Manager (b) (6), Value Stream Supervisor (b) (6), QA Manager (b) (6), QA Representative (b) (6), QA/Validation Director (b) (6), Validation Senior Manager (b) (6), and Senior Project Manager (b) (6). Decision was made to reperform sterile filtration. Bioburden and (b) (4) samples will be re-pulled. The (b) (4) will be retained for investigation.

Project code: 256-100-300P
Master Batch Record Number: 256-100-300P-101
Item Number:
Room/Location: (b) (4)
Date/time observation: 13DEC20
Date/time occurrence: 26NOV20
Batch record step / SOP step: MBR step (b) (4)

During batch record review, Senior Quality Assurance Representative (b) (6) observed that the accountability in step (b) (4) of the MBR was (b) (4) which was outside of the acceptable tolerance. Accountability should be 100%. During filling activities, a leak occurred, which caused refiltration to occur. This incident is captured in another rec. There was not original refiltered weight because of a product leak, the filling of vials before the leak occurred, and reconciliation. When refiltration occurred, there was no original tare weight for the pre-refilter product. Back calculation was performed to get the pre-refiltered weight, which could have incorrectly represented the prefiltered weight, leading to this discrepancy in

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accountability.

Classification

Classification: Major

Deviation Information

Date of Occurrence:	26-Nov-2020	Date of Detection:	26-Nov-2020
Type:	Material / Product - OOS / Defect	Sub-Type:	Non-Conforming Material / Component
Local Deviation Type:	N/A	Process:	Filling
Department:	Drug Product - Filling	Location/Area:	(b) (4)
Customer(s) Affected?	Yes	Is Equipment Involved?:	No
Product(s) Affected?:	Yes	Material(s) Affected?:	No

Immediate Actions**Immediate Actions:**

(b) (6) and (b) (6) immediately clamped off the tubing to stop the leak. Value Stream Supervisor (b) (6) and QA Representative (b) (6) were contacted and the issue was escalated.

A rapid response was held with the client and Manufacturing Technology Senior Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Manufacturing Technology Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Value Stream Manager (b) (6), Value Stream Supervisor (b) (6), QA Manager (b) (6), QA Representative (b) (6), QA/Validation Director (b) (6), Validation Senior Manager (b) (6), and Senior Project Manager (b) (6). Decision was made to reperform sterile filtration.

Bioburden and (b) (4) samples will be re-pulled. The (b) (4) will be retained for investigation.

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Impact Analysis**Impact Analysis:**

RPN Attached

Risk Analysis:

RPN Attached

Recurring Deviation?: No**Impact & Risk Attachments:** Attachment 1 to Rec 283121, RPN.pdf**Notification****Notification Required?:** No

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Investigation & Root Cause

Root Cause Analysis:

>>Man (Personnel):

- Senior Manufacturing Associate (b) (6) whom performed the connection was fully trained to applicable procedure A-SOP-21-01-040, Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing and assessment A-PBA-21-01-040-A, Performance Based Assessment for Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing. (b) (6) completed the PBA on 03APR20.
- Manufacturing Associate (b) (6) whom performed the verification was fully trained to applicable procedure A-SOP-21-01-040 and assessments A-PBA-21-01-040-A. (b) (6) completed the PBA on 01SEP20.

Human error was not a contributing factor to this deviation.

>>Method (Process):

- A-SOP-21-01-059, Inspect Pre-Sterilized Single Use Items was reviewed and provides instruction to confirm connections are secure.
- A-SOP-21-01-040, Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing was reviewed. The procedure provides instructions on how to properly perform connections involving (b) (4). The procedure also provides pictures along with text to aid associates in performing the connection. The procedure provides examples of proper connections and other potential defects/concerns related to making aseptic connections.
- A-PBA-21-01-040-A, Performance Based Assessment for Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing includes performing a connection utilizing (b) (4). Completion of the PBA consist of oral questions and behavioral tasks an employee must perform in front of a Designated Trainer. The PBA allows the employee to demonstrate competency in the performance of job-related tasks.

Method/Process was not a contributing factor for this deviation.

>>Measurement:

- There are no incorrect units of measure, calculations, or standards that impacted this event.

Measurement was not a contributing factor to this deviation.

>>Machine (Equipment/System):

- The equipment/system did not cause the damage to the (b) (4) as there is no specific Catalent equipment is used to create or alter the connection. Within the executed batch record, there was nothing indicating Catalent equipment would cause the (b) (4) to become unengaged.

Equipment/System was not a contributing factor to this deviation.

>>Materials:

- Item Number (b) (4)
- ☐ Per Material Specification Sheet (b) (4), when lots of Item (b) (4) are received, each lot undergoes incoming inspection per A-SOP-09-01-020, Quality Control Inspection of Incoming Materials. Incoming Quality Control

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Inspection for Lot (b) (4) was completed, and the lot was released on 08NOV20. All results passed and there were no non-conformance issues noted.

☐ A review of previous Supplier Complaint Reports and Non-Conforming Material Reports was completed. Within the past 12 months there were none identified for Item (b) (4) related to this issue.

- Item Number (b) (4) :

☐ Per Material Specification Sheet (b) (4), when lots of Item (b) (4) are received, each lot undergoes incoming inspection per A-SOP-09-01-020, Quality Control Inspection of Incoming Materials. Incoming Quality Control Inspection for Lot (b) (4) was completed, and the lot was released on 22NOV20. All results passed and there were no non-conformance issues noted.

☐ A review of previous Supplier Complaint Reports and Non-Conforming Material Reports was completed. Within the past 12 months there were none identified for Item (b) (4) related to this issue.

- There were no noted issues related to the handling of the material. There were no noted issues related to the engagement of the connectors as they visually appear connected properly. Associates are fully trained to performing the connection. Interviews confirmed that the leak occurred with the connectors fully engaged. Based on review of the batch record, interviews, and review of the connectors, (b) (4) are the most likely cause of the leak. Manufacturing Technology Specialist (MT) reviewed (b) (4). MT presumes that the leak most likely is due to an issue within the connector's componentry. This will be assessed with an investigation by the supplier.

Material is the most probable cause of this deviation.

>>Mother Nature (Environment):

- There was nothing unusual noted that occurred during the time of use of the (b) (4) that would impact the connection.

Environment was not a contributing factor to this deviation.

Investigation Detail & Summary:

Event Details:

- Project: 256-10-300P
- Master Batch Record (MBR): 256-100-300P-101
- Lot: 038K20
- Room/Location: (b) (4)
- Date/Time of Occurrence: 0015 on 26NOV20
- Date/Time of Observation: 0015 on 26NOV20

After completion of sterile filtration and during filling start-up activities for MBR 256-100-300P-101 Lot 038K20, Equipment Lead (b) (6) and Manufacturing Senior Associate (b) (6) noticed that product had begun to leak from the (b) (4) (b) (4). The product was connected to the product pathway and when product started to flow from the (b) (4) to the product pathway, the leak was observed.

Immediate Actions:

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(b) (6) and (b) (6) immediately clamped of the tubing to stop the leak. Value Stream Supervisor (b) (6) and QA Representative (b) (6) were contacted and the issue was escalated.

A rapid response was held with the client and Manufacturing Technology Senior Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Manufacturing Technology Manager (b) (6), Associate Manufacturing Technology Specialist (b) (6), Value Stream Manager (b) (6), Value Stream Supervisor (b) (6), QA Manager (b) (6), QA Representative (b) (6), QA/Validation Director (b) (6), Validation Senior Manager (b) (6), and Senior Project Manager (b) (6). Decision was made to reperform sterile filtration. Product was held in 2 – 8 °C storage in (b) (4). Product was placed in at 0230 on 26NOV20 and removed prior to re-filtration at 1059 on 26Nov20. Worst-case time in 2 – 8 °C storage 8 hours 29 minutes.

Re-filtration was performed following process steps outlined in MBR 256-100-300P-101. Additional pages (B pages) from the formulation section of the MBR were issued for Lot 038K20 to document the re-filtration. Bioburden and (b) (4) (b) (4) (b) (4) samples were re-pulled. Re-filtration was performed starting at 1059 on 26Nov20. The initial sterile filtration resulted in (b) (4) Sterile Filtrate Weight. The second sterile filtration resulted in (b) (4) Sterile Filtrate Weight. The (b) (4) was retained for investigation.

Background:

Master Batch Record (MBR) 256-100-300P-101 utilizes (b) (4). The filling process uses a disposable sterile assembly integrated with disposable pathways to transfer sterile product into the final container. Per step (b) (4) of MBR, prior to use, all tubing is to be inspected per A-SOP-21-01-059, Inspect Pre-Sterilized Single Use Items. The packaging is also reviewed for damage per the procedure. Damage could indicate a potential lack of integrity of the tubing assembly.

Additionally, per A-SOP-21-01-059, a gross visual inspection is conducted with ambient light and no magnification for approximately 5 minutes. A gross visual inspection is a brief, overall inspection of a single use assembly with intent to identify major issues that are clearly visible, including but not limited to large particles (>1 mm), holes, and incorrectly assembled components. The procedure also states that during installation of tubing into the peristaltic pumps, all tubing hose barb connections are to be examined to ensure they are secure.

(b) (4)

(b) (4) per A-SOP-21-01-040, Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing. Product is contained in Item Number (b) (4)

Associates whom perform the connection must be trained to procedure A-SOP-21-01-040, Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing. They must also complete a Performance Based Assessment (PBA) A-PBA-21-01-040-A, PBA for Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing.

During filling, any leaks discovered are to be addressed per A-SOP-21-01-066, Drug Product Formulation and Filling Product

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Leaks Program. Per the SOP, leaks are defined as an unintentional and negligible loss of product during processing from a closed system or from a single use assembly due to a loose connection, defect, or other source of damage to equipment that is identified and resolved in a timely manner. Per A-SOP-21-01-066, a leak (b) (4)

(b) (4) environment is an overall medium risk to product SISPQ. The procedures required a deviation to be initiated within (b) (4)

The risk level of medium was determined in RA-17-07-001, Risk Assessment for Product Leaks during Formulation and Filling for Vial, Syringe, and Flexible Filling Lines. The severity of the leak at this connection is leveled as Critical however there are existing mitigations in place to prevent and detect this failure. There are existing mitigations such as (b) (4) gowning and environment and aseptic procedures that provide a level of bioburden control to reduce potential impact to product SISPQ.

Evaluation of Leak

Manufacturing Technology Specialist (MT) reviewed the (b) (4) appear to be fully engaged when they performed a visual review of the connection. However, as a leak was observed at the (b) (4) (b) (4), MT presumes that the leak most likely is due to an issue within the connector's componentry. The visual inspection suggests that the connection was made per manufacturer instructions.

Investigation

Per step (b) (4) in MBR 256-100-300P-101, associates are to "(b) (4)." Senior Manufacturing Associate (b) (6) performed the connection and Manufacturing Associate (b) (6) performed the verification.

Employee Training Records were reviewed for associates (b) (6) who performed and verified activities per step (b) (4). Training for the associates is current on A-SOP-21-01-040, Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing and Performance Based Assessment (PBA) A-PBA-21-01-040-A, PBA for Installation and Usage of Disposable Sterile Connectors in Parenteral Manufacturing. Additionally, they are also current on A-SOP-21-01-059 Inspect Pre-Sterilized Single Use Items, (b) (4), Inspect Pre-Sterilized Single Use Items, and A-PBA-21-01-059 (A), Performance Based Assessment for Pre-Use of Pre-Sterilized Single Use Items.

There were no events record in the event log related to this step, indicating there were no issues related to the performing the connection with the exception of the leak that was observed. There was nothing unusual noted that occurred during the time of use of the (b) (4) that would impact the connection. Review of events and deviations in (b) (4) resulted in no other occurrences of leaks that occurred related to (b) (4) for lot 038K20. More than (b) (4) are made during the processing of project 256-100-300P-101. The review also did not find any other records wherein the (b) (4) leaked during use for sterile connections, yet it appeared to be fully engaged.

Per A-SOP-21-01-040, there should be a click from each side of the coupled connectors. Additionally, the procedure instructs to visually ensure that the connectors are secured by confirming the tabs are in the correct position. The associates stated that when the product was hooked up to the (b) (4), they heard the two clicks associated with (b) (4) activation. They performed the visual inspection as required by A-SOP-21-01-040 to ensure the connectors were fully engaged. The auditory and visual inspection suggested that the connection was made per manufacturer instructions. The associates also confirmed that there no issues noted with the paper strips/seals when

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removed after connection was made.

Based on review of the batch record, interviews, and review of the connectors, the (b) (4) are the most likely cause of the leak. Connection made is between Item Number (b) (4) and Item Number (b) (4). Per the batch record, the Catalent lot number of item (b) (4) used for lot 038K20 is (b) (4). The Catalent lot number of item (b) (4) used for lot 038K20 is (b) (4).

Materials History

Item Number (b) (4) :

☐ Per Material Specification Sheet (b) (4), when lots of Item (b) (4) are received, each lot undergoes incoming inspection per A-SOP-09-01-020, Quality Control Inspection of Incoming Materials. Incoming Quality Control Inspection for Lot (b) (4) was completed, and the lot was released on 08NOV20. All results passed and there were no non-conformance issues noted.

☐ A review of previous Supplier Complaint Reports and Non-Conforming Material Reports was completed. Within the past 12 months there were none identified for Item (b) (4) related to this issue.

Item Number (b) (4) :

- Per Material Specification Sheet (b) (4), when lots of Item (b) (4) are received, each lot undergoes incoming inspection per A-SOP-09-01-020, Quality Control Inspection of Incoming Materials. Incoming Quality Control Inspection for Lot (b) (4) was completed, and the lot was released on 22NOV20. All results passed and there were no non-conformance issues noted.

- A review of previous Supplier Complaint Reports and Non-Conforming Material Reports was completed. Within the past 12 months there were none identified for Item (b) (4) related to this issue.

As the issue is related to a vendor-supplied material, an action from this deviation has been created to initiate a Supplier Complaint per A-SOP-12-01-036, Vendor Complaint. On 02DEC20, QA Representative (b) (6) was notified initiate Supplier Complaint Report (SCR).

Root Cause Analysis:

Refer to Root Cause Analysis field.

Trending:

Refer to Recurring Deviation Comments field.

SISPQ Impact:

The leak potentially impacted sterility of product. The product underwent re-filtration on 26NOV20. Additional bioburden (b) (4) and (b) (4) samples were collected from the re-filtration. Finish Product samples were collected when filling was resumed after re-filtration.

CATALENT CONFIDENTIAL AND PROPRIETARY INFORMATION

Report template: (Redacted) Deviation Single Report with Family Summary v1.0

Report run by: (b) (6) on 16-Dec-2020 at 15:34 (Central Standard Time)

Page 8 of 10

Disclaimer: This is a redacted report - every effort has been made to remove fields containing confidential information from this report. Please check all written content to ensure confidential information is not included.

FDA-CBER-2022-1614-4805408

- Post initial filtration In-Process Bioburden Testing was found within specification for Sample description (b) (4) assigned LIMS (Laboratory Inventory Management System) ID 1720984 and Sample description (b) (4) assigned LIMS ID 1720985. Both samples had a bioburden count of (b) (4)
- Post re-filtration In-Process Bioburden Testing was found within specification for Sample description (b) (4) assigned LIMS ID 1727488 and Sample description (b) (4) assigned LIMS ID 1727489. Both samples had a bioburden count of (b) (4)
- Final Product Sterility Testing was found within specification for Sample description (b) (4) assigned LIMS ID (b) (4) and Sample description (b) (4) assigned LIMS IDs 1720992, 1721475, & 1721476. The sample IDs are for the Beginning, Middle, and End of filling respectively.
- Initial Product (b) (4) Testing was found within specification for Sample description (b) (4) LIMS ID 1720980. The result from the testing was reported as (b) (4)
- Post re-filtration Product (b) (4) Testing was found within specification for Sample description (b) (4) LIMS ID 1727476. The result from the testing was reported as (b) (4)

(b) (6) provided a memo (PD-MEM-0428) documenting no expected impact to the mRNA-1273 drug product due to the refiltration. Reference Attachment 3 of the record. Additionally, (b) (6) provided a memo (PD-MEM-0429) stating low risk of additional leachable impact due to the refiltration. Reference Attachment 4 of the record. All (b) (6) release testing results were within specification.

Based on product testing, there is no SISPQ impact from after completion of re-filtration for lot 038K20. The lot is recommended for release.

Conclusion

The leak was caused by the connection of the (b) (4) between Item Number (b) (4) and Item Number (b) (4). As both items are purchased materials, a Supplier Complaint to be opened and submitted to manufacturers.

Actions

- Quality Assurance Supply Chain to open an SCR to have the supplier investigate the component issue.
- Conduct awareness communication of this issue per A-SOP-03-01-008 Event and Deviation Reporting to remind operators to handle (b) (4) with care and to inspect for damaged (b) (4) prior to making the Aseptic connection.

Root Cause Attachment 3 to REC 283121 - Client Memo Reprocessing.pdf
Attachment(s): Attachment 4 to REC 283121 - Client Memo Leachables.pdf

Root Cause Grid

Row #	Cause Type	Cause Category	Cause Sub-Category
1	Possible / Probable Cause	Materials	Quality Issue

Action Information

Action Required?: Yes

CATALENT CONFIDENTIAL AND PROPRIETARY INFORMATION

Report template: (Redacted) Deviation Single Report with Family Summary v1.0

Report run by: (b) (6) on 16-Dec-2020 at 15:34 (Central Standard Time)

Page 9 of 10

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FDA-CBER-2022-1614-4805409

Effectiveness Check

Effectiveness Check Required?: Yes

Effectiveness Check Date Due: 31-May-2021

Effectiveness Check Plan:

Verify SCR has been initiated.

Verify communication related to (b) (4) has been completed.

Customer Approval

Customer Approval Required?: Yes

Customer Approval Received?: Yes

Record Signatures

Supervisor Approval By: (b) (6)

Supervisor Approval On: 16-Dec-2020 2:32 pm

Quality Approval By: (b) (6)

Quality Approval On: 16-Dec-2020 3:12 pm

Optional Approver 1 Function: Quality

Optional Approval 1 By: (b) (6)

Optional Approval 1 On: 16-Dec-2020 2:57 pm

Child Hierarchy:

This section will report dependent children and any descendants for the selected record.

<u>REC ID</u>	<u>Project</u>	<u>Date Due</u>	<u>Date Completed</u>	<u>PR State</u>	<u>Short Description</u>
283121	Deviation	26-Dec-20	16-Dec-20	Closed - Done	Leak at sterile connection and Overall Accountatbility Not in Range MBR 256-100-300P-101 Lot 038K20 WO# 4377814
291345	Action	31-Jan-21		Work in Progress	Quality Assurance Supply Chain to open an SCR to have the supplier investigate the component issue.
291349	Action	26-Feb-21		Work in Progress	Conduct awareness communication for (b) (4)

CATALENT CONFIDENTIAL AND PROPRIETARY INFORMATION

Report template: (Redacted) Deviation Single Report with Family Summary v1.0

Report run by: (b) (6) on 16-Dec-2020 at 15:34 (Central Standard Time)

Page 10 of 10

Disclaimer: This is a redacted report - every effort has been made to remove fields containing confidential information from this report. Please check all written content to ensure confidential information is not included.

FDA-CBER-2022-1614-4805410

Catalent BIOLOGICS	Document Number:	N/A	Page 1 of 3
Title: Impact Analysis and Risk Priority Number (RPN) Calculation Template			

Reference A-SOP-03-01-008, Deviation Report

Record Information		
Record #	Impacted Lot(s)	Scribe Initials/Date
283121	038K20	(b) (6) 27NOV20
RPN Attendees		
<ul style="list-style-type: none"> • Include Initial Sets/Department of all individuals present. • At minimum QA, a Supervisor or Manager from the affected department. 		
(b) (6)	(QA)	(b) (6) (MFG) N/A
	(MFG)	N/A
	(MFG)	N/A
	(ENG)	N/A

Impact Analysis Questions	
What is the potential impact to SISPQ?	No SISPQ impact to sterility, but product impact will be assessed.
Are multiple lots impacted by this event?	No.
Are the impacted products under Catalent control?	Yes.
If equipment and/or product on hold, what is the justification for moving forward with processing? (N/A if no items are on hold due to this event)	N/A
Additional Information (As Applicable)	Supply Chain Quality to be notified of potential complaint.

Attachment #:	1	Record #:	283121	Initials/Date:	(b) (6) 27NOV20
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Catalent BIOLOGICS	Document Number:	N/A	Page 2 of 3
Title: Impact Analysis and Risk Priority Number (RPN) Calculation Template			

Risk Assessment Questions	
<p>1 – Is this deviation a variation from a defined critical process or standard that could or does result in product that does not meet its regulatory filed specification and/or required quality standards in each case when that product is no longer within Catalent's control? (Note: Product shipped under quarantine is still considered within Catalent control for the purposes of this question.)</p>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<p>2 – Is this deviation a quality incident that could result in a failure to supply product which could impact patient treatment? (e.g., media fill failure or sterility test failure)</p>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<p>3 – Is this deviation a significant quality system failure that could go undetected and a significant purposeful withholding of information that may constitute fraud or falsification of products or data or give rise to the potential to harm the end user?</p>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Recurrence Check		
Legacy TW Search Parameters	Occurrence Dates	N/A
	Keywords/phrases	N/A
Global TW Search Parameters	Occurrence Dates	On or after 27NOV19
	Keywords/phrases	Leak sterile connection ①
Total # of Potentially Related Records Identified:		42 ① 0

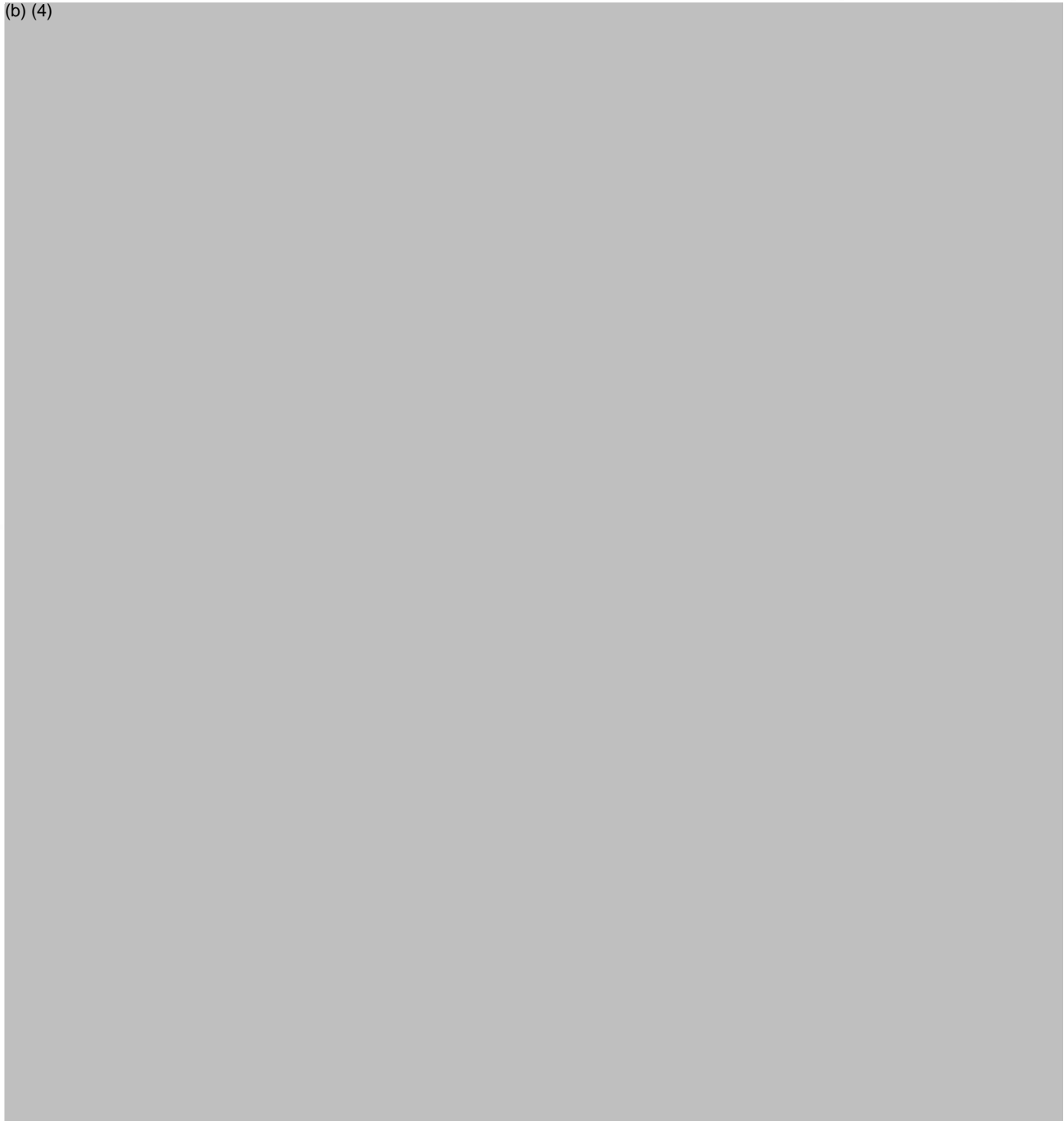
RPN Calculation and Leveling

(b) (4), (b) (6)

Catalent BIOLOGICS	Document Number:	N/A	Page 3 of 3
Title: Impact Analysis and Risk Priority Number (RPN) Calculation Template			

Risk Assessment (RPN) Calculation Tool

(b) (4)



Attachment #:	1	Record #:	283121	Initials/Date:	(b) (6) 27NOV20
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Catalent BIOLOGICS	Document Number:	N/A	Page 1 of 1
Title: Impact Analysis and Risk Priority Number (RPN) Calculation Template			

Changes and Justifications:		
1.	Change:	Removed (, and someone who can speak to the incident are required to be present.) from RPN Attendees box.
	Justification:	To align with SOP-03-01-008.
2.	Change:	Removed (What mitigations are in place?)
	Justification:	Not necessary to level deviation.
3.	Change:	Removed Impact Analysis Question (Is there any potential impact to patient safety?)
	Justification:	This information is covered in the 1 st question.

Attachment #:	1	Record #:	283121	Initials/Date:	(b) (6) 27NOV20
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1300 S Patterson Drive
Bloomington, IN 47403 USA
catalent.com

812-340-9698

Initial Notification of Major Deviation

Deviation Report Number: REC 283121

Batch Record: 256-100-300P-100

Lot Number: 038K20

Date of Recognition: 26Nov20

Description of Deviation:

Leak at sterile connection; lot 038K20, MBR 256-100-300P-100 WO# 4377814

Deviation Details:

During start-up activities for MBR 256-100-300P-101 Lot 038K20, Equipment Lead (b) (6) and Manufacturing Senior Associate (b) (6) noticed that product had begun to leak from the (b) (4) (b) (4) (b) (6) immediately clamped of the tubing to stop the leak. Value Stream Supervisor (b) (6) and QA Representative (b) (6) were contacted and the issue was escalated. A rapid response was held with the client and Manufacturing Technology Senior Manager (b) (6) Associate Manufacturing Technology Specialist (b) (6) Manufacturing Technology Manager Associate Manufacturing Technology Specialist (b) (6) Value Stream Manager (b) (6), Value Stream Supervisor (b) (6), QA Manager (b) (6) QA Representative (b) (6), QA/Validation Director (b) (6), Validation Senior Manager (b) (6), and Senior Project Manager (b) (6). Decision was made to reperform sterile filtration. Bioburden and (b) (4) samples will be re-pulled. The (b) (4) will be retained for investigation.

Deviation initiated 26Nov20, escalated to Major deviation 08Dec20 as re-filtration equates to re-processing.

(b) (6)

QA Supervisor

Technical Development Memorandum

Document #: PD-MEM-0428

To: mRNA-1273 Drug Product External Quality Assurance Team

Subject: Assessment of Impact of Sterile Filtration Reprocessing Due to Leak in (b) (4)
During Initial Sterile Filtration Process of Catalent Lot 038K20, REC 283121

Author(s): (b) (6)

Date: 15-Dec-2020

Product: mRNA-1273 DP (LDP 70065)

Executive Summary

This memorandum summarizes the assessment of mRNA-1273 Drug Product (PN 70065; Lot 038K20) that underwent sterile filtration reprocessing and determines that it is considered suitable for human use.

Background

The diluted bulk mRNA-1273 Drug Product intermediate manufactured at the fill/finish site (Catalent) is sterile filtered through (b) (4) prior to being filled into the final container closure system. This sterile filtration activity occurs at controlled room temperature.

During sterile filtration, product was identified to be leaking from the (b) (4) (b) (4) (see Catalent REC 283121, for a detailed description of the event). Operators immediately clamped the tubing to stop the leak and the issue was escalated to the rapid response team. It was determined to collect new Bioburden and (b) (4) samples from the filtered bulk prior to reprocessing the material through an additional sterile filtration assembly.

Assessment

Reprocessing of sterile filtered mRNA-1273 drug product could potentially cause changes to biophysical characteristics of lipid nanoparticles, specifically particle diameter, polydispersity, and/or mRNA encapsulation. In addition, loss of either mRNA or lipid may occur due to filter absorption.

To understand this sensitivity, a study was conducted (documented in PD-REP-0378) diluted bulk mRNA-1273 Drug Product that were passively thawed to room temperature, and sterile filtered for a total of (b) (4). Samples were collected after each of the (b) (4) filtrations and analyzed for particle diameter, encapsulation efficiency, polydispersity, subvisible particulate, RNA content and lipid content. The biophysical and content characteristics of the drug product from this study remained within acceptance criteria for all the materials generated from re-processing.



For the above-stated reasons, there is no expected impact of this event on the mRNA-1273 drug product, and material can be considered suitable for human use.

References

- PD-REP-0378: mRNA-1273 DP Reprocessing Sterile Filtration Product Impact Report
- Catalent REC # 283121

Revision History

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval in (b) (4)

Approvals

Function	Name
Drug Product Development	(b) (6)
External Quality Assurance	
Drug Product Development, Data Verifier	
CMC Development Quality	

Attachment 3 to Rec 283121
Page 3 of 4
BWS2 16DEC20

Document Approvals
Approved Date: 15 Dec 2020

Task: Approve Verdict: Approve content	(b) (6) (b) (6) @modernatx.com) Task complete 16-Dec-2020 00:23:03 GMT+0000
Task: Approve Verdict: Approve content	(b) (6) (b) (6) modernatx.com) Task complete 16-Dec-2020 00:31:14 GMT+0000
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Task: Data Verification Verdict: Data Verified	(b) (6) (b) (6) modernatx.com) Task Complete 16-Dec-2020 00:48:38 GMT+0000

Attachment 3 to Rec 283121
Page 4 of 4
BWS2 16DEC20

Document Approvals
Approved Date: 15 Dec 2020

Task: Final Approval	(b) (6)
Verdict: Approved	(b) (6) @modernatx.com)
	Task completed
	16-Dec-2020 00:50:00 GMT+0000



Technical Development Memorandum

Document #: PD-MEM-0429
To: mRNA-1273 Drug Product Tech Transfer Team
Subject: Assessment of Leachables due to Repeat Sterile Filtration of mRNA-1273 Drug Product Catalent Batch 038K20 (Catalent Rec 283121)
Author(s): (b) (6)
Date: 15-Dec-2020
Product: mRNA-1273 DP (LDP 70065)

Summary

mRNA-1273 drug product lot 038K20 (Catalent Scale B) was re-filtered through (b) (4) due to a leak being observed after sterile filtration just prior to start of filling (Catalent Rec 283121). The potential impact of additional leachables arising from the added filters is assessed here with reference to the toxicology assessment of filter leachables summarized in PD-MEM-0322 (for Catalent Scale A). A new estimate has been made of the leachables per dose for Scale B (worst-case standard process), and for lot 038K20 after re-filtration. It is concluded that re-filtration of lot 038K20 through (b) (4) does not pose any additional safety risk due to leachables from these extra filters.

Introduction

The diluted bulk mRNA-1273 Drug Product intermediate manufactured at the fill/finish site (Catalent, Bloomington, IN) is sterile filtered through (b) (4) prior to being filled into the final container closure system. This sterile filtration activity occurs at controlled room temperature.

During sterile filtration of lot 038K20, product solution was identified to be leaking from the (b) (4) (see Catalent REC 283121, for a detailed description of the event). The bulk solution was subsequently re-sterile filtered with a new single-use sterile filtration assembly prior to being filled into vials. A total bulk solution of (b) (4) (reference Attachment 3) was obtained after reprocessing although the original bulk obtained was (b) (4). Re-filtration was performed through an (b) (4) (b) (4) (b) (4).

This memo summarizes the impact of this re-filtration on the leachables profile of the final vialled mRNA-1273 drug product lot 038K20.

Background

A toxicology assessment of leachables from (b) (4) used in mRNA-1273 drug product manufacture has been completed (PD-MEM-0322). The assessment concluded that "the presence of



leachables associated with the (b) (4) pose negligible safety risk to humans at the levels currently assessed in the toxicological risk assessment for the mRNA-1273 drug product.”

The assessment in PD-MEM-0322 uses Estimated Amount (of leachables) per Dose as calculated in PD-MEM-0308 (b) (4). However, the estimate in PD-MEM-0308 was performed on Catalent Scale A process. Therefore, a new worst-case estimate for Scale B (standard process) is calculated in Appendix 1. The Estimated Amount (of Leachables) per Dose for Scale B (b) (4) which is lower than the amount estimated in PD-MEM-0308 and assessed in PD-MEM-0322 (b) (4). (b) (4) Thus, the Toxicology assessment in PD-MEM-0322 applies in the worst-case assessment of Catalent Scale B also.

The re-filtration for Lot 038K20 adds (b) (4). An Estimated Amount (of Leachables) per Dose for the 038K20 process (using original bulk obtained (b) (4) and reprocessing bulk obtained (b) (4) results in a dose of (b) (4) (see Appendix 2).

In addition, pre-use filter integrity testing is performed with water for injection (WFI) on (b) (4) (b) (4) that are used in the sterile filtration assembly followed by a filter flushing procedure with product prior to collecting filtered bulk mRNA-1273 drug product, which has the ability to flush additional leachables from the filter.

Since the process includes filter flushing steps, as described above, and the Estimated Amount (of Leachables) per Dose for the 038K20 re-filtered lot is (b) (4) assessed and found safe in PD-MEM-0322, it can be concluded that the re-filtration of Lot 038K20 does not pose any additional safety risk due to leachables from the (b) (4).

Conclusion

Re-filtration of Lot 038K20 through (b) (4) (Catalent Rec 283121) does not pose any additional safety risk due to leachables from these extra filters.



Revision History

Revision #	Change Details	Author	Effective Date
1.0	Introduction of a New Document	(b) (6)	Date of Approval in (b) (4)

Approvals

Function	Name
Data Verifier, Drug Product Development	(b) (6)
Drug Product Development	
CMC Quality Assurance	
Manager, External Quality Assurance and GMP Manufacturing Quality	



(b) (4)

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(b) (4)

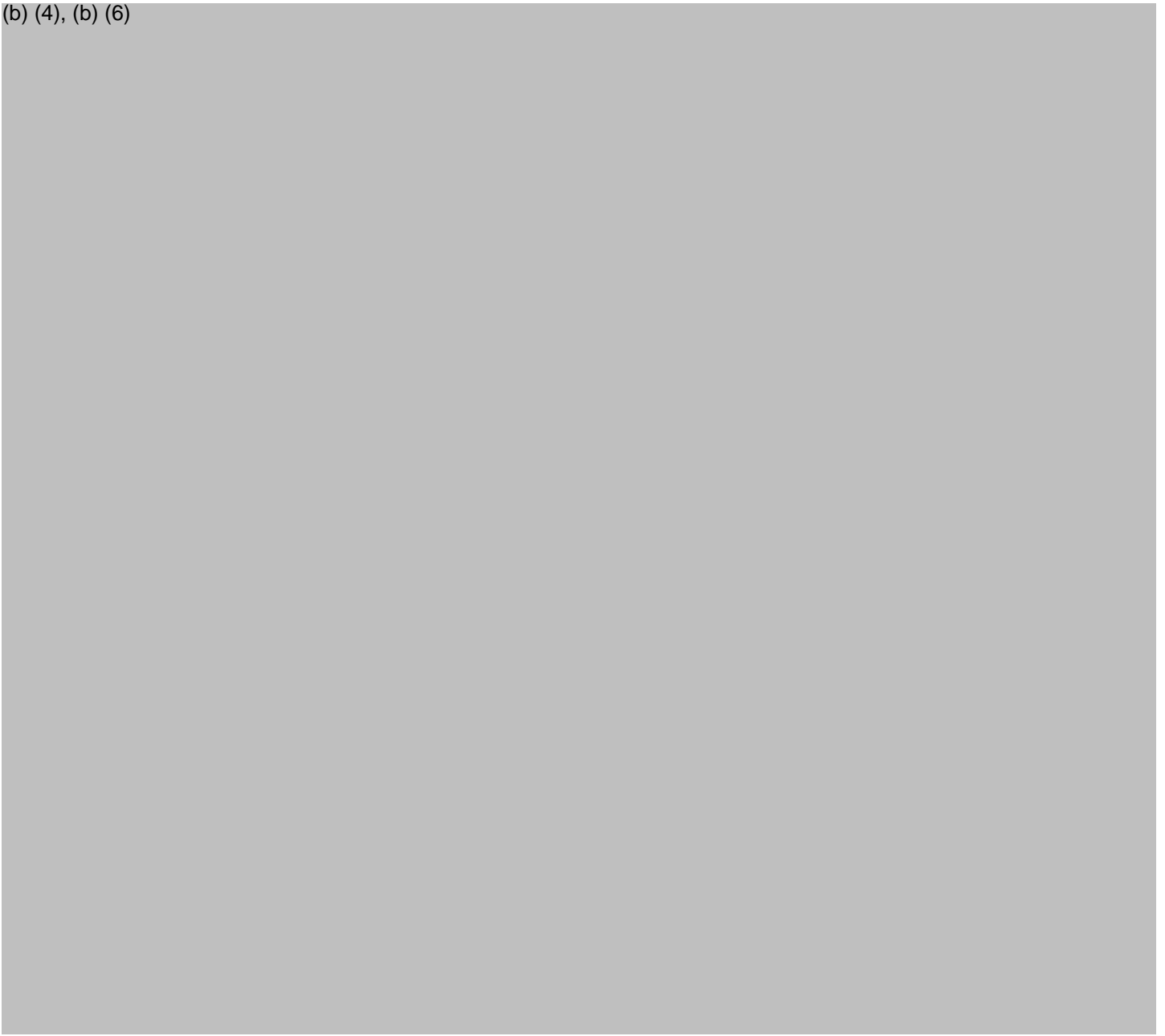
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(b) (4)

A large, solid grey rectangular box covers the majority of the page, indicating that the content has been redacted under FOIA exemption (b)(4).

(b) (4), (b) (6)





(b) (4), (b) (6)

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Attachment 4 to Rec 283121
Page 9 of 9
BWS2 16DEC20

Document Approvals
Approved Date: 16 Dec 2020

Task: Approve Verdict: Approve content	(b) (6) (b) (6) @modernatx.com) Task complete 16-Dec-2020 15:52:34 GMT+0000
Task: Approve Verdict: Approve content	(b) (6) (b) (6) @modernatx.com) Task complete 16-Dec-2020 15:53:22 GMT+0000
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Task: Data Verification Verdict: Data Verified	(b) (6) (b) (6) @modernatx.com) Task Complete 16-Dec-2020 15:54:38 GMT+0000
Task: Final Approval Verdict: Approved	(b) (6) (b) (6) @modernatx.com) Task completed 16-Dec-2020 15:55:46 GMT+0000