

Clinical Update

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Bivalent mRNA COVID-19 Vaccines: Steps Toward Simplification of Recommendations

- **Bivalent** mRNA COVID-19 vaccines authorized and recommended to be used for **all doses** administered to individuals 6 months of age and older.
 - Decisions based on review of totality of data, including safety and effectiveness, population immunity, implementation considerations
- **Monovalent** mRNA COVID-19 vaccines no longer authorized and recommended for use.
 - Deauthorization of monovalent product **not** related to safety concerns.
- Additional bivalent mRNA dose for people 65+ and with certain kinds of immunocompromise authorized
- No changes to Novavax monovalent and J&J monovalent vaccine authorizations and recommendations.

CDC Advisory Committee Updates: COVID-19 Vaccine Safety

- Safety of mRNA COVID-19 bivalent booster
 - Updated data on ischemic stroke from the Vaccine Safety Datalink (VSD) system & Vaccine Adverse Event Reporting System (VAERS)
 - No evidence of increased risk of ischemic stroke after mRNA COVID 19 bivalent boosters in U.S. & international surveillance.
- V-safe
 - COVID-19 vaccine monitoring ending soon.
 - Next generation v-safe for other vaccines under development.
- Safety monitoring continues
 - [Full list of vaccine safety monitoring systems.](#)

CDC Advisory Committee Updates: COVID-19 Vaccine Effectiveness

- Monovalent mRNA vaccines protect against symptomatic infection in children aged 6 months–4 years (Pfizer-BioNTech) and 6 months–5 years (Moderna); protection wanes over time.
- Bivalent mRNA vaccines protect against emergency department/urgent care visits and hospitalizations in adults; protection wanes over time.
- mRNA vaccines provide durable protection against invasive mechanical ventilation and death.

Implications of Updated Recommendations

- Simpler – single bivalent vaccine for most persons
- Flexibility for persons at higher risk of severe COVID-19
- Remain less simple for younger children

Summary of mRNA COVID-19 Vaccination Schedule Revision

- People ages 6 years and older who are unvaccinated or previously received only monovalent vaccine doses are recommended to receive 1 bivalent mRNA vaccine dose
- For young children, the number of bivalent doses at time of initial vaccination depends on age and vaccine product
 - Children ages 6 months–4 years are recommended to receive either 2 or 3 bivalent mRNA vaccine doses
 - Children age 5 years are recommended to receive either 1 or 2 bivalent mRNA vaccine doses
- Some people may receive an additional bivalent mRNA vaccine dose
 - Most individuals with certain kinds of immunocompromise: at least 2 months following the initial dose of a bivalent COVID-19 vaccine*
 - Adults 65+: at least 4 months following the initial dose of a bivalent COVID-19 vaccine

*Further age-appropriate doses of mRNA COVID-19 Vaccine, Bivalent may be administered at the discretion of the healthcare provider, taking into consideration the individual's clinical circumstances. See FDA fact sheets for more information

Table 1. COVID-19 vaccination schedule for people who are not moderately or severely immunocompromised by COVID-19 vaccination history, April 2023

Ages 6 months–4 years

COVID-19 vaccination history	Bivalent vaccine	Number of bivalent doses indicated	Dosage (mL/ug)	Vaccine vial cap and label colors	Interval between doses*
Unvaccinated	Moderna ___or___	2	0.25 mL/25 ug	Dark blue cap; gray label border	Dose 1 and Dose 2: 4–8 weeks
	Pfizer BioNTech [†]	3	0.2 mL/3 ug	Maroon	Dose 1 and Dose 2: 3–8 weeks Dose 2 and dose 3: At least 8 weeks
1 dose monovalent Moderna	Moderna	1	0.25 mL/25 ug	Dark blue cap; gray label border	4–8 weeks after monovalent dose
2 doses monovalent Moderna	Moderna	1	0.2 mL/10 ug	Dark pink cap; yellow label border	At least 8 weeks after last monovalent dose
2 doses monovalent Moderna and 1 dose bivalent Moderna	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA
1 dose monovalent Pfizer-BioNTech	Pfizer BioNTech [†]	2	0.2 mL/3 ug	Maroon	Dose 1: 3–8 weeks after monovalent dose Dose 1 and Dose 2: At least 8 weeks
2 doses monovalent Pfizer-BioNTech	Pfizer BioNTech	1	0.2 mL/3 ug	Maroon	At least 8 weeks after last monovalent dose
3 doses monovalent Pfizer-BioNTech	Pfizer BioNTech	1	0.2 mL/3 ug	Maroon	At least 8 weeks after last monovalent dose
2 doses monovalent Pfizer-BioNTech and 1 dose bivalent Pfizer-BioNTech	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA

Age 5 years

COVID-19 vaccination history	Bivalent vaccine	Number of bivalent doses indicated	Dosage (mL/ug)	Vaccine vial cap and label colors	Interval between doses*
Unvaccinated	Moderna ___or___	2	0.25 mL/25 ug	Dark blue cap; gray label border	Dose 1 and Dose 2: 4–8 weeks
	Pfizer BioNTech	1	0.2 mL/10 ug	Orange	
1 dose monovalent Moderna	Moderna ___or___	1	0.25 mL/25 ug	Dark blue cap; gray label border	4–8 weeks after monovalent dose
	Pfizer BioNTech	1	0.2 mL/10 ug	Orange	At least 8 weeks after monovalent dose
2 doses monovalent Moderna	Moderna ___or___	1	0.2 mL/10 ug	Dark pink cap; yellow label border	At least 8 weeks after last monovalent dose
	Pfizer BioNTech	1	0.2 mL/10 ug	Orange	At least 8 weeks after last monovalent dose
2 doses monovalent Moderna and 1 dose bivalent mRNA	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA
1 or more doses monovalent Pfizer-BioNTech	Pfizer-BioNTech	1	0.2 mL/10 ug	Orange	At least 8 weeks after last monovalent dose
2 doses monovalent Pfizer-BioNTech and 1 dose bivalent Pfizer-BioNTech	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA
Ever received 1 dose bivalent Pfizer-BioNTech (regardless of monovalent vaccine history)	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA

Table 1. COVID-19 vaccination schedule for people who are not moderately or severely immunocompromised by COVID-19 vaccination history, April 2023

Ages 6–11 years

COVID-19 vaccination history	Bivalent vaccine	Number of bivalent doses indicated	Dosage (mL/ug)	Vaccine vial cap and label colors	Interval between doses*
Unvaccinated	Moderna ___or___	1	0.25 mL/25 ug	Dark blue cap; gray label border	—
	Pfizer BioNTech	1	0.2 mL/10 ug	Orange	—
1 or more doses monovalent mRNA (no doses bivalent mRNA)	Moderna ___or___	1	0.25 mL/25 ug	Dark blue cap; gray label border	At least 8 weeks after last monovalent dose
	Pfizer BioNTech	1	0.2 mL/10 ug	Orange	At least 8 weeks after last monovalent dose
2 or more doses monovalent mRNA and 1 dose bivalent mRNA	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA
Ever received 1 dose bivalent mRNA (regardless of monovalent vaccine history)	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA

Ages 12 years and older

COVID-19 vaccination history	Bivalent vaccine	Number of bivalent doses indicated	Dosage (mL/ug)	Vaccine vial cap and label colors	Interval between doses*
Unvaccinated	Moderna ___or___	1	0.5 mL/50 ug	Dark blue cap; gray label border	—
	Pfizer BioNTech	1	0.3 mL/30 ug	Gray	—
1 or more doses monovalent mRNA (no doses bivalent mRNA)	Moderna ___or___	1	0.5 mL/50 ug	Dark blue cap; gray label border	At least 8 weeks after last monovalent dose
	Pfizer BioNTech	1	0.3 mL/30 ug	Gray	At least 8 weeks after last monovalent dose
Ever received 1 dose bivalent mRNA (regardless of monovalent vaccine history)	NA; previously received 1 bivalent vaccine dose	NA	NA	NA	NA

People ages 65 years and older have the option to receive 1 additional bivalent mRNA vaccine dose at least 4 months after the first dose of a bivalent mRNA vaccine. If Moderna is used, administer 0.5 mL/50 ug (dark blue cap and label with a gray border); if Pfizer-BioNTech is used, administer 0.3 mL/30 ug (gray cap and label with a gray border).

Guidance for Immunocompromised Young Children

- CDC guidance will be available soon
- Refer to HCP fact sheets
 - [Moderna Fact Sheet for HCP](#)
 - [Pfizer Fact Sheet for HCP](#)

Interchangeability of COVID-19 vaccines

Vaccine Status	Age	Recommendation
Children who are unvaccinated	6 months-5 years	Should receive all bivalent doses from the same manufacturer
For people who are not moderately or severely immunocompromised and previously initiated vaccination with a monovalent mRNA vaccine	6 months-4 years who received 1 or more doses of monovalent mRNA vaccine	Only bivalent mRNA vaccine dose(s) from the same vaccine manufacturer.
	5 year old who previously received 1 or more doses of Monovalent Moderna COVID-19 Vaccine	Either bivalent Moderna or bivalent Pfizer-BioNTech COVID-19 vaccine.
	5 year old who previously received 1 or more doses of Monovalent Pfizer-BioNTech COVID-19 are authorized	Only bivalent Pfizer-BioNTech COVID-19 Vaccine
	6 years and older who previously received 1 or more doses of a monovalent mRNA vaccine	Either bivalent Moderna or bivalent Pfizer-BioNTech COVID-19 vaccine.

Updated: Appendix B. People who received COVID-19 vaccine outside the United States

Table B. People who received COVID-19 vaccine outside the United States

Table B.1. Received a COVID-19 vaccine that is FDA-authorized

Vaccination history	Recommended actions
Received 1 or more monovalent mRNA vaccine dose(s)	<ul style="list-style-type: none"> Administer 1 bivalent mRNA dose.* See Table 1 if age 6 months–5 years.
Received 1 or 2 Novavax vaccine dose(s)	<ul style="list-style-type: none"> Administer 1 bivalent mRNA dose.*†
Received a bivalent mRNA dose	<ul style="list-style-type: none"> Do not repeat. See Special situation (after table footnotes).

Table B.2. Received a COVID-19 vaccine listed for emergency use by WHO but not authorized by FDA⁴⁵

Vaccination history	Recommended actions
Received all recommended primary series doses for that vaccine	<ul style="list-style-type: none"> Administer 1 bivalent mRNA dose.*†
Received partial primary series for that vaccine	<ul style="list-style-type: none"> Administer 1 bivalent mRNA dose.* See Table 1 if age 6 months–5 years.
Received a monovalent booster dose after completion of primary series	<ul style="list-style-type: none"> Administer 1 bivalent mRNA dose.*
Received a bivalent mRNA booster dose after completion of primary series	<ul style="list-style-type: none"> Do not repeat.* See Special situation (after table footnotes).

Table B.3. Received all or some of the recommended doses of COVID-19 vaccines that are NOT FDA-authorized or among those listed for emergency use by WHO

Vaccination history	Recommended actions
Received any number and combination of vaccine doses	<ul style="list-style-type: none"> Do not count doses received toward vaccination in the US. Vaccinate according to the US schedule (Table 1). Start vaccination at least 28 days after the last dose of vaccine.

Updated: Appendix D. Vaccine Administration Errors & Deviations

Table D. Interim recommendations for COVID-19 vaccine administration errors and deviations

Type	Administration error/deviation	Interim recommendation
Site/route	<ul style="list-style-type: none"> Incorrect site (i.e., site other than the deltoid muscle or vastus lateralis muscle) 	<ul style="list-style-type: none"> Do not repeat dose.
	<ul style="list-style-type: none"> Incorrect route (e.g., subcutaneous) 	<ul style="list-style-type: none"> Do not repeat dose. Inform the recipient of the potential for local and systemic adverse events.
Age	<ul style="list-style-type: none"> Unauthorized age group (recipients younger than age 6 months) 	<ul style="list-style-type: none"> Do not give another dose at this time.*
	<ul style="list-style-type: none"> Recipients transitioning from age 4 years to 5 years during the primary series who start a 3-dose Pfizer-BioNTech series with the product for ages 6 months–4 years (maroon cap and label border) and incorrectly receive the product for ages 5–11 years (orange cap and label border) for either dose 2 or 3 	<ul style="list-style-type: none"> Do not repeat dose 2 or 3. If the error occurred with dose 2, administer the bivalent Pfizer-BioNTech product for ages 6 months–4 years (maroon cap and label border) for the third dose at least 8 weeks after the second dose.
Product and dosage	<ul style="list-style-type: none"> Higher-than-authorized dose administered (e.g., incorrect dose volume, incorrect product resulting in higher-than-authorized dose) 	<ul style="list-style-type: none"> Do not repeat dose.^{4†}
	<ul style="list-style-type: none"> Lower-than-authorized dose administered (e.g., leaked out of the syringe, equipment failure, recipient pulled away, incorrect product resulting in lower-than-authorized dose) 	<ul style="list-style-type: none"> Repeat dose immediately (no minimum interval).⁴⁵ However, if a half-volume dose of vaccine is administered to a patient recommended for the full volume, another half-volume dose can be administered on the same clinic day, and the 2 doses can count as 1 full dose.
Storage and handling	<ul style="list-style-type: none"> Dose administered after improper storage and handling (i.e., temperature excursion) 	<ul style="list-style-type: none"> Contact the manufacturer for information on the stability of the vaccine.⁴ If the manufacturer does not have data to support the stability of the vaccine, repeat the dose immediately (no minimum interval).⁵
	<ul style="list-style-type: none"> Dose administered past the expiration/beyond-use date 	<ul style="list-style-type: none"> Contact the manufacturer for information on the stability of the vaccine.⁴ If the manufacturer does not have data to support the stability of the vaccine, repeat the



COVID-19 Vaccine Product Guide

COVID-19 Vaccine Product Guide Vaccinate ALL 58

Check vaccine labels and EUA fact sheets before use to avoid mix-ups.
EUA fact sheets supersede info on vials and carton. Refer to [CDC Product Guide](#) for more information.

	Pfizer			
	Infant/Toddler 6 months– 4 years*	Bivalent 6 months– 4 years	Pediatric Primary Series 5–11 years	Bivalent 5–11 years
	Deauthorized	"Bivalent" on label	Deauthorized	"Bivalent" on label
Packaging	Maroon Cap	Maroon Cap	Orange Cap	Orange Cap
Doses Per Vial	10 doses	10 doses	10 doses	10 doses
Carton Size	100 doses	100 doses	100 doses	100 doses
Min. Standard Order	Not Available	100 doses	Not Available	100 doses
NDC/Unit of Use (vial)	59267-0078-01	59267-0609-01	59267-1055-01	59267-0565-01
CVX Code	219	302	218	301
Storage Limits Before Puncture: Label vaccine with expiration and use-by dates.				
ULT (-90°C to -60°C)	Up to 18 months from manufacture date.			
Thermal Shipper				
Freezer				
Refrigerator (2–8°C)	Up to 10 weeks (write the date on carton)			
Expiration Date	18 months from manufacture date printed on vial and carton or check product website .			
Administration				
Diluent (supplied)	2.2 mL per vial	2.2 mL per vial	1.3 mL per vial	1.3 mL per vial
Dose Volume—Primary/Additional	Do not use.	0.2 mL† (3 mcg dose)	Do not use.	0.2 mL† (10 mcg dose)
Dose Volume—Booster	N/A	N/A	N/A	N/A
Refrigerator Thaw Time (2° to 8°C/ 36°F to 46°F)	Up to 2 hours in carton	Up to 2 hours in carton	Up to 4 hours in carton	Up to 4 hours in carton
(Do not refreeze)				
Room Temp Thaw Time	Vial: 30 minutes at up to 25°C (77°F)			
Total Time at Room Temp (Do not refreeze)	Up to 12 hours (including thaw time) at 8°C to 25°C (46°F to 77°F)			
Storage Limits After Puncture (Multi-dose vials): Record puncture and use-by time on vial label.				
Use-By Limit (Discard Time After 1st Puncture)	Discard after 12 hours at 2°C to 25°C (35°F to 77°F)			

* Labels for Pfizer 6 months–4 years product may not reflect expanded age ranges. Refer to [Provider Letter](#).
† Syringes in ancillary kits may require estimating volume between lines, or using private stock.

California COVID-19 Vaccination Program IMM-1399 (4/20/23) Page 1 of 3

COVID-19 Vaccine Product Guide Vaccinate ALL 58

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	Pfizer		Novavax	Janssen (J&J)
	Adol/Adult Primary Series 12+ years	Bivalent 12+ years	Primary 12+ yrs Monovalent Booster 18+	Adult 18+ years
	Deauthorized	"Bivalent" on label		
Packaging	Gray Cap	Gray Cap	Royal Blue Cap	Blue Cap
Doses Per Vial	6 doses	6 / 1 doses	5 doses	5 doses
Carton Size	60 doses	60 / 10 doses	50 doses	50 doses
Min. Standard Order	Not Available	180 / 50 doses	100 doses	Not Available
NDC/Unit of Use (vial)	00069-2025-01 (59267-1025-01)	59267-0304-01 (59267-1404-01)	80631-0102-01 (80631-0100-01)	59676-0580-05
CVX Code	217	300	211	212
Storage Limits Before Puncture: Label vaccine with expiration and use-by dates.				
ULT (-90°C to -60°C)	Until expiration			
Thermal Shipper				
Freezer				
Refrigerator (2–8°C)	Up to 10 weeks		Until expiration	Until expiration
Expiration Date	18 months from manufacture date on vial and carton. Check product website .		Check product website .	Check product website , QR code, or 800-565-4008
Administration				
Diluent (supplied)	Do not dilute		Do not dilute	Do not dilute
Dose Volume—Primary/Additional	Do not use.	0.3 mL (30 mcg dose)	Age 12+: 0.5 mL (5 mcg)	0.5 mL
Dose Volume—Booster	N/A	N/A	Age 18+: 0.5 mL (5 mcg)	0.5 mL
Refrigerator Thaw Time (2° to 8°C/ 36°F to 46°F)	Up to 6 hours in carton	In carton, Multi-dose: up to 6 hours. Single-dose: up to 2 hours.	N/A	N/A. If needed immediately, thaw at room temperature.
(Do not refreeze)			N/A	Carton: up to 4 hrs Vial: about 1 hour at 25°C (77°F) max
Room Temp Thaw Time	Vial: 30 minutes at up to 25°C (77°F)		N/A	Store up to 12 hours at 9°C to 25°C (47°F to 77°F)
Total Time at Room Temp (Do not refreeze)	Up to 12 hours (including thaw time) at 8°C to 25°C (46°F to 77°F)		N/A	
Storage Limits After Puncture (Multi-dose vials): Record puncture and use-by time on vial label.				
Use-By Limit (Discard Time After 1st Puncture)	Discard after 12 hours at 2°C to 25°C (35°F to 77°F)		Discard after 6 hours at 2° to 8°C (36° to 77°F)	Discard after 6 hours at 2° to 8°C (36°F to 77°F) or 2 hours at 25°C (77°F) max

California COVID-19 Vaccination Program IMM-1399 (4/20/23) Page 2 of 3

COVID-19 Vaccine Product Guide Vaccinate ALL 58

Check vaccine labels and EUA fact sheets before use to avoid mix-ups.
EUA fact sheets supersede info on vials and carton. Refer to [CDC Product Guide](#) for more information.

	Moderna				
	Infant/Toddler 6 months– 5 years	Bivalent 6 months– 5 years	Bivalent 6 months+	Pediatric Primary Series 6–11 years*	Adol/Adult Primary Series 12+ years
	Deauthorized	"Bivalent" On label	Gray Border	Purple Border	Light Blue Border
Packaging	Dark Blue Cap	Dark Pink Cap	Dark Blue Cap	Dark Blue Cap	Red Cap
Doses Per Vial	10 doses	2 doses	5–10 doses	5 doses	10–11 doses
Carton Size	100 doses	20 doses	50–100 doses	50 doses	100 doses
Min. Standard Order	Not Available	100 doses	100 doses	Not Available	Not Available
NDC/Unit of Use (vial)	80777-0279-05	80777-0283-02	80777-0282-05	80777-0275-05	80777-0273-10
CVX Code	228	230	229	221	207
Storage Limits Before Puncture: Label vaccine with expiration and use-by dates.					
ULT (-90°C to -60°C)					
Thermal Shipper					
Freezer	Until expiration at -50°C to -15°C (-58°F to 5°F)				
Refrigerator	Up to 30 days (not to exceed expiration date) at 2–8°C (36–46°F)				
Expiration Date	Check product website or QR code.			Expired.	Expired.
Administration					
Diluent	Do not dilute.				
Dose Volume—Primary/Additional	Do not use.	0.2 mL† (only for use after 2 monovalent doses*)	6 mo–11y: 25 mL 12+ y: 0.5 mL	Do not use.	Do not use.
Refrigerator Thaw Time (2° to 8°C/ 36°F to 46°F)	2 hours (Let vial stand at room temp for 15 min before administering.)	45 minutes (Let vial stand at room temp for 15 min before administering.)	2 hours (Let vial stand at room temp for 15 min before administering.)	2 hours (Let vial stand at room temp for 15 min before administering.)	2.5 hours (Let vial stand at room temp for 15 min before administering.)
(Do not refreeze)					
Room Temp Thaw Time	45 minutes at 15° to 25°C (59° to 77°F)	15 minutes at 15° to 25°C (59° to 77°F)	45 minutes at 15° to 25°C (59° to 77°F)	45 minutes at 15° to 25°C (59° to 77°F)	1 hour at 15° to 25°C (59° to 77°F)
Total Time at Room Temp (Do not refreeze)	Store up to 24 hours at 8°C to 25°C (46°F to 77°F)				
Storage Limits After Puncture: Record puncture and use-by time on vial label.					
Use-By Limit (Discard Time After 1st Puncture)	12 hours at 2°C to 25°C (36°F to 77°F)	8 hours at 2°C to 25°C (36°F to 77°F)	Discard after 12 hours at 2°C to 25°C (36°F to 77°F)		

* Labels for early shipments of Moderna 6–11 years product do not reflect authorized age ranges. Refer to [Provider Letter](#).
† Syringes in ancillary kits may require estimating volume between lines, or using private stock.
^ Refer to Moderna [HCP Factsheet](#) for detailed guidance.

California COVID-19 Vaccination Program IMM-1399 (4/20/23) Page 3 of 3

Looking Ahead

- June 2023: FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting
- Fall 2023: Commercialization

Resources

- Updated materials from FDA
 - [Pfizer Fact Sheet for HCP](#)
 - [Moderna Fact Sheet for HCP](#)
 - [Moderna Dear Healthcare Provider Letter](#)

- Updated materials from CDC
 - [CDC Interim Clinical Considerations for COVID-19 Vaccine](#)

