### Combination Vaccines & Invalid Doses

### Clara Alvarez, BS Quality Improvement Coordinator May 24, 2023



## Learning Objectives

- 1. Benefits of combination vaccines
- 2. Fewer shots, but same protection
- 3. Common combination vaccines for children
- 4. Why is this vaccine showing up Not Valid
- 5. Subpotent
- 6. Vaccination errors

## Benefits for children

- Fewer shots
- Less pain and discomfort
- On-time protection

### **Benefits for Parents**

- Fewer visits to doctor
- Less hassle and cost with fewer visits.
- Less time off from work or family activity

## Fewer Shots Same Protection

In order to reduce the number of shots a child receives in a doctor's visit; some vaccines are offered as combination vaccines. A combination vaccine is two or more different vaccines that have been combined into a single shot.

Combination vaccines have been in use in the United States since the mid-1940s. Examples of combination vaccines are: <u>DTap</u> (diphtheria-tetanus-pertussis), trivalent IPV (three strains of inactivated polio vaccine), <u>MMR</u> (measles-mumps-rubella).

## Common Combination Vaccines for Children

Vaccine Name	Combines	Protection from
Pediarix	DTaP + Hep B + IPV	5 diseases (Diphtheria, tetanus, pertussis, hepatitis B, and polio)
Pentacel	DTaP + IPV + Hib	<b>5 diseases</b> (Diphtheria, tetanus, pertussis, polio, and Hib ( <i>Haemophilus</i> <i>influenzae</i> type b))
Kinrix Quadracel	DTaP + IPV	<b>4 diseases</b> (Diphtheria, tetanus, pertussis, and polio)
Vaxelis	DTaP + IPV + Hib + HepB	<b>6 diseases</b> (Diphtheria, tetanus, pertussis, polio, hepatitis B, and Hib ( <i>Haemophilus influenzae</i> type b))
ProQuad	MMR + varicella (chickenpox)	<b>4 diseases</b> (measles, mumps, rubella, and varicella)

### Available Combination Vaccines

#### DTaP-IPV (Kinrix)

Ages: 4 years inrough o yea
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Use for: DTaP dose #5

IPV dose #4

Do NOT use for DTaP doses 1 through 4 OR IPV doses 1 through 3

Route: Intramuscular (IM) injection

#### **DTaP-IPV-HepB (Pediarix)**

Ages:6 weeks through 6 yearsUse for:DTaPand IPV: Doses #1, #2, and/or #3HepB: Any dose in the seriesDo NOT use for HepB birth doseRoute:Intramuscular (IM) injection

### Available Combination Vaccines

#### **DTaP-IPV-Hib (Pentacel)**

Ages: 6 weeks through 4 years Use for: DTaP and IPV: Doses #1, #2,

#3, and/or #4 Hib: Any dose in the series

Route: Intramuscular (IM) injection

Reconstitute Hib powder ONLY with manufacturer-supplied DTaP-IPV liquid diluent

Use immediately after reconstitution Do NOT administer DTaP-IPV w/o Hib

#### DTaP-IPV-HepB-Hib (Vaxelis)

Ages:	6 weeks through 4 years					
Use for:	DTaP and IPV: Doses #1, #2, and/or					
	#3					
	Hep B: Any dose in the series					
	(Do NOT use for HepB birth dose)					
	Hib: Any dose in the series					
Route:	Intramuscular (IM) injection					

### Available Combination Vaccines

#### DTaP-IPV (Quadracel)

Ages:4 years through 6 yearsUse for:DTaP dose #5IPV dose #4 or #5IPV dose #4 or #5Do NOT use for DTaP doses 1through 4 OR IPV doses 1 through 3Route:Intramuscular (IM) injection

#### MMRV (ProQuad)

Ages:12 months through 12 yearsUse for:Any dose in the seriesRoute:Subcutaneous (subcut) injection

Reconstitute MMRV powder ONLY with manufacturer-supplied sterile water diluent Beyond Use Time: Discard reconstituted vaccine if not used within 30 minutes.

#### **Immunization Schedule with Combination Vaccines**



Make sure the vaccine you administer contains the antigens on the doctor's order. Keep it simple. Stick with the same product.

This is a suggested schedule for VFC providers ordering combination vaccines. For alternatives and details, consult the latest "Recommended Immunization Schedules for persons aged 0-18 years, United States." For more info, visit EZIZ.ORG

- <sup>1</sup> A dose of Hepatitis B vaccine is not necessary at 4 months if doses are given at birth and 2 months but may be included as part of a combination vaccine.
- <sup>2</sup> The six month dose is not needed if Rotarix<sup>®</sup> was used exclusively for both dose 1 and 2 of the rotavirus vaccine series.
- <sup>3</sup> This six month Hib dose is not indicated if PedvaxHIB<sup>®</sup> is used exclusively for the 2 and 4 month infant doses.
- <sup>4</sup> CDC recommends MMR + Varicella at 12-15 months. Providers can use their discretion whether to use MMRV, however.
- <sup>5</sup> Can be administered as late as 15 months. For more information, consult the Recommended Child and Adolescent Immunization Schedule for ages 18 years or younger, United States, 2021.

- 6 Influenza vaccine is available in thimerosal-free options. See California Health and Safety Code § 124172.
- <sup>7</sup> Licensed by FDA for children 4 through 6 years with previous doses of IN-FANRIX<sup>TM</sup> or PEDIARIX<sup>TM</sup> ACIP recommends that, whenever feasible, the same manufacturer's DTaP vaccines be used for each dose in the series; however, vaccination should not be deferred because the type of DTaP previously administered is unavailable or unknown. See www.cdc.gov/mmwr/ preview/mmwrhtml/mm5739a4.htm.
- <sup>8</sup> Licensed by FDA for children 6 weeks through 4 years of age (prior to the 5th birthday).

California Department of Public Health, Immunization Branch [MM-922 (5/21)



# Can we switch back and forth from separate vaccines at one visit to combination vaccines at another visit?

Switching between combination and single-antigen vaccines poses no problem as long as you maintain the recommended minimum intervals for all vaccines and the vaccines are licensed for the age of the patient.

For example, if a child is given separate DTaP, IPV, Hib, and HepB vaccines during her 2-month visit, you could we give her either DTaP-IPV/Hib (Pentacel) or DTaP-HepB-IPV (Pediarix) at her 4-month visit.

## Combination Vaccines and Children Who Are Behind

### Can combination vaccines be used with children who have fallen behind with their vaccinations? If so, what schedule should we follow?

**Yes- Combination vaccines may used for children who have fallen behind.** The minimum interval between doses is the greatest interval between any of the individual antigens.

For example, the minimum interval between the first and second doses of MMR is 4 weeks and the minimum interval between the first and second doses of varicella vaccine is **12 weeks.** When the two vaccines are combined in MMRV (ProQuad, Merck) the minimum interval between MMRV dose #1 and dose #2 is **12 weeks**, which is the greatest of the minimum intervals of the two vaccines if given separately

## Vaccines Recommended By Selected Tracking Schedule



Select	Vaccine Group	Vaccine	Earliest Date	Recommended Date	Past Due Date
	<u>DTP/aP</u>	DTaP, NOS		Maximum Age Exceeded	
	<u>HepA</u>	HepA, NOS	11/24/2012	11/24/2012	06/24/2013
	<u>HepB</u>	HepB, NOS		Complete	
	<u>Hib</u>	Hib, NOS		Maximum Age Exceeded	
	HPV	HPV, NOS	11/24/2020	11/24/2022	12/24/2024
	<u>Influenza-seasni</u>	Flu NOS	11/24/2020	08/01/2022	11/24/2020
	<u>Meningo</u>	MCV4, NOS	11/24/2021	11/24/2022	11/24/2024
	MMR	MMR	11/24/2012	11/24/2012	03/24/2013
	<u>Polio</u>	Polio-Inject	11/24/2015	11/24/2015	11/24/2018
	<u>Td/Tdap</u>	Tdap	11/24/2018	11/24/2018	11/24/2018
	<u>Varicella</u>	Varicella	11/24/2012	11/24/2012	03/24/2013
					Add Selected

## Recommended and Minimal Ages and Intervals Between Vaccine Doses

#### Appendix A

#### Recommended and minimum ages and intervals between vaccine doses(a),(b),(c),(d)

Vaccine and dose number	Recommended age for this dose	Minimum age for this dose	Recommended interval to next dose	Minimum interval to next dose
DTaP-1(*)	2 months	6 weeks	8 weeks	4 weeks
DTaP-2	4 months	10 weeks	8 weeks	4 weeks
DTaP-3	6 months	14 weeks	6-12 months <sup>II</sup>	6 months®
DTaP-4	15-18 months	15 months <sup>(1)</sup>	3 years	6 months
DTaP-5 <sup>(g)</sup>	4-6 years	4 years	-	_
HepA-1 <sup>(e)</sup>	12-23 months	12 months	6-18 months	6 months
HepA-2	≥18 months	18 months	-	_
HepB-1 <sup>(h)</sup>	Birth	Birth	4 weeks-4 months	4 weeks
HepB-2	1-2 months	4 weeks	8 weeks-17 months	8 weeks
HepB-3 <sup>(i)</sup>	6-18 months	24 weeks	-	_
Hib-1 <sup>(i)</sup>	2 months	6 weeks	8 weeks	4 weeks
Hib-2	4 months	10 weeks	8 weeks	4 weeks
Hib-3 <sup>(k)</sup>	6 months	14 weeks	6-9 months	8 weeks
Hib-4	12-15 months	12 months	-	_
HPV-1 (Two-Dose Series) <sup>(1)</sup>	11-12 years	9 years	6 months	5 months
HPV-2	11-12 years (+6 months)	9 years +5 months <sup>(m)</sup>	-	_
HPV-1 <sup>(n)</sup> (Three-Dose Series)	11-12 years	9 years	1-2 months	4 weeks
HPV-2	11-12 years (+1-2 months)	9 years (+4 weeks)	4 months	12 weeks (n)
HPV-3 <sup>(n)</sup>	11-12 years (+6 months)	9 years (+5 months)	_	_
Influenza, inactivated <sup>(o)</sup>	≥6 months	6 months <sup>(p)</sup>	4 weeks	4 weeks
IPV-1 <sup>(e)</sup>	2 months	6 weeks	8 weeks	4 weeks
IPV-2	4 months	10 weeks	8 weeks-14 months	4 weeks
IPV-3	6-18 months	14 weeks	3-5 years	6 months
IPV-4 <sup>(q)</sup>	4-6 years	4 years	_	_
	2-49 years	2 years	4 weeks	4 weeks
MenACWY-1 <sup>(r)</sup>	11-12 years	2 months <sup>(s)</sup>	4-5 years	8 weeks
MenACWY-2	16 years	11 years (+ 8 weeks)®	_	-
MenB-1	Healthy adolescents: 16-23 years	16 years	Bexsero: 4 weeks Trumenba: 6 months <sup>[d]</sup>	Bexsero: 4 weeks Trumenba: 6 monthski
MenB-1	Persons at increased risk: ≥10 years	10 years	Bexsero: 4 weeks Trumenba: 1–2 months <sup>(c)</sup>	Bexsero: 4 weeks Trumenba: 1 month
MenB-2	Healthy adolescents: 16-23 years (+1 month)	16 years (+1 month)	-	-
MenB-2	Persons at increased risk:	10 years (+1 month)	Bexsero: —	Bexsero: —
	≥10 years (+1 month)		Trumenba: 4-5 month	Trumenba: 4 monthski
MenB-3 <sup>(u)</sup>	Persons at increased risk: ≥10 years (+6 months <sup>(c)</sup> )	10 years (+6 months네)	-	-

## Why Is This Vaccine Showing Up Invalid?

DOB 11/24/2011

Immunization Record

Vaccine Group	Date Admin	Series	Vaccine [Trade Name]	Dose Owned?
DTP/aP	01/06/2012	1 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full
	02/03/2012	2 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full
	03/01/2012	3 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full
	08/25/2012	NOT VALID	DTaP,5 pertussis antigens [DAPTACEL ®]	Full
HepB	<u>11/25/2011</u>	1 of 3	HepB-Peds [Recombivax Peds ®]	Full
	<u>01/06/2012</u>	2 of 3	HepB-Peds [Recombivax Peds ®]	Full
	05/26/2012	3 of 3	HepB-Peds [Recombivax Peds ®]	Full
Hib	01/06/2012	1 of 4	Hib-PRP-T [ActHib ®]	Full
	02/03/2012	2 of 4	Hib-PRP-T [ActHib ®]	Full
	05/26/2012	3 of 4	Hib-PRP-T [ActHib ®]	Full
	08/25/2012	NOT VALID	Hib-PRP-T [ActHib ®]	Full
Influenza- seasnl	<u>11/18/2015</u>	1 of 1	Flu quadrivalent injectable pfree [FluLaval Quad PF 0.5mL ®]	Full
MMR	08/25/2012	NOT VALID	MMR [MMR II ®]	Full
Polio	01/06/2012	1 of 4	Polio-Inject [IPOL ®]	Full
	<u>02/03/2012</u>	2 of 4	Polio-Inject [IPOL ®]	Full
	03/01/2012	3 of 4	Polio-Inject [IPOL ®]	Full
	05/25/2012	NOT VALID	Polio-Inject [IPOL ®]	Full

## Why Is This Vaccine Showing Up Invalid?

#### Immunization Record

Vaccine Group	Date Admin	Series	Vaccine [Trade Name]	Dose Owned?	Reaction Hist? Edit
DTP/aP	01/06/2012	1 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full	14
	02/03/2012	2 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full	14
	03/01/2012	3 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full	14
	08/25/2012	NOT VALID	DTaP,5 pertussis antigens [DAPTACEL ®]	Full	11

#### **Explanation of Status**

Dose was given before the earliest acceptable date. Dose was given too soon after the previous dose.

#### Series: DTaP {Vaccine Group: DTP/aP}

Dose	Min Age	Min Rec Age	Min Overdue Age	Min Valid Interval	Min Interval Between	Rec Interval Between	Overdue Interval Between	Max Age
1	42 D	2 M	3 M					7 Y
2	70 D	4 M	5 M		28 D	56 D	3 M	7 Y
3	98 D	6 M	7 M		28 D	56 D	3 M	7 Y
4	12 M	15 M	19 M	4 M	6 M	6 M	7 M	7 Y
5	4 Y	4 Y	6 Y		6 M	6 M	7 M	7 Y

### Why Is The Vaccine Invalid?

- The vaccine was given too early
- Minimal interval not met

The dose is **not** considered valid and **must** be repeated. The repeat dose should be space after the invalid dose by the recommended minimum interval. In these cases, providers should be prepared to reassure parents that the extra dose of vaccine is not harmful for their child.

### Why Is The Vaccine Invalid?

#### Trade-name vaccine is not acceptable for this dose in the series. Pentacel should not be used for any dose in the primary series for children age 5 years or older.

#### **Explanation of Status**

Trade-named vaccine is not acceptable for this dose in the series.

Dose was not given within the min/max age range for the Vaccine/Tradename combination.

The patient's age and vaccination history allowed for certain doses in the series to be skipped; however, the skip did not occur due to othe validation issues.

		•						
Dose	Min Age	Min Rec Age	Min Overdue Age	Min Valid Interval	Min Interval Between	Rec Interval Between	Overdue Interval Between	Max Age
1	42 D	2 M	3 M		28 D			
2	70 D	4 M	5 M		28 D	2 M	3 M	
3	98 D	6 M	19 M		28 D	2 M	9 M	
4		4 Y	7 Y		6 M	6 M	7 M	
5	4 Y	4 Y	7 Y		6 M	6 M	7 M	

#### Series: Polio {Vaccine Group: Polio}

### Why Is The Vaccine Invalid?

#### Using a vaccine that is not appropriate for age level

Does not need to be repeated if the minimal interval was met. Keep in mind that that vaccine is not license for that age and is considered off- label and is not recommended.

You should take measures to prevent this error in the future.

You should explain this error to the parents and assure them that the dose will cause no harm.

### It may be counted as valid.

## Invalid – Live Vaccine

#### Immunization Record

Vaccine Group	Date Admin	Series	Vaccine [Trade Name]	Dose	Owned?	Reaction	Hist? I
DTP/aP	10/19/2007	1 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full			
	03/24/2008	2 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full			
	<u>10/08/2008</u>	3 of 4	DTaP,5 pertussis antigens [DAPTACEL ®]	Full			
	<u>12/11/2008</u>	NOT VALID	DTaP,5 pertussis antigens [DAPTACEL ®]	Full			
MMR	<u>10/08/2012</u>	1 of 2	MMR [MMR II ®]	Full			
Varicella	10/23/2012	NOT VALID	Varicella [Varivax ®]	Full			

Vaccines Recommended by Selected Tracking Schedule

#### Explanation of Status

Dose was given before the earliest acceptable date.

Vaccine group Varicella has a minimum interval conflict with a dose from vaccine group Mumps.

Vaccine group Varicella has a minimum interval conflict with a dose from vaccine group Measles.

Vaccine group Varicella has a minimum interval conflict with a dose from vaccine group Rubella.

#### Series: Varicella late start 13Y {Vaccine Group: Varicella}

Dose	Min Age	Min Rec Age	Min Overdue Age	Min Valid Interval	Min Interval Between	Rec Interval Between	Overdue Interval Between	Max Age
1	13 Y	13 Y	13 Y		28 D			60 Y
2					28 D	28 D	2 M	

## Subpotent

#### **Improperly Stored Vaccine Administered:**

Contact the manufacturer for information on the stability of the vaccine. If the manufacturer does not have data to support the stability of the vaccine, repeat the dose immediately using a new vial that has been properly stored and handled, and is not past the expiration date.

Immunization Rec	ord							
Vaccine Group	Date Admin	Series	Vaccine [Trade Name]	Dose	Owned?	Reaction	Hist? Edit	
HPV	<u>05/10/2023</u>	SUBPOTENT?	HPV9 [Gardasil 9 ®]	Full			1	4

## Subpotent

Vaccine Group	Date Admin	Series	Vaccine [Trade Name]	Dose	Owned?	Reaction	Hist?	Edit
HPV	<u>05/10/2023</u>	1 of 2	HPV9 [Gardasil 9 ®]	Full				1
_								1
Edit Immur	nization							
Vaccine Group: HPV							Save	
Vaccine Display Name: HPV9							Cancel	
	Trade Name: Gardasil 9						Delete	
	Vaccine Lot Num	ber: 01215	5					
	Funding Sou	Irce: PUBL	IC					
	Dose S	<b>Size:</b> 0.5 m	l					
Do	sage From Invent	tory: Full						
	Subpotent D	ose: 🗌						
	Date Provi	ded: 05/10	0/2023					
	Vaccine Eligib	ility: V02 -	VFC Eligible - Medicaid/Maine	Care - Und	ler 19			

Check: Subpotent Dose box The Dose should be repeated as soon as possible.

Maine Center for Disease Control and Prevention

### Vaccine Administration Errors

#### **Common vaccine administration errors include:**

- Doses administered too early (e.g., before the minimum age or interval)
- Wrong vaccine (e.g., Tdap instead of DTaP)
- Wrong dosage (e.g., pediatric formulation of hepatitis B vaccine administered to an adult)
- Wrong route (e.g., MMR given by IM injection)
- Vaccine administered outside the approved age range
- Expired vaccine or diluent administered
- Improperly stored vaccine administered
- Vaccine administered to a patient with a contraindication
- Wrong diluent used to reconstitute the vaccine or only the diluent was administered

### **Reporting an Adverse Event**

• Health care providers are required by law to report certain adverse events, and encouraged to report other events, following vaccination to the Vaccine Adverse Event Reporting System (VAERS). Details on reporting adverse events after vaccination can be found at <u>https://vaers.hhs.gov</u>.

### Vaccine Administration Errors

#### Don't Be Guilty of These **Preventable** Errors in Vaccine Administration. See COVID-19 Vaccine downloads/covid19-vaccine-errors-deviations.pdf.

Is your healthcare setting making any of these frequently reported errors in administering vaccines? Although some of these errors are much more serious than others, none of them should occur. Be sure those who administer vaccines are not making any of these **preventable** errors in vaccine administration.

Note: Information about **reporting** vaccine administration errors is found at the end of this article.

#### **ERROR:** Not using a screening checklist to identify patients' contraindications and precautions to vaccination

How to Avoid This Error: Always use a reliable screening questionnaire to consistently avoid either 1) giving a vaccine to a patient for whom it is contraindicated (a serious, potentially life-threatening situation), or 2) missing opportunities to vaccinate because of false contraindications (which can also be life-threatening, as they can leave a patient exposed to a vaccine-preventable disease).

Helpful Resources: Use IAC's screening checklists, such as Screening Checklist for Contraindications to Vaccines for Children and Teens and Screening Checklist for Contraindications to Vaccines for Adults (both reviewed by CDC) available at www.immunize.org/handouts/ screening-vaccines.asp. CDC's Vaccine Contraindications and Precautions web page: www.cdc.gov/vaccines/hcp/acip-recs/ general-recs/contraindications.html.

#### **ERROR:** Using the wrong diluent or administering the diluent only

How to Avoid This Error: Use careful labeling in your vaccine storage unit. Keep vaccines and their diluents together if storage requirements are the same. Check the vial and diluents labels 3 TIMES before reconstituting vaccine. Administering the diluent *only* is most likely to happen with the two vaccines that include antigen in their liquid component, Menveo and Pentacel.

For information on how to avoid or respond to errors in

What to do after such an error: Diluent errors could affect the potency of the vaccine antigen administered, or the patient might not get the full benefit of the vaccine if the diluent not given contains antigen. If the wrong diluent is used, the vaccine needs to be repeated (except in the case of mixing up the diluent between MMR, MMRV, varicella, and zoster vaccines which are all made by Merck and use the same sterile water diluent).

If an INACTIVATED vaccine is reconstituted with the wrong diluent and is administered, the dose is invalid and should be repeated ASAP. If a LIVE vaccine is reconstituted with the wrong diluent and is administered, the dose is invalid and if it can't be repeated on the same clinic day, it needs to be repeated no earlier than four weeks after the invalid dose. This spacing is due to the effects of generating a partial immune response that could suppress the live replication of subsequent doses, even of the same live virus vaccine.

### RESOURCES

- Ask the experts: <u>Ask the Experts: Combination Vaccines (immunize.org)</u>
- Immunization Schedule with Combination Vaccines: https://eziz.org/assets/docs/IMM-922.pdf
- <u>Appendix A: Schedule and Recommendations: Recommended and minimum ages and intervals between</u> <u>vaccine doses (cdc.gov)</u>
- <u>Vaccine Label Examples (cdc.gov)</u>
- Don't Be Guilty of These Preventable Errors in Vaccine Administration! (immunize.org)
- <u>Vaccine Administration Errors and Deviations | Mpox | Poxvirus | CDC</u>
- Maine Immunization –Webinars: Information & Webinars for Providers | Immunization Program | Division of Disease Surveillance | MeCDC | Maine DHHS
- VAERS: <u>https://vaers.hhs.gov</u>.
- <u>Multiple Vaccinations at Once | Vaccine Safety | CDC</u>
- <u>ACIP Vaccine Recommendations and Schedules | CDC</u>

## Maine Immunization Program Contacts

### Website: <u>www.immunizeme.org</u> Maine Immunization Program Contact: Phone: 207-287-3746 E-mail: <u>ImmunizeME.DHHS@maine.gov</u>



Maine Center for Disease Control and Prevention