`

Biotherapeutics Pharmaceutical Sciences
Specification Review Team
INX100422573, Version 1

To: David Cirelli

From: Rebekah Ward

Date: 07-Aug-2020

Subject: Specification Report for BNT162b2 (PF-07302048) COVID-19 Vaccine Lipid Nanoparticle (LNP) Drug Product to support Emergency Use Authorization

CC: Lavinia Lewis, Mary Denton, Justin Sperry, Fanyu Meng

1.0 Notification of Changes

A summary of changes reflected throughout the document with associated rationale.

Table 1-1: Changes to DP Specifications

	Analytical Procedure	Quality Attribute	Acceptance Criteria	Procedure Number	Release, Stability, or Both	Rationale for Change	Date of Change
Previous Version	NA	NA	NA	NA	NA	Initial specification	Aug 2020
Current Version	New	New	New	New	New		

Impact assessment

Supplies in inventory:
☒ These Specification changes have **no impact** on approved supplies in inventory
☐ These Specification changes **impact** the following lots in inventory: _____
Regulatory commitments:
☒ These Specification changes have **no impact** on regulatory submissions
☐ These Specification changes **may impact** regulatory submissions

2.0 PRODUCT INFORMATION

A brief description of the product and other information relevant to establishing the specification are provided in Table 2-1.

Table 2-1: General Product Description

Product Information	
Product name	BNT162b2 (PF-07302048) COVID-19 Vaccine Lipid Nanoparticle (LNP) Drug Product
Clinical indication(s)	Vaccine
Drug Product (Lipid Nanoparticle Suspension)	DMID #D2000091, BNT162b2 Vaccine (SARS CoV 2 full spike protein S-P2 variant)
BNT Vaccine Code	BNT162b2
BNT RNA Code	RBP020.2
General Properties	
mRNA Type	modRNA
Encoded Antigen	Full Spike Protein, S-P2 Variant
mRNA Length	4,283 nt
Specific Absorption Coefficient[a]	25.0 $(mg/mL)^{-1}$ cm^{-1}
Manufacturing Process and Formulation	Product specific process involving co-mixing of lipids and mRNA drug substance, followed by TFF, dilution and fill; Formulated in 0.75X PBS, 300 mM Sucrose
Novel Raw Materials and Excipients	ALC-0315, ALC-0159
Stage of Development	Emergency Use Authorization (EUA)
Maximum Dose	30 µg flat dose

3.0 SPECIFICATIONS FOR DRUG PRODUCT

Analytical test methods contained in this section were chosen to ensure the quality, identity, purity, and potency of the BNT162b2 (PF-07302048) drug product throughout the manufacturing process and during long term storage under recommended storage conditions. The release specification for BNT162b2 drug product EUA is provided in **Table 3-1**. These are the batch release analytical requirements listed in LIMS as the Drug Product Specification. Analytical procedures and acceptance criteria applicable to the BNT162b2 drug product stability program are noted in the table. Drug product lots are additionally required to undergo 100% and acceptable quality limit visual inspections as part of product release.

Table 3-1: Drug Product Specification

Table 3-1: Drug Product Specification

Quality Attribute	Analytical Procedure	Acceptance Criteria	LIMS Target	Procedure Number	Stability Protocol
Composition and Strength					
Appearance	Appearance (Visual)	White to off-white suspension		TM100010539	Yes
Appearance (Visible Particulates)	Appearance(Particles)	Essentially free from visible particulates		TM100010539	
Subvisible particles	Subvisible particulate matter	Meets compendial requirements		USP<787> TM100010541	Yes
pH	Potentiometry	7.4 ± 0.5		TM100010538	Yes
Osmolality	Osmometry	525 ± 100 mOsmol/kg		TM100010540	No
LNP Size	Dynamic Light Scattering (DLS)	≤ 200 nm		TM100010649	Yes
LNP Polydispersity	Dynamic Light Scattering (DLS)	≤ 0.3		TM100010649	Yes
RNA Encapsulation	Fluorescence assay	≥ 80%		TM100010402	Yes
RNA Content	Fluorescence assay	0.50 ± 0.13 mg/mL		TM100010402	Yes
ALC-0315 content	HPLC-CAD	Report Result: mg/mL	Record Result: % Relative (molar), N/P Ratio	TM100010322	Yes
ALC-0159 content	HPLC-CAD	Report Result: mg/mL	Record Result: % Relative (molar)	TM100010322	Yes
DSPC content	HPLC-CAD	Report Result: mg/mL	Record Result: % Relative (molar)	TM100010322	Yes
Cholesterol content	HPLC-CAD	Report Result: mg/mL	Record Result: % Relative (molar)	TM100010322	Yes
Container content for injections	Volume of injections in containers	Not less than stated dose		USP<697> TM100010614	No
Identity					

Table 3-1: Drug Product Specification

Quality Attribute	Analytical Procedure	Acceptance Criteria	LIMS Target	Procedure Number	Stability Protocol
Lipid identities	HPLC-CAD	Retention times consistent with references (ALC-0315, ALC-0159, Cholesterol, DSPC)		TM100010322	No
Identity of encoded RNA sequence	RT-PCR	Identity confirmed		TM100010407	No
Product Purity					
RNA Integrity	Capillary Gel Electrophoresis	≥ 50% intact RNA		TM100010392	Yes
Adventitious Agents					
Bacterial Endotoxins	Endotoxin (LAL)	≤ 12.5 EU/mL		USP <85> LAB-36816 (Puurs)	Yes
Sterility	Sterility	No growth detected		USP<71>; Ph.Eur. 2.6.1	Yes
Container Closure Integrity[a]	Dye incursion	Pass		TM100010635	Yes

a. Tested at release and on stability for stability batches only

Additional analytical tests listed in **Table 3-2** are performed for each clinical drug product lot to gain further information about the normal range of drug product manufacturing process variation or to monitor the significance of the attribute(s) measured by this test.

Table 3-2: Additional Tests for Drug Product

Quality Attribute	Analytical Procedure	Acceptance Criteria	Procedure Number	Stability Protocol
5'- Cap	RP-HPLC	Report results	TM100010578	Yes
In Vitro Expression	Cell-based FACS	Report results	TM100010380	Yes
Poly(A) Tail	ddPCR	Report results	TM100010379	Yes
Residual Ethanol	GC	≤ 5000 ppm	TM100010581	No
Content	Uniformity of dosage units	Meets compendial requirements	TM100010647	No

Routine in-process tests are listed in **Table 3-3** and are performed for each clinical drug product lot. These methods may be performed at a variety of stages in the process.

Table 3-3: In-Process Tests for Drug Product

Quality Attribute	Analytical Procedure	Stage	Target	Procedure Number
Bioburden	Bioburden	Prefiltration Bioburden	≤2 CFU/20mL	LAB-12943 (Puurs)

Table 3-4 lists the analytical method(s) that will be performed for characterization purposes.

Table 3-4: Characterization Tests for Drug Product

Quality Attribute	Analytical Procedure	Acceptance Criteria	Procedure Number	Stability Protocol
Poly A Tail: Length and Distribution	RP-HPLC	Report results	TM100010391	Yes
RNA Integrity	ddPCR	Report results	TM100010379	Yes

Document Approval Record

Document Name:	INX100422573
Document Title:	Specification Report for BNT162b2 (PF-07302048) COVID-19 Vaccine Lipid Nanoparticle (LNP) Drug Product

Signed By:	Date(GMT)	Signing Capacity
Ward, Rebekah Mary	07-Aug-2020 22:37:18	Author Approval

ATTACHMENT 2: DELIVERY DOCUMENTATION

Documentation and Delivery Notes

Thermal Shipper Documentation

It is currently envisaged that the following will be provided with each shipment of the Products:

1. Authorisation Fact Sheets/Leaflets – Five (5) fact sheets folded 3x2" in a plastic bag

2. Pfizer Brochure – One (1) per Thermal Shipper container containing product storage and handling information including:
   - Dry Ice Handling Insert
   - Safety Data Sheet (SDS) for Dry Ice
   - Return instructions for GPS loggers and thermal shipping system
   - A stand-alone SDS for Dry Ice
   - Blank label – purpose of the blank label: for carriers to mark out the dry ice label to indicate that the Thermal Shipper containers are empty (not containing dry ice)

3. Return Shipping Label – One (1)

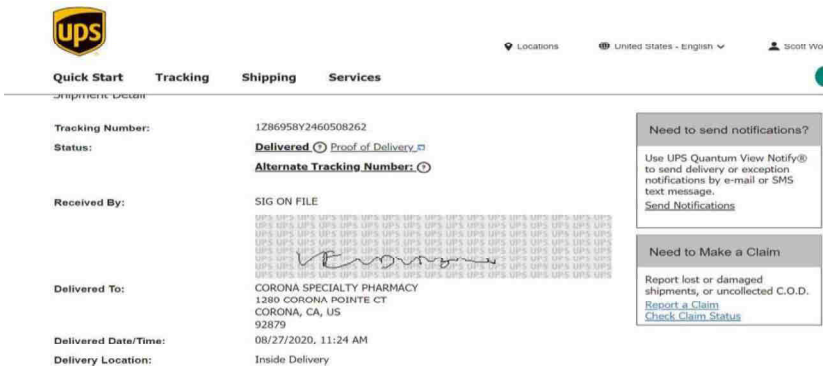
4. Outbound Shipping Label – One (1), standard label on Thermal Shipper

5. Contents Label – One (1) label on inside flap, picking label details how many carton trays are in Thermal Shipper

Proof of Delivery Documentation

Currently, the Contractor intends to use the carrier delivery signal as proof of delivery.

Proof of delivery document that can be accessed online based on track and trace number. See UPS example* below:



*The above proof of delivery image is an example only. Please note that the transport carrier selection will be based on the detail agreed in the Vaccine Order Form between the Contractor and the relevant Participating Member State.

ATTACHMENT 3: DELIVERY SPECIFICATION

Product Delivery, Storage & Handling Specifications

Product delivery, storage and handling specifications are captured below specific to the distribution model: direct shipping from the Contractor manufacturing sites direct to point of use (POU) locations or shipping to one or several central hubs per Participating Member State from which Participating Member States will ensure themselves the further delivery to the sites of use of the Vaccine.

Shipments will arrive in a long distance Thermal Shipper as provided by the Contractor in accordance with Attachment 4 (Labelling and Packaging Specifications). At this time, the minimum order quantity in any shipment shall be one (1) tray with 195 vials or 975 doses of Product. The Contractor is investigating the viability of fewer than 195 vial count SKUs and expects to determine feasibility of an alternative shipping configuration by 1H2021. The Contractor will determine order quantities for future pack sizes.

The Participating Member State shall ensure that at the expected time of arrival a dedicated person will be available to receive the Product, sign acceptance for delivery, and immediately, no later than 24 hours of delivery, switch off the temperature logger located in the Thermal Shipper, and:

1. immediately transfer the Product to:
    1. a -75 °C (+/- 15 °C) ultra-low temperature ("**ULT**") freezer; or
    2. a 2-8 °C refrigerator; or
2. maintain the Product in accordance with product storage and handling guideline captured in Pfizer's brochure and website (e.g. unpacking, storage, re-icing).

The Participating Member State acknowledges the following storage guidelines:

- As at the Effective Date, the Product has a shelf-life of up to 6 months when stored at a constant -75°C(±15°C)

- Provided the re-icing protocols are followed and re-icing occurs within 24 hours of delivery and every 5 days thereafter, the Product may be stored in the Thermal Shipper for up to 15 days

- The Product has an effective life of up to 5 days when stored at refrigerator temperatures 2-8°C

- Once the Product is defrosted and reconstituted it can be retained for up to 6 hours at standard ambient room temperatures (19-25°C)

All costs associated with receiving, handling, storing and further delivery of the Product shall be the responsibility of the Participating Member State, and the Participating Member State shall ensure that all locations where any Product is delivered shall comply with the product storage and handling specifications set forth in this Attachment 3 and shall meet the standards set forth herein.

Protocols for Unpacking Product and Re-icing: See Exhibits 1 and 2 of Attachment 3

Requirements of Delivery Location:

1. Vaccination points with -75°C (+/- 15 °C) ULT freezer
2. Vaccination points with sufficient access and supply of dry-ice
3. Vaccination points with 2-8°C refrigerator

Vaccine Preparation & Administration Instructions

Removing the Vials to Thaw

- From storage, remove 1 vial for every 5 recipients according to planned vaccinations schedule.
- Vials may be stored in the refrigerator for 5 days (120 hours).

Diluting the Vaccine

- Obtain 0.9% Sodium Chloride Injection, for use as a diluent. Do not use any alternate diluents.
- Dilute the thawed vial by adding **1.8 mL of 0.9% Sodium Chloride Injection** into the vial.
- Ensure vial pressure is equalized by **withdrawing 1.8 mL air** into the empty diluent syringe before removing the needle from the vial.

Preparing the Dose

- **Draw up 0.3 mL of the diluted dosing solution** into a new sterile dosing syringe with a needle appropriate for intramuscular injection.
- For each additional dose, use a new sterile syringe and needle and ensure the vial stopper is cleansed with antiseptic before each withdrawal.

Vaccine Administration

- Diluted vials must be used within 6 hours from the time of dilution and stored between 2-25 °C (35-77°F).
- A single 30 mcg/0.3 mL dose is followed by a second dose 21 days later.

Exhibit 1 to Attachment 3 – Unpacking and Re-icing: Thermal Shipper A

	Icing Instructions of the AeroSafe 47L7 ULT Parcel Shipper	CONFIDENTIAL

1. **Purpose**

Unpackaging and Re-Icing Instructions of the AeroSafe 47L7 ULT Parcel Shipper with version control.

2. **Appendices**

Appendix ID	Title
Appendix A	Unpackaging and Re-Icing Instructions of the AeroSafe 47L7 ULT Parcel Shipper

3. **Change History**

Issue Number	Description of Change(s)	Reason for Change(s)
1.0	Initial Release	Initial Release
2.0	Updated formatting and pictures for clarity.	Updated formatting and pictures for clarity.

4. **Approvals:**

Logistics Solutions and Compliance| Transport Qualification and Compliance Manager				
Author:	Name	Marci-Ann Ando	Sign/Date	Marci-Ann Ando Marci-Ann Ando 21 Oct 2020 18:48:024-0400 REASON: I approve this document as author. 0a1fb5f4-f692-45e0-8d06-8eb5d9529e8f
Logistics Solutions and Compliance | Sr. Manager Transport Validation & Innovation				
Approved:	Name	James Jean	Sign/Date	

DocUUID : 6ef8ea33-14ef-44c3-a1be-420f0db02480

Appendix A: Instructions
(11 Pages)

2020TA022 v2.0

Unpackaging and Re-Icing Instructions of the AeroSafe 47L7 ULT Parcel Shipper

Table Of Content

1. Purpose

The purpose of this controlled document is to provide unpackaging and re-icing requirements on the AeroSafe 47L7 Parcel Shipper with Dry Ice.

CAUTION: Use of dry ice in confined spaces (small rooms or walk-in coolers) and/or poorly ventilated areas can result in depletion of oxygen resulting in asphyxiation. Exposed skin should be protected from contact with dry ice. Eye protection is recommended (for example, safety glasses).

Appropriate training to be been conducted for personnel handling dry ice and documented within their relevant training system as required.

2. Scope

This controlled document is applicable to unpackaging and re-icing requirements using the AeroSafe 47L7 ULT Parcel Shipper with Dry Ice.

3. Reference Documents

Document Number	Description
N/A	Safe Handling Guidelines for Dry Ice
N/A	Safety Data Sheet Dry Ice

4. General Requirements

4.1. Materials

Specification Number	Description
CD-86218	SPEC – AeroSafe 47L7 Small Parcel Shipper
N/A	Insulated (Thermal) Gloves
N/A	Safety Glasses
N/A	Carton Sealing Tape
N/A	Dry Ice Pellets (10 to 16 mm)

4.2. Recommendations

Recommendations (Using Thermal Shipping Container as Temporary Storage)
• The thermal shipping container is a passive (non-compressor) device that contains dry ice as the energy source to maintain the required temperatures when maintained properly as defined by Pfizer instructions. The dry ice in the thermal shipper will deplete over a number of days (duration will vary depending on use and care), which will impact how long the shipper holds the temperatures. This differs from an ultra-low-temperature freezer, an active (electronically powered, compressor-driven) device, which when plugged in, is designed to maintain ultra-low temperatures indefinitely. The longer the thermal shipping container remains closed, the longer it will take for the dry ice to deplete. • The thermal shipping container should be stored at 15° to 25° Celsius, which is 59° to 77° Fahrenheit. • The thermal shipping container is qualified with a minimum of 22 kgs of dry ice pellets (10 mm – 16 mm pellets). Upon receipt and after opening, the box should be replenished/inspected with dry ice within 24 hours by adding dry ice to the maximum within the payload insert areas and dry ice pod. • The thermal shipping container should be re-iced every 5 days.   • This can help maintain the level of dry ice and the temperature of the vaccine product. It is recommended that the thermal shipping container **not be opened more than 2 times a day, and shouldn't be opened for** more than 1 minute at a time. If that is followed, the thermal shipping container should then be re-iced every 5 days.

Recommendations (Using Thermal Shipping Container as Temporary Storage)

• Local dry ice suppliers should be used for re-icing the thermal shipping container.
 	
• Temperature monitoring devices to be used if thermal shipping container is used as temporary storage. Sites are responsible for obtaining their own temperature monitoring devices to monitor temperatures when using the thermal shipping container as temporary storage. Temperature monitoring devices (probe or probeless) capable of being in a dry ice environment to be used and placed in the location of the vial tray payload area within the thermal shipping container.
 	
• The thermal shipping container should be returned within 20 business days of delivery, including temperature data logger.
  • If you receive a Controlant Real-Time Temperature Monitor, it must be returned with the thermal shipping container.
  • If you receive a Sensitech Temperature Monitor, it does not need to be returned.

5. Procedure

5.1. Unpackaging

Responsible Role	Action Step
Operator	1. Before opening the thermal shipping container, make sure the area in which you are working has proper ventilation. Use of dry ice in confined spaces, such as small rooms, walk-in coolers, and/or poorly ventilated areas, can result in depletion of oxygen, resulting in asphyxiation.
	2. In a well-ventilated area, open the Outer Corrugated Shipper by cutting the tape on the outside.

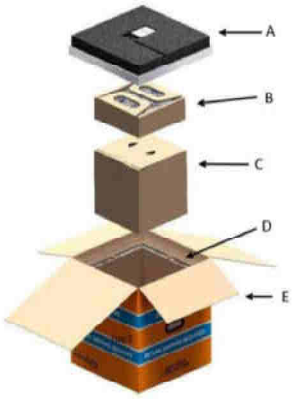
Responsible Role	Action Step
	 
	3. Remove the VIP Lid carefully as the temperature monitor probe is connected to the Payload Box. Care should be taken to not disconnect the probe from the Payload Box. 
	4. While wearing insulated (thermal) gloves, take out the Dry Ice Tray.

Responsible Role	Action Step
	
	5. Remove the Payload Box from the thermal shipper by carefully pulling directly upwards. Care should be taken to not disconnect the probe from the Payload Box. 
	6. Open the Payload Box and remove the vial tray.
	7. Take out the product for inspection and immediately (within one minute of opening) store in an ultra-low temperature freezer or prepare for use. If shipper will be used as temporary storage for remaining vials within tray, immediately re-insert the tray with vials within one minute of opening and follow the re-icing instructions. *Refer to Recommendations section of this procedure for further details on using the thermal shipping container as temporary storage.
	8. If not using the thermal shipping container as temporary storage, insert all components back into the thermal shipping container for return.

Responsible Role	Action Step
	Dry ice must be discarded in a well ventilated area before considering returning the thermal shipping container.

5.2. Re-Icing

	Description
A	VIP Lid
B	Dry Ice Tray
C	Payload Box
D	Corner Dry Ice Scaffold
E	47L7 Shipper



Responsible Role	Action Step
Operator	1. Before opening the thermal shipping container, make sure the area in which you are working has proper ventilation. Use of dry ice in confined spaces, such as small rooms, walk-in coolers, and/or poorly ventilated areas, can result in depletion of oxygen, resulting in asphyxiation.
	2. In a well-ventilated area, open the Outer Corrugated Shipper by cutting the tape on the outside.

Responsible Role	Action Step
	 
	3. Remove the VIP lid, Item A. 
	4. While wearing insulated (thermal) gloves, take out the Dry Ice Tray, Item B as required to get better access to the Scaffolding to begin re-icing.
	5. Fill the Scaffolding, Item D of the shipper with dry ice to the top of the scaffolding.

Responsible Role	Action Step
	6. Reinsert the Dry Ice Tray, Item B on top of the Payload Box, Item C. Fill the Dry Ice Tray, Item B with dry ice to the top. 
	7. Add the VIP Shipper Lid, Item A back on top. 
	8. Fold the outer corrugated flaps and reseal shipper with tape. 

6. History of changes

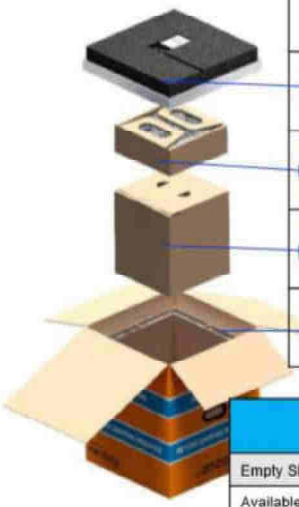
Version	History of Changes
01	Initial version
02	Updated formatting and pictures for clarity.

DocUUID : 6ef8ea33-14ef-44c3-a1be-429f0db02480

7. Appendix

7.1 Appendix 1: AeroSafe 47L7 ULT Parcel Shipper

Note: Approximate weights are based on maximum configuration of dry ice.



ITEM	DESCRIPTION
1	VIP LID
2	DRY ICE TRAY
3	PAYLOAD BOX (Takes 1 vial tray)
4	47L7 THERMAL SHIPPER

Aerosafe 47L7 Weights and Dimension	
Empty Shipper Weight	9.4 kgs
Available Payload Space	9.75" x 9.75" x 9.75"
External Dimension	17.5" x 17.5" x 21.5"
Amount of Dry Ice	22 kgs
Tare Weight w/ Dry Ice	31.4 kgs
Total weight w/ 1 vial tray	32.5 kgs

Weight of Vial Tray	1.038 kgs

DocUUID : 6ef8ea33-14ef-44c3-a1be-429f0db02480

Exhibit 2 of Attachment 3 – Unpacking and Re-icing: Thermal Shipper B

	Logistics Solutions & Compliance | Technical Assessment 2020TA021 v2.0	Page 1 of 2
	Unpackaging and Re-Icing Instructions of the Softbox Medium ULT Parcel Shipper	CONFIDENTIAL

1. **Purpose**

Unpackaging and Re-Icing Instructions of the Softbox Medium ULT Parcel Shipper with version control.

2. **Appendices**

Appendix ID	Title
Appendix A	Unpackaging and Re-Icing Instructions of the Softbox Medium ULT Parcel Shipper

3. **Change History**

Issue Number	Description of Change(s)	Reason for Change(s)
1.0	Initial Release	Initial Release
2.0	Updated formatting and pictures for clarity.	Updated formatting and pictures for clarity.

4. **Approvals:**

Logistics Solutions and Compliance| Transport Qualification and Compliance Manager				
Author:	Name	Marci-Ann Ando	Sign/Date	Marci-Ann Ando Marci-Ann Ando 21 Oct 2020 18:47:044-0400 REASON: I approve this document as author. 0a1fb5f4-f692-45e0-8d06-8eb5d9529e8f
Logistics Solutions and Compliance | Sr. Manager Transport Validation & Innovation				
Approved:	Name	James Jean	Sign/Date	James E Jean James E Jean 21 Oct 2020 19:11:006-0400 REASON: I approve this document. 524412a2-6820-4b64-8cc4-a43540e06a26

Appendix A: Instructions
(12 Pages)

2020TA021 v2.0

Unpackaging and Re-Icing Instructions of the Softbox Medium ULT Parcel Shipper

Table Of Content

1. Purpose

The purpose of this controlled document is to provide unpackaging and re-icing requirements on the Softbox Medium ULT Parcel Shipper with Dry Ice.

CAUTION: Use of dry ice in confined spaces (small rooms or walk-in coolers) and/or poorly ventilated areas can result in depletion of oxygen resulting in asphyxiation. Exposed skin should be protected from contact with dry ice. Eye protection is recommended (for example, safety glasses).

Appropriate training to be been conducted for personnel handling dry ice and documented within their relevant training system as required.

2. Scope

This controlled document is applicable to unpackaging and re-icing requirements using the Softbox Medium ULT Parcel Shipper with Dry Ice.

DocUUID : 93d2c072-1193-449d-b0fa-ef78b87c0f19

3. Reference Documents

Document Number	Description
N/A	Safe Handling Guidelines for Dry Ice
N/A	Safety Data Sheet Dry Ice

4. General Requirements

4.1. Materials

Specification Number	Description
CD-88557	SPEC – Softbox Medium ULT Parcel Shipper
N/A	Insulated (Thermal) Gloves
N/A	Safety Glasses
N/A	Carton Sealing Tape
N/A	Dry Ice Pellets (10 to 16 mm)

4.2. Recommendations

Recommendations (Using Thermal Shipping Container as Temporary Storage)
• The thermal shipping container is a passive (non-compressor) device that contains dry ice as the energy source to maintain the required temperatures when maintained properly as defined by Pfizer instructions. The dry ice in the thermal shipper will deplete over a number of days (duration will vary depending on use and care), which will impact how long the shipper holds the temperatures. This differs from an ultra-low-temperature freezer, an active (electronically powered, compressor-driven) device, which when plugged in, is designed to maintain ultra-low temperatures indefinitely. The longer the thermal shipping container remains closed, the longer it will take for the dry ice to deplete. • The thermal shipping container should be stored at 15° to 25° Celsius, which is 59° to 77° Fahrenheit. • The thermal shipping container is qualified with a minimum of 23 kgs of dry ice pellets (10 mm – 16 mm pellets). Upon receipt and after opening, the box should be replenished/inspected with dry ice within 24 hours by adding dry ice to the maximum within the payload insert areas and dry ice pod. • The thermal shipping container should be re-iced every 5 days.   • This can help maintain the level of dry ice and the temperature of the vaccine product. It is recommended that the thermal shipping container **not be opened more than 2 times a day, and shouldn't be opened for** more than 1 minute at a time. If that is followed, the thermal shipping container should then be re-iced every 5 days.

DocUUID : 93d2c072-1193-449d-b0fa-ef78b87c0f19

Recommendations (Using Thermal Shipping Container as Temporary Storage)

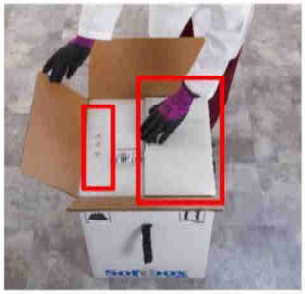
• Local dry ice suppliers should be used for re-icing the thermal shipping container.
 	
• Temperature monitoring devices to be used if thermal shipping container is used as temporary storage. Sites are responsible for obtaining their own temperature monitoring devices to monitor temperatures when using the thermal shipping container as temporary storage. Temperature monitoring devices (probe or probeless) capable of being in a dry ice environment to be used and placed in the location of the vial tray payload area within the thermal shipping container.
 	
• The thermal shipping container should be returned within 20 business days of delivery, including temperature data logger.
  • If you receive a Controlant Real-Time Temperature Monitor, it must be returned with the thermal shipping container.
  • If you receive a Sensitech Temperature Monitor, it does not need to be returned.

5. Procedure

5.1. Unpackaging

Responsible Role	**Action Step**
Operator	1. Before opening the thermal shipping container, make sure the area in which you are working has proper ventilation. Use of dry ice in confined spaces, such as small rooms, walk-in coolers, and/or poorly ventilated areas, can result in depletion of oxygen, resulting in asphyxiation.
	2. In a well-ventilated area, open the Outer Corrugated Shipper by cutting the tape on the outside.

DocUUID : 93d2c072-1193-449d-b0fa-ef78b87c0f19

Responsible Role	Action Step
	
	3. Open the lid. **Note:** One side of the thermal shipping container is permanently affixed so it is recommended to use the three finger hole die-cut on the foam.  Once the lid is opened the dry ice pod will be seen as illustrated below. 
	4. While wearing insulated (thermal) gloves, take out the Dry Ice Pod.

Responsible Role	Action Step
	
	
	5. Access the payload sleeve, which is on top of a thin layer of dry ice and open it.  **Note:** The payload sleeve does not have a bottom, so do not pull it out of the thermal shipping container.
	6. Take out the product for inspection and immediately (within one minute of opening) store in an ultra-low temperature freezer or prepare for use. If shipper will be used as temporary storage for remaining vial trays, immediately re-insert the trays within one minute of opening and follow the re-icing instructions.

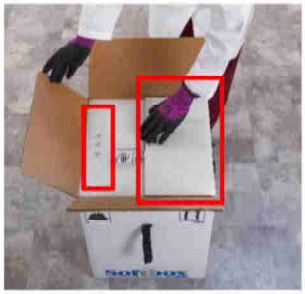
DocUUID : 93d2c072-1193-449d-b0fa-ef78b87c0f19

Responsible Role	Action Step
	 *Refer to Recommendations section of this procedure for further details on using the thermal shipping container as temporary storage.
	7. If not using the thermal shipping container as temporary storage, insert all components back into the thermal shipping container for return. Dry ice must be discarded in a well ventilated area before considering returning the thermal shipping container.

5.2. Re-Icing

Responsible Role	Action Step
Operator	1. Before opening the thermal shipping container, make sure the area in which you are working has proper ventilation. Use of dry ice in confined spaces, such as small rooms, walk-in coolers, and/or poorly ventilated areas, can result in depletion of oxygen, resulting in asphyxiation.
	2. In a well-ventilated area, open the Outer Corrugated Shipper by cutting the tape on the outside.

DocUUID : 93d2c072-1193-449d-b0fa-ef78b87c0f19

Responsible Role	Action Step
	
	3. Open the lid. **Note:** One side of the thermal shipping container is permanently affixed so it is recommended to use the three finger hole die-cut on the foam.  Once the lid is opened the dry ice pod will be seen as illustrated below. 
	4. While wearing insulated (thermal) gloves, take out the Dry Ice Pod.

Responsible Role	Action Step
	 
	5. Fill the sides of the payload sleeve with dry ice until it's equal with the corrugated structure. 

Responsible Role	Action Step
	
	6. Reinsert the Dry Ice Pod and fill with dry ice leaving room between dry ice level and sides of shipper. 
	7. Close the Dry Ice Pod. 
	8. Close the Lid, the Outer Corrugated Shipper and reseal with tape.

Responsible Role	Action Step
	 

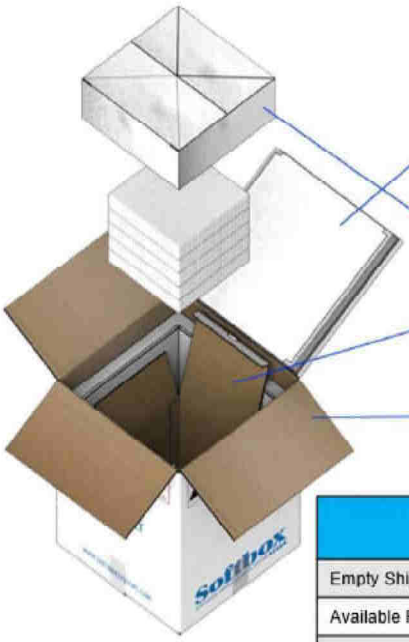
6. History of changes

Version	History of Changes
01	Initial version
02	Updated formatting and pictures for clarity.

7. Appendix

7.1 Appendix 1: Softbox Medium ULT Parcel Shipper

Note: Approximate weights are based on maximum configuration of dry ice.



ITEM	DESCRIPTION
1	VIP LID
2	DRY ICE POD
3	PAYLOAD SLEEVE (Takes 1 to 5 vial trays)
4	MEDIUM ULT THERMAL SHIPPER

Softbox Medium ULT Weights and Dimension	
Empty Shipper Weight	8.5 kgs
Available Payload Space	9.65" x 9.65" x 9.49"
External Dimension	15.75" x 15.75" x 22.04"
Amount of Dry Ice	23 kgs
Tare Weight w/ Dry Ice	31.5 kgs
Total Weight w/ 1 Vial Tray	32.6 kgs
Total Weight w/ 5 Vial Trays	36.7 kgs

Weight of Vial Tray	1.038 kgs

ATTACHMENT 4 : LABELLING AND PACKAGING SPECIFICATIONS

Product Labelling Specifications

Product labels for primary, secondary and tertiary packaging will be shared closer to regulatory filings.

It is currently envisaged that the following will be part of the initial product artwork:

Primary Packaging (Vial):

- Linear barcode: Scans as the Global Trade Item Number (GTIN) that includes the human-readable National Drug Code (NDC) number.

Secondary Packaging (Carton Tray):

- Linear barcode: Scans as the GTIN number that includes the human-readable NDC number.
- QR code: When scanned, this code links to a landing page where a copy of the Fact Sheets for the Healthcare Provider, patient/recipient, and Emergency Use Authorization Product Insert (i.e. e-leaflet) will be available.
- 2D GS1 DataMatrix: Scan of the 2D code will include the GTIN number, lot and expiry information.

Product Packaging Specifications

Primary Packaging

- 2 mL type 1 glass preservative free multi-dose vial (MDV)
- MDV has 0.45 mL frozen liquid drug product
- 5 doses per vial

Secondary Packaging "Single Tray"

- Single tray holds 195 vials
- 975 doses per tray
- Tray (white box) dimensions: 229 X 229 x 40 mm

Tertiary Container: Thermal Shipper (Softbox)

- Minimum 1 tray (975 doses) or up to 5 trays (max 4875) stacked in a payload area of the shipper
- Payload carton submerged in 23 Kg of dry ice pellets (9 mm – 16 mm pellets)
- Thermal shipper dimensions:
    - Internal Dimensions: 245mm X 245mm X 241mm
    - External Dimensions: 400mm X 400mm X 560mm

ATTACHMENT 5: RETURN AND DISPOSAL OF PRODUCT MATERIALS

A. Return

"**Logistics Delivery Equipment**" refers to the long-distance thermal shipping container ("**Thermal Shipper**") used for shipping and the temperature data logger/monitoring device attached to such Thermal Shipper.

Once dry ice is no longer needed, open the **Logistics Delivery Equipment** and leave it at room temperature in a well-ventilated area. The dry ice will readily sublime from a solid to a gas. DO NOT leave dry ice unattended.

Store the empty **Logistics Delivery Equipment** until return in an appropriate clean and secure location to protect and maintain the functionality of the equipment (e.g., do not store outside under uncontrolled conditions, exposed to weather, exposed to pests, etc.).

Return of the **Logistics Delivery Equipment** to be undertaken within 20 business days following delivery of the Product to the Participating Member State's recipient, which will be effected by collection by the Contractor within that time. Instructions and logistics for return will be provided on the interior of the Thermal Shipper and will also be available on Pfizer's website. In the event that either: (a) the **Logistics Delivery Equipment** (or any part thereof), is not made available for collection within such 20 business days; or (b) the **Logistics Delivery Equipment** (or any part thereof), is damaged in any way (determined in the Contractor's sole discretion), the Contractor shall be entitled to charge the Participating Member State $450 (exclusive of VAT) per Thermal Shipper and logger; which the Participating Member State shall pay within 30 days of the date of any invoice for such amount(s). Participating Member State acknowledges that such amount represents a reasonable pre-estimate of replacement cost for such Logistics Delivery Equipment as a result of the Participating Member State's default, act or omission.

B. Disposal

"**Primary Container Units**" refers to the vials that contain the Product.

Destruction of the **Primary Container Units** that have been opened or are unused must take place at a facility appropriately licensed to handle and destroy pharmaceutical waste, medical waste, and/or hazardous waste, and destruction must be by means of grinding or incineration.

"**Secondary Cartons**" refers to the immediate boxes that contain the vials of Product.

Secondary Cartons must be defaced and destroyed in accordance with local clinical dosing facility waste management services, and **Secondary Cartons** may not be disposed of in routine household waste collection or recycling centres.