

# **Proposed Recommendations from the ACIP Rotavirus Vaccines Working Group**

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

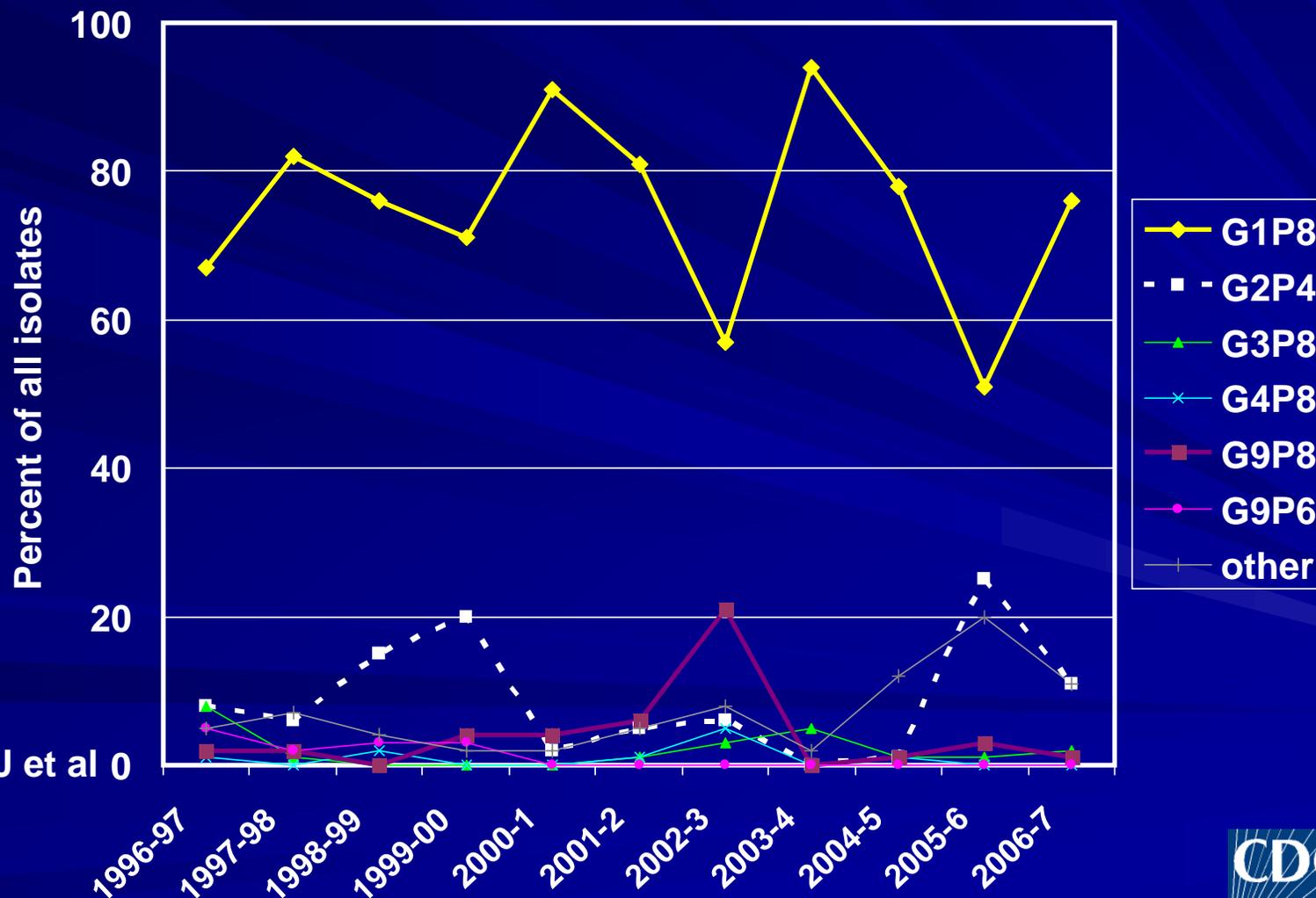


# Rotarix: Overview

- Live, attenuated human rotavirus vaccine
- Monovalent, G1P8
- Oral vaccine, 2 dose series
- BLA submitted to FDA June 1, 2007

# Rotavirus Strains in the US 1996-2007

Convenience sample of isolates from ~12 participating labs, in different US areas



Gentsch J et al

# Rotarix: Major Clinical Trials

Rotarix 023 Latin Am

1 vax : 1 plac

Rotarix 036 Europe

2 vax: 1 plac

No. infants  
studied

Safety: 63,225

Efficacy: 17,867

Efficacy: 3,874

Dose 1

Age 6 wks –13 wks 6 days

Age 6 wks – 14 wks 6 days

Dose 2

1–2 months later  
Age ≤24 wks 6 days

1–2 months later

# Rotarix: Major Clinical Trials

## Safety: Intussusception (IS)

### FDA analysis

Rotarix 023 Latin Am

1 vax : 1 plac

No. infants studied

63,225

IS Day 0–30 after any dose

7V 7P

RR = 0.996 (0.36–2.72)

IS Day 0–30 after Dose 1

1V 2P

IS Day 0–30 after Dose 2

6V 5P

# Rotarix: Major Clinical Trials

## Vaccine Efficacy

Rotarix 023 Latin Am

1 vax : 1 plac

VE to age 12 m

Rotarix 036 Europe

2 vax: 1 plac

VE to end 1<sup>st</sup> rota season

Severe Rota GE

Clinical

12V 77

**85% (72–92)**

Vesikari≥11

11V 71P

**85% (71–93)**

Vesikari≥11

5V 60P

**96% (90–99)**

Rota Hosp

9V 59P

**85% (70–94)**

0V 12P

**100% (82–100)**

Any Rota GE

24V 94P

**87% (80–92)**



# Rotarix: Major Clinical Trials

## Type-specific vaccine efficacy

	Rotarix 023 Latin Am <u>1 vax : 1 plac</u>	Rotarix 036 Europe <u>2 vax: 1 plac</u>
G1P8	Vesikari $\geq$ 11 3V 32P <b>91% (71–98)</b>	Vesikari $\geq$ 11 2V 28P <b>96% (85–100)</b>
G3P8	Clinical 1V 8P <b>88% (8–100)</b>	Vesikari $\geq$ 11 0V 5P <b>100% (45–100)</b>
G9P8	Clinical 2V 21P <b>91% (62–99)</b>	Vesikari $\geq$ 11 2V 19P <b>95% (78–99)</b>
G4P8	Clinical 1V 2P <b>VE not calculated</b>	Vesikari $\geq$ 11 0V 7P <b>100% (65–100)</b>

# Rotarix: Major Clinical Trials

## Type-specific vaccine efficacy

	Rotarix 023 Latin Am 1 vax : 1 plac	Rotarix 036 Europe 2 vax: 1 plac
G2P4	Vesikari $\geq$ 11	Vesikari $\geq$ 11
	5V 9P	1V 2P
	<b>45% (-81, 88)</b>	<b>75% (-386, 100)</b>
	To age 24m	To end 2 <sup>nd</sup> rota season
Clinical	Vesikari $\geq$ 11	
5V 8P	2V 7P	
<b>39% (-112, 84)</b>	<b>86% (24, 99)</b>	

# Proposed Recommendations

## General

“ACIP recommends routine vaccination of U.S. infants with rotavirus vaccine....  
Two different rotavirus vaccines, Rotarix (GSK) and RotaTeq (Merck), are licensed for use in infants in the U.S.”

# Proposed Recommendations

## General

“ACIP considers Rotarix and RotaTeq series equally safe and efficacious.

Efficacy studies demonstrated approximately 85-98% protection against severe rotavirus disease, and 72-87% protection against any rotavirus disease.”

# Proposed Recommendations

## General

“ACIP recommends vaccination of infants with 2 doses of Rotarix administered orally at ages 2 and 4 months.”

*ACIP recommends vaccination of infants with 3 doses of RotaTeq administered orally at ages 2, 4, and 6 months.*

# Proposed Recommendations

## Overview of ages and intervals

	Rotarix	<u>RotaTeq</u>
Number of doses in series	2	3
Recommended ages for doses	2 and 4 months	2, 4 and 6 months
Minimum age for Dose 1	6 weeks	
Maximum age for Dose 1	13 weeks (13 weeks 6 days)	
Interval between doses	4 weeks or more	
Maximum age for last dose	32 weeks (32 weeks 6 days)	

# Proposed Recommendations

## Ages in Trials vs. Proposed Recommendations

	Rotarix	<u>RotaTeq</u>
Minimum age for Dose 1	6 weeks	6 weeks
Maximum age for Dose 1	13 weeks (13 wks 6 days)	12 weeks (12 wks 0 days) <b>13 weeks (13 wks 6 days)</b>
Interval between doses	1–2 months <b>4 weeks or more</b>	4–10 weeks <b>4 weeks or more</b>
Maximum age for last dose	24 weeks (24 wks 6 days) <b>32 weeks (32 wks 6 days)</b>	32 weeks (32 wks 0 days) 32 weeks (32 wks <b>6 days</b> )

# Proposed Recommendations

## Interval between doses

	Rotarix	<u>RotaTeq</u>
Interval between doses	1–2 months <b>4 weeks or more</b>	4–10 weeks <b>4 weeks or more</b>

- “Doses of rotavirus vaccine should be separated by an interval of 4 weeks or more.”

# Proposed Recommendations

## Interval between doses

	Rotarix	<u>RotaTeq</u>
Interval between doses	1–2 months <b>4 weeks or more</b>	4–10 weeks <b>4 weeks or more</b>

### Doses separated by 4 weeks or more

- For RotaTeq
  - No change from way current ACIP recommendation is likely interpreted  
“Subsequent doses should be administered at 4-10 week intervals...”
  - Data from limited number of infants in RotaTeq trial who received vaccine doses >10 weeks apart
- Harmonization of recommendations whenever reasonable is programatically advantageous

# Proposed Recommendations

## Maximum age Dose 1

	Rotarix	<u>RotaTeq</u>
Maximum age for Dose 1	13 weeks (13 wks 6 days)	12 weeks (12 wks 0 days) <b>13 weeks (13 wks 6 days)</b>

- “The first dose of rotavirus vaccine should be administered between ages 6 and 13 weeks (maximum age for Dose 1 is 13 weeks 6 days). Vaccination should not be initiated for infants aged 14 weeks or older....”

# Proposed Recommendations

## Maximum age Dose 1

	Rotarix	<u>RotaTeq</u>
Maximum age for Dose 1	13 weeks (13 wks 6 days)	12 weeks (12 wks 0 days) <b>13 weeks (13 wks 6 days)</b>

RotaTeq: Expansion of maximum age for Dose 1 by 1-2 weeks, from that used in clinical trial

- Available data (trial, U.S. post-marketing) do not indicate RotaTeq is associated with IS in the age groups recommended for vaccination.
- Harmonization

# Proposed Recommendations

## Maximum age Last Dose

	Rotarix	<u>RotaTeq</u>
Maximum age for last dose	24 weeks (24 wks 6 days) <b>32 weeks (32 wks 6 days)</b>	32 weeks (32 wks 0 days) 32 weeks (32 wks <b>6 days</b> )

- “All doses of rotavirus vaccine should be administered by age 32 weeks (maximum age for last dose is 32 weeks 6 days).”

# Proposed Recommendations

## Maximum age Last Dose

	Rotarix	<u>RotaTeq</u>
Maximum age for last dose	24 weeks (24 wks 6 days) 32 weeks (32 wks 6 days)	32 weeks (32 wks 0 days) 32 weeks (32 wks <b>6 days</b> )

RotaTeq: Expansion of maximum age for last dose by 6 days, from that used in trial.

- No change from way current ACIP RotaTeq recommendation is likely interpreted
  - “All doses should be administered by age 32 weeks....”
- Harmonization

# Proposed Recommendations

## Maximum age Last Dose

	Rotarix	<u>RotaTeq</u>
Maximum age for last dose	24 weeks (24 wks 6 days) <b>32 weeks (32 wks 6 days)</b>	32 weeks (32 wks 0 days) 32 weeks (32 wks 6 days)

Rotarix: Expansion of maximum age for last dose by 8 weeks, from that used in trial.

- Data from trial do not suggest Rotarix is associated with IS in the age groups studied.
- Background rates of IS similar at ages 24–32 weeks.
- If mixed (or potentially mixed) series allowed and 3 doses recommended, 32 week age limit is practical
- Harmonization

# Proposed Recommendations

## Interchangeability of products in vaccine series

“It is recommended that the vaccine series be completed with the same brand of rotavirus vaccine whenever possible. However, if the product used to start the series is unknown or not available, the provider should complete the series with the product available.

If any dose in the series was or may have been RotaTeq, a total of three doses of rotavirus vaccine should be given. The interval between rotavirus vaccine doses should be 4 weeks or more, and all doses should be given by age 32 weeks (maximum age for last dose is 32 weeks 6 days).”

# Proposed Recommendations

## Interchangeability of products in vaccine series

### Allowing “mixing” in series

- No data available or expected
- WG opinion: mixed series would not pose additional risk and series would be effective against rotavirus disease
- Programmatic: practical requirement

# Proposed Recommendations

## Interchangeability of products in vaccine series

Give 3 doses of rotavirus vaccine if any dose in series was or may have been RotaTeq

- No data available or expected
- Follows general concept of ACIP Hib vaccine recommendations for mixed series, where one product (Hib-OMP) had 2-dose primary series, and other products had 3-dose primary series
  - Three doses to be given in “mixed” infant primary series
  - Some data were available on mixed series

# Additional topics to be addressed by Working Group

- Develop proposed recommendations for Rotarix (and update for RotaTeq as indicated)
  - Special populations
  - Special circumstances
  - Contraindications
  - Precautions
- Review any additional information on safety and efficacy
- Review cost-effectiveness data for Rotarix

# Thank You

## Members of ACIP Rotavirus Vaccines Working Group

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