

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. If you are using a web page screen reader and are unable to access this document, please contact the Sentinel Operations Center for assistance at info@sentinelssystem.org.

Overview for Request cder_mpl1p_wp014

Request ID: cder_mpl1p_wp014_nsdv_v01

Query Description: The goal of this query was to identify kidney, heart, and liver transplant patients within the Sentinel Distributed Database (SDD) and evaluate their follow-up time. Among these patients, this query additionally investigated the continuous use of brand and generic oral tacrolimus following the transplant event.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) module, version 5.2.1, with additional ad hoc programming.

Data Source: We included data from August 10, 2009 to October 31, 2017 from 17 Data Partners contributing to the SDD. We distributed this request on March 27, 2018. See Appendix A for a list of dates of available data for each Data Partner.

Study Design: This request was designed to describe the demographic characteristics of kidney, heart and liver transplant patients in the Sentinel database and summarize their duration of follow-up, length of treatment episodes, and gaps between treatment episodes. Baseline characteristics included patient age, sex, year of transplant, and any intravenous or parenteral tacrolimus administration during the inpatient stay. The use of the following medications was assessed within 30 days after discharge for the transplant of interest: any oral tacrolimus, oral tacrolimus coded by a procedure code, extended release oral tacrolimus, and oral immediate release tacrolimus by manufacturer. These medications were defined with National Drug Codes (NDCs) and Healthcare Common Procedure Coding System (HCPCS) codes. Please see Appendix B for the brand and generic names of medical products and Appendix C for the HCPCS codes used to define the above medications.

Events of Interest: The events of interest were kidney, heart, and liver transplants in the inpatient care setting. Claims occurring during a hospital stay, but with a care setting other than inpatient, were not included. Events of interest were defined using Current Procedural Terminology, Fourth Edition (CPT-4), International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), and International Classification of Disease, Tenth revision, Procedure Classification System (ICD-10-PCS) codes. Please refer to Appendix D for procedure codes used to define events of interest in this request.

Cohort Eligibility Criteria: We required all individuals included in the cohort to be continuously enrolled in health plans with medical and drug coverage for at least 12 months (365 days) prior to their inpatient stay admission date for the transplant event, during which gaps in coverage of up to 45 days were allowed. Members were excluded if they had a history of any organ transplant or any dispensing for tacrolimus 365 days prior to their inpatient stay admission date for the transplant of interest. History of any transplant was defined using CPT-4, ICD-9-CM, and ICD-10-PCS procedure codes. Please see Appendix E for a full list of procedure codes used to define transplant history in this request.

If a member received an outpatient dispensing of oral tacrolimus during the inpatient stay of interest, the patient was excluded. We examined only the first qualifying incident transplant, that occurred between August 10, 2009 to October 31, 2017 for each cohort member.

For oral tacrolimus continuous use evaluation, members identified with an incident transplant event were required to have a dispensing of immediate release oral tacrolimus within 30 days after the transplant of interest, beginning on the day of discharge from the inpatient stay. Please see Appendix F for a list of generic and brand names of medical products used to define oral tacrolimus for continuous use evaluation in this request. All ages were included in this evaluation.

Follow-up:

Transplant Population:

I. Total: Follow-up time began on the date of discharge from the inpatient stay of the transplant event, and continued until the first occurrence of any of the following: 1) disenrollment; 2) death; or 3) the end of Data Partner data availability.

II. Outcome: Follow-up time began on the date of discharge from the inpatient stay of the transplant event, and continued until the first dispensing of oral tacrolimus.

Overview for Request cder_mpl1p_wp014

Tacrolimus Use: Episode lengths were defined using outpatient pharmacy dispensing days supplied to create a sequence of continuous exposure. In the case of same day dispensings, the maximum days supplied was used to create the episode. No gap between episodes was allowed when defining continuous use. All valid episodes during the query period were included, starting from the first incident dispensing.

Please see Appendices G-I for the specifications of parameters used in the analyses for this request.

Limitations: Algorithms used to define exposures and outcomes are imperfect and thus, may be misclassified. Therefore, data should be interpreted with this limitation in mind.

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

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

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).

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.

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.

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

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.

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. Baseline Characteristics of Patients undergoing Inpatient Liver, Kidney, and Heart Transplant in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

Characteristic	Liver Transplant		Kidney Transplant		Heart Transplant	
	Number	Percent	Number	Percent	Number	Percent
Number of episodes	3,655	100%	27,353	100%	1,586	100%
Number of unique patients	3,655	100%	27,353	100%	1,586	100%
Demographics ²	Mean	Standard Deviation	Mean	Standard Deviation	Mean	Standard Deviation
Mean Age (Years)	58.3	11.3	51.8	14.7	56.1	13.8
Age (Years)	Number	Percent	Number	Percent	Number	Percent
0-17	65	1.8%	481	1.8%	53	3.3%
18-64	2,456	67.2%	20,898	76.4%	1,010	63.7%
65+	1,134	31.0%	5,974	21.8%	523	33.0%
Sex						
Female	1,402	38.4%	10,836	39.6%	427	26.9%
Male	2,253	61.6%	16,517	60.4%	1,159	73.1%
Year						
2009	66	1.8%	246	0.9%	32	2.0%
2010	193	5.3%	699	2.6%	61	3.8%
2011	538	14.7%	4,726	17.3%	230	14.5%
2012	541	14.8%	4,886	17.9%	228	14.4%
2013	606	16.6%	5,075	18.6%	258	16.3%
2014	661	18.1%	5,210	19.0%	318	20.1%
2015	676	18.5%	5,572	20.4%	325	20.5%
2016	246	6.7%	656	2.4%	92	5.8%
2017	128	3.5%	283	1.0%	42	2.6%
Tacrolimus administered during inpatient stay						
Intravenous Parenteral ³	0	0.0%	0	0.0%	0	0.0%
Oral Tacrolimus, Dispensed within 60 Days Post-Transplant Discharge, by Manufacturer						
All ⁴	1,388	38.0%	5,882	21.5%	446	28.1%
Brand Name						
Astellas	263	7.2%	677	2.5%	70	4.4%
Extended Release	0	0.0%	39	0.1%	0	0.0%
Generic Name						
Accord	178	4.9%	418	1.5%	73	4.6%
Dr.Reddys	181	5.0%	521	1.9%	79	5.0%
Mylan	60	1.6%	165	0.6%	17	1.1%
Panacea	*****	*****	27	0.1%	*****	*****
Sandoz	632	17.3%	1,887	6.9%	165	10.4%

Table 1. Baseline Characteristics of Patients undergoing Inpatient Liver, Kidney, and Heart Transplant in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

Characteristic	Liver Transplant		Kidney Transplant		Heart Transplant	
	Number	Percent	Number	Percent	Number	Percent
Strides	*****	*****	*****	*****	*****	*****
Watson	0	0.0%	*****	*****	0	0.0%
Procedure ⁵	299	8.2%	2,793	10.2%	118	7.4%

¹Please refer to Appendices G-H for details about specifications

²All metrics are based on total number of episodes per group, except for sex, race, and Hispanic origin which are based on total number of unique patients

³Please see Appendix C for a list of Healthcare Common Procedure Coding System (HCPCS) procedure codes used to define intravenous or parenteral tacrolimus

⁴Values in each category (“Brand Name”, “Generic Name”, and “Procedure”) do not sum up to “All” because these categories are not mutually exclusive

⁵Please see Appendix C for a list of Healthcare Common Procedure Coding System (HCPCS) procedure codes used to define oral tacrolimus

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Table 2. Time between Post-Transplant Discharge and First Dispensing for Generic or Brand Name Immediate Release Oral Tacrolimus, by Organ Type in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

Days								
Transplants by Organ	Number ²	Mean	Standard Deviation	Minimum	Q1 ³	Median	Q3 ⁴	Maximum
Liver	1403	79.1	224.3	1	1	2	32	1907
Kidney	4904	158.7	158.7	1	1	5	134.5	2647
Heart	477	151.1	151.1	1	1	8	94	1692

¹Please refer to Appendices G-H for details about specifications

²The information in this table is based on patients who had oral tacrolimus dispensed any time after transplant discharge

³Q1 represents the 25th Percentile

⁴Q3 represents the 75th Percentile

Table 3. Total Follow-Up Time after Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

Transplants by Organ	Number	Days						
		Mean	Standard Deviation	Minimum	Q1 ²	Median	Q3 ³	Maximum
Liver	3655	719.7	635	1	196	557	1099	2940
Kidney	27353	788.8	565.2	1	308	714	1149	2952
Heart	1586	710.7	614.1	1	182	564.5	1125	2916

¹Please refer to Appendices G-H for details about specifications

²Q1 represents the 25th Percentile

³Q3 represents the 75th Percentile

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap Length (Days)							
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	
Oral Tacrolimus, Prior Liver Transplant															
All Users⁵	1145	1	129	362	828	3001	575.7 (585.0)								
Users with at least 2 episodes	853	35	202	506	990	2700	679.9 (589.6)	Gap⁶ 1	853	1	6	15	31	1576	44.2 (125.8)
Users with at least 3 episodes	684	62	308	648.5	1090.5	2700	778.4 (586.6)	Gap 2	684	1	6	17	39	1683	36.6 (87.5)
Users with at least 4 episodes	563	106	390	731	1170	2628	857.1 (577.2)	Gap 3	563	1	7	19	46	714	40.0 (68.7)
Users with at least 5 episodes	481	106	450	780	1199	2628	900.7 (568.2)	Gap 4	481	1	6	20	54	891	44.4 (78.7)
Users with at least 6 episodes	396	146	546.5	888	1260	2628	985.5 (560.0)	Gap 5	396	1	5	16	51	775	41.5 (76.5)
Users with at least 7 episodes	342	185	601	952	1260	2628	1017.3 (546.7)	Gap 6	342	1	5	13	36	653	33.3 (59.1)
Users with at least 8 episodes	288	185	647.5	976.5	1313.5	2628	1053.6 (548.1)	Gap 7	288	1	5	15	38	1591	52.0 (163.2)
Users with at least 9 episodes	247	270	660	1020	1356	2628	1091.6 (540.6)	Gap 8	247	1	6	17	45	443	37.5 (57.2)
Users with at least 10 episodes	207	317	687	1050	1528	2628	1139.2 (551.8)	Gap 9	207	1	5	13	39	611	35.4 (68.8)
Users with at least 11 episodes	178	342	739	1077.5	1530	2628	1164.8 (541.4)	Gap 10	178	1	4	14.5	41	397	37.5 (61.7)
Users with at least 12 episodes	152	387	758.5	1081.5	1529	2628	1168.4 (532.5)	Gap 11	152	1	5	14	29	779	37.1 (94.8)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²								Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 13 episodes	136	387	742	1054	1542	2628	1157.3 (531.3)	Gap 12	136	1	4	14	37	341	35.7 (56.5)
Users with at least 14 episodes	102	390	762	1156.5	1575	2628	1201.6 (521.6)	Gap 13	102	1	5	15.5	38	590	37.6 (72.5)
Users with at least 15 episodes	85	421	829	1175	1575	2567	1217.1 (507.8)	Gap 14	85	1	5	18	33	259	31.2 (45.0)
Users with at least 16 episodes	65	431	886	1190	1590	2462	1251.4 (483.6)	Gap 15	65	1	5	10	20	131	19.7 (26.0)
Users with at least 17 episodes	56	431	841	1194.5	1640.5	2462	1270.2 (510.0)	Gap 16	56	1	5	11	25	216	24.8 (37.0)
Users with at least 18 episodes	42	431	1022	1260	1680	2462	1350.9 (480.6)	Gap 17	42	1	6	13	35	115	26.2 (32.3)
Users with at least 19 episodes	34	650	1022	1300	1680	2462	1371.0 (464.7)	Gap 18	34	1	11	19	46	111	30.2 (28.9)
Users with at least 20 episodes	26	650	1044	1342	1827	2462	1411.8 (483.8)	Gap 19	26	1	11	25	53	260	37.8 (50.1)
Users with at least 21 episodes	21	853	1058	1340	1827	2189	1434.2 (426.1)	Gap 20	21	2	5	12	47	333	40.2 (72.3)
Users with at least 22 episodes	19	853	1044	1584	1855	2189	1459.0 (439.1)	Gap 21	19	1	11	30	40	189	36.2 (41.0)
Users with at least 23 episodes	18	853	1059	1587	1855	2189	1483.7 (438.0)	Gap 22	18	3	8	23	45	96	30.2 (26.5)
Users with at least 24 episodes	13	853	1059	1601	1946	2189	1514.8 (482.9)	Gap 23	13	1	5	34	42	100	31.6 (28.2)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 25 episodes	11	853	1044	1601	2007	2189	1514.7 (506.7)	Gap 24	11	3	4	10	30	57	18.5 (17.2)
Users with at least 26 episodes	11	853	1044	1601	2007	2189	1514.7 (506.7)	Gap 25	11	1	3	6	38	52	17.4 (20.2)
Users with at least 27 episodes	*****	*****	*****	1714	*****	*****	1551.9 (518.1)	Gap 26	*****	*****	*****	5.5	*****	*****	16.7 (20.3)
Users with at least 28 episodes	*****	*****	*****	1714	*****	*****	1551.9 (518.1)	Gap 27	*****	*****	*****	7	*****	*****	19.8 (22.2)
Users with at least 29 episodes	*****	*****	*****	1886.5	*****	*****	1607.4 (553.6)	Gap 28	*****	*****	*****	11	*****	*****	18.4 (23.0)
Users with at least 30 episodes	*****	*****	*****	1946	*****	*****	1687.9 (545.1)	Gap 29	*****	*****	*****	8	*****	*****	20.4 (21.0)
Users with at least 31 episodes	*****	*****	*****	1946	*****	*****	1687.9 (545.1)	Gap 30	*****	*****	*****	16	*****	*****	17.7 (18.9)
Users with at least 32 episodes	*****	*****	*****	2007	*****	*****	1827.0 (492.3)	Gap 31	*****	*****	*****	6	*****	*****	43.8 (80.2)
Users with at least 33 episodes	*****	*****	*****	2019.5	*****	*****	1797.3 (563.3)	Gap 32	*****	*****	*****	9	*****	*****	10.0 (7.1)
Users with at least 34 episodes	*****	*****	*****	2032	*****	*****	1727.3 (668.3)	Gap 33	*****	*****	*****	11	*****	*****	18.0 (14.8)
Users with at least 35 episodes	*****	*****	*****	1575	*****	*****	1575.0 (868.3)	Gap 34	*****	*****	*****	31.5	*****	*****	31.5 (40.3)
Users with at least 36 episodes	*****	*****	*****	1575	*****	*****	1575.0 (868.3)	Gap 35	*****	*****	*****	12.5	*****	*****	12.5 (13.4)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap Length (Days)							
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	
Users with at least 37 episodes	*****	*****	*****	2189	*****	*****	2189.0 (.)	Gap 36	*****	*****	*****	2	*****	*****	2.0 (.)
Users with at least 38 episodes	*****	*****	*****	2189	*****	*****	2189.0 (.)	Gap 37	*****	*****	*****	1	*****	*****	1.0 (.)
Users with at least 39 episodes	*****	*****	*****	2189	*****	*****	2189.0 (.)	Gap 38	*****	*****	*****	3	*****	*****	3.0 (.)
Users with at least 40 episodes	*****	*****	*****	2189	*****	*****	2189.0 (.)	Gap 39	*****	*****	*****	2	*****	*****	2.0 (.)
Users with at least 41 episodes	*****	*****	*****	2189	*****	*****	2189.0 (.)	Gap 40	*****	*****	*****	4	*****	*****	4.0 (.)
Oral Tacrolimus, Prior Kidney Transplant															
All Users⁵	3310	1	140	450.5	1170	2877	720.5 (703.8)								
Users with at least 2 episodes	2375	14	260	650	1337	2877	855.0 (699.3)	Gap 1	2375	1	7	20	48	2496	61.9 (159.4)
Users with at least 3 episodes	1866	14	360	801.5	1481	2877	965.8 (688.7)	Gap 2	1866	1	6	18	43	2199	48.4 (138.6)
Users with at least 4 episodes	1514	14	464	910.5	1537	2831	1037.5 (668.3)	Gap 3	1514	1	6	16	37	1592	41.5 (109.0)
Users with at least 5 episodes	1233	50	540	1003	1621	2766	1109.6 (655.9)	Gap 4	1233	1	5	14	36	1268	36.5 (93.5)
Users with at least 6 episodes	1012	135	605	1088	1667	2766	1174.8 (646.5)	Gap 5	1012	1	4	12	30	719	29.8 (60.7)
Users with at least 7 episodes	823	135	670	1164	1691	2766	1208.4 (632.4)	Gap 6	823	1	4	12	32	980	31.4 (70.5)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 8 episodes	671	155	743	1186	1735	2766	1252.3 (613.4)	Gap 7	671	1	4	11	30	765	34.1 (80.0)
Users with at least 9 episodes	531	155	834	1296	1766	2730	1308.7 (588.9)	Gap 8	531	1	4	10	27	966	29.4 (72.9)
Users with at least 10 episodes	436	155	879	1334.5	1787	2730	1342.7 (568.4)	Gap 9	436	1	3	10	25	525	24.2 (47.5)
Users with at least 11 episodes	346	155	948	1378.5	1826	2730	1384.8 (550.1)	Gap 10	346	1	3	11	29	978	29.5 (66.0)
Users with at least 12 episodes	274	155	949	1400.5	1837	2730	1399.6 (553.4)	Gap 11	274	1	4	9	23	1014	26.3 (73.7)
Users with at least 13 episodes	230	155	949	1433.5	1853	2730	1407.6 (551.1)	Gap 12	230	1	4	10	22	260	21.0 (35.2)
Users with at least 14 episodes	191	155	1008	1452	1861	2730	1449.6 (536.1)	Gap 13	191	1	4	9	29	194	22.4 (32.4)
Users with at least 15 episodes	148	155	1002	1464.5	1870	2730	1462.6 (530.7)	Gap 14	148	1	4	10	27	797	28.7 (75.2)
Users with at least 16 episodes	114	155	1029	1464.5	1861	2730	1461.5 (531.1)	Gap 15	114	1	4	12.5	28	453	29.4 (60.2)
Users with at least 17 episodes	98	632	1064	1485.5	1897	2730	1493.1 (514.8)	Gap 16	98	1	4	9	27	117	18.2 (22.1)
Users with at least 18 episodes	82	650	1064	1444.5	1874	2664	1472.7 (496.8)	Gap 17	82	1	4	11	25	458	24.5 (53.9)
Users with at least 19 episodes	65	683	1074	1450	1854	2431	1469.2 (482.2)	Gap 18	65	1	4	10	25	186	19.6 (30.9)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 20 episodes	57	690	1048	1327	1826	2431	1428.6 (464.0)	Gap 19	57	1	4	11	30	567	32.0 (78.8)
Users with at least 21 episodes	49	780	1074	1410	1854	2431	1455.2 (460.4)	Gap 20	49	1	5	13	32	151	23.6 (30.7)
Users with at least 22 episodes	43	780	1048	1410	1826	2431	1441.6 (452.8)	Gap 21	43	1	5	9	24	838	36.7 (127.3)
Users with at least 23 episodes	34	780	1149	1464.5	1874	2431	1518.9 (448.5)	Gap 22	34	1	5	9.5	15	88	16.3 (19.4)
Users with at least 24 episodes	30	780	1164	1506.5	1874	2431	1550.2 (439.7)	Gap 23	30	1	6	13	33	77	20.8 (20.9)
Users with at least 25 episodes	27	780	1170	1534	1874	2431	1564.0 (434.4)	Gap 24	27	1	5	15	26	223	30.7 (49.0)
Users with at least 26 episodes	25	963	1230	1637	1874	2431	1601.6 (420.0)	Gap 25	25	1	5	9	21	116	22.1 (32.0)
Users with at least 27 episodes	22	1074	1230	1585.5	1874	2431	1608.5 (415.7)	Gap 26	22	1	4	10.5	18	40	12.8 (11.4)
Users with at least 28 episodes	18	1074	1287	1593.5	1920	2431	1648.0 (426.5)	Gap 27	18	2	5	11	20	69	15.2 (15.8)
Users with at least 29 episodes	15	1074	1410	1654	1965	2431	1725.3 (422.1)	Gap 28	15	1	4	5	15	27	9.2 (8.0)
Users with at least 30 episodes	15	1074	1410	1654	1965	2431	1725.3 (422.1)	Gap 29	15	3	6	16	20	44	15.5 (10.8)
Users with at least 31 episodes	12	1074	1445	1764	2110.5	2431	1764.4 (454.9)	Gap 30	12	1	2	6	10	57	11.2 (16.0)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap Length (Days)							
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	
Users with at least 32 episodes	11	1170	1479	1874	2256	2431	1827.2 (419.1)	Gap 31	11	1	3	5	26	52	13.8 (17.5)
Users with at least 33 episodes	*****	*****	*****	1874	*****	*****	1855.6 (449.9)	Gap 32	*****	*****	*****	12	*****	*****	15.6 (14.3)
Users with at least 34 episodes	*****	*****	*****	1874	*****	*****	1855.6 (449.9)	Gap 33	*****	*****	*****	15	*****	*****	20.6 (16.5)
Users with at least 35 episodes	*****	*****	*****	1919.5	*****	*****	1911.3 (446.6)	Gap 34	*****	*****	*****	4	*****	*****	5.4 (5.8)
Users with at least 36 episodes	*****	*****	*****	1965	*****	*****	1916.6 (482.1)	Gap 35	*****	*****	*****	4	*****	*****	9.6 (13.8)
Users with at least 37 episodes	*****	*****	*****	2110.5	*****	*****	1980.3 (494.7)	Gap 36	*****	*****	*****	14.5	*****	*****	17.8 (15.5)
Users with at least 38 episodes	*****	*****	*****	2256	*****	*****	2142.4 (330.0)	Gap 37	*****	*****	*****	4	*****	*****	6.6 (5.0)
Users with at least 39 episodes	*****	*****	*****	1965	*****	*****	2008.3 (377.9)	Gap 38	*****	*****	*****	5	*****	*****	6.3 (4.2)
Users with at least 40 episodes	*****	*****	*****	2030	*****	*****	2030.0 (531.7)	Gap 39	*****	*****	*****	8.5	*****	*****	8.5 (4.9)
Users with at least 41 episodes	*****	*****	*****	2030	*****	*****	2030.0 (531.7)	Gap 40	*****	*****	*****	8	*****	*****	8.0 (9.9)
Users with at least 42 episodes	*****	*****	*****	2030	*****	*****	2030.0 (531.7)	Gap 41	*****	*****	*****	6.5	*****	*****	6.5 (0.7)
Users with at least 43 episodes	*****	*****	*****	2030	*****	*****	2030.0 (531.7)	Gap 42	*****	*****	*****	16.5	*****	*****	16.5 (7.8)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 44 episodes	*****	*****	*****	1654	*****	*****	1654.0 (.)	Gap 43	*****	*****	*****	3	*****	*****	3.0 (.)
Users with at least 45 episodes	*****	*****	*****	1654	*****	*****	1654.0 (.)	Gap 44	*****	*****	*****	12	*****	*****	12.0 (.)
Users with at least 46 episodes	*****	*****	*****	1654	*****	*****	1654.0 (.)	Gap 45	*****	*****	*****	4	*****	*****	4.0 (.)
Oral Tacrolimus, Prior Heart Transplant															
All Users⁵	338	1	172	435.5	985	2771	683.4 (655.9)								
Users with at least 2 episodes	188	55	286	600	1190.5	2771	794.6 (676.3)	Gap 1	188	1	5	14	40	892	46.9 (110.6)
Users with at least 3 episodes	135	94	341	690	1364	2771	925.7 (702.2)	Gap 2	135	1	4	12	29	1130	53.1 (145.3)
Users with at least 4 episodes	101	94	423	766	1375	2551	973.3 (653.0)	Gap 3	101	1	4	10	32	619	27.6 (66.8)
Users with at least 5 episodes	83	164	465	776	1453	2551	1010.3 (644.1)	Gap 4	83	1	3	8	17	323	18.8 (42.2)
Users with at least 6 episodes	66	164	587	857	1483	2551	1065.5 (651.6)	Gap 5	66	1	3	9	26	1554	87.3 (277.9)
Users with at least 7 episodes	56	225	678.5	951	1599	2551	1141.4 (650.1)	Gap 6	56	1	4	8	20	273	22.3 (46.2)
Users with at least 8 episodes	51	299	676	931	1635	2551	1153.7 (663.1)	Gap 7	51	1	5	10	33	472	29.3 (68.2)
Users with at least 9 episodes	43	300	732	1110	1698	2551	1246.7 (628.8)	Gap 8	43	1	3	13	33	378	33.2 (67.5)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 10 episodes	34	465	766	1139	1698	2551	1274.1 (588.6)	Gap 9	34	1	5	9	20	182	18.2 (31.5)
Users with at least 11 episodes	30	465	766	1124.5	1827	2551	1291.8 (623.1)	Gap 10	30	1	3	11	31	95	20.8 (25.3)
Users with at least 12 episodes	24	465	746	968	1762.5	2551	1252.4 (651.4)	Gap 11	24	1	3	9.5	21	54	14.3 (13.4)
Users with at least 13 episodes	22	512	760	968	1698	2551	1256.0 (641.2)	Gap 12	22	3	11	21	36	120	27.3 (25.6)
Users with at least 14 episodes	19	512	760	1213	1827	2551	1320.9 (666.3)	Gap 13	19	1	5	11	23	40	13.9 (11.6)
Users with at least 15 episodes	18	512	776	1241	1827	2551	1352.1 (671.2)	Gap 14	18	2	7	11.5	37	82	21.8 (20.9)
Users with at least 16 episodes	14	636	900	1542.5	2061	2551	1532.3 (652.2)	Gap 15	14	2	9	26.5	37	965	91.4 (252.0)
Users with at least 17 episodes	12	776	1241	1666.5	2180	2551	1677.2 (585.0)	Gap 16	12	1	5.5	20.5	34	58	22.3 (17.9)
Users with at least 18 episodes	*****	*****	*****	1542.5	*****	*****	1576.6 (589.7)	Gap 17	*****	*****	*****	9	*****	*****	13.0 (13.1)
Users with at least 19 episodes	*****	*****	*****	1542.5	*****	*****	1576.6 (589.7)	Gap 18	*****	*****	*****	19	*****	*****	24.3 (18.0)
Users with at least 20 episodes	*****	*****	*****	1666.5	*****	*****	1722.1 (558.9)	Gap 19	*****	*****	*****	11	*****	*****	26.5 (32.3)
Users with at least 21 episodes	*****	*****	*****	1698	*****	*****	1839.6 (485.5)	Gap 20	*****	*****	*****	12	*****	*****	14.1 (12.8)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap	Gap Length (Days)						
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)		Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)
Users with at least 22 episodes	*****	*****	*****	1762.5	*****	*****	1934.7 (454.9)	Gap 21	*****	*****	*****	15	*****	*****	18.2 (16.3)
Users with at least 23 episodes	*****	*****	*****	1762.5	*****	*****	1934.7 (454.9)	Gap 22	*****	*****	*****	8.5	*****	*****	15.7 (14.8)
Users with at least 24 episodes	*****	*****	*****	1762.5	*****	*****	1934.7 (454.9)	Gap 23	*****	*****	*****	10	*****	*****	14.7 (13.6)
Users with at least 25 episodes	*****	*****	*****	1762.5	*****	*****	1934.7 (454.9)	Gap 24	*****	*****	*****	11	*****	*****	10.3 (6.3)
Users with at least 26 episodes	*****	*****	*****	1762.5	*****	*****	1934.7 (454.9)	Gap 25	*****	*****	*****	7.5	*****	*****	14.2 (19.5)
Users with at least 27 episodes	*****	*****	*****	1698	*****	*****	1832.2 (424.2)	Gap 26	*****	*****	*****	12	*****	*****	9.6 (4.9)
Users with at least 28 episodes	*****	*****	*****	1698	*****	*****	1832.2 (424.2)	Gap 27	*****	*****	*****	10	*****	*****	14.6 (11.1)
Users with at least 29 episodes	*****	*****	*****	1698	*****	*****	1832.2 (424.2)	Gap 28	*****	*****	*****	11	*****	*****	8.2 (6.5)
Users with at least 30 episodes	*****	*****	*****	1698	*****	*****	1832.2 (424.2)	Gap 29	*****	*****	*****	19	*****	*****	18.4 (15.0)
Users with at least 31 episodes	*****	*****	*****	1698	*****	*****	1720.0 (97.9)	Gap 30	*****	*****	*****	12	*****	*****	12.0 (7.0)
Users with at least 32 episodes	*****	*****	*****	1666.5	*****	*****	1666.5 (44.5)	Gap 31	*****	*****	*****	14.5	*****	*****	14.5 (12.0)
Users with at least 33 episodes	*****	*****	*****	1666.5	*****	*****	1666.5 (44.5)	Gap 32	*****	*****	*****	6	*****	*****	6.0 (5.7)

Table 4. Cumulative Length of Treatment Episode and Gap between Distinct Treatment Episodes, for Generic or Brand Name Immediate Release Oral Tacrolimus, Dispensed within 60 Days of Post-Transplant Discharge in the Sentinel Distributed Database (SDD) from August 10, 2009 to October 31, 2017¹

	Episode Length (Days) ²							Gap Length (Days)							
	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	Number	Minimum	Q1 ³	Median	Q3 ⁴	Maximum	Mean (Standard Deviation)	
Users with at least 34 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 33	*****	*****	*****	23	*****	*****	23.0 (.)
Users with at least 35 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 34	*****	*****	*****	20	*****	*****	20.0 (.)
Users with at least 36 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 35	*****	*****	*****	22	*****	*****	22.0 (.)
Users with at least 37 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 36	*****	*****	*****	22	*****	*****	22.0 (.)
Users with at least 38 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 37	*****	*****	*****	5	*****	*****	5.0 (.)
Users with at least 39 episodes	*****	*****	*****	1698	*****	*****	1698.0 (.)	Gap 38	*****	*****	*****	29	*****	*****	29.0 (.)

¹Please refer to Appendix I for details about specifications

²The length of episode calculations are cumulative across distinct episodes, and do not include the gap days

³Q1 represents the 25th Percentile

⁴Q3 represents the 75th Percentile

⁵All Users represents the number of patients with any generic or brand name immediate release tacrolimus dispensing within 60 days of post-transplant discharge, regardless of the number of subsequent episodes. This number includes those with just one episode, in addition to those with multiple episodes. Patients with at least two episodes and onward are stratified separately in subsequent rows.

⁶Gap = gap in days between exposure episode n and exposure episode n+1

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented.

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request End Date (October 31, 2017)

DP ID	DP Start Date*	DP End Date*
DP01	1/1/2008	6/30/2017
DP02	1/1/2012	6/30/2016
DP03	1/1/2006	7/31/2017
DP04	1/1/2000	6/30/2017
DP05	1/1/2000	1/31/2017
DP06	1/2/2000	5/31/2015
DP07	1/1/2000	3/31/2016
DP08	6/1/2007	7/31/2017
DP09	1/1/2000	7/31/2017
DP10	1/1/2000	7/31/2017
DP11	1/1/2005	6/30/2017
DP12	1/1/2000	7/31/2017
DP13	1/1/2000	8/31/2017
DP14	1/1/2004	10/31/2017
DP15	1/1/2008	3/31/2017
DP16	1/1/2000	12/31/2016
DP17	1/1/2010	12/31/2015

*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 Immediate Release and Extended Release Oral Tacrolimus Exposures in this Request

Generic Name	Brand Name
Tacrolimus	Prograf
Tacrolimus	Hecoria
Tacrolimus	Tacrolimus
Tacrolimus	Astagraf XL
Tacrolimus	Envarsus XR

Appendix C. List of Healthcare Common Procedure Coding System (HCPCS) Procedure Codes Used to Define Oral, Intravenous, and Parenteral Tacrolimus in this Request

Code	Description	Code Type	Code Category
Oral			
J7508	Tacrolimus, extended release, (Astagraf XL), oral, 0.1 mg	HCPCS	Procedure
J7503	Tacrolimus, extended release, oral, 0.25 mg	HCPCS	Procedure
J7507	Tacrolimus, immediate release, oral, 1 mg	HCPCS	Procedure
Intravenous or Parenteral Tacrolimus			
C9006	Injection, tacrolimus, per 5 mg (1 amp)	HCPCS	Procedure
J7525	Tacrolimus, parenteral, 5 mg	HCPCS	Procedure

Appendix D. List of Current Procedural Terminology, Fourth Edition (CPT-4), International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), and International Classification of Diseases, Tenth Revision, Procedure Classification System (ICD-10-PCS) Procedure Codes Used to Define Kidney, Liver, and Heart Transplant in this Request

Code	Description	Code Type	Code Category
Kidney Transplant			
50360	Renal allotransplantation, implantation of graft; without recipient nephrectomy	CPT-4	Procedure
50365	Renal allotransplantation, implantation of graft; with recipient nephrectomy	CPT-4	Procedure
55.69	Other kidney transplantation	ICD-9-CM	Procedure
55.6	Transplant of kidney	ICD-9-CM	Procedure
0TY1	Transplantation / Kidney, Left	ICD-10-PCS	Procedure
0TY0	Transplantation / Kidney, Right	ICD-10-PCS	Procedure
0TY10Z0	Transplantation of Left Kidney, Allogeneic, Open Approach	ICD-10-PCS	Procedure
0TY00Z0	Transplantation of Right Kidney, Allogeneic, Open Approach	ICD-10-PCS	Procedure
Heart Transplant			
33935	Heart-lung transplant with recipient cardiectomy-pneumonectomy	CPT-4	Procedure
33945	Heart transplant, with or without recipient cardiectomy	CPT-4	Procedure
33.6	Combined heart-lung transplantation	ICD- 9	Procedure
37.51	Heart transplantation	ICD- 9	Procedure
02Y	Heart and Great Vessels, Transplantation	ICD-10-PCS	Procedure
02YA	Transplantation / Heart	ICD-10-PCS	Procedure
02YA0Z0	Transplantation of Heart, Allogeneic, Open Approach	ICD-10-PCS	Procedure
Liver Transplant			
47135	Liver allotransplantation; orthotopic, partial or whole, from cadaver or living	CPT-4	Procedure
50.51	Auxiliary liver transplant	ICD-9-CM	Procedure
50.5	Liver transplant	ICD-9-CM	Procedure
50.59	Other transplant of liver	ICD-10-PCS	Procedure
0FY0	Transplantation / Liver	ICD-10-PCS	Procedure
0FY00Z0	Transplantation of Liver, Allogeneic, Open Approach	ICD-10-PCS	Procedure

Appendix E. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedure Classification System (ICD-10-PCS), and Current Procedural Terminology, Fourth Edition (CPT-4) Diagnosis and Procedure Codes Used to Define History of Transplant in this Request

Code	Description	Code Type	Code Category
V42.81	Bone marrow replaced by transplant	ICD-9-CM	Diagnosis
V42.4	Bone replaced by transplant	ICD-9-CM	Diagnosis
V42.5	Cornea replaced by transplant	ICD-9-CM	Diagnosis
V42.1	Heart replaced by transplant	ICD-9-CM	Diagnosis
V42.2	Heart valve replaced by transplant	ICD-9-CM	Diagnosis
V42.0	Kidney replaced by transplant	ICD-9-CM	Diagnosis
V42.7	Liver replaced by transplant	ICD-9-CM	Diagnosis
V42.6	Lung replaced by transplant	ICD-9-CM	Diagnosis
V42	Organ or tissue replaced by transplant	ICD-9-CM	Diagnosis
V42.84	Organ or tissue replaced by transplant, intestines	ICD-9-CM	Diagnosis
V42.89	Other organ or tissue replaced by transplant	ICD-9-CM	Diagnosis
V42.8	Other specified organ or tissue replaced by transplant	ICD-9-CM	Diagnosis
V42.83	Pancreas replaced by transplant	ICD-9-CM	Diagnosis
V42.82	Peripheral stem cells replaced by transplant	ICD-9-CM	Diagnosis
V42.3	Skin replaced by transplant	ICD-9-CM	Diagnosis
V42.9	Unspecified organ or tissue replaced by transplant	ICD-9-CM	Diagnosis
Z94.81	Bone marrow transplant status	ICD-10-CM	Diagnosis
Z94.6	Bone transplant status	ICD-10-CM	Diagnosis
Z94.7	Corneal transplant status	ICD-10-CM	Diagnosis
Z94.3	Heart and lungs transplant status	ICD-10-CM	Diagnosis
Z94.1	Heart transplant status	ICD-10-CM	Diagnosis
Z94.82	Intestine transplant status	ICD-10-CM	Diagnosis
Z94.0	Kidney transplant status	ICD-10-CM	Diagnosis
Z94.4	Liver transplant status	ICD-10-CM	Diagnosis
Z94.2	Lung transplant status	ICD-10-CM	Diagnosis
Z94.8	Other transplanted organ and tissue status	ICD-10-CM	Diagnosis
Z94.89	Other transplanted organ and tissue status	ICD-10-CM	Diagnosis
Z94.83	Pancreas transplant status	ICD-10-CM	Diagnosis
Z94.5	Skin transplant status	ICD-10-CM	Diagnosis
Z94.84	Stem cells transplant status	ICD-10-CM	Diagnosis
Z94	Transplanted organ and tissue status	ICD-10-CM	Diagnosis
Z94.9	Transplanted organ and tissue status, unspecified	ICD-10-CM	Diagnosis
V45.87	Transplanted organ removal status	ICD-9-CM	Diagnosis
Z98.85	Transplanted organ removal status	ICD-10-CM	Diagnosis
55.53	Removal of transplanted or rejected kidney	ICD-9-CM	Procedure
50380	Renal autotransplantation, reimplantation of kidney	CPT-4	Procedure
50370	Removal of transplanted renal allograft	CPT-4	Procedure
BT29	Computerized Tomography (CT Scan) / Kidney Transplant	ICD-10-PCS	Procedure
BT29ZZZ	Computerized Tomography (CT Scan) of Kidney Transplant	ICD-10-PCS	Procedure
BT29Y0Z	Computerized Tomography (CT Scan) of Kidney Transplant using Other Contrast, Unenhanced and Enhanced	ICD-10-PCS	Procedure

Appendix E. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedure Classification System (ICD-10-PCS), and Current Procedural Terminology, Fourth Edition (CPT-4) Diagnosis and Procedure Codes Used to Define History of Transplant in this Request

Code	Description	Code Type	Code Category
BT2900Z	Computerized Tomography (CT Scan) of Kidney Transplant using High Osmolar Contrast, Unenhanced and Enhanced	ICD-10-PCS	Procedure
BT2910Z	Computerized Tomography (CT Scan) of Kidney Transplant using Low Osmolar Contrast, Unenhanced and Enhanced	ICD-10-PCS	Procedure
BT290ZZ	Computerized Tomography (CT Scan) of Kidney Transplant using High Osmolar Contrast	ICD-10-PCS	Procedure
BT291ZZ	Computerized Tomography (CT Scan) of Kidney Transplant using Low Osmolar Contrast	ICD-10-PCS	Procedure
BT29YZZ	Computerized Tomography (CT Scan) of Kidney Transplant using Other Contrast	ICD-10-PCS	Procedure
BT39	Magnetic Resonance Imaging (MRI) / Kidney Transplant	ICD-10-PCS	Procedure
BT39ZZZ	Magnetic Resonance Imaging (MRI) of Kidney Transplant	ICD-10-PCS	Procedure
BT39Y0Z	Magnetic Resonance Imaging (MRI) of Kidney Transplant using Other Contrast, Unenhanced and Enhanced	ICD-10-PCS	Procedure
BT39YZZ	Magnetic Resonance Imaging (MRI) of Kidney Transplant using Other Contrast	ICD-10-PCS	Procedure
BT49	Ultrasonography / Kidney Transplant	ICD-10-PCS	Procedure
BT49ZZZ	Ultrasonography of Kidney Transplant	ICD-10-PCS	Procedure
996.81	Complications of transplanted kidney	ICD-9-CM	Diagnosis
996.82	Complications of transplanted liver	ICD-9-CM	Diagnosis
996.83	Complications of transplanted heart	ICD-9-CM	Diagnosis
T86.10	Unspecified complication of kidney transplant	ICD-10-CM	Diagnosis
T86.11	Kidney transplant rejection	ICD-10-CM	Diagnosis
T86.12	Kidney transplant failure	ICD-10-CM	Diagnosis
T86.40	Unspecified complication of liver transplant	ICD-10-CM	Diagnosis
T86.41	Liver transplant rejection	ICD-10-CM	Diagnosis
T86.42	Liver transplant failure	ICD-10-CM	Diagnosis
T86.20	Unspecified complication of heart transplant	ICD-10-CM	Diagnosis
T86.21	Heart transplant rejection	ICD-10-CM	Diagnosis
T86.22	Heart transplant failure	ICD-10-CM	Diagnosis
BT290ZZ	Computerized Tomography (CT Scan) of Kidney Transplant using High Osmolar Contrast	ICD-10-PCS	Procedure
BT291ZZ	Computerized Tomography (CT Scan) of Kidney Transplant using Low Osmolar Contrast	ICD-10-PCS	Procedure
BT29YZZ	Computerized Tomography (CT Scan) of Kidney Transplant using Other Contrast	ICD-10-PCS	Procedure
BT39	Magnetic Resonance Imaging (MRI) / Kidney Transplant	ICD-10-PCS	Procedure
BT39ZZZ	Magnetic Resonance Imaging (MRI) of Kidney Transplant	ICD-10-PCS	Procedure
BT39Y0Z	Magnetic Resonance Imaging (MRI) of Kidney Transplant using Other Contrast, Unenhanced and Enhanced	ICD-10-PCS	Procedure

Appendix E. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM), International Classification of Diseases, Tenth Revision, Procedure Classification System (ICD-10-PCS), and Current Procedural Terminology, Fourth Edition (CPT-4) Diagnosis and Procedure Codes Used to Define History of Transplant in this Request

Code	Description	Code Type	Code Category
BT39YZZ	Magnetic Resonance Imaging (MRI) of Kidney Transplant using Other Contrast	ICD-10-PCS	Procedure
BT49	Ultrasonography / Kidney Transplant	ICD-10-PCS	Procedure
BT49ZZZ	Ultrasonography of Kidney Transplant	ICD-10-PCS	Procedure
50380	Renal autotransplantation, reimplantation of kidney	CPT-4	Procedure
50370	Removal of transplanted renal allograft	CPT-4	Procedure

Appendix F. List of Generic and Brand Names of Medical Products Used to Define Immediate Release Oral Tacrolimus Outcomes in this Request

Generic Name	Brand Name
Tacrolimus	Prograf
Tacrolimus	Hecoria
Tacrolimus	Tacrolimus

Appendix G. Specifications Defining Parameters for Events and Outcome in this Request

This request used the Cohort Identification and Descriptive Analysis (CIDA) module, version 5.2.1 with additional ad hoc programming, to evaluate the feasibility of using Sentinel data to compare clinical outcomes of brand vs. individual generic products of tacrolimus oral capsule. This request identifies the kidney, liver, and heart transplant population, and their follow-up time in the Sentinel Distributed Database (SDD).

Query Period: August 10, 2009 - October 31, 2017
Coverage Requirement: Medical and Drug
Enrollment Requirement: 365 days
Enrollment Gap: 45 days
Age Groups: <18, 18-65, 65+ Years
Data Partners: All Data Partners

Scenario	Event						Covariate	Outcome	
	Event ¹	Care Setting	Incident with Respect to ²	Incidence Care Setting	Washout	Censor at Death	Cohort Definition	Conditions	Outcome ³
1	Liver Transplant	Inpatient	History of Any Transplant, Any Transplant of Interest, Any Tacrolimus	Any	365 days	Yes	First valid incident exposure	See Appendix H	Oral Tacrolimus
2	Kidney Transplant	Inpatient	History of Any Transplant, Any Transplant of Interest, Any Tacrolimus	Any	365 days	Yes	First valid incident exposure	See Appendix H	Oral Tacrolimus
3	Heart Transplant	Inpatient	History of Any Transplant, Any Transplant of Interest, Any Tacrolimus	Any	365 days	Yes	First valid incident exposure	See Appendix H	Oral Tacrolimus

¹Index Date on date of discharge from inpatient stay, containing transplant of interest

²Washout begins the day before the admission date of the inpatient stay, containing the transplant of interest

³If a patient received a dispensing of oral tacrolimus during the time of the IP stay of interest, the patient was excluded

*Envelop macro will be turned off to avoid rolling patients up to an IP stay, in which case they would not have a discharge date

International Classification of Diseases, Ninth Revision (ICD-9), International Classification of Diseases, Tenth Revision (ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus"

Appendix H. Specifications Defining Parameters for Covariates in this Request

Relative to Index Date			
Covariate	Care Setting	Look Start (day)	Look End (day)
IV or parenteral tacrolimus ¹	Inpatient	0	0
Any Oral Tacrolimus	Any	0	60
Procedure Codes	Any	0	60
Extended Release	N/A	0	60
Brand - Astellas	N/A	0	60
Generic - Sandoz	N/A	0	60
Generic - Dr Reddys	N/A	0	60
Generic - Watson	N/A	0	60
Generic - Mylan	N/A	0	60
Generic - Accord	N/A	0	60
Generic - Panacea	N/A	0	60
Generic - Strides	N/A	0	60

¹Start and End date will be assigned relative to discharge date of inpatient stay, containing the code of interest

Appendix I. Specifications Defining Parameters for Treatment Episodes in this Request

Scenario	Exposure					
	Exposure ^{1,2}	Intent to Treat	Episode Gap Type	Episode Gap (days)	Same Day Dispensings	Censor at Death
1	Oral Tacrolimus, Among Liver Transplant Cohort	N/A	Fixed	0	Use maximum days supplied	Yes
2	Oral Tacrolimus, Among Kidney Transplant Cohort	N/A	Fixed	0	Use maximum days supplied	Yes
3	Oral Tacrolimus, Among Heart Transplant Cohort	N/A	Fixed	0	Use maximum days supplied	Yes

¹ Exposure will be defined as first tacrolimus dispensing among those patients identified as incident transplant patients in the related type 2 component of this request

² For evaluation for continuous use, the tacrolimus dispensing must occur on the day of IP stay discharge or within 30 days, as established in the type 2 component of this request

International Classification of Diseases, Ninth Revision (ICD-9), International Classification of Diseases, Tenth Revision (ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDC) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus"