ADHERENCE TO ADMINISTRATION SCHEDULES OF U.S.-LICENSED ROTAVIRUS VACCINES FOR INFANTS, 2014–2018

OBJECTIVE

To assess the adherence to administration schedules of U.S.-licensed rotavirus vaccines for infants per Food and Drug Administration (FDA)-approved prescribing information and recommendations of the Advisory Committee on Immunization Practices (ACIP).

BACKGROUND

FDA-Approved Vaccination Schedules

RotaTeq®: The vaccination series consists of three doses administered orally starting at ***6 to 12 weeks*** of age, with the subsequent doses administered at intervals of ***4 to 10 weeks***. The third dose should ***not be given after 32 weeks*** of age.

Rotarix®: The vaccination series consists of two doses administered orally for infants starting at ***6 weeks*** of age, with the second dose administered after an interval of at least ***4 weeks*** and ***prior to 24 weeks*** of age.

ACIP Recommendations for Vaccination Schedules[1]

RotaTeq: The vaccination series is administered orally in a three-dose series, with doses administered at ***2, 4, and 6 months*** of age.

Rotarix: The vaccination series is administered orally in a two-dose series, with doses administered at ***2 and 4 months*** of age.

Additional ACIP recommendations for both vaccines:

- The minimum age for dose 1 of the rotavirus vaccine is 6 weeks.
- The maximum age for dose 1 is 14 weeks and 6 days. (Vaccination should not be initiated for infants aged 15 weeks and 0 days or older because of insufficient data on the safety of dose 1 of the rotavirus vaccine in older infants.)
- The minimum interval between doses of rotavirus vaccine is 4 weeks; no maximum interval is set. All doses should be administered by age 8 months and 0 days.

COHORT IDENTIFICATION

Enrollment Criteria/Cohort Identification

Cohort A: Infants born during 2014–2018 with continuous enrollment of medical benefits from birth through 365 days after birth, allowing for time gaps in coverage up to 45 days.

- Censoring Criteria: Infants in Cohort A were censored at the first occurrence of the following: disenrollment of medical benefits, reached full follow-up of 365 days post-birth, death, or reached study end date

[1] Cortese MM, Parashar UD. Prevention of rotavirus gastroenteritis among infants and children recommendations of the Advisory Committee on Immunization Practices. Morb Mortal Wkly Rep 2009; 58(RR02):1-25.

Cohort B: Infants born during 2014–2018 with at least one dose of a rotavirus vaccine.

- Censoring Criteria: Infants in Cohort B were censored at the first occurrence of the following: death or reached study end date

Data Sources and Study Period

2014–2018

IBM MarketScan® Commercial Database: January 1, 2014- September 30, 2018

Blue Health Intelligence (BHI) Commercial Database: January 1, 2014- April 21, 2018

Rotavirus Vaccine Exposure

Rotavirus vaccines will be identified using the procedure codes (Healthcare Common Procedure Coding System Level I [Current Procedural Terminology, or CPT®]) and/or National Drug Codes (NDCs) listed in Appendix A.

Statistical Methods

For Cohort A:

- Determine the proportion of infants receiving at least one dose of rotavirus vaccine within Cohort A.
- Determine the frequency of infants according to the number of rotavirus vaccination doses per infant . Rotavirus vaccine billing codes on service dates that are at least 3 days apart will be considered as separate doses. Frequencies will be reported separately for Rotarix-only, RotaTeq-only, and mixed-brand schedules (e.g., first dose RotaTeq-second dose Rotarix-third dose RotaTeq).

- For infants who have received more than one dose, determine the interval between doses and calculate mode, median, interquartile range, and range for the distribution of intervals in the study cohort. Interval distributions will be reported separately for Rotarix-only and RotaTeq-only.[2]
- Evaluate adherence to the FDA-approved vaccination schedule (for Rotarix-only and RotaTeq-only groups):
    a. Determine the proportion of infants who received the first dose between 6 to 12 weeks of age[3] (RotaTeq) or after 6 weeks of age (Rotarix).
    b. Determine the proportion of infants who received any dose after 32 weeks of age (RotaTeq) or after 24 weeks of age (Rotarix).
    c. Determine the proportion of those who have completed the dose series **within** 24 weeks of age (Rotarix) or 32 weeks of age (RotaTeq) (i.e. received 2 doses of Rotarix with 24 weeks of age and 3 doses of RotaTeq within 32 weeks of age).
    d. Determine the proportion of those who have completed the dose series **after** 24 weeks of age (Rotarix) or 32 weeks of age (RotaTeq).
- Evaluate adherence to the ACIP-recommended vaccination schedule (for Rotarix-only and RotaTeq-only groups):

[2] *Mix-brand use is not recommended or approved by FDA or ACIP. For the purposes of characterizing and understanding mixed-brand use in this study, complete series for mixed-brand schedules, are defined as combinations of RotaTeq and Rotarix—at least 1 dose of each—with the complete series administered before 32 weeks of age.*

[3] *All ages in weeks are interpreted as X weeks and 0 days.*

a. Determine the proportion of infants who received the first dose between 6 and <15 weeks of age.
b. Determine the proportion of infants who received any dose **after** 8 months of age.
c. Determine the proportion of those who have completed the dose series **within** 8 months of age.
d. Determine the proportion of those who have completed the dose series **after** 8 months of age.

For Cohort B:

- Determine the proportion of those who received any dose after 32 weeks of age (RotaTeq) or after 24 weeks of age (Rotarix).
- Determine the proportion of those who received any dose after 8 months of age stratified by Rotarix-only, RotaTeq-only, and mixed-brand groups.

Data Sources

- IBM® MarketScan® Research Databases
- Blue Health Intelligence
- Harvard Pilgrim Data Network

Stratification and report

Analysis will be conducted based on the stratification scheme specified in Table 1 for both Cohort A and Cohort B and for the Rotarix-only and RotaTeq-only groups. Appendix B shows the format of an age at dose stratification table.

Table 1. Dose Stratifications for Rotavirus Vaccines

Vaccines	Age at Dose Stratifications, Categorized by Week
• RotaTeq • Rotarix	1. Age at first dose 2. Age at second dose 3. Age at third dose **Stratify by week (in days) for the first 2 years of life** • Week 1: 0–7 days • Week 2: 8–14 days • Week 3: 15–21 days • Week 4: 22–28 days • Up through week 104 • 2–5 years • ≥6 years

APPENDIX A: CPT AND NDC CODES FOR ROTATEQ AND ROTARIX VACCINES

Code Type	Code	Vaccine Type	Long Description
CPT	90680	RotaTeq	Rotavirus vaccine, pentavalent (RV5), three-dose schedule, live, for oral use
NDC	00006-4047-20	RotaTeq	Rotavirus vaccine, live, pentavalent
NDC	00006-4047-41	RotaTeq	Rotavirus vaccine, live, pentavalent
NDC	00006-4047-01	RotaTeq	Rotavirus vaccine, live, pentavalent
CPT	90681	Rotarix	Rotavirus vaccine, human, attenuated (RV1), two-dose schedule, live, for oral use
NDC	58160-0851-01	Rotarix	Rotavirus vaccine, live
NDC	58160-0851-10	Rotarix	Rotavirus vaccine, live
NDC	58160-0854-52	Rotarix	Rotavirus vaccine, live

Abbreviations: CPT, Current Procedural Terminology; NDC, National Drug Code.

APPENDIX B: EXAMPLE OF AGE AT DOSE STRATIFICATION TABLE[a]

Timing of Doses Among Beneficiaries in Cohort A

Note: Beneficiaries must have 365 days of continuous enrollment post birth and validated estimated birth date

Weeks	Rotateq Dosing Schedule						Benes with 1 Dose		Benes with 2 Doses				Benes with 3 Doses					
	ACIP			FDA			Dose 1		Dose 1		Dose 2		Dose 1		Dose 2		Dose 3	
	1	2	3	1	2	3	#	%	#	%	#	%	#	%	#	%	#	%
Total																		
0																		
1																		
2																		
3																		
4																		
5																		
6																		
7																		
8																		
9																		
10																		
11																		
12																		
13																		
14																		
15																		
16																		
17																		
18																		
19																		
20																		
21																		
22																		
23																		
24																		
25																		
26																		
27																		
28																		
29																		

[a]Appendix B example table is truncated at week 29. The actual Timing of Doses among Beneficiaries table extends to week 52 For Cohort A and week 104 for Cohort B.