Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Overview for Request: cber_mpl1r_wp033

Request ID: cber_mpl1r_wp033_nsdp_v01

Request Description: In this request, we identified oral dose administrations of Pentavalent Rotavirus Vaccine (RV5) among infants with a birth date in the Sentinel Distributed Database (SDD) and assessed adherence measures per guidelines set by the Food and Drug Administration (FDA) and the Advisory Committee on Immunization Practices (ACIP).

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 8.1.1

Data Source: We identified infants with birth dates from January 1, 2014 to December 31, 2017. We distributed this request on September 30, 2019 to seven Data Partners contributing to the SDD. See Appendix A for a list of dates of available data for each Data Partner.

Sensitivity Analysis, Data Source: We identified infants with birth dates from January 1, 2014 to December 31, 2018.

Study Design: We identified prevalent vaccine administration by dosage number. We estimated age in weeks at administration of an indicated dosage number and provided descriptive statistics describing both the time from birth date until an indicated dosage as well as the time between dosages.

Cohort Eligibility Criteria (Primary Episode): An infant's birth date in the SDD served as the index date. To be included in the cohort, we required eligible infants to be continuously enrolled in health plans with medical coverage for at least 365 days after their index birth date, during which gaps in coverage of up to 45 days were allowed. Eligible infants could not have any evidence of Monovalent Rotavirus Vaccine (RV1) events in the 365 days after the index birth date. See Appendix B for a list of generic and brand medical product names and Appendix C for a list of Current Procedural Terminology, Fourth Edition (CPT-4) used to define exclusion criteria in this request.

Sensitivity Analysis, Cohort Eligibility Criteria (Primary Episode): An infant's birth date in the SDD served as the index date. We did not require any amount of enrollment in a health plan after the index birth date. Eligible infants could not have any evidence of RV1 events in the 365 days after the index birth date.

Censoring Criteria (Primary Episode): Infants with a primary episode were censored at the first occurrence of the following: death, disenrollment, DP end date, query end date, or 365 days.

Sensitivity Analysis, Censoring Criteria (Primary Episode): Infants with a primary episode were censored at the first occurrence of the following: death, disenrollment, DP end date, or query end date.

Exposure of Interest (Secondary Episode): We identified oral administrations of RV5 in a three-dose series. A subsequent dose must have been administered at least three days after the preceding dose to be captured as a distinct event. See Appendix B for a list of generic and brand names and Appendix C for a list of CPT-4 codes used to define vaccine administration in this request.

Multiple Events Assessment: We evaluated any RV5 events (secondary episode) among infants with one year of enrollment after their index birth date and no RV1 events (primary episode). We assessed RV5 events that occurred only within 365 days after the index birth date. RV5 events that occurred after 365 days were not retained.

Sensitivity Analysis, Multiple Events Assessment: We evaluated any RV5 events (secondary episode) among infants with a birth date and no RV1 events (primary episode, sensitivity analysis). We assessed RV5 events that occurred until the infant's primary episode was censored.

Adherence Metrics: We measured RV5 adherence by dosage number guidelines provided by the FDA and the ACIP.

--First dose: The FDA recommends that the first dose be administered between 6 to 12 weeks[1] and the ACIP between 6 to <15 weeks[2].

--Third dose: The FDA recommends that the third dose be administered within 32 weeks of birth[3] and the ACIP within 8 months of birth[4].

Sensitivity Analysis, Non-Adherence Metrics: We evaluated non-adherence measures for any RV5 dose administration outside of the FDA and the ACIP recommendations via baseline characteristics.

--FDA: We considered any administration of RV5 >32 weeks, 0 days after birth date[5] to be non-adherent per FDA recommendations.

--ACIP: We considered any administration of RV5 >8 months, 0 days after birth date[6] to be non-adherent per ACIP recommendations.

Multiple Events Assessment of Any Rotavirus Administration: We identified any Rotavirus vaccine event (RV1 or RV5) among infants with a birth date and various enrollment requirements. See Appendix F for any RV1 or RV5 events among infants with one year of enrollment after birth date and Appendix G for any RV1 or RV5 events among infants with a birth date and any amount of enrollment.

Please see Appendices H.1 and H.2 for detailed specifications in this request. See Appendix I for the parameters to define baseline characteristics. See Appendix J for a design diagram detailing our assessment of multiple events and time to event metrics.

Limitation: Algorithms to define exposures have not been validated. Therefore, data should be interpreted with this limitation in mind.

Strength: All infants enrolled in a health plan in the SDD have a birth date; thus, age at vaccine administration from birth date is accurately measured.

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document.

[1]FDA adherence for first dose measured days 42 to 84.

[2]ACIP adherence for first dose measured days 42 to 104.

[3]FDA adherence for third dose measured from birth date to day 224.

[4]ACIP adherence for third dose measured from birth date to day 244.

[5]FDA non-adherence measured day 225 until end of enrollment.

[6]ACIP non-adherence measured day 245 until end of enrollment.

Sentinel

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Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Module*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.
Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

- **Ambulatory Visit (AV) -** includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.
- **Emergency Department (ED) -** includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.
- **Inpatient Hospital Stay (IP) -** includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.
- **Non-Acute Institutional Stay (IS) -** includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.
- **Other Ambulatory Visit (OA) -** includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

Code Days - the minimum number of times the diagnosis must be found during the evaluation period in order to fulfill the algorithm to identify the corresponding patient characteristic.
Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario) within each Data Partner site.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.
Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.
Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a “continuously enrolled” sequence.

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the same treatment episode.

Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.
Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*all terms may not be used in this report

Table 1. Summary of Pentavalent Rotavirus Vaccine (RV5) Events among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Infants	Infants with no vaccinations	Infants with the indicated dose number	Percent of infants with the indicated dose number per all infants with one year of enrollment following birth date and no RV1
Infants with one year of enrollment, no evidence of RV1	1,143,330	208,099	n/a	n/a
Pentavalent Rotavirus Vaccine (RV5) events among infants with one year of enrollment				
At least one dose	n/a	n/a	935,231	81.8%
At least two doses	n/a	n/a	875,928	76.6%
At least three doses	n/a	n/a	757,034	66.2%

Table 2a. Descriptive Statistics of Time to Pentavalent Rotavirus Vaccine (RV5) Events and Adherence Measures per Food and Drug Administration (FDA) Guidelines among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Infants with the indicated dose number	Descriptive statistics of time to indicated dose number from birth date (days)							Number of infants who meet adherence definition	Percent of infants who meet FDA adherence per all infants who received the indicated dose number and no RV1
		Mean	Standard Deviation	Minimum	Q1	Median	Q3	Maximum		
Pentavalent Rotavirus Vaccine (RV5) events among infants with one year of enrollment										
First dose, among those with 1+ dose(s); Adherence: between 6 to 12 weeks[1]	935,231	68	20	0	61	63	68	361	866,649	92.7%
Second dose, among those with 2+ doses	875,928	132	19	14	123	126	133	359	n/a	n/a
Third dose, among those with 3+ doses; Adherence: within 32 weeks[2]									735,111	97.1%
Third dose, among those with 3+ doses; Non-adherence: after 32 weeks[3]	757,034	192	13	34	185	188	196	362	21,923	2.9%

[1]FDA adherence measured days 42 to 84.

[2]FDA adherence measured birth date to day 224.

[3]FDA non-adherence measured days 225 to 365.

Table 2b. Descriptive Statistics of Time to Pentavalent Rotavirus Vaccine (RV5) Events and Adherence Measures per Advisory Committee on Immunization Practices (ACIP) Guidelines among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Infants with the indicated dose number	Descriptive statistics of time to indicated dose number from birth date (days)							Number of infants who meet adherence definition	Percent of infants who meet ACIP adherence per all infants who received the indicated dose number and no RV1
		Mean	Standard Deviation	Minimum	Q1	Median	Q3	Maximum		
Pentavalent Rotavirus Vaccine (RV5) events among infants with one year of enrollment										
First dose, among those with 1+ dose(s); Adherence: between 6 to <15 weeks[1]	935,231	68	20	0	61	63	68	361	889,986	95.2%
Second dose, among those with 2+ doses	875,928	132	19	14	123	126	133	359	n/a	n/a
Third dose, among those with 3+ doses; Adherence: within 8 months[2]	757,034	192	13	34	185	188	196	362	752,962	99.5%
Third dose, among those with 3+ doses; Non-adherence: after 8 months[3]									4,072	0.5%

[1]ACIP adherence measured days 42 to 104.

[2]ACIP adherence measured birth date to day 244.

[3]ACIP non-adherence measured days 245 to 365.

Table 3. Time to Pentavalent Rotavirus Vaccine (RV5) Events among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017, by Age Week

	First RV5 dose, among those with 1+ dose(s)*		Second RV5 dose, among those with 2+ doses*		Third RV5 dose, among those with 3+ doses*	
Age Week	Infants with a first RV5 dose	Percent of the total number of infants with a first RV5 dose and no RV1	Infants with a second RV5 dose	Percent of the total number of infants with a second RV5 dose and no RV1	Infants with a third RV5 dose	Percent of the total number of infants with a third RV5 dose and no RV1
Total infants:	**935,231**	**n/a**	**875,928**	**n/a**	**757,034**	**n/a**
<1 week	73	0.0%	-	0.0%	-	0.0%
1-<2 weeks	47	0.0%	-	0.0%	-	0.0%
2-<3 weeks	35	0.0%	1	0.0%	-	0.0%
3-<4 weeks	34	0.0%	-	0.0%	-	0.0%
4-<5 weeks	210	0.0%	1	0.0%	1	0.0%
5-<6 weeks	634	0.1%	5	0.0%	-	0.0%
6-<7 weeks	24,628	2.6%	12	0.0%	-	0.0%
7-<8 weeks	29,900	3.2%	11	0.0%	-	0.0%
8-<9 weeks	324,866	34.7%	130	0.0%	3	0.0%
9-<10 weeks	362,273	38.7%	254	0.0%	4	0.0%
10-<11 weeks	91,500	9.8%	630	0.1%	3	0.0%
11-<12 weeks	30,736	3.3%	728	0.1%	9	0.0%
12-<13 weeks	12,776	1.4%	1,355	0.2%	7	0.0%
13-<14 weeks	8,678	0.9%	3,130	0.4%	11	0.0%
14-<15 weeks	4,629	0.5%	3,206	0.4%	58	0.0%
15-<16 weeks	2,200	0.2%	6,913	0.8%	81	0.0%
16-<17 weeks	2,065	0.2%	27,039	3.1%	138	0.0%
17-<18 weeks	11,119	1.2%	348,704	39.8%	684	0.1%
18-<19 weeks	8,765	0.9%	258,296	29.5%	833	0.1%
19-<20 weeks	4,003	0.4%	93,907	10.7%	621	0.1%
20-<21 weeks	2,240	0.2%	38,498	4.4%	610	0.1%
21-<22 weeks	1,391	0.1%	19,465	2.2%	984	0.1%
22-<23 weeks	1,024	0.1%	12,323	1.4%	1,666	0.2%
23-<24 weeks	704	0.1%	6,962	0.8%	1,883	0.2%
24-<25 weeks	508	0.1%	4,234	0.5%	4,419	0.6%
25-<26 weeks	724	0.1%	4,441	0.5%	36,187	4.8%
26-<27 weeks	3,404	0.4%	17,255	2.0%	331,757	43.8%
27-<28 weeks	2,151	0.2%	10,471	1.2%	185,260	24.5%

*The green heat map highlights the largest proportion of age weeks that infants received the indicated dose number.

Table 3. Time to Pentavalent Rotavirus Vaccine (RV5) Events among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017, by Age Week

	First RV5 dose, among those with 1+ dose(s)		Second RV5 dose, among those with 2+ doses		Third RV5 dose, among those with 3+ doses	
Age Week	Infants with a first RV5 dose	% of the total number of infants with a first RV5 dose and no RV1	Infants with a second RV5 dose	% of the total number of infants with a second RV5 dose and no RV1	Infants with a third RV5 dose	% of the total number of infants with a third RV5 dose and no RV1
Total infants:	**935,231**	**n/a**	**875,928**	**n/a**	**757,034**	**n/a**
28-<29 weeks	1,177	0.1%	5,882	0.7%	85,265	11.3%
29-<30 weeks	774	0.1%	3,654	0.4%	41,818	5.5%
30-<31 weeks	577	0.1%	2,550	0.3%	25,164	3.3%
31-<32 weeks	408	0.0%	1,915	0.2%	15,780	2.1%
32-<33 weeks	295	0.0%	1,370	0.2%	9,500	1.3%
33-<34 weeks	221	0.0%	1,045	0.1%	6,196	0.8%
34-<35 weeks	181	0.0%	696	0.1%	4,020	0.5%
35-<36 weeks	65	0.0%	198	0.0%	1,210	0.2%
36-<37 weeks	32	0.0%	144	0.0%	692	0.1%
37-<38 weeks	26	0.0%	90	0.0%	426	0.1%
38-<39 weeks	23	0.0%	81	0.0%	318	0.0%
39-<40 weeks	27	0.0%	81	0.0%	449	0.1%
40-<41 weeks	23	0.0%	60	0.0%	286	0.0%
41-<42 weeks	18	0.0%	43	0.0%	174	0.0%
42-<43 weeks	10	0.0%	29	0.0%	126	0.0%
43-<44 weeks	16	0.0%	26	0.0%	104	0.0%
44-<45 weeks	10	0.0%	18	0.0%	74	0.0%
45-<46 weeks	4	0.0%	25	0.0%	57	0.0%
46-<47 weeks	4	0.0%	13	0.0%	45	0.0%
47-<48 weeks	11	0.0%	12	0.0%	44	0.0%
48-<49 weeks	4	0.0%	6	0.0%	30	0.0%
49-<50 weeks	1	0.0%	9	0.0%	19	0.0%
50-<51 weeks	4	0.0%	8	0.0%	10	0.0%
51 weeks - <365 days	3	0.0%	2	0.0%	8	0.0%

*The green heat map highlights the largest proportion of age weeks that infants received the indicated dose number.

Table 4a. Descriptive Statistics of the Gap Length Between the First and Second Pentavalent Rotavirus Vaccine (RV5) Events among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Total number of infants with 2+ RV5 doses	Descriptive statistics of time between first and second dose (days)						
	Number	Mean	Standard Deviation	Minimum	Q1	Median	Q3	Maximum
First and Second Dose	875,928	64	15	3	59	62	67	298

Table 4b. Descriptive Statistics of the Gap Length Between the Second and Third Pentavalent Rotavirus Vaccine (RV5) Events among Infants with One Year of Enrollment and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Total number of infants with 3+ RV5 doses	Descriptive statistics of time between second and third dose (days)						
	Number	Mean	Standard Deviation	Minimum	Q1	Median	Q3	Maximum
Second and Third Dose	757,034	63	11	3	58	62	66	224

Table 5. Summary of Pentavalent Rotavirus Vaccine (RV5) Events among Infants with a Birth Date, Any Amount of Enrollment, and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2018

	Infants	Infants with no vaccinations	Infants with the indicated dose number	Percent of infants with at least one dose per all infants with a birth date and no RV1
Infants with a birth date, no evidence of RV1	2,269,114	765,462	n/a	n/a
Pentavalent Rotavirus Vaccine (RV5) events among infants with a birth date				
At least one dose	n/a	n/a	1,503,652	66.3%

Table 6. Summary of Any Pentavalent Rotavirus Vaccine (RV5) Events Outside of the Food and Drug Administration (FDA) or Advisory Committee on Immunization Practices (ACIP) Guidelines among Infants with at Least a First RV5 Dose, Any Amount of Enrollment, and No Evidence of Monovalent Rotavirus Vaccine (RV1) Events in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2018

	Number	Percent
Infants with at least a first RV5 dose	1,503,652	n/a
Baseline characteristics		
Any RV5 dose after 32 weeks[1]; Outside of the FDA guidelines	37,329	2.5%
Any RV5 dose after 8 months[2]; Outside of the ACIP guidelines	8,208	0.5%

[1]FDA non-adherence measured day 225 until end of enrollment.

[2]ACIP non-adherence measured day 245 until end of enrollment.

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (September 30, 2019)

DP ID	Start Date[1]	End Date[1]
DP01	01/06/2007	01/31/2019
DP02	01/01/2008	11/30/2018
DP03	01/01/2008	06/30/2018
DP04	01/01/2012	06/30/2017
DP05	01/01/2000	12/31/2017
DP06	01/01/2006	12/31/2018
DP07	01/01/2000	06/30/2018

[1]The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

Appendix B. List of Generic and Brand Names of Medical Products Used to Define Exclusion Criteria in this Request

Generic Name	Brand Name
Monovalent Rotavirus Vaccine (RV1)	
rotavirus vaccine, live oral attenuated,89-12 strain, G1P(8)	Rotarix

Appendix C. List of Current Procedural Terminology, Fourth Edition (CPT-4) Procedure Codes Used to Define Exclusion Criteria in this Request

Code	Description	Code Type	Code Category
	Monovalent Rotavirus Vaccine (RV1)		
90681	rotavirus vaccine, human, attenuated (RV1), 2 dose schedule, live, for oral use	Procedure	CPT-4

Appendix D. List of Generic and Brand Names of Medical Products Used to Define Vaccine Administration in this Request

Generic Name	Brand Name
Pentavalent Rotavirus Vaccine (RV5)	
rotavirus vaccine, live oral pentavalent	RotaTeq Vaccine

Appendix E. List of Current Procedural Terminology, Fourth Edition (CPT-4) Procedure Codes Used to Define Vaccine Administration in this Request

Code	Description	Code Type	Code Category
	Pentavalent Rotavirus Vaccine (RV5)		
90680	Rotavirus vaccine, pentavalent (RV5), 3 dose schedule, live, for oral use	Procedure	CPT-4

Appendix F. Summary of Monovalent or Pentavalent Rotavirus Vaccine (RV1 or RV5) Events among Infants with One Year of Enrollment in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2017

	Infants	Infants with no vaccinations	Infants with the indicated dose number	Percent of infants with the indicated dose number per all infants with one year of enrollment following birth date
Infants with one year of enrollment	1,374,944	213,465	n/a	n/a
Monovalent or Pentavalent Rotavirus Vaccine (RV1 or RV5) events among infants with one year of enrollment				
At least one dose	n/a	n/a	1,161,479	84.5%
At least two doses	n/a	n/a	1,078,064	78.4%
At least three doses[1]	n/a	n/a	775,140	56.4%

[1]Infants receiving only doses of RV1 would not be expected to contribute to this category.

Appendix G. Summary of Monovalent or Pentavalent Rotavirus Vaccine (RV1 or RV5) Events among Infants with a Birth Date and Any Amount of Enrollment in the Sentinel Distributed Database (SDD), Birth Dates from January 1, 2014 to December 31, 2018

	Infants	Infants with no vaccinations	Infants with the indicated dose number	Percent of infants with at least one dose per all infants with a birth date
Infants with a birth date	2,629,931	767,485	n/a	n/a
Monovalent or Pentavalent Rotavirus Vaccine (RV1 or RV5) events among infants with one year of enrollment				
At least one dose	n/a	n/a	1,862,446	70.8%

Appendix H.1. Specifications Defining Parameters for this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) module to identify multiple pentavalent rotavirus vaccine events and adherence measures among infants with one year of enrollment after birth date.

Query period: January 1, 2014 - December 31, 2017
Coverage requirement: Medical & Drug Coverage
Pre-index enrollment requirement: 0 days
Post-index enrollment requirement: 365 days (for primary episode)
Enrollment gap: 45 days
Age groups: N/A
Stratifications: Age group at dose number (time to secondary episode)
Restrictions: None
Envelope macro: No reclassification

			Episode Parameters										Exclusion Criteria		
Scenario	Recommendations	Episode of Interest	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	User-defined exposure episode length (days)	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration (days)	Care setting	Censor treatment episode at evidence of:	Exclusion Condition	Evaluation Window Start	Evaluation Window End
1	FDA	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	n/a	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
1	FDA	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
2	FDA	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
2	FDA	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--

		Episode Parameters											Exclusion Criteria		
Scenario	Recommendations	Episode of Interest	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	User-defined exposure episode length (days)	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration (days)	Care setting	Censor treatment episode at evidence of:	Exclusion Condition	Evaluation Window Start	Evaluation Window End
3	FDA	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
3	FDA	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
4	FDA	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
4	FDA	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
5	ACIP	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
5	ACIP	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--

			Episode Parameters										Exclusion Criteria		
Scenario	Recommendations	Episode of Interest	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	User-defined exposure episode length (days)	Minimum exposure episode duration	Minimum days supplied	Maximum exposure episode duration (days)	Care setting	Censor treatment episode at evidence of:	Exclusion Condition	Evaluation Window Start	Evaluation Window End
6	ACIP	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
6	ACIP	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
7	ACIP	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
7	ACIP	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
8	ACIP	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
8	ACIP	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--

			Episode Parameters										Exclusion Criteria		
Scenario	**Recommendations**	**Episode of Interest**	**Index Exposure**	**Cohort definition**	**Incident exposure washout period**	**Incident with respect to:**	**User-defined exposure episode length (days)**	**Minimum exposure episode duration**	**Minimum days supplied**	**Maximum exposure episode duration (days)**	**Care setting**	**Censor treatment episode at evidence of:**	**Exclusion Condition**	**Evaluation Window Start**	**Evaluation Window End**
9	n/a	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	365	n/a	n/a	365	n/a	*Death; *Disenrollment; *DP end date; *Query end date	n/a	--	--
9	n/a	Secondary Episode	RotaTeq or Rotarix	All valid exposure episodes during query period	3	RotaTeq or Rotarix	none	1 day	none	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--

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National Drug Codes (NDCs) are checked against First Data Bank's “National Drug Data File (NDDF®) Plus.”

Appendix H.1.1. Specifications Defining Parameters for this Request

This request executed the Cohort Identification and Descriptive Analysis (CIDA) module to identify multiple pentavalent rotavirus vaccine events and adherence measures among infants with one year of enrollment after birth date.

Query period: January 1, 2014 - December 31, 2017
Coverage requirement: Medical & Drug Coverage
Pre-index enrollment requirement: 0 days
Post-index enrollment requirement: 365 days (for primary episode)
Enrollment gap: 45 days
Age groups: N/A
Stratifications: Age group at dose number (time to secondary episode)
Restrictions: None
Envelope macro: No reclassification

	Multiple Events Assessment							Adherence					Stratifications
									Count of Secondary Episodes		Time to Secondary		
Scenario	Observation Window Start Anchor	Number of Days from Obs. Window Start Anchor to Start Obs. Window	Observation Window End Anchor	Number of Days from Obs. Window End Anchor to End Obs. Window	Secondary (Sec.) episode (Ep.) to use for Time to Sec. Ep.Output	Minimum Adherence Criteria	Adherence Scale Evaluate adherence by...	Analysis Group	Minimum Number of Sec. Episodes	Maximum Number of Sec. Episodes	Episode Start	Episode End	Output levels
1	Primary episode index date	0	Primary episode end date: 365 days	0	First episode	At least 1 episode	Days	FDA_CA_Teq1	1	n/a	42 (6 weeks * 7 days)	84 (12 weeks * 7 days)	Overall, Time to first secondary episode, Adherence
2	Primary episode index date	0	Primary episode end date: 365 days	0	Second episode	At least 2 episodes	Days						Overall, Time to second secondary episode, Gap between first and second secondary episode
3	Primary episode index date	0	Primary episode end date: 365 days	0	Third episode	3 episodes	Days	FDA_CA_Teq3_Within	3	n/a	0	224 (32 weeks * 7 days)	Overall, Time to third secondary episode, Adherence, Gap between second and third secondary episode

	Multiple Events Assessment							Adherence					Stratifications
									Count of Secondary Episodes		Time to Secondary		
Scenario	Observation Window Start Anchor	Number of Days from Obs. Window Start Anchor to Start Obs. Window	Observation Window End Anchor	Number of Days from Obs. Window End Anchor to End Obs. Window	Secondary (Sec.) episode (Ep.) to use for Time to Sec. Ep.Output	Minimum Adherence Criteria	Adherence Scale Evaluate adherence by...	Analysis Group	Minimum Number of Sec. Episodes	Maximum Number of Sec. Episodes	Episode Start	Episode End	Output levels
4	Primary episode index date	0	Primary episode end date: 365 days	0	Third episode	3 episodes	Days	FDA_CA_Teq3_After	3	n/a	225 (32 weeks * 7 days + 1 day)	365	Overall, Time to third secondary episode, Adherence, Gap between second and third secondary episode
5	Primary episode index date	0	Primary episode end date: 365 days	0	First episode	At least 1 episode	Days	ACIP_CA_Teq1	1	n/a	42 (6 weeks * 7 days)	104 (14 weeks * 7 days + 6 days)	Overall, Time to first secondary episode, Adherence
6	Primary episode index date	0	Primary episode end date: 365 days	0	Second episode	At least 2 episodes	Days						Overall, Time to second secondary episode, Gap between first and second secondary episode
7	Primary episode index date	0	Primary episode end date: 365 days	0	Third episode	3 episodes	Days	ACIP_CA_Teq3_Within	3	n/a	0	244 (estimation for 8 months)	Overall, Time to third secondary episode, Adherence, Gap between second and third secondary episode
8	Primary episode index date	0	Primary episode end date: 365 days	0	Third episode	3 episodes	Days	ACIP_CA_Teq3_After	3	n/a	245 (after 8 months estimation)	365	Overall, Time to third secondary episode, Adherence, Gap between second and third secondary episode

	Multiple Events Assessment							Adherence					Stratifications
									Count of Secondary Episodes		Time to Secondary		
Scenario	Observation Window Start Anchor	Number of Days from Obs. Window Start Anchor to Start Obs. Window	Observation Window End Anchor	Number of Days from Obs. Window End Anchor to End Obs. Window	Secondary (Sec.) episode (Ep.) to use for Time to Sec. Ep.Output	Minimum Adherence Criteria	Adherence Scale Evaluate adherence by...	Analysis Group	Minimum Number of Sec. Episodes	Maximum Number of Sec. Episodes	Episode Start	Episode End	Output levels
9	Primary episode index date	0	Primary episode end date: 365 days	0	First episode	At least 1 episode	Days	Rotavirus _NoExcl_ CA					Overall, Time to third secondary episode, Adherence, Gap between second and third secondary episode

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Appendix H.2: Specifications for Multiple Events Identification and Adherence Measures of Pentavalent Rotavirus Vaccine (RV5) Events among Infants with Any Amount of Enrollment

This request executed the Cohort Identification and Descriptive Analysis (CIDA) module to identify multiple pentavalent rotavirus vaccine events and adherence measures among infants with a birth date.

Query period: January 1, 2014 - December 31, 2018
Coverage requirement: Medical & Drug Coverage
Pre-index enrollment requirement: 0 days
Post-index enrollment requirement: 0 days
Enrollment gap: 45 days
Age groups: N/A
Stratifications: None
Restrictions: None
Envelope macro: No reclassification

			Episode Parameters									Exclusion Criteria		
Scenario	Recommendations	Episode of Interest	Index Exposure	Cohort definition	Incident exposure washout period	Incident with respect to:	User-defined exposure episode length	Minimum exposure episode duration	Maximum exposure episode duration	Care setting	Censor treatment episode at evidence of:	Exclusion Condition	Evaluation Window Start	Evaluation Window End
1	FDA vs. ACIP recommendations to be measured via Baseline Characteristics	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	2,000	n/a	n/a	n/a	*Death; *Disenrollment; *DP end date; *Query end date	Rotarix vaccination event	0	365
1	FDA vs. ACIP recommendations to be measured via Baseline Characteristics	Secondary Episode	RotaTeq	All valid exposure episodes during query period	3	RotaTeq	none	1 day	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--
2	n/a	Primary Episode	Infant birth date	First valid exposure episode during query period	n/a	n/a	2,000	n/a	n/a	n/a	*Death; *Disenrollment; *DP end date; *Query end date	n/a	--	--
2	n/a	Secondary Episode	RotaTeq or Rotavirus	All valid exposure episodes during query period	3	RotaTeq or Rotavirus	none	1 day	none	All	*Death; *Disenrollment; *DP end date; *Query end date	--	--	--

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Appendix H.2.1: Specifications for Multiple Events Identification and Adherence Measures of Pentavalent Rotavirus Vaccine (RV5) Events among Infants with Any Amount of Enrollment

This request executed the Cohort Identification and Descriptive Analysis (CIDA) module to identify multiple pentavalent rotavirus vaccine events and adherence measures among infants with a birth date.

Query period: January 1, 2014 - December 31, 2018
Coverage requirement: Medical & Drug Coverage
Pre-index enrollment requirement: 0 days
Post-index enrollment requirement: 0 days
Enrollment gap: 45 days
Age groups: N/A
Stratifications: None
Restrictions: None
Envelope macro: No reclassification

	Multiple Events Assessment							Stratifications	Adherence
Scenario	Observation (Obs.) Window Start Anchor	Number of Days from Obs. Window Start Anchor to Start Obs. Window	Observation (Obs.) Window End Anchor	Number of Days from Obs. Window End Anchor to End Obs. Window	Secondary (Sec.) episode (Ep.) to use for Time to Sec. Ep.Output	Minimum Adherence Criteria	Adherence Scale Evaluate adherence by...	Output levels	Adherence Measures
1 1	Primary episode index date	0	Primary episode end date; end of available follow-up time	0	1st episode	At least 1 episode	Days	Overall, Time to 1st secondary episode	See Appendix I for Cohort B metrics; FDA vs. ACIP
2 2	Primary episode index date	0	Primary episode end date; end of available follow-up time	0	1st episode	At least 1 episode	Days	Overall, Time to 1st secondary episode	See Appendix I tab for Cohort B metrics; FDA vs. ACIP

International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology, Fourth Edition (CPT-4) codes are provided by Optum360.

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Appendix I: Baseline Characteristics to Measure Non-Adherence among Infants with Any Amount of Enrollment

Baseline Characteristics

Recommendation	Baseline Characteristic	Cohort	Care setting	Principal diagnosis position	Evaluation period start (days)	Evaluation period end
FDA	Any RotaTeq dose after 32 weeks of age	Sensitivity Analysis	Any care setting	Any diagnosis position	225	end of available follow-up
ACIP	Any RotaTeq dose after 8 months of age	Sensitivity Analysis	Any care setting	Any diagnosis position	245	end of available follow-up

Appendix J: Design Diagram Detailing Multiple Events Assessment and Time to Event Metrics