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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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Table 2. Summary of Use of Selected Drugs in the Sentinel Distributed Database (SDD) between January 1, 2011 and December 31, 2015, by Drug, Year, and Age Group

Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2011-2015										
Atenolol, Metoprolol, Nebivolol, Propranolol										
00-21 Years	77,055	340,778	10,993,108	21,586,424	27,178,643	51,047,090.4	2.84	142.67	4.42	32.26
22-44 Years	799,079	5,362,096	194,053,129	254,626,662	38,224,633	62,804,523.7	20.90	242.85	6.71	36.19
45-64 Years	2,584,520	25,665,188	1,108,152,878	1,457,778,691	28,333,576	56,529,815.5	91.22	428.77	9.93	43.18
65+ Years	2,255,149	24,415,446	1,392,462,136	1,921,829,022	9,260,114	22,831,377.9	243.53	617.46	10.83	57.03
Atenolol										
00-21 Years	17,122	94,385	3,308,711	4,758,413	27,178,643	51,047,090.4	0.63	193.24	5.51	35.06
22-44 Years	202,596	1,427,236	59,694,052	67,648,414	38,224,633	62,804,523.7	5.30	294.65	7.04	41.82
45-64 Years	783,954	7,833,375	398,372,719	458,987,038	28,333,576	56,529,815.5	27.67	508.16	9.99	50.86
65+ Years	721,458	7,866,445	519,556,316	613,122,746	9,260,114	22,831,377.9	77.91	720.15	10.90	66.05
Metoprolol										
00-21 Years	13,168	56,202	1,852,521	2,507,755	27,178,643	51,047,090.4	0.48	140.68	4.27	32.96
22-44 Years	346,426	2,444,061	85,852,527	119,729,185	38,224,633	62,804,523.7	9.06	247.82	7.06	35.13
45-64 Years	1,474,689	14,089,302	571,771,555	822,865,309	28,333,576	56,529,815.5	52.05	387.72	9.55	40.58
65+ Years	1,453,194	14,733,639	790,344,895	1,197,288,787	9,260,114	22,831,377.9	156.93	543.87	10.14	53.64
Nebivolol										
00-21 Years	1,347	6,448	206,913	218,455	27,178,643	51,047,090.4	0.05	153.61	4.79	32.09
22-44 Years	67,679	528,389	17,466,950	18,387,939	38,224,633	62,804,523.7	1.77	258.09	7.81	33.06
45-64 Years	211,166	2,150,876	78,014,243	83,507,192	28,333,576	56,529,815.5	7.45	369.45	10.19	36.27
65+ Years	106,579	1,063,070	44,957,172	48,614,258	9,260,114	22,831,377.9	11.51	421.82	9.97	42.29
Propranolol										
00-21 Years	47,538	183,743	5,624,963	14,101,801	27,178,643	51,047,090.4	1.75	118.33	3.87	30.61
22-44 Years	214,135	962,410	31,039,600	48,861,123	38,224,633	62,804,523.7	5.60	144.95	4.49	32.25
45-64 Years	212,093	1,591,635	59,994,361	92,419,151	28,333,576	56,529,815.5	7.49	282.87	7.50	37.69
65+ Years	87,522	752,292	37,603,753	62,803,231	9,260,114	22,831,377.9	9.45	429.65	8.60	49.99

Table 3. Summary of Use of Selected Drugs in the Sentinel Distributed Database (SDD) between January 1, 2011 and December 31, 2015, by Drug, Year, and Sex

Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2011										
Propranolol, Metoprolol, Atenolol, Nebivolol										
Female	1,253,946	6,017,980	286,222,181	385,438,824	24,758,280	20,439,743.4	50.65	228.26	4.80	47.56
Male	1,126,912	5,365,696	255,483,880	342,238,529	23,830,255	19,458,864.3	47.29	226.71	4.76	47.61
Unknown	122	586	27,036	37,240	2,354	1,879.3	51.83	221.61	4.80	46.14
Atenolol										
Female	495,632	2,234,302	124,581,561	147,661,134	24,758,280	20,439,743.4	20.02	251.36	4.51	55.76
Male	393,103	1,737,596	98,125,797	112,923,910	23,830,255	19,458,864.3	16.50	249.62	4.42	56.47
Unknown	36	180	9,206	8,971	2,354	1,879.3	15.29	255.72	5.00	51.14
Metoprolol										
Female	596,805	2,980,991	131,251,706	195,487,515	24,758,280	20,439,743.4	24.11	219.92	4.99	44.03
Male	617,986	3,026,619	134,938,154	200,016,015	23,830,255	19,458,864.3	25.93	218.35	4.90	44.58
Unknown	70	339	14,812	23,626	2,354	1,879.3	29.74	211.60	4.84	43.69
Nebivolol										
Female	65,080	325,191	12,090,447	12,671,251	24,758,280	20,439,743.4	2.63	185.78	5.00	37.18
Male	72,294	367,237	13,552,104	14,184,328	23,830,255	19,458,864.3	3.03	187.46	5.08	36.90
Unknown	7	29	1,325	2,380	2,354	1,879.3	2.97	189.29	4.14	45.69
Propranolol										
Female	118,079	477,496	18,298,467	29,618,925	24,758,280	20,439,743.4	4.77	154.97	4.04	38.32
Male	61,550	234,244	8,867,825	15,114,276	23,830,255	19,458,864.3	2.58	144.08	3.81	37.86
Unknown	11	38	1,693	2,263	2,354	1,879.3	4.67	153.91	3.45	44.55

Table 3. Summary of Use of Selected Drugs in the Sentinel Distributed Database (SDD) between January 1, 2011 and December 31, 2015, by Drug, Year, and Sex

Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2012										
Atenolol, Metoprolol, Nebivolol, Propranolol										
Female	1,318,970	6,237,939	304,423,548	410,621,009	25,432,727	21,029,503.4	51.86	230.80	4.73	48.80
Male	1,198,696	5,642,229	274,426,052	368,720,699	24,567,557	20,116,040.2	48.79	228.94	4.71	48.64
Unknown	135	632	29,957	42,251	2,647	2,107.3	51.00	221.90	4.68	47.40
Atenolol										
Female	488,177	2,173,856	123,483,896	146,033,260	25,432,727	21,029,503.4	19.19	252.95	4.45	56.80
Male	384,082	1,686,888	96,483,815	110,834,001	24,567,557	20,116,040.2	15.63	251.21	4.39	57.20
Unknown	37	202	9,318	9,479	2,647	2,107.3	13.98	251.84	5.46	46.13
Metoprolol										
Female	661,706	3,197,563	147,648,985	219,504,402	25,432,727	21,029,503.4	26.02	223.13	4.83	46.18
Male	688,094	3,277,393	152,423,801	225,324,029	24,567,557	20,116,040.2	28.01	221.52	4.76	46.51
Unknown	80	354	16,979	27,432	2,647	2,107.3	30.22	212.24	4.43	47.96
Nebivolol										
Female	74,919	380,759	14,467,710	15,177,716	25,432,727	21,029,503.4	2.95	193.11	5.08	38.00
Male	83,935	435,251	16,259,492	17,020,927	24,567,557	20,116,040.2	3.42	193.72	5.19	37.36
Unknown	9	40	2,040	2,790	2,647	2,107.3	3.40	226.67	4.44	51.00
Propranolol										
Female	116,913	485,761	18,822,957	29,905,630	25,432,727	21,029,503.4	4.60	161.00	4.15	38.75
Male	61,547	242,697	9,258,944	15,541,741	24,567,557	20,116,040.2	2.51	150.44	3.94	38.15
Unknown	9	36	1,620	2,550	2,647	2,107.3	3.40	180.00	4.00	45.00

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Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2013										
Atenolol, Metoprolol, Nebivolol, Propranolol										
Female	1,337,844	6,399,199	316,126,479	426,378,977	25,429,877	20,893,234.8	52.61	236.30	4.78	49.40
Male	1,228,921	5,865,279	288,492,987	387,404,544	24,659,733	20,039,309.0	49.84	234.75	4.77	49.19
Unknown	145	643	31,354	41,757	2,431	1,786.4	59.65	216.23	4.43	48.76
Atenolol										
Female	463,447	2,072,167	119,140,846	140,675,708	25,429,877	20,893,234.8	18.22	257.08	4.47	57.50
Male	364,893	1,610,682	92,911,201	106,579,541	24,659,733	20,039,309.0	14.80	254.63	4.41	57.68
Unknown	37	172	8,935	8,988	2,431	1,786.4	15.22	241.49	4.65	51.95
Metoprolol										
Female	702,784	3,438,188	162,431,959	239,484,941	25,429,877	20,893,234.8	27.64	231.13	4.89	47.24
Male	733,882	3,541,696	168,476,501	246,621,171	24,659,733	20,039,309.0	29.76	229.57	4.83	47.57
Unknown	86	385	18,634	27,680	2,431	1,786.4	35.38	216.67	4.48	48.40
Nebivolol										
Female	78,565	413,073	15,822,001	16,653,178	25,429,877	20,893,234.8	3.09	201.39	5.26	38.30
Male	87,935	473,448	17,816,945	18,706,907	24,659,733	20,039,309.0	3.57	202.61	5.38	37.63
Unknown	14	51	2,054	2,520	2,431	1,786.4	5.76	146.71	3.64	40.27
Propranolol										
Female	116,294	475,771	18,731,673	29,565,149	25,429,877	20,893,234.8	4.57	161.07	4.09	39.37
Male	61,513	239,453	9,288,340	15,496,926	24,659,733	20,039,309.0	2.49	151.00	3.89	38.79
Unknown	8	35	1,731	2,569	2,431	1,786.4	3.29	216.38	4.38	49.46

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Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2014										
Atenolol, Metoprolol, Nebivolol, Propranolol										
Female	1,389,862	6,407,819	321,831,316	438,919,809	26,474,584	21,486,218.3	52.50	231.56	4.61	50.22
Male	1,269,290	5,835,935	292,547,773	396,846,972	25,715,224	20,643,097.6	49.36	230.48	4.60	50.13
Unknown	133	528	25,574	35,236	2,367	1,685.5	56.19	192.29	3.97	48.44
Atenolol										
Female	452,628	1,945,563	113,915,112	134,834,926	26,474,584	21,486,218.3	17.10	251.67	4.30	58.55
Male	352,349	1,494,995	87,779,746	100,476,380	25,715,224	20,643,097.6	13.70	249.13	4.24	58.72
Unknown	36	116	6,286	5,888	2,367	1,685.5	15.21	174.61	3.22	54.19
Metoprolol										
Female	751,487	3,536,098	171,393,683	253,703,456	26,474,584	21,486,218.3	28.39	228.07	4.71	48.47
Male	781,795	3,624,885	177,041,364	260,178,131	25,715,224	20,643,097.6	30.40	226.45	4.64	48.84
Unknown	80	349	16,561	25,682	2,367	1,685.5	33.80	207.01	4.36	47.45
Nebivolol										
Female	75,190	395,740	15,402,264	16,463,716	26,474,584	21,486,218.3	2.84	204.84	5.26	38.92
Male	83,641	446,991	17,151,387	18,366,494	25,715,224	20,643,097.6	3.25	205.06	5.34	38.37
Unknown	9	39	1,622	1,712	2,367	1,685.5	3.80	180.22	4.33	41.59
Propranolol										
Female	133,344	530,418	21,120,257	33,917,710	26,474,584	21,486,218.3	5.04	158.39	3.98	39.82
Male	70,538	269,064	10,575,276	17,825,966	25,715,224	20,643,097.6	2.74	149.92	3.81	39.30
Unknown	11	24	1,105	1,954	2,367	1,685.5	4.65	100.45	2.18	46.04

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Year	New Users	Dispensings	Days Supplied	Amount Supplied	Eligible Members	Member- Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
2015										
Atenolol, Metoprolol, Nebivolol, Propranolol										
Female	1,220,696	4,188,524	192,078,170	262,130,379	24,392,996	14,787,700.3	50.04	157.35	3.43	45.86
Male	1,115,612	3,820,303	173,905,253	236,951,001	23,856,625	14,310,501.0	46.76	155.88	3.42	45.52
Unknown	89	216	9,691	13,573	2,411	1,136.6	36.91	108.89	2.43	44.87
Atenolol										
Female	381,616	1,280,919	70,295,782	82,589,532	24,392,996	14,787,700.3	15.64	184.21	3.36	54.88
Male	293,785	983,759	54,177,920	61,872,522	23,856,625	14,310,501.0	12.31	184.41	3.35	55.07
Unknown	19	44	2,377	2,372	2,411	1,136.6	7.88	125.11	2.32	54.02
Metoprolol										
Female	679,632	2,313,957	100,388,152	148,994,186	24,392,996	14,787,700.3	27.86	147.71	3.40	43.38
Male	705,975	2,384,239	103,753,935	152,963,123	23,856,625	14,310,501.0	29.59	146.97	3.38	43.52
Unknown	62	148	6,272	9,646	2,411	1,136.6	25.72	101.16	2.39	42.38
Nebivolol										
Female	59,765	239,521	8,553,194	10,055,997	24,392,996	14,787,700.3	2.45	143.11	4.01	35.71
Male	66,595	271,394	9,521,995	11,416,991	23,856,625	14,310,501.0	2.79	142.98	4.08	35.09
Unknown	5	19	698	938	2,411	1,136.6	2.07	139.60	3.80	36.74
Propranolol										
Female	113,158	354,127	12,841,042	20,490,665	24,392,996	14,787,700.3	4.64	113.48	3.13	36.26
Male	60,403	180,911	6,451,403	10,698,365	23,856,625	14,310,501.0	2.53	106.81	3.00	35.66
Unknown	3	5	344	617	2,411	1,136.6	1.24	114.67	1.67	68.80

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2011-2015										
Atenolol, Metoprolol, Nebivolol, Propranolol										
Female	2,837,480	29,251,461	1,420,681,694	1,923,488,997	48,090,136	98,636,400.3	59.00	500.68	10.31	48.57
Male	2,598,085	26,529,442	1,284,855,945	1,732,161,744	47,099,887	94,567,812.2	55.16	494.54	10.21	48.43
Unknown	268	2,605	123,612	170,057	5,263	8,595.1	50.92	461.24	9.72	47.45
Atenolol										
Female	905,863	9,706,807	551,417,197	651,794,560	48,090,136	98,636,400.3	18.84	608.72	10.72	56.81
Male	717,549	7,513,920	429,478,479	492,686,355	47,099,887	94,567,812.2	15.23	598.54	10.47	57.16
Unknown	65	714	36,122	35,698	5,263	8,595.1	12.35	555.72	10.98	50.59
Metoprolol										
Female	1,537,796	15,466,797	713,114,485	1,057,174,501	48,090,136	98,636,400.3	31.98	463.73	10.06	46.11
Male	1,609,326	15,854,832	736,633,755	1,085,102,469	47,099,887	94,567,812.2	34.17	457.73	9.85	46.46
Unknown	165	1,575	73,258	114,066	5,263	8,595.1	31.35	443.99	9.55	46.51
Nebivolol										
Female	175,307	1,754,284	66,335,616	71,021,857	48,090,136	98,636,400.3	3.65	378.40	10.01	37.81
Male	193,926	1,994,321	74,301,923	79,695,647	47,099,887	94,567,812.2	4.12	383.15	10.28	37.26
Unknown	23	178	7,739	10,340	5,263	8,595.1	4.37	336.48	7.74	43.48
Propranolol										
Female	354,245	2,323,573	89,814,396	143,498,079	48,090,136	98,636,400.3	7.37	253.54	6.56	38.65
Male	189,506	1,166,369	44,441,788	74,677,274	47,099,887	94,567,812.2	4.02	234.51	6.15	38.10
Unknown	24	138	6,493	9,953	5,263	8,595.1	4.56	270.54	5.75	47.05

Appendix A. Start and End Dates for Each Data Partner (DP) up to Request Distribution Date (June 17, 2016)

DP ID	Start Date¹	End Date¹
DP0001	1/1/2011	7/31/2015
DP0002	1/1/2011	10/31/2014
DP0003	1/1/2011	9/30/2015
DP0004	1/1/2011	12/31/2015
DP0005	1/1/2011	2/28/2015
DP0006	1/1/2011	10/31/2015
DP0007	1/1/2011	12/31/2014
DP0008	1/1/2011	11/30/2015
DP0009	1/1/2011	11/30/2015
DP0010	1/1/2011	9/30/2015
DP0011	1/1/2011	6/30/2015
DP0012	1/1/2011	6/30/2015
DP0013	1/1/2011	6/30/2012
DP0014	1/1/2011	7/31/2014
DP0015	1/1/2011	4/30/2015

¹The 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 Name Medical Products Used to Define Beta Blockers of Interest in this Request

Generic Name	Brand Name
Atenolol	
Atenolol	Atenolol
Atenolol	Tenormin
Metoprolol	
Metoprolol Succinate	Metoprolol Succinate
Metoprolol Succinate	Toprol XL
Metoprolol Tartrate	Metoprolol Tartrate
Metoprolol Tartrate	Lopressor
Nebivolol	
Nebivolol HCl	Bystolic
Propranolol	
Propranolol HCl	Propranolol HCl
Propranolol HCl	Propranolol HCl ER
Propranolol HCl	Hemangeol
Propranolol HCl	Inderal LA
Propranolol HCl	Inderal XL
Propranolol HCl	Innopran XL

Appendix C. Specifications Defining Parameters in this Request

Scenario	Drug/Exposure			Pre-Existing Condition	Event/Outcome	
	Exposure	Incident with respect to:	Washout (days)	Cohort Definition	Pre-Existing Condition	Event/Outcome
22	Infliximab, Etanercept, Adalimumab, Golimumab, Certolizumab	NA	0	02	None	Dummy
23	Infliximab	NA	0	02	None	Dummy
24	Etanercept	NA	0	02	None	Dummy
25	Adalimumab	NA	0	02	None	Dummy
26	Golimumab	NA	0	02	None	Dummy
27	Certolizumab	NA	0	02	None	Dummy
28	Filgrastim, Pegfilgrastim, GM-CSF	NA	0	02	None	Dummy
29	Filgrastim	NA	0	02	None	Dummy
30	Pegfilgrastim	NA	0	02	None	Dummy
31	GM-CSF	NA	0	02	None	Dummy

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

NOTE: Other scenarios can be viewed in the two other reports in this request.