COVID-19 Vaccine Handling Toolkit:

Operational Considerations for Healthcare Practitioners

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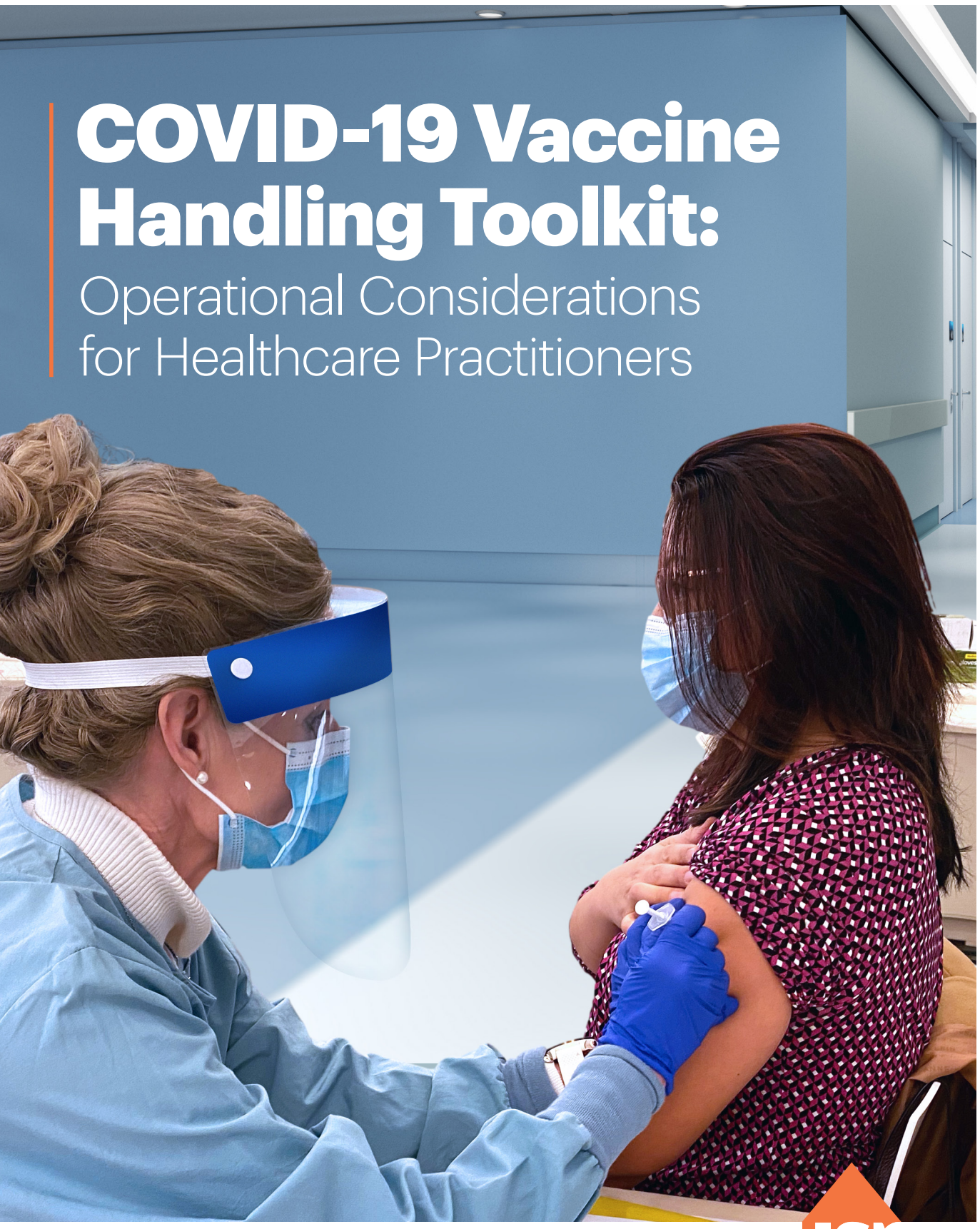

COVID-19 Vaccine Information continues to evolve. Please scan the QR code to visit the USP COVID-19 Vaccine Handling Toolkit website for the latest information.

Introduction

The Food and Drug Administration (FDA) has issued three approved or authorized COVID-19 vaccines in the United States. *(Updated 11/12/21)* The Moderna and Pfizer-BioNTech COVID-19 vaccines are mRNA-based vaccines. The Janssen Ad26 COVID-19 vaccine is an adenovirus type 26 (Ad26) vectored vaccine encoding a stabilized variant of the COVID-19 spike protein (Janssen is a subsidiary of Johnson & Johnson). These COVID-19 vaccines are now available for primary and booster doses. The same vaccine should be used for the primary and additional doses of vaccine administered to people who likely did not mount a protective immune response. A different COVID-19 vaccine can be used for booster doses to eligible individuals.[1] *(Updated 11/12/21)*

COVID-19 Vaccines	Primary Series Dose	Booster Dose
Janssen	0.5 mL	0.5 mL
Moderna	0.5 mL	0.25 mL
Pfizer-BioNTech 12 years of age and older, **purple cap** (must dilute)	0.3 mL	0.3 mL
Pfizer-BioNTech 12 years of age and older, **gray cap** (no dilution)	0.3 mL	0.3 mL
Pfizer-BioNTech 5 - 11 years of age, **orange cap** (must dilute)	0.2 mL	N/A

The USP Healthcare Safety and Quality Expert Committee (HSQ EC) with experts from the Package and Distribution (PD EC), Nomenclature and Labeling (NL EC), Health Information and Technology (HIT EC) and Compounding (CMP EC) Expert Committees have developed the following operational strategies based on stakeholder input and in anticipation of challenges that may arise during the preparation of these COVID-19 vaccines.

In light of the public health emergency posed by COVID-19, this document was developed without a public comment period. This document is not a USP compendial standard; rather, it reflects considerations developed by the USP HSQ EC and other EC members, based on their scientific and professional expertise, and with input from stakeholders and regulatory agencies.

Disclaimer: This document is for informational purposes only and is intended to address operational considerations for COVID-19 vaccine preparation during the COVID-19 pandemic. This does not reflect the USP Healthcare Safety and Quality Expert Committee's opinions on future revisions to official text of the *USP–NF*. Parties relying on the information in this document bear independent responsibility for awareness of, and compliance with, any applicable federal, state, or local laws and requirements. USP is actively monitoring the evolving situation and will update this document accordingly.

1 Preparation

Operational Considerations for COVID-19 Vaccine Preparation

Background

Preparing a conventionally manufactured COVID-19 vaccine, such as a vaccine that has received an EUA or approval from the FDA, should be performed in accordance with the directions in the manufacturer's approved labeling.[2,3,4] This section focuses on considerations for preparation of COVID-19 vaccines for administration and can be used to supplement a manufacturer's approved labeling, but not replace it. In addition, this information should not replace a facility's policies and procedures.

Environmental Considerations for Vaccine Preparation

Achieving and maintaining sterility and overall freedom from contamination of the vaccines is dependent on the environmental conditions under which the preparation process is performed. The following considerations should be made when selecting an environment for preparation of vaccines:

- A dedicated area or room should be utilized for vaccine preparation.
  - The dedicated area or room should be a clean, uncluttered, functionally separate workspace.
  - Whenever possible, the dedicated area or room should be away from windows, doors, air vents, etc. to minimize airflow disruptions.
  - Whenever possible, the area dedicated for vaccine preparation should not be located in or close to where environmental control challenges could negatively affect the air quality (e.g., restrooms, warehouses, or food preparation areas).
  - Items that are not necessary for vaccine preparation should be removed from the vaccine preparation area (e.g., food, drinks, and other materials).
  - Whenever possible, there should be a sink, water, and soap for hand hygiene in the proximity of the area for vaccine preparation. If not possible, alcohol-based hand sanitizer (see USP Hand Sanitizer Toolkit[5], WHO guidance[6]) should be available. For alcohol-based hand sanitizers, the Centers for Disease Control & Prevention (CDC) recommends a concentration of 60% to 95% ethanol or isopropanol (i.e., isopropyl)[7] alcohol.[8]
- Equipment available in the dedicated area or room may include sharps containers, alcohol swabs, sink and/or hand sanitizer, and materials for personnel hygiene and garbing.
- When manufacturer labeling permits, COVID-19 vaccines can be prepared in ambient air without using a Primary Engineering Control (PEC) device (e.g., prepared outside of an ISO Class 5 air environment).
  - A PEC is defined as a device or zone that provides an ISO Class 5 air environment which minimizes the risk of microbial contamination.
  - ISO Class 5 describes the concentration of total particulates per unit volume in the air.[7] (see USP General Chapter <1116> Microbiological control and monitoring of aseptic processing environments). *(Added 6/17/21)*
- Understanding that the vaccine preparation will take place across a variety of practice settings, it is important to adhere to aseptic technique to ensure the quality and safety of the preparation of these vaccine products.
  - Clean and disinfect the surface where the vaccine preparation will take place using a solution of at least 70% isopropyl alcohol or optionally utilize clean preparation mats per your facility's policy and procedures.

Personnel Hygiene and Garbing

Healthcare workers who supervise the preparation of the vaccines should ensure that personnel are adequately skilled, educated, and trained to correctly perform preparation of the COVID-19 vaccines. Before beginning preparation of COVID-19 vaccines, personnel should consider the following aspects of hygiene and garbing:

- Personnel should remove hand, wrist, and other exposed jewelry that could interfere with the effectiveness of garbing or otherwise increase the risk of contamination of the vaccines.
- Fingernails should be clean and neatly trimmed to minimize particle shedding and avoid glove punctures.
- Personnel should perform hand hygiene by washing hands with soap and water for at least 30 seconds or use hand sanitizer rubbed between hands and fingers and allowed to dry.
- Personnel should don powder-free gloves before preparing vaccines for administration. Powder-free gloves should be inspected regularly for holes, punctures or tears and must be replaced immediately if such defects are detected.
- Personnel should don and replace garb (e.g., masks, freshly laundered lab coat, powder-free gloves, clean scrubs) immediately if it becomes visibly soiled or if its integrity is compromised.

Basic Aseptic Considerations for Vaccine Preparation

Aseptic technique is a set of processes used to keep objects and areas free of microorganisms and thereby minimize infection risk to patients. Aseptic technique should be utilized to prepare vaccines for administration in order to prevent the vaccines from being contaminated with microorganisms from the environment or from the persons preparing them. Manufacturer supplied information on the steps for thawing, storage temperatures, and preparation of the available COVID-19 vaccines are provided on the Janssen Ad26, Moderna, and Pfizer-BioNTech COVID-19 resource webpages.[2,3,4] Aseptic technique considerations for vaccine preparation should include the following:

- Follow facility and regulatory requirements related to competency, training, or certification of vaccine preparation and administration, as appropriate.
- Inspect vials for cracks or leaks prior to proceeding further.
- Disinfect entry points on the diluent and vaccine vials (e.g., vial stoppers) by wiping the vials with single-use alcohol swabs. Allow the alcohol to dry before piercing stoppers with sterile needles.
- During preparation of the vaccine, personnel should avoid touching critical parts of the components being used for preparation of the vaccines (e.g., needles, disinfected vial stoppers) in order to minimize microbial contamination.
- Place all used syringes, needles, and vials into puncture-proof containers (e.g., sharps container) and dispose of the containers according to regulatory requirements.
    - The disposal of COVID-19 vaccine vials should be secured in a way to mitigate potential tampering.

Withdrawing Doses

Manufacturer supplied information on the steps for preparation of the available COVID-19 vaccines are provided on the Janssen Ad26, Moderna, and Pfizer-BioNTech COVID-19 vaccine resource webpages.[2,3,4] Additional considerations, including how to ensure complete doses are withdrawn and safe practices include the following:

- If applicable, ensure needle and syringe are tightly luer-locked together.
- Consider using the smallest syringe appropriate for the dose to improve dose accuracy. For example, a 0.3 mL or 0.5 mL dose should be drawn up using a 1 mL syringe or 3 mL syringe, respectively, based on ancillary kit syringe supply availability.
- Also consider using a syringe with appropriate measuring lines on the barrel of the syringe to further improve dose accuracy. *(Added 11/12/21)*
- The same needle should be used for withdrawal and administration. This eliminates the need to change needles and therefore reduces the risk of touch contamination to the vaccine and potential loss of volume. More information is provided in the FAQ for Optimizing COVID-19 Vaccine Preparation and Safety.[9]
    - Use the correct needle gauge and length for the recipient patient based on age, gender and weight recommendations in CDC's Vaccine Administration: Needle Gauge and Length.[10]
- Exercise care to avoid contaminating or bending the needle if being used for both withdrawal and administration.

- Do not fill syringes with air in preparation for later dose or diluent withdrawal due to potential for error of injecting air instead of the dose or diluent. *(Added 11/12/21)*
- Refrain from using transfer devices (e.g., mini spikes, dispensing pins) or using one needle to prepare multiple syringes due to potential loss of medicine in dead space or damage to the stopper and loss of integrity of the vial.
- Use a new needle, preferably a smaller needle (e.g., 25 gauge), for each vial puncture to preserve vial septum integrity. *(Added 6/17/21)*
- Utilize safe practices when recapping the needle after withdrawing and before administration.
- While small air bubbles can be ignored, large air bubbles can lead to underdosing and should be addressed. For example image of small versus large bubble, see the FAQ for Optimizing COVID-19 Vaccine Preparation and Safety. *(Updated 6/17/21)*
  - If diluent is required, slowly inject the diluent, aiming towards the wall of the vial to prevent excess foaming or bubbling.
  - Minimize tapping of the syringe due to theoretical risk of inactivating the vaccine or degrading quality.
  - Slowly withdraw the vaccine to prevent excess foaming or bubbling.
- Rotate the insertion point of the needle across various locations of the vial septum for each withdrawal to reduce leakage of vaccine.
- **Independent double check** is preferred when resources are available. This is best practice to incorporate a process for checking that the correct dose and vaccine is prepared particularly in a multi-vaccine environment (i.e., sites where more than one vaccine type are administered).
- According to the Institute for Safe Medication Practices (ISMP), further mix-ups have been reported between COVID-19 vaccines, influenza vaccines and COVID-19 specific monoclonal antibodies which further highlights the importance of checking the correct dose and medicine.[11,13] *(Updated 11/12/21)*
  - With the increased demand and coadministration of vaccines, vaccine mix-ups have been attributed to some of the following contributing factors[13]:
    - Syringes near each other
    - Unlabeled syringes
    - Distractions
    - Staffing shortages
    - Inappropriately trained staff
- Additional mitigating strategies that can be derived from USP General Chapter <1066> *Physical Environments that Promote Safe Medication Use and the Institute for Safe Medication Practices (ISMP)* to minimize medication errors in a multi-vaccine environment include: *(Added 11/12/21)*
  - Decreasing interruptions and distractions including visual cues (such as wearing clean orange safety vests) and physical barriers while preparing vaccine
  - Dedicating personnel assignments for preparation, transport, and administration to a single vaccine
  - Minimizing traffic in the preparation area, with only authorized individuals allowed access
  - Segregating preparation of different vaccines in separate workspaces
  - Segregating administration of different vaccines with separate designated signage at mass vaccination sites
  - Utilizing technology for product verification (e.g., affix barcoded labels to vials and syringes.)
  - Immediately before vaccination, ask the patient/caregiver to provide at least two patient identifiers (i.e., full name and date of birth) and verify the patient's vaccine(s)[13]
  - Prior to vaccine administration, ask the patient/caregiver to read the syringe label (and vial if present) and expiration date aloud to confirm the correct vaccine[13]

Pfizer-BioNTech COVID-19 Vaccine Considerations[4]

- As of October 29, 2021, there are three Pfizer-BioNTech COVID-19 vaccine presentations visually distinguishable by the vial cap and label border color. At the time of this revision, the **gray** vial cap formulation, which does not require dilution, is not available in the United States *(Added 11/12/21)*:
  - **Purple** Vial Cap and Label Border (must dilute) for 12 years and older (final diluted conc: 30 mcg/ 0.3 mL)
  - **Gray** Vial Cap and Label Border (no dilution) for 12 years and older (final conc: 30 mcg/ 0.3 mL)
  - **Orange** Vial Cap and Label Border (must dilute) for 5 through 11 years (final diluted conc: 10 mcg/ 0.2 mL)
- The Pfizer-BioNTech COVID-19 Vaccine that is supplied in vials with **purple** vial cap and label border should not be used for individuals 5 through 11 years of age because of the potential for vaccine administration errors, including dosing errors. The effects of using a more concentrated vaccine in individuals 5 through 11 years of age has not been studied.

  - Furthermore, there are limits to the number of times the vial septum can be punctured without losing integrity or compromising sterility. The use of a vial of Pfizer-BioNTech (**purple**/**gray** vial cap and label border) 12 years and older vaccine for 5-11 years would require three times as many punctures of a vial. The ability of the septum to withstand these additional punctures has not been studied.
- Maximize doses withdrawn from vials (at least 6 doses for the **purple** and **gray** vial cap and label border formulations, and at least 10 doses for the **orange** vial cap and label formulation) by utilizing low dead-volume syringes and needles, whenever possible. *(Updated 11/12/21)*
  - Dead volume (commonly referred to as dead space) is the volume of medical product remaining in the needle and the hub of a syringe after an injection. Low Dead-Volume (LDV) Syringe and needle combinations are those that have 0.035 mL or less of dead volume.[14]
  - A LDV is designed to limit dead space that exists between the syringe hub and needle. A LDV is designed with less space between the needle and the plunger.
- Practice settings that may not have adequate quantities of LDV syringes can maximize doses by utilizing a combination of LDV and non-LDV syringes (e.g., 3 LDV syringes and 3 non-LDV syringes for **purple** and **gray** vial cap and label border formulations). The ratio of LDV to non-LDV syringes should be dependent on the type of syringe and needle used.
- For the **purple** vial cap and label border formulation, regardless of diluent vial size, only a single needle entry can be used to withdraw a single 1.8 mL volume of 0.9% sodium chloride injection, preservative-free, diluent to prepare one vial of the Pfizer-BioNTech COVID-19 vaccine. Any excess diluent must be discarded. *(Updated 11/12/21)*
- For the **gray** vial cap and label border formulation, no dilution is required. *(Added 11/12/21)*
- For the **orange** vial cap and label border formulation, regardless of diluent vial size, only a single needle entry can be used to withdraw a single 1.3 mL volume of 0.9% sodium chloride injection, preservative-free, diluent to prepare one vial of the Pfizer-BioNTech COVID-19 vaccine. Any excess diluent must be discarded. *(Added 11/12/21)*
- 0.9% sodium chloride injection, preservative-free, diluent should not be drawn up in advance as it is preservative-free.
- The manufacturer states that for dose preparation, a 21-gauge or narrower needle helps prevent leaking from the stopper when doses are withdrawn.
- The Pfizer-BioNTech COVID-19 Vaccine resource webpage provides preparation instruction that should be reviewed to ensure quality vaccine preparation.[4]

The following are additional considerations for withdrawing doses including optimizing vial pressure to ensure maximizing doses for each Pfizer-BioNTech COVID-19 Vaccine vials.

Follow aseptic technique throughout vaccine preparation.

For the purple vial cap and label border formulation:

Step 1: Prepare for Dilution

- A Pfizer-BioNTech COVID-19 vaccine vial must reach room temperature before dilution and be diluted within 2 hours of removal from frozen or refrigerated storage.
- Inspect liquid to ensure it is a white to off-white suspension which may contain white to off-white opaque amorphous particles.
- Invert vaccine vial gently 10 times. Do not shake.

Step 2: Dilute the vaccine

- Visually inspect vial for cracks and leaks.
- Wipe diluent vial stopper using sterile 70% isopropyl alcohol swab and allow to dry.
- If applicable, ensure needle and syringe are tightly luer-locked together.
- Withdraw 1.8 mL 0.9% sodium chloride injection, preservative free, diluent into syringe. Discard vial after diluent withdrawal.
- To prevent excess foaming or bubbling, slowly inject 1.8 mL of 0.9% sodium chloride injection, preservative free, diluent onto the wall of the vaccine vial.
- Before removing the needle from the vaccine vial, move needle tip to the air headspace of the vial and draw out 2.1 mL of air to optimize vial pressure.
  - The vial pressure must at least be equalized by withdrawing 1.8 mL of air into the empty diluent syringe per the labeling. Various pharmacy settings report withdrawal of 2.1 mL of air optimizes vial pressure for more consistent 6th dose withdrawal.
- Gently invert the diluted vial 10 times to mix. Do not shake.
- Record dilution date and time on vaccine vial and store diluted vaccine for up to 6 hours at 2°C to 25°C (35°F to 77°F).

Step 3: Draw up each dose of the vaccine

- Wipe vaccine vial stopper using sterile 70% isopropyl alcohol swab and allow to dry.
- If applicable, ensure needle and syringe are tightly luer-locked together.
- Inject 0.2 mL of air into the vial of reconstituted vaccine to optimize vial pressure.
- Slowly withdraw 0.3 mL of vaccine into the administration syringe.
- While small air bubbles can be ignored, large air bubbles can lead to underdosing and should be addressed. Minimize tapping of the syringe due to theoretical risk of inactivating the vaccine or degrading quality.
- Utilize safe practices when recapping the needle after withdrawing and before administrating.
- Rotate the insertion point of the needle across various locations of the vial septum for each withdrawal to reduce leakage of vaccine.

For the orange vial cap and label border formulation: *(Added 11/12/21)*

Step 1: Prepare for Dilution

- A Pfizer-BioNTech COVID-19 vaccine **orange** cap vial must reach room temperature before dilution and be diluted within 12 hours of removal from frozen or refrigerated storage.
- Inspect liquid to ensure it is a white to off-white suspension which may contain white to off-white opaque amorphous particles.
- Invert vaccine vial gently 10 times. Do not shake.

Step 2: Dilute the vaccine

- Visually inspect vial for cracks and leaks.
- Wipe diluent vial stopper using sterile 70% isopropyl alcohol swab and allow to dry.
- If applicable, ensure needle and syringe are tightly luer-locked together.
- Withdraw 1.3 mL 0.9% sodium chloride injection, preservative free, diluent into syringe. Discard vial after diluent withdrawal.
- To prevent excess foaming or bubbling, slowly inject 1.3 mL of 0.9% sodium chloride injection, preservative free, diluent onto the wall of the vaccine vial.
- Gently invert the diluted vial 10 times to mix. Do not shake.
- Record dilution date and time on vaccine vial and store diluted vaccine for up to 12 hours at 2°C to 25°C (35°F to 77°F).

Step 3: Draw up each dose of the vaccine

- Wipe vaccine vial stopper using sterile 70% isopropyl alcohol swab and allow to dry.
- If applicable, ensure needle and syringe are tightly luer-locked together.
- Inject 0.2 mL of air into the vial of reconstituted vaccine to optimize vial pressure.
- Slowly withdraw 0.2 mL of vaccine into the administration syringe.
- While small air bubbles can be ignored, large air bubbles can lead to underdosing and should be addressed. Minimize tapping of the syringe due to theoretical risk of inactivating the vaccine or degrading quality.
- Utilize safe practices when recapping the needle after withdrawing and before administrating.
- Rotate the insertion point of the needle across various locations of the vial septum for each withdrawal to reduce leakage of vaccine.

Moderna COVID-19 Vaccine Considerations *(Updated 6/17/21)*

- As of October 2021, there are two multi-dose presentations:
  - 5.5 mL vials that are currently available, in that the maximum number of extractable doses is 11, with a range of 10-11 doses.
  - 7.5 mL vial in which each vial contains a maximum of 15 doses (Moderna COVID-19 vaccine Max 15 doses), with a range of 13-15 doses that can be potentially extracted.[12]
- Maximize doses withdrawn from either vial by utilizing LDV syringes/needles whenever possible to minimize drug loss in syringe/needles.
- Practice settings with adequate quantities of LDV syringes, utilizing only LDV syringes should consistently withdraw the maximum number of extractable doses (11 or 15).

- Practice settings that may not have adequate quantities of LDV syringes can consistently achieve 14 doses from the Moderna COVID-19 vaccine Max 15 doses vial by utilizing a combination of LDV and non-LDV syringes (e.g., 7 LDV syringes and 7 non-LDV conventional or luer-locked needles/syringes). The ratio of LDV to non-LDV syringes should be dependent on the type of syringe and needle used.
- The Moderna COVID-19 Vaccine resource webpage provides preparation instruction that should be reviewed to ensure quality vaccine preparation.[3]

The following are additional considerations for withdrawing doses, including optimizing vial pressure to help maximize doses for the Moderna COVID-19 vaccine Max 15 dose vial.

Follow aseptic technique throughout vaccine preparation.

Step 1: Prepare

- Thaw each vial before use. Vials may be thawed:
  - In the refrigerator at 2°C to 8°C (36°F to 46°F) for 3 hours.
  - At room temperature at 15°C to 25°C (59°F to 77°F) for 1 hour and 30 minutes.

Step 2: Draw up each dose of the vaccine

- Visually inspect vial for cracks and leaks.
- Swirl vial gently after thawing and between each withdrawal. Do not shake.
- Wipe vaccine vial stopper using sterile 70% isopropyl alcohol swab. Allow to air dry before inserting needle.
- If applicable, ensure needle and syringe are tightly luer-locked together.
- Inject 0.2 mL of air into the vial of vaccine to optimize vial pressure.
- For primary series doses, slowly withdraw 0.5 mL of vaccine into the administration syringe. For booster doses, slowly withdraw 0.25 mL of vaccine into the administration syringe.
- While small air bubbles can be ignored, large air bubbles can lead to underdosing and should be addressed. Minimize tapping of the syringe due to theoretical risk of inactivating the vaccine or degrading quality.
- Rotating the insertion point of the needle across various locations of the vial septum for each withdrawal to reduce leakage of vaccine.
- Gently swirl and tilt the vial to withdraw the final dose to maximize the volume of vaccine withdrawn. Be careful not to bend the needle.
- Do not puncture the vial stopper more than 20 times.
- Utilize safe practices when recapping the needle after withdrawing and before administering.

Janssen Ad26 COVID-19 Vaccine Considerations
(Updated 6/17/21)

- Visually inspect vial for cracks and leaks.
- Wipe vaccine vial stopper using a sterile 70% isopropyl alcohol swab. Allow to air dry before inserting a needle.
- Before withdrawing each dose of vaccine, carefully mix the contents of the multi-dose vial by swirling gently in an upright position for 10 seconds. Do not shake.
- The same needle should be used for withdrawal and administration. This eliminates the need to change needles and therefore reduces the risk of touch contamination to the vaccine and potential loss of volume.
  - Use the correct needle gauge and length for the recipient patient based on age, gender and weight recommendations in CDC's Vaccine Administration: Needle Gauge and Length.[10]
- Rotate the insertion point of the needle across various locations of the vial septum for each withdrawal to reduce leakage of vaccine.

Beyond-Use Dating Considerations for Pre-drawn Syringes

We recognize that practice settings may benefit from certain operational efficiencies that support a separation of the vaccine preparation steps from vaccine administration to the patient. For example, this may occur when a practice setting prepares and pre-draws the vaccine into syringes in one area and then transports the pre-drawn syringes to a different site for administration. If pre-drawn syringes are used, consider the following manufacturer-released information supporting stability data of the vaccine pre-drawn into syringes:

Pfizer-BioNTech COVID-19 Vaccine > 12 years

- For the **purple** vial cap and label border formulations, Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all its measured quality attributes when diluted vaccine is stored in polycarbonate and polypropylene syringes with stainless steel needles for 6 hours at 2°C to 25°C (35°F to 77°F) after the source vial is diluted.
- Microbiological risk was assessed through a microbiological challenge study which showed that microbiological growth has a greater potential to occur after 6 hours. The hold time of 6 hours, from the time the source vial is diluted, is not specifically tied to a preparation environment and can be applied to doses prepared outside of ISO Class 5 environment (PEC).
- 0.9% sodium chloride injection, preservative-free, diluent should not be drawn up in advance as it is preservative-free.
- Keep out of direct sunlight and ultraviolet light.

Pfizer-BioNTech COVID-19 Vaccine 5 – 11 years

- For the **orange** vial cap and label border formulation, Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all of its measured quality attributes when the diluted vaccine is stored in polycarbonate or polypropylene syringes for a cumulative time up to 24 hours post-dilution with no more than 12 hours at room temperature (up to 30°C or 86F). *(updated 11/12/21)*
- Microbiological risk was assessed through a microbiological challenge study which showed that microbial growth has a greater potential to occur after 12 hours. Although no logarithmic growth of spiked microorganisms was seen until 24 hours at 25°C, a 2x safety factor was applied resulting in the 12 hours in use period. *(updated 11/12/21)*
- 0.9% sodium chloride injection, preservative-free, diluent should not be drawn up in advance as it is preservative-free.
- Keep out of direct sunlight and ultraviolet light.

Moderna COVID-19 Vaccine

- According to the Chemistry, Manufacturing and Control (CMC) department at Moderna, pre-drawn syringes can be stored in the refrigerator to ambient room temperature at 2°C to 25°C (35° to 77°F), provided they are administered within 12 hours of the first time the source vial is punctured. *(Updated 6/17/21)*
- Per Moderna, common disposable syringes made of polypropylene or polycarbonate are suitable for use.
- Keep out of direct sunlight and ultraviolet light.

Janssen Ad26 COVID-19 Vaccine

- According to Janssen, based on data on file, pre-drawn syringes can be stored:
  - In the refrigerator at 2°C to 8°C (36° to 46°F), provided they are administered within 6 hours of the first time the source vial is punctured.
  - In ambient room temperature up to 25°C (77°F), provided they are administered within 2 hours of the first time the source vial is punctured.
- Per Janssen, common disposable syringes made of polypropylene or polycarbonate are suitable for use.
- Keep out of direct sunlight and ultraviolet light.

Labeling Considerations

When the COVID-19 vaccines are not being prepared for immediate administration, appropriate labeling considerations should be undertaken. If the vaccines are sent outside the facility in which they were prepared for administration, a designated person must ensure that contact information of the preparation facility is conveyed and available at the site where they will be administered. Labels should be adhered to the container(s) (e.g., light protected zip-lock bag in which pre-drawn syringes are stored and transported). Pre-drawn syringes prepared for administration must be labeled with legible identifying information to prevent errors during storage, dispensing, transport and use.

Personnel should consider adding the following labeling components to the containers in which the pre-drawn vaccine syringes are stored, as well as the pre-drawn vaccine syringe.

Container labeling components:

- Facility name and phone number
- Quantity of syringes
- Name and amount of vaccine
- Primary or Booster dose (if applicable)
- Age range (if applicable)
- The exact beyond-use date and time
- Lot number
- Initials of preparer(s)

Examples of pre-drawn syringe storage container labels

Pfizer-BioNTech COVID-19 Vaccine IM suspension
Age 5-11 years (10 mcg / 0.2 mL) or Age >12 years (30 mcg / 0.3 mL)
Facility name and phone number:
Quantity of syringes:
Date & Time to discard (For 5-11 years: 12 hours after dilution;
For >12 years purple cap: 6 hours after dilution):
Lot no:
Initials of preparer(s):

Moderna COVID-19 Vaccine IM suspension
Primary dose (100 mcg/ 0.5 mL) or Booster dose (50 mcg/ 0.25 mL)
Facility name and phone number:
Quantity of syringes:
Date & Time to discard (12 hours after vial puncture):
Lot no:
Initials of preparer(s):

Janssen Ad26 COVID-19 Vaccine (5×10^{10}vp / 0.5 mL) IM suspension
Facility name and phone number:
Quantity of syringes:
Date & Time to discard:
(6 hours after vial puncture at 2°C to 8°C (36° to 46°F) or
2 hours after vial puncture at up to 25°C (77°F))
Lot no:
Initials of preparer(s):

Pre-drawn syringe labeling components:

- Name and amount of vaccine
- The exact beyond-use date and time
- Primary or Booster dose
- Age range (if applicable)
- Lot number
- Initials of preparer(s)

Examples of pre-drawn syringe labels

Pfizer-BioNTech COVID-19 Vaccine IM suspension
Age 5-11 years (10 mcg / 0.2 mL) or Age >12 years (30 mcg / 0.3 mL)
Date & Time to discard (For 5-11 years: 12 hours after dilution;
For >12 years purple cap: 6 hours after dilution):
Lot no:
Initials of preparer(s):

Moderna COVID-19 Vaccine IM suspension
Primary dose (100 mcg / 0.5 mL) or Booster dose (50 mcg / 0.25 mL)
Date & Time to discard (12 hours after vial puncture):
Lot no:
Initials of preparer(s):

Janssen Ad26 COVID-19 Vaccine (5×10^{10}vp / 0.5 mL) IM suspension
Date & Time to discard:
(6 hours after vial puncture at 2°C to 8°C (36° to 46°F) or
2 hours after vial puncture at up to 25°C (77°F))
Lot no:
Initials of preparer(s):

References

1. https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html#Interchangeability
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2 Storage and Transportation

Operational Considerations for Storing, Handling and Transporting COVID-19 Vaccines

Background

Proper storage, handling, and transportation of COVID-19 vaccines are critical activities in their integrated supply chain. Failure to store and handle vaccines properly can potentially reduce potency, leading to inadequate immune response in patients and poor protection against COVID-19. Proper storage, handling, and transportation of the COVID-19 vaccines begins with an effective cold chain process, which is temperature-controlled, using related equipment and procedures. It begins with cold storage at the manufacturing facility and extends to the proper receiving, storage, and handling of the vaccine at the provider facility, and in some situations, transporting off-site or to satellite facilities.

Manufacturer supplied information for storing and handling the new COVID-19 vaccines in the United States are provided on the Janssen Ad26, Moderna, and Pfizer-BioNTech COVID-19 resource webpages.[1,2,3] This document focuses on considerations for storing, handling, and transporting vaccines and can be used to supplement a manufacturer's labeling, but not replace them. In addition, this document should not replace a facility's policies and procedures.

Quality Management System (QMS)

Developing and maintaining clearly written, detailed, and up-to-date receiving, storage, handling, and transporting standard operating procedures (SOPs) are essential. This occurs within the framework of a robust Quality Management System (QMS), which is a set of policies, processes, and procedures required to execute core activities. Due to the risk associated with vaccine transport caused by improper packing or storage unit failure, it is necessary to include detailed packing and transport protocols in the organization's storage and handling SOPs (including those that address inclement weather, natural disasters, and traffic disruptions). State immunization or local programs may be able to provide sample SOPs for vaccine storage and handling, which may vary from state to state. In addition, sample SOPs, for example purposes only, are available online.[4,5] The QMS, along with related SOPs, helps ensure proper procedures are followed and problems (e.g., damaged packages or vials) are identified, reported, and corrected. SOPs should also provide direction for handling emergencies, such as equipment malfunctions, power failures, or natural disasters. All staff members who come in contact with the vaccines, or who administer the vaccines should be trained on all relevant practices and procedures. The objective of the training should be to reduce the gap between existing staff competencies and those required to perform the job (see USP General Chapter <1079> *Risks and Mitigation Strategies for the Storage and Transportation of Finished Drug Products*).

Receiving Vaccine

When vaccines arrive at the facility, they should be transferred as quickly as possible to a designated storage area and stored at the recommended temperature. Receiving areas should protect the product from inclement weather during unloading, and the receiving area should limit access to authorized persons only. Deliveries should be examined at receipt in order to check that shipping containers are not damaged, and that the shipment corresponds to the order. Check the temperature monitoring device, if applicable, for any indication of temperature excursion(s) during transit. Each organization should have a receiving procedure that determines the appropriate checks

for this operation. A checklist can be used as a reminder of what to inspect and what to record (see USP General Chapter <1079> *Risks and Mitigation Strategies for the Storage and Transportation of Finished Drug Products*).

Vaccine Storage

Storage units are required to maintain the product temperature between the limits defined on the product label (see USP General Chapter <695> *Packaging and Storage Requirements*). Detailed information on vaccine storage and temperature monitoring equipment is included in section 3 of the CDC Vaccine and Storage Handling Toolkit.[6] Manufacturer supplied information for storing the authorized COVID-19 vaccines in the United States are provided on the Janssen Ad26, Moderna, and Pfizer-BioNTech COVID-19 resource webpages.[1,2,3]

On February 25, 2021, the U.S. Food and Drug Administration announced that it is allowing undiluted frozen vials of the Pfizer-BioNTech COVID-19 Vaccine 12 years and older, **purple** vial cap and label border, to be transported and stored at conventional pharmaceutical freezers for a period of up to two weeks at the freezer temperature of -25°C to -15°C (-13°F to 5°F). The frozen vaccine may be returned one time to the recommended storage condition of -90°C to -60°C (-130°F to -76°F). Total cumulative time the **purple** vial cap and label border formulation are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.[7]

According to the CDC Storage and Handling Toolkit, COVID-19 Vaccine Addendum section, it is essential to utilize continuous temperature monitoring systems to ensure the vaccines are stored within the correct temperature range and a specific device, a digital data logger (DDL) with an external display is preferred.[6] A DDL is an electronic device that records data digitally over time or in relation to location either with a built-in or external instrument or sensor. Although automated systems monitor temperature continuously, manual checks must be performed as appropriate to ensure functionality and when the vaccine is removed from storage. Temperature monitoring devices should be calibrated (NIST traceable)[6] against nationally accepted standards to ensure accuracy of readings (see USP General Chapter <1118> *Monitoring Devices—Time, Temperature, and Humidity*). Calibration testing should be done every one to two years or according to the manufacturer's suggested timeline. Alarm systems may be part of the temperature monitoring system.

Pharmaceutical-grade refrigerators and freezers are preferred because they are designed specifically for storing biopharmaceuticals, including vaccines. Per CDC guidance, "household-grade units can be an acceptable alternative for refrigeration in some situations. However, the freezer compartment of household-grade units is not recommended to store vaccines and there may be other areas of the refrigerated compartment that should be avoided as well. If your facility provides frozen vaccine, a separate freezer unit is necessary."[6] Under no circumstance should a vaccine be stored in a dormitory-style refrigerator/freezer unit. Food and drinks and/or biological specimens should not be stored in the same unit as the vaccine.

Standard operating procedures (SOPs) should be in place to ensure power supply or alternative options when power outage occurs. Routine maintenance should be conducted to ensure proper function of the refrigeration unit. Depending on the time of year (e.g., summer, winter), or room temperature, the thermostats may need to be reset.

Typically, a refrigeration unit specification would be set to 5°C (41°F) with an allowable range of ± 3°C (2°C to 8°C or 38°F to 44°F) to store products labeled 2°to 8°C (36 to 46°F). Freezer temperatures may vary and typically range from -25°C to -10°C (-13°F to 14°F). Most standard freezer units do not meet ultra-cold freezer requirements for storing vaccines between -60°C and -80°C (-76°F and -112°F).

If ultra-low freezer temperatures are required and the manufacturer provides or specifies the use of dry ice (e.g., Pfizer-BioNTech COVID-19 vaccine), additional handling precautions should be taken, such as the following:

1. Store thermal shippers containing dry ice, as well as dry ice replenishment containers, in a well-ventilated area. Because frozen carbon dioxide changes phase (i.e., melts) into a gaseous state, elevated levels of carbon dioxide can be dangerous to personnel operating within a poorly ventilated area, which may lead to asphyxiation.
2. Because of thermal expansion of dry ice as it changes phases from frozen to gaseous, it should never be stored in a tightly sealed device.
3. Wear impermeable loose-fitting gloves (e.g., leather, lined oven mitts, etc.) to protect from contact freezing (similar to a burn). Gloves must be insulated to protect from general freezing temperatures (dry ice is -78.5°C or -109.3°F).
4. Wear goggles or a face shield to protect your eyes.

For maintaining temperatures at outdoor venues, keep opened vials or pre-drawn syringes at temperatures at or below 25°C (77°F) within the beyond-use date until the time of administration to the patient. For further information, see the Transporting COVID-19 Vaccines Off-Site guide accessible on pg. 17. *(Updated 6/17/21)*

Temperature Excursions

Inclement weather, natural disasters, and traffic disruption can cause receiving delays and potential temperature excursions. A temperature excursion is any temperature reading outside of the recommended range for vaccine storage as defined in the manufacturer's package insert. Temperature excursions or inappropriate storage conditions require immediate action. Each excursion should be documented, including the magnitude of the temperature excursion, and the total amount of time that temperatures were out of range. For refrigerated vaccines, Mean Kinetic Temperature may be calculated (see USP General Chapter <1079.2> *Mean Kinetic Temperature in the Evaluation of Temperature Excursions During Storage and Transportation of Drug Products*). To determine the impact of an excursion, and whether the vaccines are still viable, contact the manufacturer for guidance on whether the affected vaccines should be discarded or can be utilized. While this determination is being made, the vaccines should be maintained at the appropriate temperature and clearly labeled "**DO NOT USE pending guidance by the manufacturer.**" Place them in a separate container apart from other vaccines and do not discard these vaccines. The ability of the manufacturer to determine the excursion impact will depend on the information provided and so as much information as possible regarding the excursion should be provided. Each excursion event is unique and a manufacturer's recommendation for a specific excursion event should not be applied to future events that appear to be similar.

Temperature excursion labeling

DO NOT USE pending guidance by the manufacturer.

Vaccine Transport (Off-site or Satellite Facilities)

Vaccine transport off-site or to satellite facilities involves the process of transporting vaccines over short distances and time frames in accordance with practice setting SOPs. When vaccine transport is necessary, transport the vaccines using a portable refrigerator and/or freezer unit with a temperature monitoring device. If a portable refrigerator and/or freezer unit is not available, qualified containers and packouts with a temperature monitoring device can be used. A container or packout is 'qualified' through laboratory testing under controlled conditions to ensure they achieve and maintain desired temperatures for a set amount of time and are available through packaging suppliers. When transporting the vaccine, the temperature should be validated whenever the storage container is opened. The manufacturer supplied packaging can be used in accordance with the directions in the manufacturer's labeling.

The total time for transport should be minimized to reduce potential risk for a temperature excursion due to a storage unit or thermal packaging system failure. Sufficient transport supplies (e.g., materials and equipment) are needed. These can include portable refrigerator/freezer units, qualified containers, coolant materials, insulating materials, and the required temperature monitoring devices.

Vaccines must be secured from theft and tampering, as other medications, when not under supervision of healthcare personnel. Strategies to ensure secure transport can include the use of 'tamper proof' or 'tamper evident' measures (e.g., locks, tape) on these containers as appropriate per the health professional's judgment. For additional information on tampering/damage, see the Visual Inspection Guide linked on pg. 17. *(Added 6/17/21)*

The redistribution of vaccine supply to other in-network settings for preparation and administration also requires the redistribution of adequate ancillary supplies for preparation and administration. For the Pfizer-BioNTech COVID-19 Vaccine, the following are additional considerations for redistribution of ancillary supplies:

- Ensure adequate number of preservative-free sodium chloride 0.9% sterile diluent for vaccine preparation.
- Ancillary supply redistribution example is provided in *Appendix II: Example of Pfizer-BioNTech COVID-19 Vaccine Ancillary Kit Redistribution*.

Transport of frozen solid vaccine vials

Pfizer-BioNTech COVID-19 Vaccine[3]

- Use a temperature monitoring device, with continuous monitoring being preferred, to ensure consistent temperature monitoring during transport.
- Frozen Pfizer-BioNTech COVID-19 Vaccine **purple**, **gray**, and **orange** vial cap and label formulations can be transported at ultra-low-temperature of -90ºC to -60ºC (-130ºF to -76ºF).
- Frozen Pfizer-BioNTech COVID-19 Vaccine **purple** vial cap and label formulation can be transported and stored at conventional pharmaceutical freezers for a period of up to two weeks at the freezer temperature of -25°C to -15°C (-13°F to 5°F). The frozen vaccine may be returned one time to the recommended storage condition of -90ºC to -60ºC (-130ºF to -76ºF). Total cumulative time the **purple** vial cap and label formulation are stored at -25°C to -15°C (-13°F to 5°F) should be tracked and should not exceed 2 weeks.[7] *(Updated 11/12/21)*
- Per manufacturer labeling, the only allowable containers for frozen transfer are: 1) portable ultra-low freezers, 2) portable pharmaceutical grade freezers, or 3) original thermal shipper containers, if following re-icing guidelines.
  - Pfizer provides detailed instructions for *Dry Ice Replenishment* when stored in the original thermal shipper (including information on dry ice replenishment, pellet size, and pack-out instructions for re-icing thermal packaging).[10]
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- If the storage condition is changed to an unmonitored temperature container, this is when the allowable storage time for non-frozen condition begins for the **purple** vial cap and label formulation at 1 month at refrigeration temperatures) and for **gray** and **orange** vial cap and label formulations at 10 weeks. *(Updated 11/12/21)*
- When the vaccine's storage condition is changed, it is critical to utilize appropriate labeling to indicate the beyond-use date, per the manufacturer. The CDC offers manufacturer-specific vaccine labels for beyond-use date tracking.[11]

Moderna COVID-19 Vaccine[2]

- Use a temperature monitoring device, with continuous monitoring being preferred, to ensure consistent temperature monitoring during transport.
- Frozen Moderna COVID-19 Vaccine multiple-dose vials is maintained at a temperature of -50ºC to -15ºC (-58ºF to 5ºF). *(Updated 11/12/21)*
- Transporting Moderna COVID-19 Vaccine in vials is preferred.[12] *(Updated 6/17/21)*
- A portable freezer can be utilized to transport frozen vaccine product.
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- Per manufacturer labeling, dry ice should not be used in transferring vaccine product.
- If the storage condition is changed to an unmonitored temperature container, this is when allowable storage time for non-frozen condition starts (e.g., 30 days in refrigerated temperatures).
- When the vaccine's storage condition is changed, it is critical to utilize appropriate labeling to indicate beyond-use date, per the manufacturer. The CDC offers manufacturer-specific vaccine labels for beyond-use date tracking.[13]

Transport of multidose vaccine vials outside of frozen state or those that do not require freezing

Pfizer-BioNTech COVID-19 Vaccine[3]

- Use a temperature monitoring device, with a continuous monitoring device being preferred, to ensure consistent temperature monitoring during transport.
- Undiluted vials can be maintained at refrigeration temperatures at 2ºC to 8ºC (35ºF to 46ºF) for 1 month for **purple** vial cap and label formulation and 10 weeks for **gray** and **orange** vial cap and label formulations. *(Updated 11/12/21)*
- Undiluted vials can be maintained at room temperature for up to 25ºC (77ºF) for 2 hours for **purple** vial cap and label formulation and 12 hours prior to first puncture for **gray** and **orange** vial cap and label formulations. *(Updated 11/12/21)*
- Diluted vials can be maintained at room temperature for up to 25ºC (77ºF) for 6 hours and must be discarded after 6 hours for the **purple** vial cap and label formulation and for up to 12 hours for **gray** and **orange** vial cap and label formulations. *(Updated 11/12/21)*

- A portable refrigerator unit can be utilized to transport thawed vaccine product.
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- Expanded polystyrene foam containers can be used for maintaining cold chain/temperature consistency across transport to administration site.
  - In addition, to protect from damage during transport, a hard-plastic container should be considered to carry the expanded polystyrene foam container (NOTE: A hard-sided plastic container alone may not be sufficient to maintain temperature control). A soft-sided container can also be considered if it is a qualified container or packout.
- If a cooling agent is used, a thick barrier (at least 1 inch) of bubble wrap or corrugated cardboard may be utilized as a barrier between the transport container cooling agent and the container with thawed vials. This is to prevent direct contact between vials and the cooling agent that may cause the vaccine to freeze or deviate from appropriate cold chain.[14]
- When the product is thawed, do not refreeze.
- When the vaccine's storage condition is changed, it is critical to utilize appropriate labeling to indicate beyond-use date, per the manufacturer. The CDC offers manufacturer-specific vaccine labels for beyond-use date tracking.[11]

Moderna COVID-19 Vaccine[2]

- Use a temperature monitoring device, with a continuous monitoring device being preferred, to ensure consistent temperature monitoring during transport.
- Vials can be maintained at refrigeration temperatures between 2°C to 8°C (36°F to 46°F) for up to 30 days prior to initial vial puncture. Use Moderna's tool to determine expiration date.[15] *(Updated 6/17/21)*
- Available data supports transportation of one or more thawed vials for up to 12 hours at 2°C to 8°C (36°F to 46°F) when shipped using shipping containers which have been qualified to maintain 2°C to 8°C (36°F to 46°F) and under routine road and air transport conditions with shaking and vibration minimized. *(Added 11/12/21)*
- A portable refrigerator unit can be utilized to transport thawed vaccine product.
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- Expanded polystyrene foam containers can be used for maintaining cold chain/temperature consistency across transport to administration site.
  - In addition, to protect from damage during transport, a hard-sided plastic or soft-sided qualified container or packout should be considered to carry the expanded polystyrene foam container. (NOTE: A hard-sided plastic or soft-sided qualified container alone may not be sufficient to maintain temperature control).

- If a cooling agent is used, a thick barrier (at least 1 inch) of bubble wrap or corrugated cardboard may be utilized as a barrier between the transport container cooling agent and the container with thawed vials. This is to prevent direct contact between vials and the cooling agent that may cause the vaccine to freeze or deviate from appropriate cold chain.[14]
- When the product is thawed, do not refreeze.
- When the vaccine's storage condition is changed, it is critical to utilize appropriate labeling to indicate beyond-use date, per the manufacturer. The CDC offers manufacturer-specific vaccine labels for beyond-use date tracking.[13]

Janssen Ad26 COVID-19 Vaccine[1]

- Use a temperature monitoring device, with a continuous monitoring device being preferred, to ensure consistent temperature monitoring during transport.
- Vials can be maintained at refrigeration temperatures between 2°C to 8°C (36°F to 46°F) until expiry date prior to initial vial puncture. Use Janssen's tool to determine expiration date.[16] *(Updated 6/17/21)*
- A portable refrigerator unit can be utilized to transport vaccine product.
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- Expanded polystyrene foam containers can be used for maintaining cold chain/temperature consistency across transport to administration site.
  - In addition, to protect from damage during transport, a hard-plastic container should be considered to carry the expanded polystyrene foam container (NOTE: A hard-sided plastic container alone may not be sufficient to maintain temperature control). A soft-sided container can also be considered if it is a qualified container or packout.
- If a cooling agent is used, a thick barrier (at least 1 inch) of bubble wrap or corrugated cardboard may be utilized as a barrier between the transport container cooling agent and the container with vials. This is to prevent direct contact between vials and the cooling agent that may cause the vaccine to freeze or deviate from appropriate cold chain.[14]
- When the vaccine's storage condition is changed, it is critical to utilize appropriate labeling to indicate beyond-use date, per the manufacturer. The CDC offers manufacturer-specific vaccine labels for beyond-use date tracking.[17]

Transfer of pre-drawn syringes

The following operational considerations are offered for the Janssen Ad26, Moderna, and Pfizer-BioNTec COVID-19 vaccines according to the temperatures defined below for pre-drawn syringe stability provided by the manufacturer:

- Use a temperature monitoring device, with continuous monitoring being preferred, to ensure consistent temperature monitoring during transport.
- Portable refrigerated units may be used to transport the vaccine.
  - Appropriate measures should be taken to ensure the vaccine is cushioned and protected from agitation during transport.
- Expanded polystyrene foam containers can be used for maintaining cold chain/temperature consistency across transport to administration site.
  - In addition, to protect from damage during transport, a hard-plastic container should be considered to carry the expanded polystyrene foam container (NOTE: A hard-sided plastic container alone may not be sufficient to maintain temperature control). A soft-sided container can also be considered if it is a qualified container or packout.
- If a cooling agent is used, a thick barrier (at least 1 inch) of bubble wrap or corrugated cardboard may be utilized as a barrier between the transport container cooling agent and the container with pre-drawn syringes. This is to prevent direct contact between pre-drawn syringes and the cooling agent that may cause the vaccine to freeze or deviate from appropriate cold chain.[14]

Pfizer-BioNTech COVID-19 Vaccine

- For the **purple** vial cap and label formulation, Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all its measured quality attributes when the diluted vaccine is stored in polycarbonate and polypropylene syringes with stainless steel needles for 6 hours at 2°C to 25°C (35°F to 77°F) after the source vial is diluted.
- For the **purple** vial cap and label border formulation, microbiological risk was assessed through a microbiological challenge study which showed that microbiological growth has a greater potential to occur after 6 hours. The hold time of 6 hours, from the time the source vial is diluted, is not specifically tied to a preparation environment and can be applied to doses prepared outside of ISO Class 5 environment (PEC).
- For the **orange** vial cap and label border formulation, Pfizer has conducted physical and chemical stability studies which have shown that the vaccine maintains all of its measured quality attributes when the diluted vaccine is stored in polycarbonate or polypropylene syringes for a cumulative time up to 24 hours post-dilution with no more than 12 hours at room temperature (up to 30°C). *(Updated 11/12/21)*
- For the **orange** vial cap and label border formulation, microbiological risk was assessed through a microbiological challenge study which showed that microbial growth has a greater potential to occur after 12 hours. Although no logarithmic growth of spiked microorganisms was seen until 24 hours at 25°C, a 2x safety factor was applied resulting in the 12 hours in use period. *(Updated 11/12/21)*

Moderna COVID-19 Vaccine

- According to the Chemistry, Manufacturing and Control (CMC) department at Moderna, pre-drawn syringes can be stored in the refrigerator to ambient room temperature at 2°C to 25°C (35°F to 77°F), provided they are administered within 12 hours of the first time the source vial is punctured.

Janssen Ad26 COVID-19 Vaccine

- According to Janssen, based on data on file, pre-drawn syringes can be stored:
  - In the refrigerator at 2°C to 8°C (36°F to 46°F), provided they are administered within 6 hours of the first time the source vial is punctured.
  - In ambient room temperature up to 25°C (77°F) provided they are administered within 2 hours of the first time the source vial is punctured.

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3 Waste Minimization and Ancillary Supply Disposal

Operational Considerations for Waste Minimization and Ancillary Supply Disposal for COVID-19 Vaccines

Background

The variety of COVID-19 vaccines in the manufacturing pipeline will continue to pose challenges for the safe and proper minimization of waste of unused vaccine and safe disposal of ancillary supplies (e.g., dry ice, syringes, needles). Disposal of unused vaccine or ancillary supply waste from a COVID-19 vaccine that has been authorized by local regulators should be performed in accordance with the directions in the manufacturer's labeling.[1,2,3] USP supports the Occupational Safety and Health Administration (OSHA) and other regulators setting and enforcing standards to ensure safe and healthful working conditions during the COVID-19 pandemic. This document focuses on considerations for disposal of unused or ancillary supply waste of COVID-19 vaccines and can be used to supplement a manufacturer's labeling, but not replace them. In addition, this document should not replace a facility's policies and procedures.

COVID-19 Vaccine Waste Minimization

Given the critical shortage of COVID-19 vaccines worldwide, sites should accordingly plan and build standard operating considerations (SOPs) to minimize loss of doses following local regulatory guidance. The following considerations should be made to minimize or control vaccine waste:

- A site should have plans in place to minimize waste of usable vaccine (e.g., waiting list for vaccines, plans to distribute vaccines if individuals do not keep appointments, agreements with pharmacies and other local centers for vaccine transport, etc.)
- Ensure cold chain is properly maintained with proper storage conditions and continuous temperature monitoring to prevent the need to discard any product due to temperature excursions.
- Ensure vaccine preparers are properly trained and demonstrate competency for proper aseptic technique to minimize the risk of contaminating the product.
- Maximize doses withdrawn from vials (6 doses from the Pfizer-BioNTech COVID-19 vaccine vial, 11 or 15 doses from the Moderna COVID-19 vaccine vial, and 5 doses from the Janssen Ad26 COVID-19 vaccine vials) by utilizing low dead volume (LDV) syringes/needles, whenever possible. A LDV syringe is designed to limit dead space that exists between the syringe hub and needle. A LDV needle is designed with less space between the needle and the plunger.
- For the Pfizer-BioNTech COVID-19 Vaccine, to ensure practice settings that may not have adequate quantities of LDV syringes to more consistently achieve the maximum doses withdrawn, a combination of LDV syringes and non-LDV syringes could also maximize doses withdrawn (e.g., 3 low dead-volume syringes and 3 non-low dead-volume syringes).
  - Inserting the needle in various locations of the vial septum can reduce leaking of vaccine and maximize doses withdrawn.
- For the Moderna COVID-19 Vaccine Max 15 dose vial, practice settings that may not have adequate quantities of LDV syringes may use a combination of 7 LDV syringes and 7 non-LDV syringes to consistently withdraw 14 doses. *(Added 6/17/21)*
- Carefully consider the number of pre-drawn syringes to prepare to avoid drawing up unnecessary doses.

- Use pre-drawn syringes with earliest discard time first to avoid waste.
- Carefully insert and withdraw needle from vial septum to not bend the needle which could lead to wastage. *(Added 6/17/21)*
- Ensure safe practices when recapping the needle and utilizing safety shields to reduce need to discard product due to microbiological risks. *(Added 6/17/21)*

Considerations for the Disposal of Vaccines and Ancillary Supplies

The authorized Janssen Ad26, Moderna, and Pfizer-BioNTech COVID-19 vaccines do not meet criteria for hazardous waste and their disposal should follow policies for disposal of medical waste. Medical waste is healthcare waste that may be contaminated by blood, body fluids, or other potentially infectious materials.[4] Medical waste disposal requirements are set by regulatory agencies. Thus, follow regulatory or facility policies for appropriate disposal. Empty vaccine vials are usually not considered hazardous or medical waste and do not require disposal in a biomedical waste container.[5]

Needles must be discarded in biohazard containers that are closable, puncture-resistant, leakproof on sides and bottom, labeled, and color-coded (e.g., sharps container). This is important to prevent an accidental needlestick, which can lead to transmission of infection. Then, dispose of the biohazard containers according to facility and regulatory requirements.

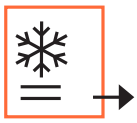
Thermal shipping containers should be returned to the manufacturer following instructions provided in the manufacturer pamphlet:

- Pfizer BioNTech COVID-19 vaccine thermal shipping container is to be returned with data loggers.
- Moderna COVID-19 vaccine thermal shipping container is to be returned alone.
- Janssen Ad26 COVID-19 vaccine's shipping container does not need to be returned.

Items to be discarded immediately after use or recommended double check when the vaccine exceeds the beyond-use-date and time may include:

- Empty vials
- Vials with unused vaccine
- Vials with unused diluent
- Pre-drawn syringes and needles
- Used syringes and needles (e.g., post patient injection, used in dilution process, etc.)

Facilities should have policies and procedures for security and storage for the COVID-19 vaccines. ASHP provides guidance on this topic.[6] In addition, the disposal of COVID-19 vaccine vials should be secured in a way to mitigate potential tampering.



Considerations for the Disposal of Dry Ice Product

(applicable for Pfizer-BioNTech COVID-19 Vaccine storage)

Centers for Disease Control and Prevention (CDC) guidance on the storage and safe disposal of dry ice is available at the healthcare practitioner portal of the CDC, which can be accessed here,[7] or as posted by the manufacturer (e.g., Pfizer-BioNTech Dry Ice Disposal Guidance).[8] Use of dry ice in confined spaces (small rooms or walk-in coolers) and/or poorly ventilated areas can result in depletion of oxygen, causing asphyxiation. Exposed skin should be protected from contact with dry ice. Considerations include the following:

- Once dry ice is no longer needed (vaccine has been removed), open the container and leave it at room temperature in a well-ventilated area. It will readily sublime from a solid to a gas.
- DO NOT leave dry ice in an unsecured area.
- DO NOT place dry ice in a drain or flush in the toilet.
- DO NOT dispose dry ice in the trash.
- DO NOT place dry ice in a closed area, such as an airtight container or walk-in cooler.

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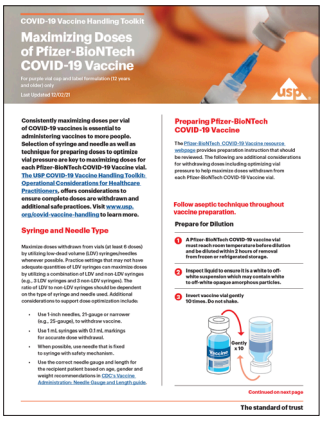
Supplemental content is also available

Handouts and related content intended to highlight key information and visually represent techniques discussed in this toolkit are also available by clicking on the links below. These handouts include:



Maximizing Doses of Pfizer-BioNTech COVID-19 Vaccine

Updated December 2021

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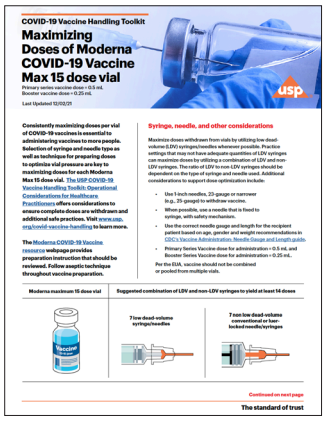
View the Video



Maximizing Doses of Moderna COVID-19 Vaccine Max 15 dose vial

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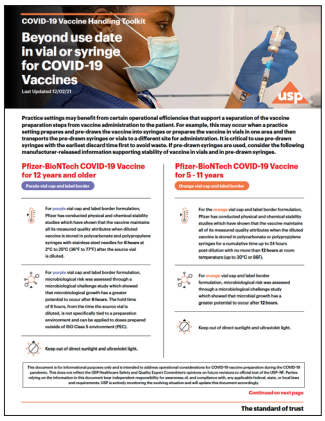

Beyond use date in vial or syringe for COVID-19 Vaccines

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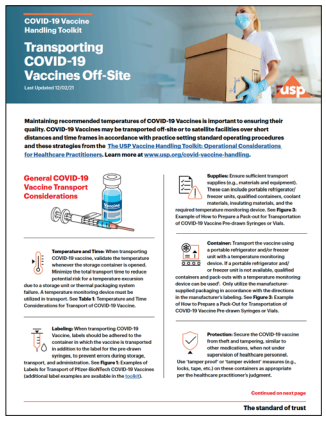

Transporting COVID-19 Vaccines Off-Site

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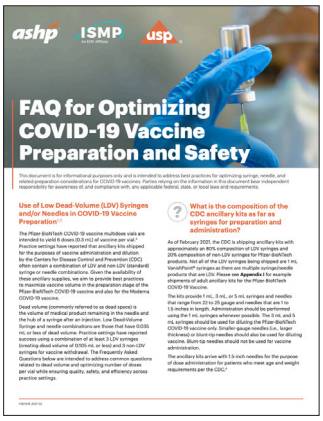

ASHP| ISMP | USP FAQs for Optimizing COVID-19 Vaccine Preparation and Safety

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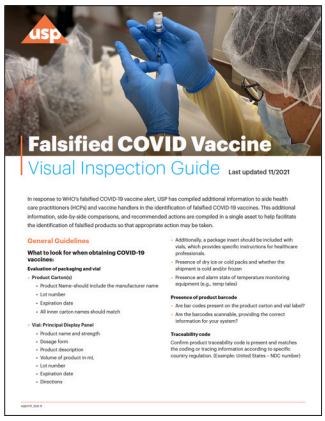

Falsified COVID Vaccine Visual Inspection Guide

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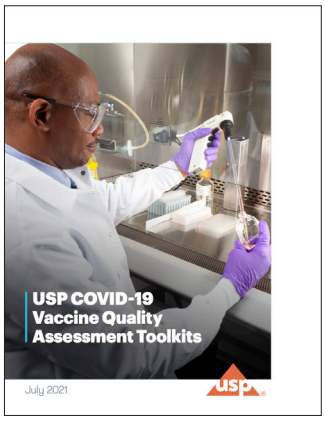

COVID-19 Vaccine Quality Assessment Toolkits

Download the guide

Your feedback helps us improve the content that we offer.

Please submit any questions or comments, including if this toolkit has been helpful to you, to COVID-19@usp.org.

Appendix I: Independent Expert Volunteers and Other Contributors to the COVID-19 Vaccine Handling Toolkit

The Toolkit's development was led by USP's Healthcare Safety & Quality Expert Committee, with input from other USP Expert Committees, government liaisons, observers, and USP staff. Participants as of June 2021:

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Appendix II: Example of Pfizer-BioNTech COVID-19 Vaccine Ancillary Kit Redistribution

Item Name	Quantity	Considerations
Pfizer-BioNTech COVID-19 vaccine vial	45	
0.9% sodium chloride, preservative free, sterile diluent	45	These are single use diluents
3 mL syringes, for dilution of vaccine	45	These are non-safety 3 mL or 5 mL syringes that are used in diluting the vaccine and not for administration (since they are *not* safety devices)
1 mL syringe/needle combination, for vaccine withdrawal and administration	45 * 6 = 270 doses total Will need at least 270 syringes/needles (rarely, some sites report a 7th dose of the Pfizer-BioNTech COVID-19 vaccine per vial). **Suggested ratio:** 80% LDV = 216 syringes/needles for administration 20% non-LDV = 54 syringes/needles for administration (non-low dead volume/standard)	The ancillary kits arrive with 80% low dead volume syringes and 20% non-low dead volume or standard syringes. Utilize at least 3 LDV and 3 non-LDV syringes for vaccine preparation to help maximize the 6th dose from the Pfizer-BioNTech COVID-19 vaccine vials If adequate supplies of LDV syringes are available, all LDV syringes can be utilized for vaccine withdrawal and administration
1.5 inch needles	The kits arrive with approximately 20% 1.5 inch needles for vaccine administration for patients who meet age, gender, and weight requirements for 1.5 inch based on CDC's Vaccine Administration: Needle Gauge and Length guide.[1]	Ensure adequate supply of needles for patients for redistribution
Immunization record cards	At least 270	
Other supplies include face shields, face masks, alcohol prep pads, and containers that may be redistributed based on existing site available supplies.		
Other supplies not included in the ancillary kits that sites should have on-hand are, for example, sharps containers, gloves, band-aids, and hand sanitizer.		

1. https://www.cdc.gov/vaccines/hcp/admin/downloads/vaccine-administration-needle-length.pdf

NOTE: PED (Pfizer age 5-11 Years Old) example kits would include 1" needles and 1 mL syringes, as well as the diluent required.
(Updated 11/12/21)