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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 opi_ahr_wp002_nsdp_v01

Request ID: opi_ahr_wp002_nsdp_v01

Report Description: This report provides the number and proportion of "opioid-tolerant-only" episodes of transdermal fentanyl that were prescribed to patients with evidence of prior-established "opioid tolerance" by dose of transdermal fentanyl. This analysis only assesses the first eligible transdermal fentanyl episode per user, by dose.

Sentinel Modular Program Tool Used: Ad Hoc Programming

Data Source: Data from January 1, 2009 to December 31, 2013 from 15 Data Partners contributing to the Mini-Sentinel Distributed Database (MSDD) were included in this report. This is the period during which new opioid-tolerant-only dose product treatment episodes started. The request was distributed to two Data Partners in March 2016 and to the remaining 13 participating Data Partners in April 2016. Please see Appendix A for the latest date of available data for each Data Partner.

Study Design: The first eligible transdermal fentanyl episode per user, by dose, was identified and assessed for evidence of prior opioid tolerance, by each of the four tolerance definitions. Two washout periods were used to define new use: [1] No use of transdermal fentanyl in 183 days prior (primary analysis) and [2] No use of transdermal fentanyl in 91 days prior (sensitivity analysis).

Cohort Eligibility Criteria: Individuals included in the cohort were required to be continuously enrolled in plans with both medical and drug coverage for at least 183 days (for primary analysis) or 91 days (sensitivity analysis) prior to their first eligible transdermal fentanyl episode, during which gaps in coverage of up to 45 days were allowed. Individuals ages 0 through 64 years were included in the analysis. Age groupings are as follows: 0-11, 12-17, 18-24, 25-34, 35-44, 45-54, and 55-64 years. Patients were excluded if they were diagnosed with opioid poisoning in the 183 days (or 91 days for sensitivity analysis) prior to their first eligible transdermal fentanyl episode or if they were hospitalized (inpatient stay) in the 30 days prior to cohort entry. Opioid poisoning was defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Please see Appendix C for a list of codes.

Exposures of Interest: The exposure of interest was new use of opioid-tolerant-only transdermal fentanyl. The exposure was defined using National Drug Codes (NDCs). Please see Appendix B for a list of drugs.

Definition of opioid-tolerant-only doses: All dose formulations are opioid-tolerant-only doses, but results are stratified by dose: 12, 25, 50, 75, and 100mcg/hr, as well as any outlier doses.

Definitions of opioid tolerance:

Primary: ≥ 30 mg oxycodone equivalents per day for seven days consecutively in the seven days prior to new opioid-tolerant-only dose index date

Secondary: ≥ 30 mg oxycodone equivalents per day for seven days in the 30 days prior to new opioid-tolerant-only dose index date (seven days not required to be consecutive)

Tertiary: > 0 mg (i.e., any dose of oxycodone equivalent) for seven days in the seven consecutive days prior to new opioid-tolerant-only dose index date

Quaternary: > 0 mg (i.e., any dose of oxycodone equivalent) for seven days in the 30 days prior to new opioid-tolerant-only dose index date (seven days not required to be consecutive). All dose formulations are opioid-tolerant-only doses, but results are stratified by dose: 12, 25, 50, 75, and 100mcg/hr, as well as any outlier doses.

Limitations: Algorithms to define exposures and events are imperfect and, therefore, may be misclassified.

Notes: Please contact the Sentinel Operations Center Query Fulfillment Team (qf@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. This is equivalent to the "RxAmt"
- 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). Along with the Principal Diagnosis Indicator, forms the Care Setting/PDX parameter.
- Cohort Definition (drug/exposure)**- indicates how the cohort will be defined: (1) 01: Cohort includes only the first valid incident treatment episode during the query period; (2) 02: Cohort includes all valid incident treatment episodes during the query period; (3) 03: Cohort includes all valid incident treatment episodes during the query period until an event occurs.
- Days Supplied** - number of days supplied for all dispensings in qualifying treatment episodes.
- Enrollment Gap** - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled"
- Episodes** - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by
- Episode Gap** - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered the
- Event Deduplication** - specifies how events are counted by the MP algorithm: (0) 0: Counts all occurrences of an HOI during an exposure episode; (1) 1: de-duplicates occurrences of the same HOI code and code type on the same day; (2) 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).
- Exposure Extension Period** - number of days post treatment period in which the outcomes/events are counted for a treatment episode.
- Exposure Episode Length** - number of days after exposure initiation that is considered "exposed time."
- Lookback Period (pre-existing condition)** - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).
- 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.
- 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
- Query Period** - period in which the modular program looks for exposures and outcomes of interest.
- Treatment Episode Truncation Indicator** - indicates whether observation of the incident query code during follow-up requires truncation of valid treatment episodes. A value of Y indicates that the treatment episodes should be truncated at the first occurrence of an incident query code. A value of N indicates that the treatment episodes should not be truncated at the occurrence of the incident query code.
- Users** - number of members with exposure during the query period. Member must have no evidence of exposure(s) of interest (defined by incidence criteria) in the prior washout period. A user may only be counted once in a query period.
- 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

**incident treatment episodes must be incident to both the exposure and the event

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	16,379	4,699	28.7%	3	1	33%	44,450	16,623	37.4%	1	0	0%	298	160	54%
	0 - 11 years	32	-	0.0%	-	-	0%	23	2	8.7%	0	0	0%	1	-	0%
	12 - 17 years	75	6	8.0%	-	-	0%	79	15	19.0%	0	0	0%	2	-	0%
	18 - 24 years	375	96	25.6%	-	-	0%	827	314	38.0%	0	0	0%	8	3	38%
	25 - 34 years	1,464	539	36.8%	-	-	0%	3,731	1,688	45.2%	1	0	0%	24	16	67%
	35 - 44 years	2,841	955	33.6%	2	1	50%	7,954	3,325	41.8%	0	0	0%	63	33	52%
	45 - 54 years	5,214	1,532	29.4%	-	-	0%	14,785	5,707	38.6%	0	0	0%	87	47	54%
	55 - 64 years	6,378	1,571	24.6%	1	-	0%	17,051	5,572	32.7%	0	0	0%	113	61	54%
Gender	Male	5,124	1,537	30.0%	1	1	100%	18,327	7,100	38.7%	0	0	0%	133	73	55%
	Female	11,255	3,162	28.1%	2	-	0%	26,123	9,523	36.5%	1	0	0%	165	87	53%
	Ambiguous	-	-	0.0%	-	-	0%	-	-	0.0%	0	0	0%	-	-	0%
	Unknown	0	0	0	0	-	0%	-	0	0	0	0	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	220	66	30.0%	-	-	0%	953	316	33.2%	0	0	0%	4	3	75%
	Feb 2009	206	51	24.8%	-	-	0%	890	312	35.1%	0	0	0%	8	3	38%
	Mar 2009	267	72	27.0%	-	-	0%	982	334	34.0%	0	0	0%	5	3	60%
	Apr 2009	220	52	23.6%	-	-	0%	969	334	34.5%	1	0	0%	4	1	25%
	May 2009	248	61	24.6%	-	-	0%	875	330	37.7%	0	0	0%	6	5	83%
	Jun 2009	258	65	25.2%	-	-	0%	909	312	34.3%	0	0	0%	5	4	80%
	Jul 2009	249	67	26.9%	-	-	0%	870	301	34.6%	0	0	0%	6	2	33%
	Aug 2009	268	71	26.5%	-	-	0%	881	289	32.8%	0	0	0%	2	1	50%
	Sep 2009	295	86	29.2%	-	-	0%	943	331	35.1%	0	0	0%	4	3	75%
	Oct 2009	261	69	26.4%	-	-	0%	857	292	34.1%	0	0	0%	1	1	100%
	Nov 2009	231	67	29.0%	-	-	0%	818	274	33.5%	0	0	0%	8	4	50%
	Dec 2009	244	74	30.3%	-	-	0%	900	337	37.4%	0	0	0%	7	3	43%
	Jan 2010	226	55	24.3%	-	-	0%	827	271	32.8%	0	0	0%	6	-	0%
	Feb 2010	238	79	33.2%	-	-	0%	753	270	35.9%	0	0	0%	8	6	75%
	Mar 2010	268	76	28.4%	-	-	0%	791	294	37.2%	0	0	0%	8	3	38%
	Apr 2010	257	71	27.6%	-	-	0%	833	277	33.3%	0	0	0%	3	2	67%
	May 2010	227	73	32.2%	-	-	0%	738	299	40.5%	0	0	0%	5	1	20%
	Jun 2010	246	68	27.6%	-	-	0%	746	281	37.7%	0	0	0%	4	1	25%
	Jul 2010	223	62	27.8%	-	-	0%	764	305	39.9%	0	0	0%	5	3	60%
	Aug 2010	260	73	28.1%	-	-	0%	810	281	34.7%	0	0	0%	3	2	67%
	Sep 2010	301	91	30.2%	-	-	0%	833	323	38.8%	0	0	0%	2	2	100%
	Oct 2010	288	70	24.3%	-	-	0%	777	292	37.6%	0	0	0%	5	3	60%
	Nov 2010	290	87	30.0%	-	-	0%	824	306	37.1%	0	0	0%	9	4	44%
	Dec 2010	291	87	29.9%	-	-	0%	731	294	40.2%	0	0	0%	3	1	33%
	Jan 2011	252	67	26.6%	-	-	0%	724	272	37.6%	0	0	0%	1	1	100%
	Feb 2011	264	61	23.1%	-	-	0%	639	235	36.8%	0	0	0%	3	2	67%
	Mar 2011	279	73	26.2%	-	-	0%	802	309	38.5%	0	0	0%	9	5	56%
	Apr 2011	269	80	29.7%	-	-	0%	710	281	39.6%	0	0	0%	10	9	90%
	May 2011	261	73	28.0%	-	-	0%	700	256	36.6%	0	0	0%	3	2	67%
	Jun 2011	276	76	27.5%	-	-	0%	678	272	40.1%	0	0	0%	4	2	50%
	Jul 2011	282	81	28.7%	-	-	0%	679	249	36.7%	0	0	0%	3	2	67%
	Aug 2011	314	106	33.8%	-	-	0%	758	265	35.0%	0	0	0%	4	2	50%
	Sep 2011	291	85	29.2%	-	-	0%	730	280	38.4%	0	0	0%	7	3	43%
	Oct 2011	263	79	30.0%	-	-	0%	711	283	39.8%	0	0	0%	3	2	67%
	Nov 2011	288	96	33.3%	-	-	0%	659	275	41.7%	0	0	0%	8	2	25%
	Dec 2011	307	93	30.3%	-	-	0%	689	261	37.9%	0	0	0%	5	3	60%
	Jan 2012	279	80	28.7%	-	-	0%	720	278	38.6%	0	0	0%	2	2	100%
	Feb 2012	255	67	26.3%	-	-	0%	638	222	34.8%	0	0	0%	7	3	43%
	Mar 2012	294	83	28.2%	-	-	0%	683	252	36.9%	0	0	0%	6	4	67%
	Apr 2012	251	83	33.1%	-	-	0%	650	249	38.3%	0	0	0%	3	2	67%
	May 2012	324	88	27.2%	-	-	0%	631	249	39.5%	0	0	0%	8	5	63%
	Jun 2012	242	68	28.1%	-	-	0%	564	219	38.8%	0	0	0%	3	2	67%
	Jul 2012	295	90	30.5%	-	-	0%	617	244	39.5%	0	0	0%	5	2	40%
	Aug 2012	304	111	36.5%	-	-	0%	787	306	38.9%	0	0	0%	2	1	50%
	Sep 2012	279	75	26.9%	-	-	0%	645	239	37.1%	0	0	0%	5	4	80%
	Oct 2012	304	91	29.9%	-	-	0%	699	304	43.5%	0	0	0%	3	1	33%
	Nov 2012	313	82	26.2%	-	-	0%	712	241	33.8%	0	0	0%	6	3	50%
	Dec 2012	293	78	26.6%	-	-	0%	631	251	39.8%	0	0	0%	8	3	38%
	Jan 2013	277	87	31.4%	-	-	0%	593	220	37.1%	0	0	0%	4	3	75%
	Feb 2013	254	76	29.9%	-	-	0%	638	270	42.3%	0	0	0%	3	2	67%
	Mar 2013	253	85	33.6%	-	-	0%	585	246	42.1%	0	0	0%	4	3	75%
	Apr 2013	289	99	34.3%	-	-	0%	617	243	39.4%	0	0	0%	9	4	44%
	May 2013	261	80	30.7%	-	-	0%	640	261	40.8%	0	0	0%	8	4	50%
	Jun 2013	271	69	25.5%	1	-	0%	602	242	40.2%	0	0	0%	4	2	50%
	Jul 2013	331	95	28.7%	-	-	0%	663	264	39.8%	0	0	0%	8	5	63%
	Aug 2013	341	97	28.4%	-	-	0%	735	300	40.8%	0	0	0%	3	1	33%
	Sep 2013	302	78	25.8%	-	-	0%	645	252	39.1%	0	0	0%	3	2	67%
	Oct 2013	331	99	29.9%	1	1	100%	714	285	39.9%	0	0	0%	3	1	33%
	Nov 2013	310	89	28.7%	1	-	0%	651	255	39.2%	0	0	0%	5	1	20%
	Dec 2013	298	86	28.9%	0	-	0%	637	238	37.4%	0	0	0%	5	4	80%

Table 1a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	18,527	8,871	48%	22	6	27%	5,118	2,756	54%	8	2	25%	3,507	1,991	57%
	0 - 11 years	7	2	29%	1	-	0%	2	-	0%	-	-	0%	4	-	0%
	12 - 17 years	32	9	28%	-	-	0%	11	3	27%	-	-	0%	8	2	25%
	18 - 24 years	380	161	42%	1	-	0%	99	52	53%	-	-	0%	77	38	49%
	25 - 34 years	1,614	900	56%	2	-	0%	523	309	59%	1	1	100%	290	179	62%
	35 - 44 years	3,502	1,846	53%	4	1	25%	1,011	553	55%	1	-	0%	686	403	59%
	45 - 54 years	6,358	3,055	48%	11	3	27%	1,785	966	54%	4	1	25%	1,276	744	58%
	55 - 64 years	6,634	2,898	44%	3	2	67%	1,687	873	52%	2	-	0%	1,166	625	54%
Gender	Male	8,727	4,377	50%	11	5	45%	2,510	1,428	57%	4	1	25%	1,839	1,111	60%
	Female	9,800	4,494	46%	11	1	9%	2,608	1,328	51%	4	1	25%	1,668	880	53%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	412	185	45%	2	2	100%	145	61	42%	1	-	0%	94	42	45%
	Feb 2009	414	199	48%	-	-	0%	118	65	55%	-	-	0%	98	55	56%
	Mar 2009	424	208	49%	-	-	0%	112	55	49%	-	-	0%	79	38	48%
	Apr 2009	423	215	51%	-	-	0%	108	62	57%	-	-	0%	88	50	57%
	May 2009	368	166	45%	-	-	0%	101	50	50%	-	-	0%	84	42	50%
	Jun 2009	409	176	43%	-	-	0%	111	53	48%	-	-	0%	75	49	65%
	Jul 2009	376	170	45%	2	-	0%	89	41	46%	-	-	0%	86	48	56%
	Aug 2009	348	165	47%	-	-	0%	97	53	55%	-	-	0%	72	41	57%
	Sep 2009	396	180	45%	-	-	0%	95	63	66%	2	-	0%	72	37	51%
	Oct 2009	433	190	44%	-	-	0%	100	52	52%	-	-	0%	90	50	56%
	Nov 2009	366	172	47%	1	1	100%	94	51	54%	-	-	0%	77	46	60%
	Dec 2009	379	170	45%	-	-	0%	113	59	52%	-	-	0%	74	40	54%
	Jan 2010	359	158	44%	-	-	0%	101	52	51%	-	-	0%	89	55	62%
	Feb 2010	325	143	44%	1	-	0%	84	39	46%	1	-	0%	60	31	52%
	Mar 2010	331	142	43%	-	-	0%	113	63	56%	-	-	0%	62	35	56%
	Apr 2010	307	134	44%	-	-	0%	100	57	57%	-	-	0%	67	45	67%
	May 2010	326	147	45%	-	-	0%	84	38	45%	-	-	0%	60	39	65%
	Jun 2010	340	167	49%	-	-	0%	77	40	52%	-	-	0%	49	38	78%
	Jul 2010	342	180	53%	-	-	0%	92	45	49%	-	-	0%	55	37	67%
	Aug 2010	325	158	49%	-	-	0%	98	50	51%	-	-	0%	71	44	62%
	Sep 2010	343	165	48%	1	1	100%	93	57	61%	-	-	0%	70	41	59%
	Oct 2010	340	174	51%	-	-	0%	95	54	57%	-	-	0%	58	42	72%
	Nov 2010	326	163	50%	-	-	0%	93	56	60%	-	-	0%	63	37	59%
	Dec 2010	356	156	44%	-	-	0%	78	44	56%	-	-	0%	64	30	47%
	Jan 2011	306	130	42%	-	-	0%	112	54	48%	-	-	0%	90	52	58%
	Feb 2011	277	148	53%	-	-	0%	96	59	61%	-	-	0%	66	38	58%
	Mar 2011	338	174	51%	1	-	0%	94	61	65%	-	-	0%	79	43	54%
	Apr 2011	322	147	46%	-	-	0%	86	44	51%	-	-	0%	52	24	46%
	May 2011	280	126	45%	-	-	0%	86	47	55%	-	-	0%	52	28	54%
	Jun 2011	286	123	43%	-	-	0%	75	45	60%	1	-	0%	41	23	56%
	Jul 2011	309	146	47%	-	-	0%	70	48	69%	-	-	0%	48	26	54%
	Aug 2011	322	148	46%	-	-	0%	78	38	49%	-	-	0%	45	30	67%
	Sep 2011	310	153	49%	-	-	0%	78	44	56%	-	-	0%	42	23	55%
	Oct 2011	269	129	48%	2	-	0%	77	48	62%	-	-	0%	56	32	57%
	Nov 2011	274	140	51%	-	-	0%	77	43	56%	-	-	0%	47	26	55%
	Dec 2011	286	135	47%	-	-	0%	72	36	50%	-	-	0%	59	37	63%
	Jan 2012	273	132	48%	-	-	0%	88	48	55%	-	-	0%	53	27	51%
	Feb 2012	266	146	55%	1	-	0%	75	45	60%	-	-	0%	53	34	64%
	Mar 2012	282	141	50%	-	-	0%	76	43	57%	-	-	0%	48	28	58%
	Apr 2012	277	143	52%	1	-	0%	86	40	47%	-	-	0%	48	26	54%
	May 2012	287	149	52%	1	-	0%	71	40	56%	-	-	0%	52	36	69%
	Jun 2012	234	111	47%	1	-	0%	60	34	57%	-	-	0%	49	30	61%
	Jul 2012	307	156	51%	-	-	0%	87	43	49%	-	-	0%	37	17	46%
	Aug 2012	284	142	50%	1	-	0%	89	54	61%	-	-	0%	51	35	69%
	Sep 2012	254	131	52%	1	-	0%	77	49	64%	1	1	100%	38	20	53%
	Oct 2012	251	108	43%	-	-	0%	69	40	58%	-	-	0%	47	20	43%
	Nov 2012	296	137	46%	-	-	0%	90	39	43%	2	1	50%	62	32	52%
	Dec 2012	261	141	54%	-	-	0%	54	22	41%	-	-	0%	46	19	41%
	Jan 2013	254	132	52%	2	1	50%	87	39	45%	-	-	0%	42	25	60%
	Feb 2013	212	117	55%	2	-	0%	56	31	55%	-	-	0%	44	27	61%
	Mar 2013	236	118	50%	-	-	0%	72	38	53%	-	-	0%	36	19	53%
	Apr 2013	226	108	48%	-	-	0%	68	33	49%	-	-	0%	37	23	62%
	May 2013	250	130	52%	1	1	100%	65	41	63%	-	-	0%	42	24	57%
	Jun 2013	244	116	48%	-	-	0%	69	36	52%	-	-	0%	34	17	50%
	Jul 2013	239	119	50%	-	-	0%	78	45	58%	-	-	0%	43	20	47%
	Aug 2013	272	130	48%	-	-	0%	61	26	43%	-	-	0%	31	14	45%
	Sep 2013	245	119	49%	-	-	0%	66	38	58%	-	-	0%	44	22	50%
	Oct 2013	242	130	54%	-	-	0%	67	41	61%	-	-	0%	47	32	68%
	Nov 2013	241	115	48%	-	-	0%	58	33	57%	-	-	0%	47	24	51%
	Dec 2013	247	118	48%	1	-	0%	57	31	54%	-	-	0%	42	26	62%

Table 1a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)																
	Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	3	3	100%	137	68	50%	2	1	50%	172	103	60%	2	1	50%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%	0	0	0%	0	0	0%
	12 - 17 years	-	-	0%	1	-	0%	-	-	0%	1	0	0%	0	0	0%
	18 - 24 years	-	-	0%	2	2	100%	-	-	0%	5	4	80%	1	0	0%
	25 - 34 years	-	-	0%	9	7	78%	-	-	0%	12	6	50%	0	0	0%
	35 - 44 years	-	-	0%	20	8	40%	-	-	0%	30	21	70%	0	0	0%
	45 - 54 years	1	1	100%	57	29	51%	1	-	0%	60	36	60%	0	0	0%
	55 - 64 years	2	2	100%	48	22	46%	1	1	100%	64	36	56%	1	1	100%
Gender	Male	1	1	100%	69	33	48%	-	-	0%	95	61	64%	2	1	50%
	Female	2	2	100%	68	35	51%	2	1	50%	77	42	55%	0	0	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%	0	0	0%	0	0	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%	0	0	0%	0	0	0%
Month and Year of Episode Start Date	Jan 2009	1	1	100%	4	2	50%	-	-	0%	6	2	33%	0	0	0%
	Feb 2009	-	-	0%	3	1	33%	-	-	0%	2	1	50%	0	0	0%
	Mar 2009	-	-	0%	3	-	0%	-	-	0%	1	1	100%	0	0	0%
	Apr 2009	-	-	0%	2	1	50%	-	-	0%	1	1	100%	0	0	0%
	May 2009	-	-	0%	3	3	100%	-	-	0%	6	4	67%	0	0	0%
	Jun 2009	-	-	0%	2	2	100%	-	-	0%	7	6	86%	0	0	0%
	Jul 2009	-	-	0%	1	1	100%	-	-	0%	3	1	33%	0	0	0%
	Aug 2009	-	-	0%	1	-	0%	-	-	0%	4	0	0%	0	0	0%
	Sep 2009	-	-	0%	-	-	0%	-	-	0%	5	3	60%	0	0	0%
	Oct 2009	-	-	0%	1	-	0%	-	-	0%	4	2	50%	0	0	0%
	Nov 2009	-	-	0%	2	1	50%	-	-	0%	7	5	71%	0	0	0%
	Dec 2009	-	-	0%	2	1	50%	-	-	0%	7	5	71%	0	0	0%
	Jan 2010	-	-	0%	7	2	29%	-	-	0%	5	3	60%	0	0	0%
	Feb 2010	-	-	0%	6	1	17%	-	-	0%	5	3	60%	0	0	0%
	Mar 2010	-	-	0%	2	-	0%	-	-	0%	4	3	75%	0	0	0%
	Apr 2010	-	-	0%	4	1	25%	-	-	0%	4	3	75%	0	0	0%
	May 2010	-	-	0%	2	1	50%	-	-	0%	4	2	50%	0	0	0%
	Jun 2010	-	-	0%	5	2	40%	-	-	0%	2	1	50%	0	0	0%
	Jul 2010	-	-	0%	1	-	0%	-	-	0%	5	4	80%	0	0	0%
	Aug 2010	-	-	0%	2	1	50%	-	-	0%	2	0	0%	0	0	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%	3	0	0%	0	0	0%
	Oct 2010	-	-	0%	3	3	100%	1	1	100%	3	3	100%	0	0	0%
	Nov 2010	-	-	0%	2	2	100%	-	-	0%	2	1	50%	0	0	0%
	Dec 2010	-	-	0%	1	1	100%	-	-	0%	4	2	50%	0	0	0%
	Jan 2011	-	-	0%	3	1	33%	-	-	0%	4	2	50%	1	0	0%
	Feb 2011	1	1	100%	3	-	0%	-	-	0%	3	1	33%	0	0	0%
	Mar 2011	-	-	0%	2	1	50%	-	-	0%	2	1	50%	0	0	0%
	Apr 2011	-	-	0%	3	1	33%	-	-	0%	4	4	100%	0	0	0%
	May 2011	-	-	0%	5	1	20%	-	-	0%	2	1	50%	0	0	0%
	Jun 2011	-	-	0%	2	1	50%	-	-	0%	0	0	0%	0	0	0%
	Jul 2011	-	-	0%	2	-	0%	-	-	0%	4	4	100%	0	0	0%
	Aug 2011	-	-	0%	1	1	100%	-	-	0%	1	1	100%	0	0	0%
	Sep 2011	-	-	0%	4	2	50%	1	-	0%	3	3	100%	1	1	100%
	Oct 2011	-	-	0%	1	1	100%	-	-	0%	1	0	0%	0	0	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%	1	1	100%	0	0	0%
	Dec 2011	-	-	0%	3	2	67%	-	-	0%	1	1	100%	0	0	0%
	Jan 2012	-	-	0%	2	1	50%	-	-	0%	2	2	100%	0	0	0%
	Feb 2012	-	-	0%	2	1	50%	-	-	0%	5	4	80%	0	0	0%
	Mar 2012	-	-	0%	3	3	100%	-	-	0%	2	1	50%	0	0	0%
	Apr 2012	1	1	100%	5	5	100%	-	-	0%	3	2	67%	0	0	0%
	May 2012	-	-	0%	4	-	0%	-	-	0%	0	0	0%	0	0	0%
	Jun 2012	-	-	0%	-	-	0%	-	-	0%	2	1	50%	0	0	0%
	Jul 2012	-	-	0%	1	1	100%	-	-	0%	0	0	0%	0	0	0%
	Aug 2012	-	-	0%	4	3	75%	-	-	0%	1	1	100%	0	0	0%
	Sep 2012	-	-	0%	1	1	100%	-	-	0%	2	1	50%	0	0	0%
	Oct 2012	-	-	0%	2	2	100%	-	-	0%	2	2	100%	0	0	0%
	Nov 2012	-	-	0%	2	2	100%	-	-	0%	5	2	40%	0	0	0%
	Dec 2012	-	-	0%	3	1	33%	-	-	0%	0	0	0%	0	0	0%
	Jan 2013	-	-	0%	2	-	0%	-	-	0%	4	0	0%	0	0	0%
	Feb 2013	-	-	0%	3	1	33%	-	-	0%	0	0	0%	0	0	0%
	Mar 2013	-	-	0%	2	1	50%	-	-	0%	3	1	33%	0	0	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%	3	2	67%	0	0	0%
	May 2013	-	-	0%	1	1	100%	-	-	0%	0	0	0%	0	0	0%
	Jun 2013	-	-	0%	-	-	0%	-	-	0%	3	1	33%	0	0	0%
	Jul 2013	-	-	0%	3	3	100%	-	-	0%	2	2	100%	0	0	0%
	Aug 2013	-	-	0%	2	2	100%	-	-	0%	3	1	33%	0	0	0%
	Sep 2013	-	-	0%	1	1	100%	-	-	0%	2	1	50%	0	0	0%
	Oct 2013	-	-	0%	4	1	25%	-	-	0%	1	1	100%	0	0	0%
	Nov 2013	-	-	0%	1	1	100%	-	-	0%	3	2	67%	0	0	0%
	Dec 2013	-	-	0%	1	-	0%	-	-	0%	2	1	50%	0	0	0%

Table 1a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)										
		Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr		
		Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Age (years)	Total	33	16	48%	4	3	75%	2	0	0%
	0 - 11 years	0	0	0%	0	0	0%	0	0	0%
	12 - 17 years	1	1	100%	0	0	0%	0	0	0%
	18 - 24 years	3	3	100%	0	0	0%	0	0	0%
	25 - 34 years	1	0	0%	0	0	0%	1	0	0%
	35 - 44 years	4	3	75%	3	2	67%	0	0	0%
	45 - 54 years	9	4	44%	1	1	100%	0	0	0%
	55 - 64 years	15	5	33%	0	0	0%	1	0	0%
Gender	Male	11	9	82%	4	3	75%	2	0	0%
	Female	22	7	32%	0	0	0%	0	0	0%
	Ambiguous	0	0	0%	0	0	0%	0	0	0%
	Unknown	0	0	0%	0	0	0%	0	0	0%
Month and Year of Episode Start Date	Jan 2009	1	0	0%	0	0	0%	0	0	0%
	Feb 2009	1	1	100%	0	0	0%	0	0	0%
	Mar 2009	1	1	100%	0	0	0%	0	0	0%
	Apr 2009	3	3	100%	1	1	100%	0	0	0%
	May 2009	0	0	0%	0	0	0%	0	0	0%
	Jun 2009	0	0	0%	0	0	0%	0	0	0%
	Jul 2009	2	0	0%	0	0	0%	1	0	0%
	Aug 2009	0	0	0%	0	0	0%	0	0	0%
	Sep 2009	1	1	100%	0	0	0%	0	0	0%
	Oct 2009	1	0	0%	0	0	0%	0	0	0%
	Nov 2009	0	0	0%	0	0	0%	0	0	0%
	Dec 2009	1	0	0%	0	0	0%	0	0	0%
	Jan 2010	0	0	0%	0	0	0%	0	0	0%
	Feb 2010	0	0	0%	0	0	0%	0	0	0%
	Mar 2010	1	1	100%	1	1	100%	0	0	0%
	Apr 2010	0	0	0%	0	0	0%	0	0	0%
	May 2010	0	0	0%	0	0	0%	0	0	0%
	Jun 2010	1	0	0%	0	0	0%	0	0	0%
	Jul 2010	0	0	0%	0	0	0%	0	0	0%
	Aug 2010	1	1	100%	0	0	0%	0	0	0%
	Sep 2010	0	0	0%	0	0	0%	0	0	0%
	Oct 2010	1	1	100%	0	0	0%	0	0	0%
	Nov 2010	0	0	0%	0	0	0%	0	0	0%
	Dec 2010	1	1	100%	0	0	0%	0	0	0%
	Jan 2011	0	0	0%	0	0	0%	0	0	0%
	Feb 2011	2	1	50%	0	0	0%	0	0	0%
	Mar 2011	1	1	100%	0	0	0%	0	0	0%
	Apr 2011	1	0	0%	0	0	0%	0	0	0%
	May 2011	0	0	0%	0	0	0%	0	0	0%
	Jun 2011	2	1	50%	0	0	0%	0	0	0%
	Jul 2011	0	0	0%	0	0	0%	0	0	0%
	Aug 2011	1	0	0%	0	0	0%	0	0	0%
	Sep 2011	2	1	50%	0	0	0%	0	0	0%
	Oct 2011	2	0	0%	0	0	0%	0	0	0%
	Nov 2011	0	0	0%	0	0	0%	0	0	0%
	Dec 2011	0	0	0%	0	0	0%	0	0	0%
	Jan 2012	0	0	0%	0	0	0%	0	0	0%
	Feb 2012	0	0	0%	0	0	0%	0	0	0%
	Mar 2012	1	0	0%	0	0	0%	0	0	0%
	Apr 2012	1	0	0%	0	0	0%	0	0	0%
	May 2012	0	0	0%	0	0	0%	0	0	0%
	Jun 2012	0	0	0%	0	0	0%	0	0	0%
	Jul 2012	0	0	0%	0	0	0%	0	0	0%
	Aug 2012	0	0	0%	0	0	0%	0	0	0%
	Sep 2012	0	0	0%	0	0	0%	0	0	0%
	Oct 2012	0	0	0%	0	0	0%	0	0	0%
	Nov 2012	0	0	0%	0	0	0%	1	0	0%
	Dec 2012	0	0	0%	0	0	0%	0	0	0%
Jan 2013	0	0	0%	0	0	0%	0	0	0%	
Feb 2013	1	0	0%	0	0	0%	0	0	0%	
Mar 2013	0	0	0%	0	0	0%	0	0	0%	
Apr 2013	0	0	0%	0	0	0%	0	0	0%	
May 2013	0	0	0%	0	0	0%	0	0	0%	
Jun 2013	1	0	0%	2	1	50%	0	0	0%	
Jul 2013	0	0	0%	0	0	0%	0	0	0%	
Aug 2013	0	0	0%	0	0	0%	0	0	0%	
Sep 2013	1	1	100%	0	0	0%	0	0	0%	
Oct 2013	0	0	0%	0	0	0%	0	0	0%	
Nov 2013	0	0	0%	0	0	0%	0	0	0%	
Dec 2013	1	1	100%	0	0	0%	0	0	0%	

Table 1b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	16,379	7,855	48.0%	3	2	67%	44,450	26,009	58.5%	1	0	0%	298	210	70%
	0 - 11 years	32	1	3.1%	-	0	0%	23	4	17.4%	0	0	0%	1	0	0%
	12 - 17 years	75	16	21.3%	-	0	0%	79	23	29.1%	0	0	0%	2	0	0%
	18 - 24 years	375	151	40.3%	-	0	0%	827	440	53.2%	0	0	0%	8	5	63%
	25 - 34 years	1,464	822	56.1%	-	0	0%	3,731	2,488	66.7%	1	0	0%	24	20	83%
	35 - 44 years	2,841	1,500	52.8%	2	1	50%	7,954	4,989	62.7%	0	0	0%	63	43	68%
	45 - 54 years	5,214	2,529	48.5%	-	0	0%	14,785	8,764	59.3%	0	0	0%	87	64	74%
	55 - 64 years	6,378	2,836	44.5%	1	1	100%	17,051	9,301	54.5%	0	0	0%	113	78	69%
Gender	Male	5,124	2,569	50.1%	1	1	100%	18,327	11,006	60.1%	0	0	0%	133	96	72%
	Female	11,255	5,286	47.0%	2	1	50%	26,123	15,003	57.4%	1	0	0%	165	114	69%
	Ambiguous	-	-	0.0%	-	0	0%	-	-	0.0%	0	0	0%	0	0	0%
	Unknown	0	0	0	0	0	0%	-	0	0	0	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	220	106	48.2%	-	0	0%	953	539	56.6%	0	0	0%	4	4	100%
	Feb 2009	206	95	46.1%	-	0	0%	890	519	58.3%	0	0	0%	8	4	50%
	Mar 2009	267	121	45.3%	-	0	0%	982	547	55.7%	0	0	0%	5	5	100%
	Apr 2009	220	100	45.5%	-	0	0%	969	526	54.3%	1	0	0%	4	2	50%
	May 2009	248	118	47.6%	-	0	0%	875	510	58.3%	0	0	0%	6	5	83%
	Jun 2009	258	106	41.1%	-	0	0%	909	521	57.3%	0	0	0%	5	4	80%
	Jul 2009	249	115	46.2%	-	0	0%	870	485	55.7%	0	0	0%	6	4	67%
	Aug 2009	268	129	48.1%	-	0	0%	881	472	53.6%	0	0	0%	2	1	50%
	Sep 2009	295	141	47.8%	-	0	0%	943	545	57.8%	0	0	0%	4	4	100%
	Oct 2009	261	127	48.7%	-	0	0%	857	494	57.6%	0	0	0%	1	1	100%
	Nov 2009	231	106	45.9%	-	0	0%	818	441	53.9%	0	0	0%	8	5	63%
	Dec 2009	244	118	48.4%	-	0	0%	900	523	58.1%	0	0	0%	7	4	57%
	Jan 2010	226	94	41.6%	-	0	0%	827	457	55.3%	0	0	0%	6	0	0%
	Feb 2010	238	119	50.0%	-	0	0%	753	432	57.4%	0	0	0%	8	6	75%
	Mar 2010	268	119	44.4%	-	0	0%	791	445	56.3%	0	0	0%	8	6	75%
	Apr 2010	257	129	50.2%	-	0	0%	833	467	56.1%	0	0	0%	3	2	67%
	May 2010	227	122	53.7%	-	0	0%	738	467	63.3%	0	0	0%	5	1	20%
	Jun 2010	246	116	47.2%	-	0	0%	746	434	58.2%	0	0	0%	4	1	25%
	Jul 2010	223	101	45.3%	-	0	0%	764	468	61.3%	0	0	0%	5	4	80%
	Aug 2010	260	119	45.8%	-	0	0%	810	459	56.7%	0	0	0%	3	2	67%
	Sep 2010	301	153	50.8%	-	0	0%	833	506	60.7%	0	0	0%	2	2	100%
	Oct 2010	288	122	42.4%	-	0	0%	777	452	58.2%	0	0	0%	5	5	100%
	Nov 2010	290	147	50.7%	-	0	0%	824	497	60.3%	0	0	0%	9	7	78%
	Dec 2010	291	143	49.1%	-	0	0%	731	436	59.6%	0	0	0%	3	2	67%
	Jan 2011	252	116	46.0%	-	0	0%	724	424	58.6%	0	0	0%	1	1	100%
	Feb 2011	264	114	43.2%	-	0	0%	639	376	58.8%	0	0	0%	3	3	100%
	Mar 2011	279	122	43.7%	-	0	0%	802	485	60.5%	0	0	0%	9	6	67%
	Apr 2011	269	134	49.8%	-	0	0%	710	422	59.4%	0	0	0%	10	9	90%
	May 2011	261	118	45.2%	-	0	0%	700	388	55.4%	0	0	0%	3	3	100%
	Jun 2011	276	137	49.6%	-	0	0%	678	398	58.7%	0	0	0%	4	2	50%
	Jul 2011	282	134	47.5%	-	0	0%	679	392	57.7%	0	0	0%	3	2	67%
	Aug 2011	314	166	52.9%	-	0	0%	758	411	54.2%	0	0	0%	4	3	75%
	Sep 2011	291	140	48.1%	-	0	0%	730	446	61.1%	0	0	0%	7	5	71%
	Oct 2011	263	135	51.3%	-	0	0%	711	432	60.8%	0	0	0%	3	2	67%
	Nov 2011	288	142	49.3%	-	0	0%	659	408	61.9%	0	0	0%	8	4	50%
	Dec 2011	307	152	49.5%	-	0	0%	689	400	58.1%	0	0	0%	5	4	80%
	Jan 2012	279	125	44.8%	-	0	0%	720	426	59.2%	0	0	0%	2	2	100%
	Feb 2012	255	124	48.6%	-	0	0%	638	356	55.8%	0	0	0%	7	5	71%
	Mar 2012	294	138	46.9%	-	0	0%	683	409	59.9%	0	0	0%	6	5	83%
	Apr 2012	251	125	49.8%	-	0	0%	650	381	58.6%	0	0	0%	3	2	67%
	May 2012	324	142	43.8%	-	0	0%	631	384	60.9%	0	0	0%	8	6	75%
	Jun 2012	242	114	47.1%	-	0	0%	564	337	59.8%	0	0	0%	3	3	100%
	Jul 2012	295	159	53.9%	-	0	0%	617	361	58.5%	0	0	0%	5	4	80%
	Aug 2012	304	161	53.0%	-	0	0%	787	474	60.2%	0	0	0%	2	2	100%
	Sep 2012	279	138	49.5%	-	0	0%	645	389	60.3%	0	0	0%	5	5	100%
	Oct 2012	304	147	48.4%	-	0	0%	699	438	62.7%	0	0	0%	3	1	33%
	Nov 2012	313	152	48.6%	-	0	0%	712	398	55.9%	0	0	0%	6	3	50%
	Dec 2012	293	143	48.8%	-	0	0%	631	373	59.1%	0	0	0%	8	5	63%
	Jan 2013	277	133	48.0%	-	0	0%	593	354	59.7%	0	0	0%	4	3	75%
	Feb 2013	254	126	49.6%	-	0	0%	638	393	61.6%	0	0	0%	3	3	100%
	Mar 2013	253	129	51.0%	-	0	0%	585	358	61.2%	0	0	0%	4	4	100%
	Apr 2013	289	159	55.0%	-	0	0%	617	375	60.8%	0	0	0%	9	6	67%
	May 2013	261	119	45.6%	-	0	0%	640	389	60.8%	0	0	0%	8	5	63%
	Jun 2013	271	121	44.6%	1	0	0%	602	375	62.3%	0	0	0%	4	3	75%
	Jul 2013	331	164	49.5%	-	0	0%	663	407	61.4%	0	0	0%	8	7	88%
	Aug 2013	341	157	46.0%	-	0	0%	735	439	59.7%	0	0	0%	3	2	67%
	Sep 2013	302	142	47.0%	-	0	0%	645	375	58.1%	0	0	0%	3	2	67%
	Oct 2013	331	165	49.8%	1	1	100%	714	437	61.2%	0	0	0%	3	2	67%
	Nov 2013	310	148	47.7%	1	1	100%	651	391	60.1%	0	0	0%	5	1	20%
	Dec 2013	298	148	49.7%	0	0	0%	637	366	57.5%	0	0	0%	5	4	80%

Table 1b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	18,527	12,461	67%	22	7	32%	5,118	3,578	70%	8	5	63%	3,507	2,447	70%
	0 - 11 years	7	2	29%	1	0	0%	2	-	0%	0	0	0%	4	-	0%
	12 - 17 years	32	15	47%	0	0	0%	11	3	27%	0	0	0%	8	3	38%
	18 - 24 years	380	228	60%	1	0	0%	99	63	64%	0	0	0%	77	45	58%
	25 - 34 years	1,614	1,187	74%	2	0	0%	523	384	73%	1	1	100%	290	223	77%
	35 - 44 years	3,502	2,528	72%	4	1	25%	1,011	719	71%	1	0	0%	686	493	72%
	45 - 54 years	6,358	4,270	67%	11	4	36%	1,785	1,265	71%	4	3	75%	1,276	908	71%
	55 - 64 years	6,634	4,231	64%	3	2	67%	1,687	1,144	68%	2	1	50%	1,166	775	66%
Gender	Male	8,727	6,009	69%	11	6	55%	2,510	1,812	72%	4	3	75%	1,839	1,331	72%
	Female	9,800	6,452	66%	11	1	9%	2,608	1,766	68%	4	2	50%	1,668	1,116	67%
	Ambiguous	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
	Unknown	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	412	272	66%	2	2	100%	145	85	59%	1	0	0%	94	58	62%
	Feb 2009	414	299	72%	0	0	0%	118	84	71%	0	0	0%	98	70	71%
	Mar 2009	424	291	69%	0	0	0%	112	69	62%	0	0	0%	79	46	58%
	Apr 2009	423	288	68%	0	0	0%	108	82	76%	0	0	0%	88	62	70%
	May 2009	368	226	61%	0	0	0%	101	67	66%	0	0	0%	84	56	67%
	Jun 2009	409	259	63%	0	0	0%	111	76	68%	0	0	0%	75	56	75%
	Jul 2009	376	245	65%	2	0	0%	89	59	66%	0	0	0%	86	58	67%
	Aug 2009	348	233	67%	0	0	0%	97	70	72%	0	0	0%	72	50	69%
	Sep 2009	396	263	66%	0	0	0%	95	74	78%	2	1	50%	72	47	65%
	Oct 2009	433	266	61%	0	0	0%	100	72	72%	0	0	0%	90	61	68%
	Nov 2009	366	238	65%	1	1	100%	94	70	74%	0	0	0%	77	52	68%
	Dec 2009	379	247	65%	0	0	0%	113	80	71%	0	0	0%	74	50	68%
	Jan 2010	359	228	64%	0	0	0%	101	65	64%	0	0	0%	89	65	73%
	Feb 2010	325	206	63%	1	0	0%	84	52	62%	1	1	100%	60	39	65%
	Mar 2010	331	215	65%	0	0	0%	113	77	68%	0	0	0%	62	40	65%
	Apr 2010	307	201	65%	0	0	0%	100	77	77%	0	0	0%	67	50	75%
	May 2010	326	212	65%	0	0	0%	84	52	62%	0	0	0%	60	45	75%
	Jun 2010	340	229	67%	0	0	0%	77	56	73%	0	0	0%	49	40	82%
	Jul 2010	342	235	69%	0	0	0%	92	63	68%	0	0	0%	55	44	80%
	Aug 2010	325	217	67%	0	0	0%	98	67	68%	0	0	0%	71	54	76%
	Sep 2010	343	229	67%	1	1	100%	93	72	77%	0	0	0%	70	49	70%
	Oct 2010	340	241	71%	0	0	0%	95	68	72%	0	0	0%	58	49	84%
	Nov 2010	326	228	70%	0	0	0%	93	73	78%	0	0	0%	63	47	75%
	Dec 2010	356	229	64%	0	0	0%	78	58	74%	0	0	0%	64	36	56%
	Jan 2011	306	198	65%	0	0	0%	112	71	63%	0	0	0%	90	62	69%
	Feb 2011	277	191	69%	0	0	0%	96	71	74%	0	0	0%	66	47	71%
	Mar 2011	338	231	68%	1	0	0%	94	73	78%	0	0	0%	79	55	70%
	Apr 2011	322	205	64%	0	0	0%	86	58	67%	0	0	0%	52	33	63%
	May 2011	280	175	63%	0	0	0%	86	59	69%	0	0	0%	52	32	62%
	Jun 2011	286	187	65%	0	0	0%	75	57	76%	1	1	100%	41	29	71%
	Jul 2011	309	201	65%	0	0	0%	70	54	77%	0	0	0%	48	36	75%
	Aug 2011	322	215	67%	0	0	0%	78	52	67%	0	0	0%	45	38	84%
	Sep 2011	310	223	72%	0	0	0%	78	56	72%	0	0	0%	42	26	62%
	Oct 2011	269	179	67%	2	0	0%	77	58	75%	0	0	0%	56	39	70%
	Nov 2011	274	194	71%	0	0	0%	77	55	71%	0	0	0%	47	32	68%
	Dec 2011	286	193	67%	0	0	0%	72	47	65%	0	0	0%	59	46	78%
	Jan 2012	273	198	73%	0	0	0%	88	65	74%	0	0	0%	53	34	64%
	Feb 2012	266	197	74%	1	0	0%	75	54	72%	0	0	0%	53	43	81%
	Mar 2012	282	201	71%	0	0	0%	76	58	76%	0	0	0%	48	39	81%
	Apr 2012	277	199	72%	1	0	0%	86	59	69%	0	0	0%	48	34	71%
	May 2012	287	185	64%	1	0	0%	71	49	69%	0	0	0%	52	39	75%
	Jun 2012	234	157	67%	1	0	0%	60	43	72%	0	0	0%	49	37	76%
	Jul 2012	307	208	68%	0	0	0%	87	56	64%	0	0	0%	37	22	59%
	Aug 2012	284	195	69%	1	1	100%	89	63	71%	0	0	0%	51	39	76%
	Sep 2012	254	184	72%	1	0	0%	77	57	74%	1	1	100%	38	30	79%
	Oct 2012	251	157	63%	0	0	0%	69	51	74%	0	0	0%	47	28	60%
	Nov 2012	296	186	63%	0	0	0%	90	52	58%	2	1	50%	62	40	65%
	Dec 2012	261	185	71%	0	0	0%	54	30	56%	0	0	0%	46	27	59%
	Jan 2013	254	177	70%	2	1	50%	87	54	62%	0	0	0%	42	30	71%
	Feb 2013	212	165	78%	2	0	0%	56	41	73%	0	0	0%	44	35	80%
	Mar 2013	236	154	65%	0	0	0%	72	46	64%	0	0	0%	36	27	75%
	Apr 2013	226	158	70%	0	0	0%	68	47	69%	0	0	0%	37	29	78%
	May 2013	250	173	69%	1	1	100%	65	53	82%	0	0	0%	42	26	62%
	Jun 2013	244	172	70%	0	0	0%	69	45	65%	0	0	0%	34	23	68%
	Jul 2013	239	168	70%	0	0	0%	78	62	79%	0	0	0%	43	29	67%
	Aug 2013	272	184	68%	0	0	0%	61	38	62%	0	0	0%	31	16	52%
	Sep 2013	245	174	71%	0	0	0%	66	47	71%	0	0	0%	44	28	64%
	Oct 2013	242	175	72%	0	0	0%	67	45	67%	0	0	0%	47	35	74%
	Nov 2013	241	153	63%	0	0	0%	58	43	74%	0	0	0%	47	30	64%
	Dec 2013	247	167	68%	1	0	0%	57	41	72%	0	0	0%	42	28	67%

Table 1b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
	Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Total	3	3	100%	137	83	61%	2	1	50%	172	119	69%	2	2	100%	
Age (years)																
0 - 11 years	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%	
12 - 17 years	0	0	0%	1	-	0%	-	-	0%	1	-	0%	-	-	0%	
18 - 24 years	0	0	0%	2	2	100%	-	-	0%	5	4	80%	1	1	100%	
25 - 34 years	0	0	0%	9	7	78%	-	-	0%	12	8	67%	-	-	0%	
35 - 44 years	0	0	0%	20	13	65%	-	-	0%	30	24	80%	-	-	0%	
45 - 54 years	1	1	100%	57	34	60%	1	-	0%	60	41	68%	-	-	0%	
55 - 64 years	2	2	100%	48	27	56%	1	1	100%	64	42	66%	1	1	100%	
Gender																
Male	1	1	100%	69	39	57%	-	-	0%	95	74	78%	2	2	100%	
Female	2	2	100%	68	44	65%	2	1	50%	77	45	58%	-	-	0%	
Ambiguous	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%	
Unknown	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%	
Month and Year of Episode Start Date																
Jan 2009	1	1	100%	4	2	50%	-	-	0%	6	2	33%	-	-	0%	
Feb 2009	0	0	0%	3	2	67%	-	-	0%	2	2	100%	-	-	0%	
Mar 2009	0	0	0%	3	1	33%	-	-	0%	1	1	100%	-	-	0%	
Apr 2009	0	0	0%	2	1	50%	-	-	0%	1	1	100%	-	-	0%	
May 2009	0	0	0%	3	3	100%	-	-	0%	6	4	67%	-	-	0%	
Jun 2009	0	0	0%	2	2	100%	-	-	0%	7	6	86%	-	-	0%	
Jul 2009	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%	
Aug 2009	0	0	0%	1	1	100%	-	-	0%	4	1	25%	-	-	0%	
Sep 2009	0	0	0%	-	-	0%	-	-	0%	5	4	80%	-	-	0%	
Oct 2009	0	0	0%	1	-	0%	-	-	0%	4	2	50%	-	-	0%	
Nov 2009	0	0	0%	2	1	50%	-	-	0%	7	5	71%	-	-	0%	
Dec 2009	0	0	0%	2	1	50%	-	-	0%	7	5	71%	-	-	0%	
Jan 2010	0	0	0%	7	3	43%	-	-	0%	5	3	60%	-	-	0%	
Feb 2010	0	0	0%	6	2	33%	-	-	0%	5	4	80%	-	-	0%	
Mar 2010	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%	
Apr 2010	0	0	0%	4	1	25%	-	-	0%	4	3	75%	-	-	0%	
May 2010	0	0	0%	2	1	50%	-	-	0%	4	3	75%	-	-	0%	
Jun 2010	0	0	0%	5	4	80%	-	-	0%	2	2	100%	-	-	0%	
Jul 2010	0	0	0%	1	-	0%	-	-	0%	5	4	80%	-	-	0%	
Aug 2010	0	0	0%	2	1	50%	-	-	0%	2	1	50%	-	-	0%	
Sep 2010	0	0	0%	-	-	0%	-	-	0%	3	1	33%	-	-	0%	
Oct 2010	0	0	0%	3	3	100%	1	1	100%	3	3	100%	-	-	0%	
Nov 2010	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%	
Dec 2010	0	0	0%	1	1	100%	-	-	0%	4	2	50%	-	-	0%	
Jan 2011	0	0	0%	3	1	33%	-	-	0%	4	3	75%	1	1	100%	
Feb 2011	1	1	100%	3	1	33%	-	-	0%	3	1	33%	-	-	0%	
Mar 2011	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%	
Apr 2011	0	0	0%	3	1	33%	-	-	0%	4	4	100%	-	-	0%	
May 2011	0	0	0%	5	3	60%	-	-	0%	2	2	100%	-	-	0%	
Jun 2011	0	0	0%	2	1	50%	-	-	0%	-	-	0%	-	-	0%	
Jul 2011	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%	
Aug 2011	0	0	0%	1	1	100%	-	-	0%	1	1	100%	-	-	0%	
Sep 2011	0	0	0%	4	2	50%	1	-	0%	3	3	100%	1	1	100%	
Oct 2011	0	0	0%	1	1	100%	-	-	0%	1	-	0%	-	-	0%	
Nov 2011	0	0	0%	-	-	0%	-	-	0%	1	1	100%	-	-	0%	
Dec 2011	0	0	0%	3	2	67%	-	-	0%	1	1	100%	-	-	0%	
Jan 2012	0	0	0%	2	1	50%	-	-	0%	2	2	100%	-	-	0%	
Feb 2012	0	0	0%	2	2	100%	-	-	0%	5	4	80%	-	-	0%	
Mar 2012	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%	
Apr 2012	1	1	100%	5	5	100%	-	-	0%	3	3	100%	-	-	0%	
May 2012	0	0	0%	4	1	25%	-	-	0%	-	-	0%	-	-	0%	
Jun 2012	0	0	0%	-	-	0%	-	-	0%	2	1	50%	-	-	0%	
Jul 2012	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%	
Aug 2012	0	0	0%	4	4	100%	-	-	0%	1	1	100%	-	-	0%	
Sep 2012	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%	
Oct 2012	0	0	0%	2	2	100%	-	-	0%	2	2	100%	-	-	0%	
Nov 2012	0	0	0%	2	2	100%	-	-	0%	5	3	60%	-	-	0%	
Dec 2012	0	0	0%	3	1	33%	-	-	0%	-	-	0%	-	-	0%	
Jan 2013	0	0	0%	2	-	0%	-	-	0%	4	1	25%	-	-	0%	
Feb 2013	0	0	0%	3	2	67%	-	-	0%	-	-	0%	-	-	0%	
Mar 2013	0	0	0%	2	1	50%	-	-	0%	3	1	33%	-	-	0%	
Apr 2013	0	0	0%	-	-	0%	-	-	0%	3	3	100%	-	-	0%	
May 2013	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%	
Jun 2013	0	0	0%	-	-	0%	-	-	0%	3	1	33%	-	-	0%	
Jul 2013	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%	
Aug 2013	0	0	0%	2	2	100%	-	-	0%	3	1	33%	-	-	0%	
Sep 2013	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%	
Oct 2013	0	0	0%	4	1	25%	-	-	0%	1	1	100%	-	-	0%	
Nov 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%	
Dec 2013	0	0	0%	1	-	0%	-	-	0%	2	1	50%	-	-	0%	

Table 1b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)										
		Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr		
		Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Age (years)	Total	33	18	55%	4	3	75%	2	1	50%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	1	1	100%	-	-	0%	-	-	0%
	18 - 24 years	3	3	100%	-	-	0%	-	-	0%
	25 - 34 years	1	-	0%	-	-	0%	1	1	100%
	35 - 44 years	4	3	75%	3	2	67%	-	-	0%
	45 - 54 years	9	6	67%	1	1	100%	-	-	0%
	55 - 64 years	15	5	33%	-	-	0%	1	-	0%
Gender	Male	11	9	82%	4	3	75%	2	1	50%
	Female	22	9	41%	-	-	0%	-	-	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	-	0%	-	-	0%	-	-	0%
	Feb 2009	1	1	100%	-	-	0%	-	-	0%
	Mar 2009	1	1	100%	-	-	0%	-	-	0%
	Apr 2009	3	3	100%	1	1	100%	-	-	0%
	May 2009	-	-	0%	-	-	0%	-	-	0%
	Jun 2009	-	-	0%	-	-	0%	-	-	0%
	Jul 2009	2	2	100%	-	-	0%	1	1	100%
	Aug 2009	-	-	0%	-	-	0%	-	-	0%
	Sep 2009	1	1	100%	-	-	0%	-	-	0%
	Oct 2009	1	-	0%	-	-	0%	-	-	0%
	Nov 2009	-	-	0%	-	-	0%	-	-	0%
	Dec 2009	1	-	0%	-	-	0%	-	-	0%
	Jan 2010	-	-	0%	-	-	0%	-	-	0%
	Feb 2010	-	-	0%	-	-	0%	-	-	0%
	Mar 2010	1	1	100%	1	1	100%	-	-	0%
	Apr 2010	-	-	0%	-	-	0%	-	-	0%
	May 2010	-	-	0%	-	-	0%	-	-	0%
	Jun 2010	1	-	0%	-	-	0%	-	-	0%
	Jul 2010	-	-	0%	-	-	0%	-	-	0%
	Aug 2010	1	1	100%	-	-	0%	-	-	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%
	Oct 2010	1	1	100%	-	-	0%	-	-	0%
	Nov 2010	-	-	0%	-	-	0%	-	-	0%
	Dec 2010	1	1	100%	-	-	0%	-	-	0%
	Jan 2011	-	-	0%	-	-	0%	-	-	0%
	Feb 2011	2	1	50%	-	-	0%	-	-	0%
	Mar 2011	1	1	100%	-	-	0%	-	-	0%
	Apr 2011	1	-	0%	-	-	0%	-	-	0%
	May 2011	-	-	0%	-	-	0%	-	-	0%
	Jun 2011	2	1	50%	-	-	0%	-	-	0%
	Jul 2011	-	-	0%	-	-	0%	-	-	0%
	Aug 2011	1	-	0%	-	-	0%	-	-	0%
	Sep 2011	2	1	50%	-	-	0%	-	-	0%
	Oct 2011	2	-	0%	-	-	0%	-	-	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%
	Dec 2011	-	-	0%	-	-	0%	-	-	0%
	Jan 2012	-	-	0%	-	-	0%	-	-	0%
	Feb 2012	-	-	0%	-	-	0%	-	-	0%
	Mar 2012	1	-	0%	-	-	0%	-	-	0%
	Apr 2012	1	-	0%	-	-	0%	-	-	0%
	May 2012	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	-	-	0%	-	-	0%	-	-	0%
	Jul 2012	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	-	-	0%	-	-	0%	-	-	0%
	Sep 2012	-	-	0%	-	-	0%	-	-	0%
	Oct 2012	-	-	0%	-	-	0%	-	-	0%
	Nov 2012	-	-	0%	-	-	0%	1	-	0%
	Dec 2012	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	-	-	0%	-	-	0%	-	-	0%
	Feb 2013	1	-	0%	-	-	0%	-	-	0%
	Mar 2013	-	-	0%	-	-	0%	-	-	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%
	May 2013	-	-	0%	-	-	0%	-	-	0%
	Jun 2013	1	-	0%	2	1	50%	-	-	0%
	Jul 2013	-	-	0%	-	-	0%	-	-	0%
	Aug 2013	-	-	0%	-	-	0%	-	-	0%
	Sep 2013	1	1	100%	-	-	0%	-	-	0%
	Oct 2013	-	-	0%	-	-	0%	-	-	0%
	Nov 2013	-	-	0%	-	-	0%	-	-	0%
	Dec 2013	1	1	100%	-	-	0%	-	-	0%

Table 1c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	16,379	8,076	49.3%	3	2	67%	44,450	23,730	53.4%	1	0	0%	298	181	61%
	0 - 11 years	32	6	18.8%	-	0	0%	23	6	26.1%	0	0	0%	1	0	0%
	12 - 17 years	75	23	30.7%	-	0	0%	79	28	35.4%	0	0	0%	2	0	0%
	18 - 24 years	375	167	44.5%	-	0	0%	827	427	51.6%	0	0	0%	8	3	38%
	25 - 34 years	1,464	870	59.4%	-	0	0%	3,731	2,285	61.2%	1	0	0%	24	17	71%
	35 - 44 years	2,841	1,561	54.9%	2	2	100%	7,954	4,564	57.4%	0	0	0%	63	37	59%
	45 - 54 years	5,214	2,603	49.9%	-	0	0%	14,785	8,065	54.5%	0	0	0%	87	54	62%
	55 - 64 years	6,378	2,846	44.6%	1	0	0%	17,051	8,355	49.0%	0	0	0%	113	70	62%
Gender	Male	5,124	2,585	50.4%	1	1	100%	18,327	9,822	53.6%	0	0	0%	133	85	64%
	Female	11,255	5,491	48.8%	2	1	50%	26,123	13,908	53.2%	1	0	0%	165	96	58%
	Ambiguous	-	-	0.0%	-	0	0%	-	-	0.0%	0	0	0%	0	0	0%
	Unknown	0	0	0	0	0	0%	-	0	0	0	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	220	117	53.2%	-	0	0%	953	470	49.3%	0	0	0%	4	3	75%
	Feb 2009	206	97	47.1%	-	0	0%	890	438	49.2%	0	0	0%	8	3	38%
	Mar 2009	267	118	44.2%	-	0	0%	982	496	50.5%	0	0	0%	5	3	60%
	Apr 2009	220	105	47.7%	-	0	0%	969	503	51.9%	1	0	0%	4	2	50%
	May 2009	248	119	48.0%	-	0	0%	875	490	56.0%	0	0	0%	6	5	83%
	Jun 2009	258	115	44.6%	-	0	0%	909	443	48.7%	0	0	0%	5	5	100%
	Jul 2009	249	124	49.8%	-	0	0%	870	443	50.9%	0	0	0%	6	2	33%
	Aug 2009	268	122	45.5%	-	0	0%	881	432	49.0%	0	0	0%	2	1	50%
	Sep 2009	295	145	49.2%	-	0	0%	943	481	51.0%	0	0	0%	4	4	100%
	Oct 2009	261	114	43.7%	-	0	0%	857	423	49.4%	0	0	0%	1	1	100%
	Nov 2009	231	109	47.2%	-	0	0%	818	412	50.4%	0	0	0%	8	4	50%
	Dec 2009	244	115	47.1%	-	0	0%	900	497	55.2%	0	0	0%	7	3	43%
	Jan 2010	226	109	48.2%	-	0	0%	827	414	50.1%	0	0	0%	6	0	0%
	Feb 2010	238	128	53.8%	-	0	0%	753	400	53.1%	0	0	0%	8	8	100%
	Mar 2010	268	126	47.0%	-	0	0%	791	411	52.0%	0	0	0%	8	5	63%
	Apr 2010	257	119	46.3%	-	0	0%	833	418	50.2%	0	0	0%	3	2	67%
	May 2010	227	122	53.7%	-	0	0%	738	407	55.1%	0	0	0%	5	1	20%
	Jun 2010	246	117	47.6%	-	0	0%	746	391	52.4%	0	0	0%	4	1	25%
	Jul 2010	223	104	46.6%	-	0	0%	764	423	55.4%	0	0	0%	5	3	60%
	Aug 2010	260	130	50.0%	-	0	0%	810	420	51.9%	0	0	0%	3	2	67%
	Sep 2010	301	136	45.2%	-	0	0%	833	463	55.6%	0	0	0%	2	2	100%
	Oct 2010	288	134	46.5%	-	0	0%	777	410	52.8%	0	0	0%	5	3	60%
	Nov 2010	290	141	48.6%	-	0	0%	824	421	51.1%	0	0	0%	9	5	56%
	Dec 2010	291	138	47.4%	-	0	0%	731	398	54.4%	0	0	0%	3	1	33%
	Jan 2011	252	116	46.0%	-	0	0%	724	372	51.4%	0	0	0%	1	1	100%
	Feb 2011	264	121	45.8%	-	0	0%	639	329	51.5%	0	0	0%	3	2	67%
	Mar 2011	279	144	51.6%	-	0	0%	802	433	54.0%	0	0	0%	9	5	56%
	Apr 2011	269	135	50.2%	-	0	0%	710	381	53.7%	0	0	0%	10	9	90%
	May 2011	261	120	46.0%	-	0	0%	700	371	53.0%	0	0	0%	3	3	100%
	Jun 2011	276	123	44.6%	-	0	0%	678	377	55.6%	0	0	0%	4	2	50%
	Jul 2011	282	145	51.4%	-	0	0%	679	355	52.3%	0	0	0%	3	2	67%
	Aug 2011	314	162	51.6%	-	0	0%	758	389	51.3%	0	0	0%	4	2	50%
	Sep 2011	291	138	47.4%	-	0	0%	730	392	53.7%	0	0	0%	7	4	57%
	Oct 2011	263	133	50.6%	-	0	0%	711	404	56.8%	0	0	0%	3	2	67%
	Nov 2011	288	147	51.0%	-	0	0%	659	383	58.1%	0	0	0%	8	2	25%
	Dec 2011	307	145	47.2%	-	0	0%	689	357	51.8%	0	0	0%	5	3	60%
	Jan 2012	279	125	44.8%	-	0	0%	720	394	54.7%	0	0	0%	2	2	100%
	Feb 2012	255	128	50.2%	-	0	0%	638	340	53.3%	0	0	0%	7	5	71%
	Mar 2012	294	145	49.3%	-	0	0%	683	358	52.4%	0	0	0%	6	5	83%
	Apr 2012	251	126	50.2%	-	0	0%	650	353	54.3%	0	0	0%	3	2	67%
	May 2012	324	159	49.1%	-	0	0%	631	341	54.0%	0	0	0%	8	6	75%
	Jun 2012	242	127	52.5%	-	0	0%	564	310	55.0%	0	0	0%	3	2	67%
	Jul 2012	295	149	50.5%	-	0	0%	617	342	55.4%	0	0	0%	5	2	40%
	Aug 2012	304	169	55.6%	-	0	0%	787	437	55.5%	0	0	0%	2	1	50%
	Sep 2012	279	131	47.0%	-	0	0%	645	333	51.6%	0	0	0%	5	4	80%
	Oct 2012	304	160	52.6%	-	0	0%	699	426	60.9%	0	0	0%	3	2	67%
	Nov 2012	313	161	51.4%	-	0	0%	712	373	52.4%	0	0	0%	6	4	67%
	Dec 2012	293	141	48.1%	-	0	0%	631	347	55.0%	0	0	0%	8	3	38%
	Jan 2013	277	143	51.6%	-	0	0%	593	320	54.0%	0	0	0%	4	3	75%
	Feb 2013	254	131	51.6%	-	0	0%	638	377	59.1%	0	0	0%	3	3	100%
	Mar 2013	253	137	54.2%	-	0	0%	585	346	59.1%	0	0	0%	4	3	75%
	Apr 2013	289	159	55.0%	-	0	0%	617	353	57.2%	0	0	0%	9	5	56%
	May 2013	261	135	51.7%	-	0	0%	640	362	56.6%	0	0	0%	8	5	63%
	Jun 2013	271	146	53.9%	1	1	100%	602	339	56.3%	0	0	0%	4	2	50%
	Jul 2013	331	162	48.9%	-	0	0%	663	386	58.2%	0	0	0%	8	7	88%
	Aug 2013	341	160	46.9%	-	0	0%	735	403	54.8%	0	0	0%	3	1	33%
	Sep 2013	302	149	49.3%	-	0	0%	645	348	54.0%	0	0	0%	3	2	67%
	Oct 2013	331	173	52.3%	1	1	100%	714	397	55.6%	0	0	0%	3	1	33%
	Nov 2013	310	166	53.5%	1	0	0%	651	353	54.2%	0	0	0%	5	1	20%
	Dec 2013	298	161	54.0%	0	0	0%	637	345	54.2%	0	0	0%	5	4	80%

Table 1c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	18,527	11,000	59%	22	6	27%	5,118	3,122	61%	8	2	25%	3,507	2,125	61%
	0 - 11 years	7	2	29%	1	0	0%	2	-	0%	0	0	0%	4	-	0%
	12 - 17 years	32	10	31%	0	0	0%	11	3	27%	0	0	0%	8	2	25%
	18 - 24 years	380	205	54%	1	0	0%	99	55	56%	0	0	0%	77	39	51%
	25 - 34 years	1,614	1,055	65%	2	0	0%	523	337	64%	1	1	100%	290	191	66%
	35 - 44 years	3,502	2,240	64%	4	1	25%	1,011	613	61%	1	0	0%	686	424	62%
	45 - 54 years	6,358	3,779	59%	11	3	27%	1,785	1,110	62%	4	1	25%	1,276	790	62%
	55 - 64 years	6,634	3,709	56%	3	2	67%	1,687	1,004	60%	2	0	0%	1,166	679	58%
Gender	Male	8,727	5,343	61%	11	5	45%	2,510	1,590	63%	4	1	25%	1,839	1,171	64%
	Female	9,800	5,657	58%	11	1	9%	2,608	1,532	59%	4	1	25%	1,668	954	57%
	Ambiguous	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
	Unknown	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	412	223	54%	2	2	100%	145	76	52%	1	0	0%	94	46	49%
	Feb 2009	414	251	61%	0	0	0%	118	68	58%	0	0	0%	98	59	60%
	Mar 2009	424	263	62%	0	0	0%	112	67	60%	0	0	0%	79	40	51%
	Apr 2009	423	262	62%	0	0	0%	108	68	63%	0	0	0%	88	56	64%
	May 2009	368	208	57%	0	0	0%	101	52	51%	0	0	0%	84	46	55%
	Jun 2009	409	227	56%	0	0	0%	111	58	52%	0	0	0%	75	56	75%
	Jul 2009	376	214	57%	2	0	0%	89	48	54%	0	0	0%	86	55	64%
	Aug 2009	348	212	61%	0	0	0%	97	58	60%	0	0	0%	72	43	60%
	Sep 2009	396	233	59%	0	0	0%	95	69	73%	2	0	0%	72	40	56%
	Oct 2009	433	241	56%	0	0	0%	100	59	59%	0	0	0%	90	54	60%
	Nov 2009	366	213	58%	1	1	100%	94	63	67%	0	0	0%	77	48	62%
	Dec 2009	379	216	57%	0	0	0%	113	67	59%	0	0	0%	74	44	59%
	Jan 2010	359	200	56%	0	0	0%	101	59	58%	0	0	0%	89	58	65%
	Feb 2010	325	176	54%	1	0	0%	84	44	52%	1	0	0%	60	35	58%
	Mar 2010	331	195	59%	0	0	0%	113	71	63%	0	0	0%	62	37	60%
	Apr 2010	307	172	56%	0	0	0%	100	67	67%	0	0	0%	67	48	72%
	May 2010	326	188	58%	0	0	0%	84	47	56%	0	0	0%	60	41	68%
	Jun 2010	340	206	61%	0	0	0%	77	42	55%	0	0	0%	49	39	80%
	Jul 2010	342	216	63%	0	0	0%	92	51	55%	0	0	0%	55	37	67%
	Aug 2010	325	191	59%	0	0	0%	98	58	59%	0	0	0%	71	47	66%
	Sep 2010	343	206	60%	1	1	100%	93	61	66%	0	0	0%	70	41	59%
	Oct 2010	340	215	63%	0	0	0%	95	64	67%	0	0	0%	58	43	74%
	Nov 2010	326	207	63%	0	0	0%	93	62	67%	0	0	0%	63	41	65%
	Dec 2010	356	203	57%	0	0	0%	78	46	59%	0	0	0%	64	30	47%
	Jan 2011	306	165	54%	0	0	0%	112	60	54%	0	0	0%	90	55	61%
	Feb 2011	277	171	62%	0	0	0%	96	64	67%	0	0	0%	66	39	59%
	Mar 2011	338	211	62%	1	0	0%	94	64	68%	0	0	0%	79	46	58%
	Apr 2011	322	173	54%	0	0	0%	86	56	65%	0	0	0%	52	30	58%
	May 2011	280	156	56%	0	0	0%	86	54	63%	0	0	0%	52	31	60%
	Jun 2011	286	157	55%	0	0	0%	75	53	71%	1	0	0%	41	27	66%
	Jul 2011	309	185	60%	0	0	0%	70	52	74%	0	0	0%	48	28	58%
	Aug 2011	322	185	57%	0	0	0%	78	44	56%	0	0	0%	45	31	69%
	Sep 2011	310	186	60%	0	0	0%	78	49	63%	0	0	0%	42	25	60%
	Oct 2011	269	156	58%	2	0	0%	77	56	73%	0	0	0%	56	33	59%
	Nov 2011	274	165	60%	0	0	0%	77	47	61%	0	0	0%	47	28	60%
	Dec 2011	286	167	58%	0	0	0%	72	41	57%	0	0	0%	59	38	64%
	Jan 2012	273	167	61%	0	0	0%	88	60	68%	0	0	0%	53	27	51%
	Feb 2012	266	168	63%	1	0	0%	75	49	65%	0	0	0%	53	36	68%
	Mar 2012	282	179	63%	0	0	0%	76	48	63%	0	0	0%	48	30	63%
	Apr 2012	277	175	63%	1	0	0%	86	50	58%	0	0	0%	48	29	60%
	May 2012	287	181	63%	1	0	0%	71	46	65%	0	0	0%	52	37	71%
	Jun 2012	234	144	62%	1	0	0%	60	38	63%	0	0	0%	49	32	65%
	Jul 2012	307	189	62%	0	0	0%	87	48	55%	0	0	0%	37	18	49%
	Aug 2012	284	170	60%	1	0	0%	89	59	66%	0	0	0%	51	35	69%
	Sep 2012	254	159	63%	1	0	0%	77	55	71%	1	1	100%	38	22	58%
	Oct 2012	251	145	58%	0	0	0%	69	47	68%	0	0	0%	47	21	45%
	Nov 2012	296	165	56%	0	0	0%	90	46	51%	2	1	50%	62	33	53%
	Dec 2012	261	171	66%	0	0	0%	54	26	48%	0	0	0%	46	20	43%
	Jan 2013	254	156	61%	2	1	50%	87	45	52%	0	0	0%	42	26	62%
	Feb 2013	212	134	63%	2	0	0%	56	33	59%	0	0	0%	44	29	66%
	Mar 2013	236	148	63%	0	0	0%	72	45	63%	0	0	0%	36	19	53%
	Apr 2013	226	129	57%	0	0	0%	68	39	57%	0	0	0%	37	25	68%
	May 2013	250	160	64%	1	1	100%	65	43	66%	0	0	0%	42	26	62%
	Jun 2013	244	141	58%	0	0	0%	69	44	64%	0	0	0%	34	18	53%
	Jul 2013	239	141	59%	0	0	0%	78	49	63%	0	0	0%	43	22	51%
	Aug 2013	272	169	62%	0	0	0%	61	29	48%	0	0	0%	31	15	48%
	Sep 2013	245	152	62%	0	0	0%	66	41	62%	0	0	0%	44	25	57%
	Oct 2013	242	152	63%	0	0	0%	67	43	64%	0	0	0%	47	32	68%
	Nov 2013	241	142	59%	0	0	0%	58	37	64%	0	0	0%	47	26	55%
	Dec 2013	247	148	60%	1	0	0%	57	37	65%	0	0	0%	42	27	64%

Table 1c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	3	3	100%	137	73	53%	2	1	50%	172	104	60%	2	1	50%
	0 - 11 years	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	0	0	0%	1	-	0%	-	-	0%	1	-	0%	-	-	0%
	18 - 24 years	0	0	0%	2	2	100%	-	-	0%	5	4	80%	1	-	0%
	25 - 34 years	0	0	0%	9	7	78%	-	-	0%	12	6	50%	-	-	0%
	35 - 44 years	0	0	0%	20	8	40%	-	-	0%	30	21	70%	-	-	0%
	45 - 54 years	1	1	100%	57	31	54%	1	-	0%	60	37	62%	-	-	0%
	55 - 64 years	2	2	100%	48	25	52%	1	1	100%	64	36	56%	1	1	100%
Gender	Male	1	1	100%	69	35	51%	-	-	0%	95	61	64%	2	1	50%
	Female	2	2	100%	68	38	56%	2	1	50%	77	43	56%	-	-	0%
	Ambiguous	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	1	100%	4	2	50%	-	-	0%	6	2	33%	-	-	0%
	Feb 2009	0	0	0%	3	1	33%	-	-	0%	2	1	50%	-	-	0%
	Mar 2009	0	0	0%	3	1	33%	-	-	0%	1	1	100%	-	-	0%
	Apr 2009	0	0	0%	2	1	50%	-	-	0%	1	1	100%	-	-	0%
	May 2009	0	0	0%	3	3	100%	-	-	0%	6	4	67%	-	-	0%
	Jun 2009	0	0	0%	2	2	100%	-	-	0%	7	6	86%	-	-	0%
	Jul 2009	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%
	Aug 2009	0	0	0%	1	1	100%	-	-	0%	4	-	0%	-	-	0%
	Sep 2009	0	0	0%	-	-	0%	-	-	0%	5	3	60%	-	-	0%
	Oct 2009	0	0	0%	1	-	0%	-	-	0%	4	2	50%	-	-	0%
	Nov 2009	0	0	0%	2	1	50%	-	-	0%	7	5	71%	-	-	0%
	Dec 2009	0	0	0%	2	1	50%	-	-	0%	7	5	71%	-	-	0%
	Jan 2010	0	0	0%	7	2	29%	-	-	0%	5	3	60%	-	-	0%
	Feb 2010	0	0	0%	6	1	17%	-	-	0%	5	3	60%	-	-	0%
	Mar 2010	0	0	0%	2	-	0%	-	-	0%	4	3	75%	-	-	0%
	Apr 2010	0	0	0%	4	1	25%	-	-	0%	4	3	75%	-	-	0%
	May 2010	0	0	0%	2	1	50%	-	-	0%	4	2	50%	-	-	0%
	Jun 2010	0	0	0%	5	2	40%	-	-	0%	2	1	50%	-	-	0%
	Jul 2010	0	0	0%	1	-	0%	-	-	0%	5	4	80%	-	-	0%
	Aug 2010	0	0	0%	2	1	50%	-	-	0%	2	-	0%	-	-	0%
	Sep 2010	0	0	0%	-	-	0%	-	-	0%	3	-	0%	-	-	0%
	Oct 2010	0	0	0%	3	3	100%	1	1	100%	3	3	100%	-	-	0%
	Nov 2010	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Dec 2010	0	0	0%	1	1	100%	-	-	0%	4	2	50%	-	-	0%
	Jan 2011	0	0	0%	3	1	33%	-	-	0%	4	2	50%	1	-	0%
	Feb 2011	1	1	100%	3	1	33%	-	-	0%	3	1	33%	-	-	0%
	Mar 2011	0	0	0%	2	1	50%	-	-	0%	2	1	50%	-	-	0%
	Apr 2011	0	0	0%	3	2	67%	-	-	0%	4	4	100%	-	-	0%
	May 2011	0	0	0%	5	1	20%	-	-	0%	2	1	50%	-	-	0%
	Jun 2011	0	0	0%	2	1	50%	-	-	0%	-	-	0%	-	-	0%
	Jul 2011	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%
	Aug 2011	0	0	0%	1	1	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2011	0	0	0%	4	3	75%	1	-	0%	3	3	100%	1	1	100%
	Oct 2011	0	0	0%	1	1	100%	-	-	0%	1	-	0%	-	-	0%
	Nov 2011	0	0	0%	-	-	0%	-	-	0%	1	1	100%	-	-	0%
	Dec 2011	0	0	0%	3	2	67%	-	-	0%	1	1	100%	-	-	0%
	Jan 2012	0	0	0%	2	1	50%	-	-	0%	2	2	100%	-	-	0%
	Feb 2012	0	0	0%	2	1	50%	-	-	0%	5	4	80%	-	-	0%
	Mar 2012	0	0	0%	3	3	100%	-	-	0%	2	1	50%	-	-	0%
	Apr 2012	1	1	100%	5	5	100%	-	-	0%	3	2	67%	-	-	0%
	May 2012	0	0	0%	4	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	0	0	0%	-	-	0%	-	-	0%	2	1	50%	-	-	0%
	Jul 2012	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	0	0	0%	4	3	75%	-	-	0%	1	1	100%	-	-	0%
	Sep 2012	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2012	0	0	0%	2	2	100%	-	-	0%	2	2	100%	-	-	0%
	Nov 2012	0	0	0%	2	2	100%	-	-	0%	5	3	60%	-	-	0%
	Dec 2012	0	0	0%	3	1	33%	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	0	0	0%	2	-	0%	-	-	0%	4	-	0%	-	-	0%
	Feb 2013	0	0	0%	3	1	33%	-	-	0%	-	-	0%	-	-	0%
	Mar 2013	0	0	0%	2	1	50%	-	-	0%	3	1	33%	-	-	0%
	Apr 2013	0	0	0%	-	-	0%	-	-	0%	3	2	67%	-	-	0%
	May 2013	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Jun 2013	0	0	0%	-	-	0%	-	-	0%	3	1	33%	-	-	0%
	Jul 2013	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%
	Aug 2013	0	0	0%	2	2	100%	-	-	0%	3	1	33%	-	-	0%
	Sep 2013	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2013	0	0	0%	4	1	25%	-	-	0%	1	1	100%	-	-	0%
	Nov 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2013	0	0	0%	1	-	0%	-	-	0%	2	1	50%	-	-	0%

Table 1c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)									
	Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr		
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Total	33	16	48%	4	3	75%	2	-	0%
Age (years)									
0 - 11 years	-	-	0%	-	-	0%	-	-	0%
12 - 17 years	1	1	100%	-	-	0%	-	-	0%
18 - 24 years	3	3	100%	-	-	0%	-	-	0%
25 - 34 years	1	-	0%	-	-	0%	1	-	0%
35 - 44 years	4	3	75%	3	2	67%	-	-	0%
45 - 54 years	9	4	44%	1	1	100%	-	-	0%
55 - 64 years	15	5	33%	-	-	0%	1	-	0%
Gender									
Male	11	9	82%	4	3	75%	2	-	0%
Female	22	7	32%	-	-	0%	-	-	0%
Ambiguous	-	-	0%	-	-	0%	-	-	0%
Unknown	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date									
Jan 2009	1	-	0%	-	-	0%	-	-	0%
Feb 2009	1	1	100%	-	-	0%	-	-	0%
Mar 2009	1	1	100%	-	-	0%	-	-	0%
Apr 2009	3	3	100%	1	1	100%	-	-	0%
May 2009	-	-	0%	-	-	0%	-	-	0%
Jun 2009	-	-	0%	-	-	0%	-	-	0%
Jul 2009	2	-	0%	-	-	0%	1	-	0%
Aug 2009	-	-	0%	-	-	0%	-	-	0%
Sep 2009	1	1	100%	-	-	0%	-	-	0%
Oct 2009	1	-	0%	-	-	0%	-	-	0%
Nov 2009	-	-	0%	-	-	0%	-	-	0%
Dec 2009	1	-	0%	-	-	0%	-	-	0%
Jan 2010	-	-	0%	-	-	0%	-	-	0%
Feb 2010	-	-	0%	-	-	0%	-	-	0%
Mar 2010	1	1	100%	1	1	100%	-	-	0%
Apr 2010	-	-	0%	-	-	0%	-	-	0%
May 2010	-	-	0%	-	-	0%	-	-	0%
Jun 2010	1	-	0%	-	-	0%	-	-	0%
Jul 2010	-	-	0%	-	-	0%	-	-	0%
Aug 2010	1	1	100%	-	-	0%	-	-	0%
Sep 2010	-	-	0%	-	-	0%	-	-	0%
Oct 2010	1	1	100%	-	-	0%	-	-	0%
Nov 2010	-	-	0%	-	-	0%	-	-	0%
Dec 2010	1	1	100%	-	-	0%	-	-	0%
Jan 2011	-	-	0%	-	-	0%	-	-	0%
Feb 2011	2	1	50%	-	-	0%	-	-	0%
Mar 2011	1	1	100%	-	-	0%	-	-	0%
Apr 2011	1	-	0%	-	-	0%	-	-	0%
May 2011	-	-	0%	-	-	0%	-	-	0%
Jun 2011	2	1	50%	-	-	0%	-	-	0%
Jul 2011	-	-	0%	-	-	0%	-	-	0%
Aug 2011	1	-	0%	-	-	0%	-	-	0%
Sep 2011	2	1	50%	-	-	0%	-	-	0%
Oct 2011	2	-	0%	-	-	0%	-	-	0%
Nov 2011	-	-	0%	-	-	0%	-	-	0%
Dec 2011	-	-	0%	-	-	0%	-	-	0%
Jan 2012	-	-	0%	-	-	0%	-	-	0%
Feb 2012	-	-	0%	-	-	0%	-	-	0%
Mar 2012	1	-	0%	-	-	0%	-	-	0%
Apr 2012	1	-	0%	-	-	0%	-	-	0%
May 2012	-	-	0%	-	-	0%	-	-	0%
Jun 2012	-	-	0%	-	-	0%	-	-	0%
Jul 2012	-	-	0%	-	-	0%	-	-	0%
Aug 2012	-	-	0%	-	-	0%	-	-	0%
Sep 2012	-	-	0%	-	-	0%	-	-	0%
Oct 2012	-	-	0%	-	-	0%	-	-	0%
Nov 2012	-	-	0%	-	-	0%	1	-	0%
Dec 2012	-	-	0%	-	-	0%	-	-	0%
Jan 2013	-	-	0%	-	-	0%	-	-	0%
Feb 2013	1	-	0%	-	-	0%	-	-	0%
Mar 2013	-	-	0%	-	-	0%	-	-	0%
Apr 2013	-	-	0%	-	-	0%	-	-	0%
May 2013	-	-	0%	-	-	0%	-	-	0%
Jun 2013	1	-	0%	2	1	50%	-	-	0%
Jul 2013	-	-	0%	-	-	0%	-	-	0%
Aug 2013	-	-	0%	-	-	0%	-	-	0%
Sep 2013	1	1	100%	-	-	0%	-	-	0%
Oct 2013	-	-	0%	-	-	0%	-	-	0%
Nov 2013	-	-	0%	-	-	0%	-	-	0%
Dec 2013	1	1	100%	-	-	0%	-	-	0%

Table 1d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg for seven days in the 30 days prior)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	16,379	11,725	71.6%	3	3	100%	44,450	34,055	76.6%	1	0	0%	298	226	76%
	0 - 11 years	32	13	40.6%	-	0	0%	23	9	39.1%	0	0	0%	1	0	0%
	12 - 17 years	75	34	45.3%	-	0	0%	79	35	44.3%	0	0	0%	2	0	0%
	18 - 24 years	375	244	65.1%	-	0	0%	827	573	69.3%	0	0	0%	8	5	63%
	25 - 34 years	1,464	1,149	78.5%	-	0	0%	3,731	3,036	81.4%	1	0	0%	24	20	83%
	35 - 44 years	2,841	2,145	75.5%	2	2	100%	7,954	6,322	79.5%	0	0	0%	63	45	71%
	45 - 54 years	5,214	3,758	72.1%	-	0	0%	14,785	11,417	77.2%	0	0	0%	87	66	76%
	55 - 64 years	6,378	4,382	68.7%	1	1	100%	17,051	12,663	74.3%	0	0	0%	113	90	80%
Gender	Male	5,124	3,737	72.9%	1	1	100%	18,327	14,155	77.2%	0	0	0%	133	105	79%
	Female	11,255	7,988	71.0%	2	2	100%	26,123	19,900	76.2%	1	0	0%	165	121	73%
	Ambiguous	-	-	0.0%	-	-	0%	-	-	0.0%	0	0	0%	0	0	0%
	Unknown	0	0	0	0	0	0%	-	0	0	0	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	220	165	75.0%	-	0	0%	953	703	73.8%	0	0	0%	4	4	100%
	Feb 2009	206	140	68.0%	-	0	0%	890	672	75.5%	0	0	0%	8	4	50%
	Mar 2009	267	174	65.2%	-	0	0%	982	739	75.3%	0	0	0%	5	5	100%
	Apr 2009	220	159	72.3%	-	0	0%	969	725	74.8%	1	0	0%	4	2	50%
	May 2009	248	182	73.4%	-	0	0%	875	689	78.7%	0	0	0%	6	6	100%
	Jun 2009	258	172	66.7%	-	0	0%	909	689	75.8%	0	0	0%	5	5	100%
	Jul 2009	249	174	69.9%	-	0	0%	870	643	73.9%	0	0	0%	6	4	67%
	Aug 2009	268	191	71.3%	-	0	0%	881	641	72.8%	0	0	0%	2	1	50%
	Sep 2009	295	219	74.2%	-	0	0%	943	717	76.0%	0	0	0%	4	4	100%
	Oct 2009	261	172	65.9%	-	0	0%	857	631	73.6%	0	0	0%	1	1	100%
	Nov 2009	231	157	68.0%	-	0	0%	818	598	73.1%	0	0	0%	8	5	63%
	Dec 2009	244	167	68.4%	-	0	0%	900	687	76.3%	0	0	0%	7	5	71%
	Jan 2010	226	156	69.0%	-	0	0%	827	607	73.4%	0	0	0%	6	0	0%
	Feb 2010	238	171	71.8%	-	0	0%	753	562	74.6%	0	0	0%	8	8	100%
	Mar 2010	268	184	68.7%	-	0	0%	791	601	76.0%	0	0	0%	8	6	75%
	Apr 2010	257	179	69.6%	-	0	0%	833	621	74.5%	0	0	0%	3	2	67%
	May 2010	227	179	78.9%	-	0	0%	738	595	80.6%	0	0	0%	5	1	20%
	Jun 2010	246	171	69.5%	-	0	0%	746	557	74.7%	0	0	0%	4	1	25%
	Jul 2010	223	155	69.5%	-	0	0%	764	593	77.6%	0	0	0%	5	4	80%
	Aug 2010	260	186	71.5%	-	0	0%	810	623	76.9%	0	0	0%	3	2	67%
	Sep 2010	301	213	70.8%	-	0	0%	833	643	77.2%	0	0	0%	2	2	100%
	Oct 2010	288	196	68.1%	-	0	0%	777	586	75.4%	0	0	0%	5	5	100%
	Nov 2010	290	210	72.4%	-	0	0%	824	621	75.4%	0	0	0%	9	7	78%
	Dec 2010	291	209	71.8%	-	0	0%	731	567	77.6%	0	0	0%	3	2	67%
	Jan 2011	252	169	67.1%	-	0	0%	724	547	75.6%	0	0	0%	1	1	100%
	Feb 2011	264	177	67.0%	-	0	0%	639	490	76.7%	0	0	0%	3	3	100%
	Mar 2011	279	193	69.2%	-	0	0%	802	622	77.6%	0	0	0%	9	6	67%
	Apr 2011	269	199	74.0%	-	0	0%	710	553	77.9%	0	0	0%	10	10	100%
	May 2011	261	184	70.5%	-	0	0%	700	527	75.3%	0	0	0%	3	3	100%
	Jun 2011	276	192	69.6%	-	0	0%	678	521	76.8%	0	0	0%	4	3	75%
	Jul 2011	282	193	68.4%	-	0	0%	679	515	75.8%	0	0	0%	3	2	67%
	Aug 2011	314	237	75.5%	-	0	0%	758	559	73.7%	0	0	0%	4	3	75%
	Sep 2011	291	208	71.5%	-	0	0%	730	565	77.4%	0	0	0%	7	5	71%
	Oct 2011	263	194	73.8%	-	0	0%	711	555	78.1%	0	0	0%	3	2	67%
	Nov 2011	288	204	70.8%	-	0	0%	659	529	80.3%	0	0	0%	8	4	50%
	Dec 2011	307	215	70.0%	-	0	0%	689	517	75.0%	0	0	0%	5	5	100%
	Jan 2012	279	190	68.1%	-	0	0%	720	562	78.1%	0	0	0%	2	2	100%
	Feb 2012	255	189	74.1%	-	0	0%	638	492	77.1%	0	0	0%	7	6	86%
	Mar 2012	294	218	74.1%	-	0	0%	683	538	78.8%	0	0	0%	6	5	83%
	Apr 2012	251	180	71.7%	-	0	0%	650	494	76.0%	0	0	0%	3	3	100%
	May 2012	324	225	69.4%	-	0	0%	631	486	77.0%	0	0	0%	8	7	88%
	Jun 2012	242	179	74.0%	-	0	0%	564	443	78.5%	0	0	0%	3	3	100%
	Jul 2012	295	225	76.3%	-	0	0%	617	464	75.2%	0	0	0%	5	4	80%
	Aug 2012	304	230	75.7%	-	0	0%	787	625	79.4%	0	0	0%	2	2	100%
	Sep 2012	279	199	71.3%	-	0	0%	645	496	76.9%	0	0	0%	5	5	100%
	Oct 2012	304	223	73.4%	-	0	0%	699	565	80.8%	0	0	0%	3	2	67%
	Nov 2012	313	227	72.5%	-	0	0%	712	553	77.7%	0	0	0%	6	4	67%
	Dec 2012	293	214	73.0%	-	0	0%	631	478	75.8%	0	0	0%	8	5	63%
	Jan 2013	277	200	72.2%	-	0	0%	593	452	76.2%	0	0	0%	4	3	75%
	Feb 2013	254	182	71.7%	-	0	0%	638	516	80.9%	0	0	0%	3	3	100%
	Mar 2013	253	185	73.1%	-	0	0%	585	470	80.3%	0	0	0%	4	4	100%
	Apr 2013	289	219	75.8%	-	0	0%	617	486	78.8%	0	0	0%	9	7	78%
	May 2013	261	185	70.9%	-	0	0%	640	500	78.1%	0	0	0%	8	6	75%
	Jun 2013	271	197	72.7%	1	1	100%	602	482	80.1%	0	0	0%	4	3	75%
	Jul 2013	331	241	72.8%	-	0	0%	663	530	79.9%	0	0	0%	8	7	88%
	Aug 2013	341	244	71.6%	-	0	0%	735	582	79.2%	0	0	0%	3	2	67%
	Sep 2013	302	221	73.2%	-	0	0%	645	489	75.8%	0	0	0%	3	2	67%
	Oct 2013	331	248	74.9%	1	1	100%	714	550	77.0%	0	0	0%	3	2	67%
	Nov 2013	310	236	76.1%	1	1	100%	651	501	77.0%	0	0	0%	5	2	40%
	Dec 2013	298	222	74.5%	0	0	0%	637	491	77.1%	0	0	0%	5	4	80%

Table 1d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg for seven days in the 30 days prior)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Total	18,527	14,686	79%	22	8	36%	5,118	3,944	77%	8	5	63%	3,507	2,603	74%	
Age (years)																
0 - 11 years	7	3	43%	1	0	0%	2	1	50%	0	0	0%	4	-	0%	
12 - 17 years	32	17	53%	0	0	0%	11	4	36%	0	0	0%	8	3	38%	
18 - 24 years	380	277	73%	1	0	0%	99	70	71%	0	0	0%	77	48	62%	
25 - 34 years	1,614	1,331	82%	2	0	0%	523	409	78%	1	1	100%	290	231	80%	
35 - 44 years	3,502	2,886	82%	4	2	50%	1,011	771	76%	1	0	0%	686	518	76%	
45 - 54 years	6,358	5,038	79%	11	4	36%	1,785	1,396	78%	4	3	75%	1,276	960	75%	
55 - 64 years	6,634	5,134	77%	3	2	67%	1,687	1,293	77%	2	1	50%	1,166	843	72%	
Gender																
Male	8,727	7,004	80%	11	6	55%	2,510	1,966	78%	4	3	75%	1,839	1,404	76%	
Female	9,800	7,682	78%	11	2	18%	2,608	1,978	76%	4	2	50%	1,668	1,199	72%	
Ambiguous	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%	
Unknown	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%	
Month and Year of Episode Start Date																
Jan 2009	412	313	76%	2	2	100%	145	98	68%	1	0	0%	94	65	69%	
Feb 2009	414	346	84%	0	0	0%	118	90	76%	0	0	0%	98	75	77%	
Mar 2009	424	348	82%	0	0	0%	112	80	71%	0	0	0%	79	52	66%	
Apr 2009	423	337	80%	0	0	0%	108	88	81%	0	0	0%	88	68	77%	
May 2009	368	269	73%	0	0	0%	101	74	73%	0	0	0%	84	62	74%	
Jun 2009	409	311	76%	0	0	0%	111	83	75%	0	0	0%	75	66	88%	
Jul 2009	376	294	78%	2	0	0%	89	62	70%	0	0	0%	86	63	73%	
Aug 2009	348	285	82%	0	0	0%	97	75	77%	0	0	0%	72	52	72%	
Sep 2009	396	312	79%	0	0	0%	95	81	85%	2	1	50%	72	49	68%	
Oct 2009	433	322	74%	0	0	0%	100	77	77%	0	0	0%	90	64	71%	
Nov 2009	366	287	78%	1	1	100%	94	78	83%	0	0	0%	77	57	74%	
Dec 2009	379	295	78%	0	0	0%	113	86	76%	0	0	0%	74	55	74%	
Jan 2010	359	269	75%	0	0	0%	101	70	69%	0	0	0%	89	67	75%	
Feb 2010	325	241	74%	1	0	0%	84	60	71%	1	1	100%	60	43	72%	
Mar 2010	331	260	79%	0	0	0%	113	86	76%	0	0	0%	62	43	69%	
Apr 2010	307	240	78%	0	0	0%	100	84	84%	0	0	0%	67	53	79%	
May 2010	326	250	77%	0	0	0%	84	60	71%	0	0	0%	60	46	77%	
Jun 2010	340	272	80%	0	0	0%	77	61	79%	0	0	0%	49	42	86%	
Jul 2010	342	276	81%	0	0	0%	92	69	75%	0	0	0%	55	44	80%	
Aug 2010	325	258	79%	0	0	0%	98	72	73%	0	0	0%	71	57	80%	
Sep 2010	343	271	79%	1	1	100%	93	78	84%	0	0	0%	70	51	73%	
Oct 2010	340	278	82%	0	0	0%	95	77	81%	0	0	0%	58	50	86%	
Nov 2010	326	269	83%	0	0	0%	93	77	83%	0	0	0%	63	49	78%	
Dec 2010	356	281	79%	0	0	0%	78	61	78%	0	0	0%	64	38	59%	
Jan 2011	306	232	76%	0	0	0%	112	78	70%	0	0	0%	90	67	74%	
Feb 2011	277	217	78%	0	0	0%	96	76	79%	0	0	0%	66	49	74%	
Mar 2011	338	270	80%	1	0	0%	94	78	83%	0	0	0%	79	57	72%	
Apr 2011	322	244	76%	0	0	0%	86	67	78%	0	0	0%	52	38	73%	
May 2011	280	211	75%	0	0	0%	86	67	78%	0	0	0%	52	34	65%	
Jun 2011	286	220	77%	0	0	0%	75	65	87%	1	1	100%	41	31	76%	
Jul 2011	309	244	79%	0	0	0%	70	59	84%	0	0	0%	48	39	81%	
Aug 2011	322	256	80%	0	0	0%	78	58	74%	0	0	0%	45	39	87%	
Sep 2011	310	253	82%	0	0	0%	78	63	81%	0	0	0%	42	31	74%	
Oct 2011	269	210	78%	2	0	0%	77	64	83%	0	0	0%	56	41	73%	
Nov 2011	274	221	81%	0	0	0%	77	59	77%	0	0	0%	47	34	72%	
Dec 2011	286	236	83%	0	0	0%	72	52	72%	0	0	0%	59	48	81%	
Jan 2012	273	226	83%	0	0	0%	88	74	84%	0	0	0%	53	35	66%	
Feb 2012	266	219	82%	1	0	0%	75	56	75%	0	0	0%	53	45	85%	
Mar 2012	282	237	84%	0	0	0%	76	64	84%	0	0	0%	48	40	83%	
Apr 2012	277	221	80%	1	0	0%	86	66	77%	0	0	0%	48	37	77%	
May 2012	287	222	77%	1	0	0%	71	56	79%	0	0	0%	52	39	75%	
Jun 2012	234	193	82%	1	0	0%	60	49	82%	0	0	0%	49	39	80%	
Jul 2012	307	245	80%	0	0	0%	87	64	74%	0	0	0%	37	22	59%	
Aug 2012	284	225	79%	1	1	100%	89	68	76%	0	0	0%	51	39	76%	
Sep 2012	254	213	84%	1	0	0%	77	64	83%	1	1	100%	38	31	82%	
Oct 2012	251	202	80%	0	0	0%	69	57	83%	0	0	0%	47	32	68%	
Nov 2012	296	211	71%	0	0	0%	90	60	67%	2	1	50%	62	43	69%	
Dec 2012	261	209	80%	0	0	0%	54	34	63%	0	0	0%	46	31	67%	
Jan 2013	254	202	80%	2	1	50%	87	62	71%	0	0	0%	42	31	74%	
Feb 2013	212	180	85%	2	0	0%	56	46	82%	0	0	0%	44	36	82%	
Mar 2013	236	187	79%	0	0	0%	72	52	72%	0	0	0%	36	27	75%	
Apr 2013	226	183	81%	0	0	0%	68	54	79%	0	0	0%	37	29	78%	
May 2013	250	205	82%	1	1	100%	65	56	86%	0	0	0%	42	27	64%	
Jun 2013	244	203	83%	0	0	0%	69	51	74%	0	0	0%	34	24	71%	
Jul 2013	239	192	80%	0	0	0%	78	67	86%	0	0	0%	43	30	70%	
Aug 2013	272	229	84%	0	0	0%	61	41	67%	0	0	0%	31	17	55%	
Sep 2013	245	204	83%	0	0	0%	66	50	76%	0	0	0%	44	33	75%	
Oct 2013	242	197	81%	0	0	0%	67	50	75%	0	0	0%	47	35	74%	
Nov 2013	241	189	78%	0	0	0%	58	47	81%	0	0	0%	47	31	66%	
Dec 2013	247	194	79%	1	1	100%	57	43	75%	0	0	0%	42	31	74%	

Table 1d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg for seven days in the 30 days prior)																
	Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	3	3	100%	137	94	69%	2	1	50%	172	124	72%	2	2	100%
	0 - 11 years	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	0	0	0%	1	1	100%	-	-	0%	1	-	0%	-	-	0%
	18 - 24 years	0	0	0%	2	2	100%	-	-	0%	5	4	80%	1	1	100%
	25 - 34 years	0	0	0%	9	7	78%	-	-	0%	12	8	67%	-	-	0%
	35 - 44 years	0	0	0%	20	15	75%	-	-	0%	30	24	80%	-	-	0%
	45 - 54 years	1	1	100%	57	38	67%	1	-	0%	60	44	73%	-	-	0%
	55 - 64 years	2	2	100%	48	31	65%	1	1	100%	64	44	69%	1	1	100%
Gender	Male	1	1	100%	69	46	67%	-	-	0%	95	75	79%	2	2	100%
	Female	2	2	100%	68	48	71%	2	1	50%	77	49	64%	-	-	0%
	Ambiguous	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	1	100%	4	3	75%	-	-	0%	6	2	33%	-	-	0%
	Feb 2009	0	0	0%	3	2	67%	-	-	0%	2	2	100%	-	-	0%
	Mar 2009	0	0	0%	3	1	33%	-	-	0%	1	1	100%	-	-	0%
	Apr 2009	0	0	0%	2	1	50%	-	-	0%	1	1	100%	-	-	0%
	May 2009	0	0	0%	3	3	100%	-	-	0%	6	4	67%	-	-	0%
	Jun 2009	0	0	0%	2	2	100%	-	-	0%	7	6	86%	-	-	0%
	Jul 2009	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%
	Aug 2009	0	0	0%	1	1	100%	-	-	0%	4	1	25%	-	-	0%
	Sep 2009	0	0	0%	-	-	0%	-	-	0%	5	4	80%	-	-	0%
	Oct 2009	0	0	0%	1	-	0%	-	-	0%	4	2	50%	-	-	0%
	Nov 2009	0	0	0%	2	1	50%	-	-	0%	7	5	71%	-	-	0%
	Dec 2009	0	0	0%	2	1	50%	-	-	0%	7	6	86%	-	-	0%
	Jan 2010	0	0	0%	7	4	57%	-	-	0%	5	3	60%	-	-	0%
	Feb 2010	0	0	0%	6	3	50%	-	-	0%	5	4	80%	-	-	0%
	Mar 2010	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%
	Apr 2010	0	0	0%	4	2	50%	-	-	0%	4	3	75%	-	-	0%
	May 2010	0	0	0%	2	1	50%	-	-	0%	4	3	75%	-	-	0%
	Jun 2010	0	0	0%	5	4	80%	-	-	0%	2	2	100%	-	-	0%
	Jul 2010	0	0	0%	1	1	100%	-	-	0%	5	4	80%	-	-	0%
	Aug 2010	0	0	0%	2	1	50%	-	-	0%	2	1	50%	-	-	0%
	Sep 2010	0	0	0%	-	-	0%	-	-	0%	3	1	33%	-	-	0%
	Oct 2010	0	0	0%	3	3	100%	1	1	100%	3	3	100%	-	-	0%
	Nov 2010	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Dec 2010	0	0	0%	1	1	100%	-	-	0%	4	2	50%	-	-	0%
	Jan 2011	0	0	0%	3	1	33%	-	-	0%	4	3	75%	1	1	100%
	Feb 2011	1	1	100%	3	2	67%	-	-	0%	3	2	67%	-	-	0%
	Mar 2011	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Apr 2011	0	0	0%	3	2	67%	-	-	0%	4	4	100%	-	-	0%
	May 2011	0	0	0%	5	3	60%	-	-	0%	2	2	100%	-	-	0%
	Jun 2011	0	0	0%	2	2	100%	-	-	0%	-	-	0%	-	-	0%
	Jul 2011	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%
	Aug 2011	0	0	0%	1	1	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2011	0	0	0%	4	3	75%	1	-	0%	3	3	100%	1	1	100%
	Oct 2011	0	0	0%	1	1	100%	-	-	0%	1	-	0%	-	-	0%
	Nov 2011	0	0	0%	-	-	0%	-	-	0%	1	1	100%	-	-	0%
	Dec 2011	0	0	0%	3	2	67%	-	-	0%	1	1	100%	-	-	0%
	Jan 2012	0	0	0%	2	1	50%	-	-	0%	2	2	100%	-	-	0%
	Feb 2012	0	0	0%	2	2	100%	-	-	0%	5	4	80%	-	-	0%
	Mar 2012	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%
	Apr 2012	1	1	100%	5	5	100%	-	-	0%	3	3	100%	-	-	0%
	May 2012	0	0	0%	4	2	50%	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	0	0	0%	-	-	0%	-	-	0%	2	1	50%	-	-	0%
	Jul 2012	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	0	0	0%	4	4	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2012	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2012	0	0	0%	2	2	100%	-	-	0%	2	2	100%	-	-	0%
	Nov 2012	0	0	0%	2	2	100%	-	-	0%	5	4	80%	-	-	0%
	Dec 2012	0	0	0%	3	1	33%	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	0	0	0%	2	-	0%	-	-	0%	4	1	25%	-	-	0%
	Feb 2013	0	0	0%	3	2	67%	-	-	0%	-	-	0%	-	-	0%
	Mar 2013	0	0	0%	2	2	100%	-	-	0%	3	1	33%	-	-	0%
	Apr 2013	0	0	0%	-	-	0%	-	-	0%	3	3	100%	-	-	0%
	May 2013	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Jun 2013	0	0	0%	-	-	0%	-	-	0%	3	3	100%	-	-	0%
	Jul 2013	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%
	Aug 2013	0	0	0%	2	2	100%	-	-	0%	3	1	33%	-	-	0%
	Sep 2013	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2013	0	0	0%	4	1	25%	-	-	0%	1	1	100%	-	-	0%
	Nov 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2013	0	0	0%	1	-	0%	-	-	0%	2	1	50%	-	-	0%

Table 1d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 183-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg for seven days in the 30 days prior)										
		Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr		
		Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Age (years)	Total	33	20	61%	4	3	75%	2	1	50%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	1	1	100%	-	-	0%	-	-	0%
	18 - 24 years	3	3	100%	-	-	0%	-	-	0%
	25 - 34 years	1	-	0%	-	-	0%	1	1	100%
	35 - 44 years	4	4	100%	3	2	67%	-	-	0%
	45 - 54 years	9	6	67%	1	1	100%	-	-	0%
	55 - 64 years	15	6	40%	-	-	0%	1	-	0%
Gender	Male	11	9	82%	4	3	75%	2	1	50%
	Female	22	11	50%	-	-	0%	-	-	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	-	0%	-	-	0%	-	-	0%
	Feb 2009	1	1	100%	-	-	0%	-	-	0%
	Mar 2009	1	1	100%	-	-	0%	-	-	0%
	Apr 2009	3	3	100%	1	1	100%	-	-	0%
	May 2009	-	-	0%	-	-	0%	-	-	0%
	Jun 2009	-	-	0%	-	-	0%	-	-	0%
	Jul 2009	2	2	100%	-	-	0%	1	1	100%
	Aug 2009	-	-	0%	-	-	0%	-	-	0%
	Sep 2009	1	1	100%	-	-	0%	-	-	0%
	Oct 2009	1	-	0%	-	-	0%	-	-	0%
	Nov 2009	-	-	0%	-	-	0%	-	-	0%
	Dec 2009	1	-	0%	-	-	0%	-	-	0%
	Jan 2010	-	-	0%	-	-	0%	-	-	0%
	Feb 2010	-	-	0%	-	-	0%	-	-	0%
	Mar 2010	1	1	100%	1	1	100%	-	-	0%
	Apr 2010	-	-	0%	-	-	0%	-	-	0%
	May 2010	-	-	0%	-	-	0%	-	-	0%
	Jun 2010	1	1	100%	-	-	0%	-	-	0%
	Jul 2010	-	-	0%	-	-	0%	-	-	0%
	Aug 2010	1	1	100%	-	-	0%	-	-	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%
	Oct 2010	1	1	100%	-	-	0%	-	-	0%
	Nov 2010	-	-	0%	-	-	0%	-	-	0%
	Dec 2010	1	1	100%	-	-	0%	-	-	0%
	Jan 2011	-	-	0%	-	-	0%	-	-	0%
	Feb 2011	2	1	50%	-	-	0%	-	-	0%
	Mar 2011	1	1	100%	-	-	0%	-	-	0%
	Apr 2011	1	-	0%	-	-	0%	-	-	0%
	May 2011	-	-	0%	-	-	0%	-	-	0%
	Jun 2011	2	1	50%	-	-	0%	-	-	0%
	Jul 2011	-	-	0%	-	-	0%	-	-	0%
	Aug 2011	1	-	0%	-	-	0%	-	-	0%
	Sep 2011	2	1	50%	-	-	0%	-	-	0%
	Oct 2011	2	-	0%	-	-	0%	-	-	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%
	Dec 2011	-	-	0%	-	-	0%	-	-	0%
	Jan 2012	-	-	0%	-	-	0%	-	-	0%
	Feb 2012	-	-	0%	-	-	0%	-	-	0%
	Mar 2012	1	1	100%	-	-	0%	-	-	0%
	Apr 2012	1	-	0%	-	-	0%	-	-	0%
	May 2012	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	-	-	0%	-	-	0%	-	-	0%
	Jul 2012	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	-	-	0%	-	-	0%	-	-	0%
	Sep 2012	-	-	0%	-	-	0%	-	-	0%
	Oct 2012	-	-	0%	-	-	0%	-	-	0%
	Nov 2012	-	-	0%	-	-	0%	1	-	0%
	Dec 2012	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	-	-	0%	-	-	0%	-	-	0%
	Feb 2013	1	-	0%	-	-	0%	-	-	0%
	Mar 2013	-	-	0%	-	-	0%	-	-	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%
	May 2013	-	-	0%	-	-	0%	-	-	0%
	Jun 2013	1	-	0%	2	1	50%	-	-	0%
	Jul 2013	-	-	0%	-	-	0%	-	-	0%
	Aug 2013	-	-	0%	-	-	0%	-	-	0%
	Sep 2013	1	1	100%	-	-	0%	-	-	0%
	Oct 2013	-	-	0%	-	-	0%	-	-	0%
	Nov 2013	-	-	0%	-	-	0%	-	-	0%
	Dec 2013	1	1	100%	-	-	0%	-	-	0%

Table 2a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)													
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	17,812	5,093	28.6%	3	1	33%	49,148	18,322	37.3%	1	0	0%
	0 - 11 years	34	1	2.9%	-	-	0%	25	2	8.0%	0	0	0%
	12 - 17 years	81	6	7.4%	-	-	0%	85	16	18.8%	0	0	0%
	18 - 24 years	412	104	25.2%	-	-	0%	925	345	37.3%	0	0	0%
	25 - 34 years	1,605	582	36.3%	-	-	0%	4,297	1,931	44.9%	1	0	0%
	35 - 44 years	3,153	1,065	33.8%	2	1	50%	8,915	3,696	41.5%	0	0	0%
	45 - 54 years	5,672	1,650	29.1%	-	-	0%	16,409	6,277	38.3%	0	0	0%
	55 - 64 years	6,855	1,685	24.6%	1	-	0%	18,492	6,055	32.7%	0	0	0%
Gender	Male	5,595	1,675	29.9%	1	1	100%	20,233	7,836	38.7%	0	0	0%
	Female	12,217	3,418	28.0%	2	-	0%	28,915	10,486	36.3%	1	0	0%
	Ambiguous	-	-	0.0%	-	-	0%	-	-	0.0%	0	0	0%
	Unknown	0	0	0	0	-	0%	-	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	238	72	30.3%	-	-	0%	1,070	365	34.1%	0	0	0%
	Feb 2009	227	53	23.3%	-	-	0%	992	346	34.9%	0	0	0%
	Mar 2009	284	76	26.8%	-	-	0%	1,072	369	34.4%	0	0	0%
	Apr 2009	251	57	22.7%	-	-	0%	1,147	388	33.8%	1	0	0%
	May 2009	283	73	25.8%	-	-	0%	1,039	386	37.2%	0	0	0%
	Jun 2009	300	72	24.0%	-	-	0%	1,080	368	34.1%	0	0	0%
	Jul 2009	267	73	27.3%	-	-	0%	966	335	34.7%	0	0	0%
	Aug 2009	284	74	26.1%	-	-	0%	946	307	32.5%	0	0	0%
	Sep 2009	318	89	28.0%	-	-	0%	1,007	357	35.5%	0	0	0%
	Oct 2009	278	78	28.1%	-	-	0%	948	328	34.6%	0	0	0%
	Nov 2009	244	71	29.1%	-	-	0%	898	294	32.7%	0	0	0%
	Dec 2009	261	74	28.4%	-	-	0%	970	363	37.4%	0	0	0%
	Jan 2010	245	59	24.1%	-	-	0%	881	292	33.1%	0	0	0%
	Feb 2010	254	84	33.1%	-	-	0%	790	282	35.7%	0	0	0%
	Mar 2010	283	79	27.9%	-	-	0%	853	317	37.2%	0	0	0%
	Apr 2010	289	78	27.0%	-	-	0%	958	331	34.6%	0	0	0%
	May 2010	261	84	32.2%	-	-	0%	845	342	40.5%	0	0	0%
	Jun 2010	285	81	28.4%	-	-	0%	884	341	38.6%	0	0	0%
	Jul 2010	239	68	28.5%	-	-	0%	837	333	39.8%	0	0	0%
	Aug 2010	270	77	28.5%	-	-	0%	871	310	35.6%	0	0	0%
	Sep 2010	320	96	30.0%	-	-	0%	908	348	38.3%	0	0	0%
	Oct 2010	313	74	23.6%	-	-	0%	843	312	37.0%	0	0	0%
	Nov 2010	306	91	29.7%	-	-	0%	889	334	37.6%	0	0	0%
	Dec 2010	307	90	29.3%	-	-	0%	796	321	40.3%	0	0	0%
	Jan 2011	264	69	26.1%	-	-	0%	774	284	36.7%	0	0	0%
	Feb 2011	279	66	23.7%	-	-	0%	674	246	36.5%	0	0	0%
	Mar 2011	292	82	28.1%	-	-	0%	845	331	39.2%	0	0	0%
	Apr 2011	307	97	31.6%	-	-	0%	812	324	39.9%	0	0	0%
	May 2011	299	84	28.1%	-	-	0%	795	286	36.0%	0	0	0%
	Jun 2011	316	85	26.9%	-	-	0%	777	311	40.0%	0	0	0%
	Jul 2011	294	82	27.9%	-	-	0%	728	263	36.1%	0	0	0%
	Aug 2011	328	112	34.1%	-	-	0%	820	290	35.4%	0	0	0%
	Sep 2011	307	90	29.3%	-	-	0%	795	300	37.7%	0	0	0%
	Oct 2011	279	87	31.2%	-	-	0%	768	308	40.1%	0	0	0%
	Nov 2011	306	100	32.7%	-	-	0%	718	293	40.8%	0	0	0%
	Dec 2011	323	96	29.7%	-	-	0%	747	283	37.9%	0	0	0%
	Jan 2012	298	87	29.2%	-	-	0%	776	301	38.8%	0	0	0%
	Feb 2012	269	68	25.3%	-	-	0%	696	236	33.9%	0	0	0%
	Mar 2012	307	88	28.7%	-	-	0%	738	271	36.7%	0	0	0%
	Apr 2012	316	96	30.4%	-	-	0%	803	302	37.6%	0	0	0%
	May 2012	389	107	27.5%	-	-	0%	786	313	39.8%	0	0	0%
	Jun 2012	293	82	28.0%	-	-	0%	683	263	38.5%	0	0	0%
	Jul 2012	315	96	30.5%	-	-	0%	672	264	39.3%	0	0	0%
	Aug 2012	324	116	35.8%	-	-	0%	857	328	38.3%	0	0	0%
	Sep 2012	290	76	26.2%	-	-	0%	705	264	37.4%	0	0	0%
	Oct 2012	330	100	30.3%	-	-	0%	754	325	43.1%	0	0	0%
	Nov 2012	332	85	25.6%	-	-	0%	775	261	33.7%	0	0	0%
	Dec 2012	316	84	26.6%	-	-	0%	666	266	39.9%	0	0	0%
	Jan 2013	296	93	31.4%	-	-	0%	650	242	37.2%	0	0	0%
	Feb 2013	275	81	29.5%	-	-	0%	675	281	41.6%	0	0	0%
	Mar 2013	274	95	34.7%	-	-	0%	632	256	40.5%	0	0	0%
	Apr 2013	327	112	34.3%	-	-	0%	724	284	39.2%	0	0	0%
	May 2013	293	85	29.0%	-	-	0%	754	303	40.2%	0	0	0%
	Jun 2013	306	83	27.1%	1	-	0%	701	278	39.7%	0	0	0%
	Jul 2013	345	99	28.7%	-	-	0%	719	282	39.2%	0	0	0%
	Aug 2013	358	108	30.2%	-	-	0%	780	314	40.3%	0	0	0%
	Sep 2013	323	85	26.3%	-	-	0%	687	269	39.2%	0	0	0%
	Oct 2013	366	107	29.2%	1	1	100%	784	307	39.2%	0	0	0%
	Nov 2013	344	96	27.9%	1	-	0%	702	272	38.7%	0	0	0%
	Dec 2013	325	91	28.0%	0	-	0%	686	252	36.7%	0	0	0%

Table 2a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)																
	Dose 37 mcg/hr			Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	339	174	51%	21,245	10,088	47%	26	7	27%	6,215	3,197	51%	14	4	29%
	0 - 11 years	1	-	0%	8	3	38%	1	-	0%	3	-	0%	-	-	0%
	12 - 17 years	2	-	0%	37	11	30%	-	-	0%	14	4	29%	-	-	0%
	18 - 24 years	9	3	33%	423	182	43%	2	-	0%	121	61	50%	-	-	0%
	25 - 34 years	27	16	59%	1,911	1,051	55%	2	-	0%	614	355	58%	2	2	100%
	35 - 44 years	71	35	49%	4,031	2,108	52%	6	2	33%	1,229	649	53%	1	-	0%
	45 - 54 years	99	51	52%	7,320	3,506	48%	11	3	27%	2,201	1,141	52%	6	2	33%
	55 - 64 years	130	69	53%	7,515	3,227	43%	4	2	50%	2,033	987	49%	5	-	0%
Gender	Male	145	77	53%	9,916	4,945	50%	13	6	46%	2,974	1,629	55%	6	2	33%
	Female	194	97	50%	11,329	5,143	45%	13	1	8%	3,241	1,568	48%	8	2	25%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	6	3	50%	490	217	44%	2	2	100%	189	79	42%	1	-	0%
	Feb 2009	9	4	44%	484	231	48%	-	-	0%	152	73	48%	-	-	0%
	Mar 2009	5	3	60%	492	236	48%	-	-	0%	140	67	48%	-	-	0%
	Apr 2009	4	1	25%	532	265	50%	-	-	0%	147	80	54%	-	-	0%
	May 2009	6	5	83%	470	213	45%	-	-	0%	146	69	47%	-	-	0%
	Jun 2009	8	6	75%	496	215	43%	-	-	0%	138	64	46%	1	-	0%
	Jul 2009	8	2	25%	440	196	45%	2	-	0%	112	53	47%	1	1	100%
	Aug 2009	3	1	33%	398	182	46%	-	-	0%	129	66	51%	-	-	0%
	Sep 2009	5	3	60%	457	210	46%	-	-	0%	108	69	64%	2	-	0%
	Oct 2009	1	1	100%	486	215	44%	1	-	0%	123	60	49%	-	-	0%
	Nov 2009	8	4	50%	402	185	46%	1	1	100%	108	56	52%	-	-	0%
	Dec 2009	8	4	50%	429	191	45%	-	-	0%	135	67	50%	1	-	0%
	Jan 2010	6	-	0%	406	177	44%	-	-	0%	120	54	45%	-	-	0%
	Feb 2010	9	7	78%	362	159	44%	1	-	0%	100	46	46%	1	-	0%
	Mar 2010	8	3	38%	354	153	43%	-	-	0%	132	67	51%	-	-	0%
	Apr 2010	4	2	50%	368	166	45%	-	-	0%	122	66	54%	-	-	0%
	May 2010	6	2	33%	388	172	44%	-	-	0%	109	49	45%	1	-	0%
	Jun 2010	7	3	43%	402	195	49%	1	-	0%	103	55	53%	-	-	0%
	Jul 2010	5	3	60%	371	196	53%	-	-	0%	98	45	46%	-	-	0%
	Aug 2010	3	2	67%	363	170	47%	-	-	0%	116	58	50%	-	-	0%
	Sep 2010	2	2	100%	373	176	47%	1	1	100%	105	62	59%	-	-	0%
	Oct 2010	5	3	60%	383	193	50%	-	-	0%	115	60	52%	-	-	0%
	Nov 2010	8	4	50%	353	175	50%	-	-	0%	102	61	60%	1	-	0%
	Dec 2010	3	1	33%	404	178	44%	-	-	0%	90	50	56%	-	-	0%
	Jan 2011	1	1	100%	346	148	43%	1	1	100%	138	63	46%	-	-	0%
	Feb 2011	3	2	67%	305	166	54%	-	-	0%	109	64	59%	-	-	0%
	Mar 2011	9	5	56%	371	192	52%	-	-	0%	103	65	63%	-	-	0%
	Apr 2011	10	9	90%	386	175	45%	-	-	0%	124	67	54%	-	-	0%
	May 2011	4	2	50%	346	158	46%	-	-	0%	98	53	54%	-	-	0%
	Jun 2011	4	2	50%	344	144	42%	1	-	0%	96	54	56%	1	-	0%
	Jul 2011	4	2	50%	350	170	49%	-	-	0%	80	51	64%	-	-	0%
	Aug 2011	5	2	40%	342	157	46%	-	-	0%	94	41	44%	-	-	0%
	Sep 2011	6	3	50%	337	161	48%	-	-	0%	87	47	54%	-	-	0%
	Oct 2011	3	2	67%	306	143	47%	2	-	0%	86	51	59%	-	-	0%
	Nov 2011	7	2	29%	300	155	52%	-	-	0%	85	46	54%	-	-	0%
	Dec 2011	5	4	80%	312	146	47%	-	-	0%	88	42	48%	-	-	0%
	Jan 2012	3	2	67%	310	148	48%	-	-	0%	108	54	50%	-	-	0%
	Feb 2012	7	3	43%	300	161	54%	1	-	0%	86	51	59%	-	-	0%
	Mar 2012	7	4	57%	314	157	50%	-	-	0%	84	47	56%	-	-	0%
	Apr 2012	7	3	43%	359	184	51%	1	-	0%	118	56	47%	1	1	100%
	May 2012	8	5	63%	363	189	52%	1	-	0%	98	52	53%	-	-	0%
	Jun 2012	4	2	50%	299	141	47%	1	-	0%	82	45	55%	-	-	0%
	Jul 2012	5	2	40%	331	170	51%	-	-	0%	103	52	50%	-	-	0%
	Aug 2012	2	1	50%	297	147	49%	1	-	0%	102	59	58%	-	-	0%
	Sep 2012	5	4	80%	283	135	48%	1	-	0%	89	47	53%	1	1	100%
	Oct 2012	3	1	33%	285	127	45%	-	-	0%	83	45	54%	-	-	0%
	Nov 2012	6	3	50%	336	157	47%	-	-	0%	105	48	46%	2	1	50%
	Dec 2012	9	3	33%	286	156	55%	-	-	0%	64	26	41%	-	-	0%
	Jan 2013	5	3	60%	302	146	48%	2	1	50%	103	43	42%	-	-	0%
	Feb 2013	3	2	67%	246	131	53%	2	-	0%	64	35	55%	-	-	0%
	Mar 2013	4	3	75%	248	123	50%	-	-	0%	80	40	50%	-	-	0%
	Apr 2013	11	4	36%	280	137	49%	-	-	0%	93	43	46%	-	-	0%
	May 2013	9	5	56%	307	152	50%	1	1	100%	83	46	55%	-	-	0%
	Jun 2013	5	3	60%	288	135	47%	-	-	0%	89	49	55%	-	-	0%
	Jul 2013	9	5	56%	272	134	49%	-	-	0%	88	48	55%	-	-	0%
	Aug 2013	7	2	29%	300	146	49%	-	-	0%	75	29	39%	-	-	0%
	Sep 2013	5	3	60%	276	131	47%	1	-	0%	75	38	51%	-	-	0%
	Oct 2013	4	1	25%	274	145	53%	-	-	0%	78	45	58%	-	-	0%
	Nov 2013	7	1	14%	265	125	47%	-	-	0%	71	42	59%	-	-	0%
	Dec 2013	6	4	67%	276	130	47%	1	-	0%	67	37	55%	-	-	0%

Table 2a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)																
	Dose 100 mcg/hr			Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	4,524	2,410	53%	5	4	80%	179	88	49%	2	1	50%	233	119	51%
	0 - 11 years	6	-	0%	-	-	0%	-	-	0%	-	-	0%	0	0	0%
	12 - 17 years	9	2	22%	-	-	0%	1	-	0%	-	-	0%	2	0	0%
	18 - 24 years	91	43	47%	-	-	0%	2	2	100%	-	-	0%	5	4	80%
	25 - 34 years	375	226	60%	-	-	0%	10	8	80%	-	-	0%	13	6	46%
	35 - 44 years	870	492	57%	1	1	100%	30	15	50%	-	-	0%	37	22	59%
	45 - 54 years	1,644	892	54%	1	1	100%	72	33	46%	1	-	0%	88	45	51%
	55 - 64 years	1,529	755	49%	3	2	67%	64	30	47%	1	1	100%	88	42	48%
Gender	Male	2,316	1,323	57%	2	2	100%	83	43	52%	-	-	0%	125	70	56%
	Female	2,208	1,087	49%	3	2	67%	96	45	47%	2	1	50%	108	49	45%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%	-	-	0%	0	0	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%	-	-	0%	0	0	0%
Month and Year of Episode Start Date	Jan 2009	131	56	43%	1	1	100%	5	3	60%	-	-	0%	7	3	43%
	Feb 2009	132	69	52%	-	-	0%	5	1	20%	-	-	0%	3	2	67%
	Mar 2009	101	48	48%	-	-	0%	4	1	25%	-	-	0%	2	1	50%
	Apr 2009	120	66	55%	-	-	0%	5	3	60%	-	-	0%	7	3	43%
	May 2009	122	57	47%	-	-	0%	4	3	75%	-	-	0%	8	5	63%
	Jun 2009	107	64	60%	-	-	0%	4	3	75%	-	-	0%	9	6	67%
	Jul 2009	114	57	50%	-	-	0%	1	1	100%	-	-	0%	3	1	33%
	Aug 2009	98	49	50%	-	-	0%	3	1	33%	-	-	0%	5	0	0%
	Sep 2009	89	42	47%	-	-	0%	1	-	0%	-	-	0%	5	3	60%
	Oct 2009	108	58	54%	-	-	0%	2	-	0%	-	-	0%	6	2	33%
	Nov 2009	93	50	54%	-	-	0%	3	2	67%	-	-	0%	7	5	71%
	Dec 2009	96	52	54%	-	-	0%	5	2	40%	-	-	0%	7	5	71%
	Jan 2010	115	63	55%	-	-	0%	10	2	20%	-	-	0%	7	3	43%
	Feb 2010	74	35	47%	-	-	0%	6	1	17%	-	-	0%	5	3	60%
	Mar 2010	71	38	54%	-	-	0%	3	-	0%	-	-	0%	5	3	60%
	Apr 2010	98	64	65%	-	-	0%	3	1	33%	-	-	0%	6	5	83%
	May 2010	75	44	59%	-	-	0%	2	1	50%	-	-	0%	5	3	60%
	Jun 2010	71	47	66%	-	-	0%	6	3	50%	-	-	0%	5	2	40%
	Jul 2010	66	41	62%	-	-	0%	4	3	75%	-	-	0%	6	4	67%
	Aug 2010	86	52	60%	1	-	0%	3	1	33%	-	-	0%	3	0	0%
	Sep 2010	84	47	56%	-	-	0%	1	-	0%	-	-	0%	3	0	0%
	Oct 2010	75	53	71%	-	-	0%	7	6	86%	1	1	100%	5	4	80%
	Nov 2010	70	37	53%	-	-	0%	2	2	100%	-	-	0%	3	2	67%
	Dec 2010	77	35	45%	-	-	0%	1	1	100%	-	-	0%	4	2	50%
	Jan 2011	115	59	51%	-	-	0%	3	1	33%	-	-	0%	5	2	40%
	Feb 2011	77	45	58%	1	1	100%	2	-	0%	-	-	0%	3	1	33%
	Mar 2011	101	56	55%	-	-	0%	3	1	33%	-	-	0%	4	1	25%
	Apr 2011	70	31	44%	-	-	0%	5	2	40%	-	-	0%	7	4	57%
	May 2011	69	38	55%	-	-	0%	5	1	20%	-	-	0%	4	1	25%
	Jun 2011	59	31	53%	-	-	0%	2	1	50%	-	-	0%	0	0	0%
	Jul 2011	53	28	53%	-	-	0%	2	-	0%	-	-	0%	4	4	100%
	Aug 2011	52	34	65%	-	-	0%	1	1	100%	-	-	0%	1	1	100%
	Sep 2011	55	31	56%	-	-	0%	4	2	50%	1	-	0%	5	4	80%
	Oct 2011	68	37	54%	-	-	0%	2	2	100%	-	-	0%	1	0	0%
	Nov 2011	62	29	47%	-	-	0%	1	1	100%	-	-	0%	2	1	50%
	Dec 2011	73	41	56%	-	-	0%	4	2	50%	-	-	0%	2	2	100%
	Jan 2012	69	35	51%	-	-	0%	3	2	67%	-	-	0%	3	2	67%
	Feb 2012	60	37	62%	-	-	0%	2	1	50%	-	-	0%	6	4	67%
	Mar 2012	61	35	57%	-	-	0%	3	3	100%	-	-	0%	2	1	50%
	Apr 2012	74	37	50%	1	1	100%	5	5	100%	-	-	0%	6	3	50%
	May 2012	77	43	56%	-	-	0%	4	-	0%	-	-	0%	0	0	0%
	Jun 2012	64	37	58%	-	-	0%	2	2	100%	-	-	0%	6	1	17%
	Jul 2012	52	22	42%	-	-	0%	1	1	100%	-	-	0%	0	0	0%
	Aug 2012	61	39	64%	-	-	0%	4	3	75%	-	-	0%	1	1	100%
	Sep 2012	48	26	54%	-	-	0%	2	2	100%	-	-	0%	2	1	50%
	Oct 2012	60	23	38%	-	-	0%	4	2	50%	-	-	0%	2	2	100%
	Nov 2012	77	39	51%	-	-	0%	2	2	100%	-	-	0%	5	2	40%
	Dec 2012	54	23	43%	-	-	0%	3	1	33%	-	-	0%	1	0	0%
	Jan 2013	64	30	47%	-	-	0%	4	-	0%	-	-	0%	4	0	0%
	Feb 2013	52	27	52%	1	1	100%	3	1	33%	-	-	0%	0	0	0%
	Mar 2013	40	21	53%	-	-	0%	2	1	50%	-	-	0%	3	1	33%
	Apr 2013	59	30	51%	-	-	0%	-	-	0%	-	-	0%	5	2	40%
	May 2013	54	30	56%	-	-	0%	1	1	100%	-	-	0%	3	1	33%
	Jun 2013	55	28	51%	-	-	0%	-	-	0%	-	-	0%	5	1	20%
	Jul 2013	60	25	42%	-	-	0%	2	2	100%	-	-	0%	3	2	67%
	Aug 2013	39	17	44%	-	-	0%	2	2	100%	-	-	0%	2	1	50%
	Sep 2013	52	25	48%	-	-	0%	1	-	0%	-	-	0%	3	1	33%
	Oct 2013	56	35	63%	-	-	0%	3	1	33%	-	-	0%	1	1	100%
	Nov 2013	57	30	53%	-	-	0%	1	1	100%	-	-	0%	3	2	67%
	Dec 2013	52	32	62%	-	-	0%	1	-	0%	-	-	0%	3	2	67%

Table 2a: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Primary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Primary Tolerance Definition (≥30 mg per day in the prior 7 consecutive days)													
	Dose 162 mcg/hr			Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	2	1	50%	52	25	48%	5	3	60%	4	0	0%
	0 - 11 years	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	12 - 17 years	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	18 - 24 years	1	0	0%	3	3	100%	0	0	0%	0	0	0%
	25 - 34 years	0	0	0%	3	2	67%	0	0	0%	1	0	0%
	35 - 44 years	0	0	0%	7	4	57%	3	2	67%	1	0	0%
	45 - 54 years	0	0	0%	17	7	41%	2	1	50%	0	0	0%
	55 - 64 years	1	1	100%	21	8	38%	0	0	0%	2	0	0%
Gender	Male	2	1	50%	17	11	65%	5	3	60%	2	0	0%
	Female	0	0	0%	35	14	40%	0	0	0%	2	0	0%
	Ambiguous	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Unknown	0	0	0%	0	0	0%	0	0	0%	0	0	0%
Month and Year of Episode Start Date	Jan 2009	0	0	0%	2	0	0%	0	0	0%	0	0	0%
	Feb 2009	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	Mar 2009	0	0	0%	2	2	100%	1	0	0%	1	0	0%
	Apr 2009	0	0	0%	4	4	100%	1	1	100%	0	0	0%
	May 2009	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Jun 2009	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Jul 2009	0	0	0%	2	0	0%	0	0	0%	1	0	0%
	Aug 2009	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Sep 2009	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	Oct 2009	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Nov 2009	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Dec 2009	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Jan 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Feb 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Mar 2010	0	0	0%	1	1	100%	1	1	100%	0	0	0%
	Apr 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	May 2010	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Jun 2010	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Jul 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Aug 2010	0	0	0%	2	2	100%	0	0	0%	1	0	0%
	Sep 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Oct 2010	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Nov 2010	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Dec 2010	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Jan 2011	1	0	0%	1	0	0%	0	0	0%	0	0	0%
	Feb 2011	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	Mar 2011	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	Apr 2011	0	0	0%	2	0	0%	0	0	0%	0	0	0%
	May 2011	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Jun 2011	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	Jul 2011	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Aug 2011	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Sep 2011	1	1	100%	3	1	33%	0	0	0%	0	0	0%
	Oct 2011	0	0	0%	2	0	0%	0	0	0%	0	0	0%
	Nov 2011	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Dec 2011	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Jan 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Feb 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Mar 2012	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Apr 2012	0	0	0%	2	1	50%	0	0	0%	0	0	0%
	May 2012	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Jun 2012	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Jul 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Aug 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Sep 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Oct 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Nov 2012	0	0	0%	1	0	0%	0	0	0%	1	0	0%
	Dec 2012	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Jan 2013	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Feb 2013	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Mar 2013	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Apr 2013	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	May 2013	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Jun 2013	0	0	0%	1	0	0%	2	1	50%	0	0	0%
	Jul 2013	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Aug 2013	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Sep 2013	0	0	0%	1	1	100%	0	0	0%	0	0	0%
	Oct 2013	0	0	0%	1	0	0%	0	0	0%	0	0	0%
	Nov 2013	0	0	0%	0	0	0%	0	0	0%	0	0	0%
	Dec 2013	0	0	0%	1	1	100%	0	0	0%	0	0	0%

Table 2b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	17,812	8,518	47.8%	3	2	67%	49,148	28,665	58.3%	1	0	0%	339	233	69%
	0 - 11 years	34	2	5.9%	-	0	0%	25	4	16.0%	0	0	0%	1	0	0%
	12 - 17 years	81	18	22.2%	-	0	0%	85	25	29.4%	0	0	0%	2	0	0%
	18 - 24 years	412	164	39.8%	-	0	0%	925	494	53.4%	0	0	0%	9	6	67%
	25 - 34 years	1,605	898	56.0%	-	0	0%	4,297	2,845	66.2%	1	0	0%	27	22	81%
	35 - 44 years	3,153	1,661	52.7%	2	1	50%	8,915	5,544	62.2%	0	0	0%	71	45	63%
	45 - 54 years	5,672	2,741	48.3%	-	0	0%	16,409	9,658	58.9%	0	0	0%	99	72	73%
	55 - 64 years	6,855	3,034	44.3%	1	1	100%	18,492	10,095	54.6%	0	0	0%	130	88	68%
Gender	Male	5,595	2,786	49.8%	1	1	100%	20,233	12,138	60.0%	0	0	0%	145	104	72%
	Female	12,217	5,732	46.9%	2	1	50%	28,915	16,527	57.2%	1	0	0%	194	129	66%
	Ambiguous	-	-	0.0%	-	0	0%	-	-	0.0%	0	0	0%	0	0	0%
	Unknown	0	0	0	0	0	0%	-	0	0	0	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	238	115	48.3%	-	0	0%	1,070	609	56.9%	0	0	0%	6	6	100%
	Feb 2009	227	107	47.1%	-	0	0%	992	576	58.1%	0	0	0%	9	5	56%
	Mar 2009	284	128	45.1%	-	0	0%	1,072	596	55.6%	0	0	0%	5	5	100%
	Apr 2009	251	108	43.0%	-	0	0%	1,147	618	53.9%	1	0	0%	4	2	50%
	May 2009	283	136	48.1%	-	0	0%	1,039	603	58.0%	0	0	0%	6	5	83%
	Jun 2009	300	120	40.0%	-	0	0%	1,080	624	57.8%	0	0	0%	8	6	75%
	Jul 2009	267	124	46.4%	-	0	0%	966	539	55.8%	0	0	0%	8	5	63%
	Aug 2009	284	135	47.5%	-	0	0%	946	503	53.2%	0	0	0%	3	2	67%
	Sep 2009	318	149	46.9%	-	0	0%	1,007	585	58.1%	0	0	0%	5	5	100%
	Oct 2009	278	136	48.9%	-	0	0%	948	549	57.9%	0	0	0%	1	1	100%
	Nov 2009	244	112	45.9%	-	0	0%	898	471	52.4%	0	0	0%	8	5	63%
	Dec 2009	261	125	47.9%	-	0	0%	970	562	57.9%	0	0	0%	8	5	63%
	Jan 2010	245	100	40.8%	-	0	0%	881	487	55.3%	0	0	0%	6	0	0%
	Feb 2010	254	125	49.2%	-	0	0%	790	458	58.0%	0	0	0%	9	7	78%
	Mar 2010	283	123	43.5%	-	0	0%	853	479	56.2%	0	0	0%	8	6	75%
	Apr 2010	289	139	48.1%	-	0	0%	958	549	57.3%	0	0	0%	4	2	50%
	May 2010	261	141	54.0%	-	0	0%	845	528	62.5%	0	0	0%	6	2	33%
	Jun 2010	285	136	47.7%	-	0	0%	884	511	57.8%	0	0	0%	7	4	57%
	Jul 2010	239	110	46.0%	-	0	0%	837	507	60.6%	0	0	0%	5	4	80%
	Aug 2010	270	124	45.9%	-	0	0%	871	502	57.6%	0	0	0%	3	2	67%
	Sep 2010	320	162	50.6%	-	0	0%	908	557	61.3%	0	0	0%	2	2	100%
	Oct 2010	313	130	41.5%	-	0	0%	843	483	57.3%	0	0	0%	5	5	100%
	Nov 2010	306	154	50.3%	-	0	0%	889	538	60.5%	0	0	0%	8	6	75%
	Dec 2010	307	147	47.9%	-	0	0%	796	474	59.5%	0	0	0%	3	2	67%
	Jan 2011	264	122	46.2%	-	0	0%	774	447	57.8%	0	0	0%	1	1	100%
	Feb 2011	279	122	43.7%	-	0	0%	674	398	59.1%	0	0	0%	3	3	100%
	Mar 2011	292	132	45.2%	-	0	0%	845	516	61.1%	0	0	0%	9	6	67%
	Apr 2011	307	156	50.8%	-	0	0%	812	473	58.3%	0	0	0%	10	9	90%
	May 2011	299	140	46.8%	-	0	0%	795	438	55.1%	0	0	0%	4	3	75%
	Jun 2011	316	154	48.7%	-	0	0%	777	458	58.9%	0	0	0%	4	2	50%
	Jul 2011	294	136	46.3%	-	0	0%	728	419	57.6%	0	0	0%	4	2	50%
	Aug 2011	328	176	53.7%	-	0	0%	820	450	54.9%	0	0	0%	5	3	60%
	Sep 2011	307	149	48.5%	-	0	0%	795	480	60.4%	0	0	0%	6	5	83%
	Oct 2011	279	145	52.0%	-	0	0%	768	469	61.1%	0	0	0%	3	2	67%
	Nov 2011	306	147	48.0%	-	0	0%	718	437	60.9%	0	0	0%	7	4	57%
	Dec 2011	323	159	49.2%	-	0	0%	747	436	58.4%	0	0	0%	5	5	100%
	Jan 2012	298	136	45.6%	-	0	0%	776	464	59.8%	0	0	0%	3	2	67%
	Feb 2012	269	127	47.2%	-	0	0%	696	384	55.2%	0	0	0%	7	5	71%
	Mar 2012	307	146	47.6%	-	0	0%	738	441	59.8%	0	0	0%	7	5	71%
	Apr 2012	316	152	48.1%	-	0	0%	803	465	57.9%	0	0	0%	7	3	43%
	May 2012	389	174	44.7%	-	0	0%	786	476	60.6%	0	0	0%	8	6	75%
	Jun 2012	293	140	47.8%	-	0	0%	683	404	59.2%	0	0	0%	4	3	75%
	Jul 2012	315	168	53.3%	-	0	0%	672	394	58.6%	0	0	0%	5	4	80%
	Aug 2012	324	172	53.1%	-	0	0%	857	508	59.3%	0	0	0%	2	2	100%
	Sep 2012	290	144	49.7%	-	0	0%	705	424	60.1%	0	0	0%	5	5	100%
	Oct 2012	330	161	48.8%	-	0	0%	754	468	62.1%	0	0	0%	3	1	33%
	Nov 2012	332	160	48.2%	-	0	0%	775	435	56.1%	0	0	0%	6	3	50%
	Dec 2012	316	156	49.4%	-	0	0%	666	394	59.2%	0	0	0%	9	5	56%
	Jan 2013	296	143	48.3%	-	0	0%	650	383	58.9%	0	0	0%	5	3	60%
	Feb 2013	275	136	49.5%	-	0	0%	675	419	62.1%	0	0	0%	3	3	100%
	Mar 2013	274	142	51.8%	-	0	0%	632	382	60.4%	0	0	0%	4	4	100%
	Apr 2013	327	179	54.7%	-	0	0%	724	440	60.8%	0	0	0%	11	7	64%
	May 2013	293	131	44.7%	-	0	0%	754	448	59.4%	0	0	0%	9	6	67%
	Jun 2013	306	140	45.8%	1	0	0%	701	428	61.1%	0	0	0%	5	4	80%
	Jul 2013	345	170	49.3%	-	0	0%	719	434	60.4%	0	0	0%	9	7	78%
	Aug 2013	358	169	47.2%	-	0	0%	780	460	59.0%	0	0	0%	7	4	57%
	Sep 2013	323	152	47.1%	-	0	0%	687	402	58.5%	0	0	0%	5	3	60%
	Oct 2013	366	178	48.6%	1	1	100%	784	475	60.6%	0	0	0%	4	2	50%
	Nov 2013	344	162	47.1%	1	1	100%	702	418	59.5%	0	0	0%	7	2	29%
	Dec 2013	325	156	48.0%	0	0	0%	686	390	56.9%	0	0	0%	6	5	83%

Table 2b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	21,245	14,126	66%	26	8	31%	6,215	4,211	68%	14	7	50%	4,524	3,032	67%
	0 - 11 years	8	3	38%	1	0	0%	3	-	0%	0	0	0%	6	1	17%
	12 - 17 years	37	17	46%	0	0	0%	14	4	29%	0	0	0%	9	3	33%
	18 - 24 years	423	254	60%	2	0	0%	121	76	63%	0	0	0%	91	52	57%
	25 - 34 years	1,911	1,387	73%	2	0	0%	614	443	72%	2	2	100%	375	284	76%
	35 - 44 years	4,031	2,875	71%	6	2	33%	1,229	857	70%	1	0	0%	870	607	70%
	45 - 54 years	7,320	4,882	67%	11	4	36%	2,201	1,507	68%	6	4	67%	1,644	1,121	68%
	55 - 64 years	7,515	4,708	63%	4	2	50%	2,033	1,324	65%	5	1	20%	1,529	964	63%
Gender	Male	9,916	6,779	68%	13	7	54%	2,974	2,091	70%	6	4	67%	2,316	1,621	70%
	Female	11,329	7,347	65%	13	1	8%	3,241	2,120	65%	8	3	38%	2,208	1,411	64%
	Ambiguous	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
	Unknown	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	490	318	65%	2	2	100%	189	112	59%	1	0	0%	131	79	60%
	Feb 2009	484	338	70%	0	0	0%	152	99	65%	0	0	0%	132	92	70%
	Mar 2009	492	332	67%	0	0	0%	140	85	61%	0	0	0%	101	60	59%
	Apr 2009	532	355	67%	0	0	0%	147	104	71%	0	0	0%	120	85	71%
	May 2009	470	290	62%	0	0	0%	146	91	62%	0	0	0%	122	76	62%
	Jun 2009	496	317	64%	0	0	0%	138	93	67%	1	0	0%	107	72	67%
	Jul 2009	440	280	64%	2	0	0%	112	75	67%	1	1	100%	114	70	61%
	Aug 2009	398	259	65%	0	0	0%	129	89	69%	0	0	0%	98	61	62%
	Sep 2009	457	302	66%	0	0	0%	108	82	76%	2	1	50%	89	55	62%
	Oct 2009	486	297	61%	1	0	0%	123	83	67%	0	0	0%	108	73	68%
	Nov 2009	402	257	64%	1	1	100%	108	79	73%	0	0	0%	93	60	65%
	Dec 2009	429	278	65%	0	0	0%	135	90	67%	1	0	0%	96	67	70%
	Jan 2010	406	255	63%	0	0	0%	120	72	60%	0	0	0%	115	76	66%
	Feb 2010	362	226	62%	1	0	0%	100	61	61%	1	1	100%	74	46	62%
	Mar 2010	354	229	65%	0	0	0%	132	87	66%	0	0	0%	71	44	62%
	Apr 2010	368	244	66%	0	0	0%	122	91	75%	0	0	0%	98	74	76%
	May 2010	388	250	64%	0	0	0%	109	66	61%	1	0	0%	75	54	72%
	Jun 2010	402	267	66%	1	0	0%	103	77	75%	0	0	0%	71	53	75%
	Jul 2010	371	255	69%	0	0	0%	98	64	65%	0	0	0%	66	51	77%
	Aug 2010	363	239	66%	0	0	0%	116	76	66%	0	0	0%	86	62	72%
	Sep 2010	373	249	67%	1	1	100%	105	78	74%	0	0	0%	84	59	70%
	Oct 2010	383	268	70%	0	0	0%	115	78	68%	0	0	0%	75	61	81%
	Nov 2010	353	243	69%	0	0	0%	102	79	77%	1	0	0%	70	50	71%
	Dec 2010	404	256	63%	0	0	0%	90	67	74%	0	0	0%	77	42	55%
	Jan 2011	346	220	64%	1	1	100%	138	88	64%	0	0	0%	115	77	67%
	Feb 2011	305	213	70%	0	0	0%	109	78	72%	0	0	0%	77	53	69%
	Mar 2011	371	252	68%	0	0	0%	103	79	77%	0	0	0%	101	70	69%
	Apr 2011	386	245	63%	0	0	0%	124	83	67%	0	0	0%	70	44	63%
	May 2011	346	215	62%	0	0	0%	98	65	66%	0	0	0%	69	44	64%
	Jun 2011	344	224	65%	1	0	0%	96	69	72%	1	1	100%	59	38	64%
	Jul 2011	350	229	65%	0	0	0%	80	63	79%	0	0	0%	53	38	72%
	Aug 2011	342	228	67%	0	0	0%	94	59	63%	0	0	0%	52	44	85%
	Sep 2011	337	237	70%	0	0	0%	87	63	72%	0	0	0%	55	36	65%
	Oct 2011	306	202	66%	2	0	0%	86	63	73%	0	0	0%	68	45	66%
	Nov 2011	300	210	70%	0	0	0%	85	60	71%	0	0	0%	62	41	66%
	Dec 2011	312	210	67%	0	0	0%	88	56	64%	0	0	0%	73	51	70%
	Jan 2012	310	219	71%	0	0	0%	108	74	69%	0	0	0%	69	43	62%
	Feb 2012	300	218	73%	1	0	0%	86	60	70%	0	0	0%	60	48	80%
	Mar 2012	314	222	71%	0	0	0%	84	62	74%	0	0	0%	61	48	79%
	Apr 2012	359	251	70%	1	0	0%	118	79	67%	1	1	100%	74	48	65%
	May 2012	363	241	66%	1	0	0%	98	66	67%	0	0	0%	77	51	66%
	Jun 2012	299	203	68%	1	0	0%	82	58	71%	0	0	0%	64	47	73%
	Jul 2012	331	226	68%	0	0	0%	103	68	66%	0	0	0%	52	30	58%
	Aug 2012	297	202	68%	1	1	100%	102	70	69%	0	0	0%	61	44	72%
	Sep 2012	283	195	69%	1	0	0%	89	58	65%	1	1	100%	48	38	79%
	Oct 2012	285	179	63%	0	0	0%	83	57	69%	0	0	0%	60	35	58%
	Nov 2012	336	211	63%	0	0	0%	105	63	60%	2	1	50%	77	48	62%
	Dec 2012	286	200	70%	0	0	0%	64	37	58%	0	0	0%	54	33	61%
	Jan 2013	302	198	66%	2	1	50%	103	62	60%	0	0	0%	64	37	58%
	Feb 2013	246	185	75%	2	0	0%	64	46	72%	0	0	0%	52	39	75%
	Mar 2013	248	161	65%	0	0	0%	80	50	63%	0	0	0%	40	30	75%
	Apr 2013	280	197	70%	0	0	0%	93	63	68%	0	0	0%	59	39	66%
	May 2013	307	203	66%	1	1	100%	83	60	72%	0	0	0%	54	33	61%
	Jun 2013	288	199	69%	0	0	0%	89	60	67%	0	0	0%	55	36	65%
	Jul 2013	272	192	71%	0	0	0%	88	66	75%	0	0	0%	60	36	60%
	Aug 2013	300	204	68%	0	0	0%	75	44	59%	0	0	0%	39	21	54%
	Sep 2013	276	190	69%	1	0	0%	75	50	67%	0	0	0%	52	32	62%
	Oct 2013	274	193	70%	0	0	0%	78	52	67%	0	0	0%	56	38	68%
	Nov 2013	265	166	63%	0	0	0%	71	52	73%	0	0	0%	57	37	65%
	Dec 2013	276	182	66%	1	0	0%	67	50	75%	0	0	0%	52	38	73%

Table 2b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)																
		Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr		
		Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Age (years)	Total	5	4	80%	179	108	60%	2	1	50%	233	143	61%	2	2	100%
	0 - 11 years	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	0	0	0%	1	-	0%	-	-	0%	2	-	0%	-	-	0%
	18 - 24 years	0	0	0%	2	2	100%	-	-	0%	5	4	80%	1	1	100%
	25 - 34 years	0	0	0%	10	8	80%	-	-	0%	13	9	69%	-	-	0%
	35 - 44 years	1	1	100%	30	22	73%	-	-	0%	37	26	70%	-	-	0%
	45 - 54 years	1	1	100%	72	38	53%	1	-	0%	88	54	61%	-	-	0%
	55 - 64 years	3	2	67%	64	38	59%	1	1	100%	88	50	57%	1	1	100%
Gender	Male	2	2	100%	83	50	60%	-	-	0%	125	85	68%	2	2	100%
	Female	3	2	67%	96	58	60%	2	1	50%	108	58	54%	-	-	0%
	Ambiguous	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	1	100%	5	3	60%	-	-	0%	7	3	43%	-	-	0%
	Feb 2009	0	0	0%	5	2	40%	-	-	0%	3	3	100%	-	-	0%
	Mar 2009	0	0	0%	4	2	50%	-	-	0%	2	1	50%	-	-	0%
	Apr 2009	0	0	0%	5	3	60%	-	-	0%	7	4	57%	-	-	0%
	May 2009	0	0	0%	4	3	75%	-	-	0%	8	5	63%	-	-	0%
	Jun 2009	0	0	0%	4	3	75%	-	-	0%	9	7	78%	-	-	0%
	Jul 2009	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%
	Aug 2009	0	0	0%	3	2	67%	-	-	0%	5	1	20%	-	-	0%
	Sep 2009	0	0	0%	1	-	0%	-	-	0%	5	4	80%	-	-	0%
	Oct 2009	0	0	0%	2	1	50%	-	-	0%	6	2	33%	-	-	0%
	Nov 2009	0	0	0%	3	2	67%	-	-	0%	7	5	71%	-	-	0%
	Dec 2009	0	0	0%	5	4	80%	-	-	0%	7	5	71%	-	-	0%
	Jan 2010	0	0	0%	10	3	30%	-	-	0%	7	3	43%	-	-	0%
	Feb 2010	0	0	0%	6	2	33%	-	-	0%	5	4	80%	-	-	0%
	Mar 2010	0	0	0%	3	-	0%	-	-	0%	5	4	80%	-	-	0%
	Apr 2010	0	0	0%	3	1	33%	-	-	0%	6	5	83%	-	-	0%
	May 2010	0	0	0%	2	1	50%	-	-	0%	5	4	80%	-	-	0%
	Jun 2010	0	0	0%	6	5	83%	-	-	0%	5	3	60%	-	-	0%
	Jul 2010	0	0	0%	4	3	75%	-	-	0%	6	4	67%	-	-	0%
	Aug 2010	1	0	0%	3	1	33%	-	-	0%	3	1	33%	-	-	0%
	Sep 2010	0	0	0%	1	-	0%	-	-	0%	3	1	33%	-	-	0%
	Oct 2010	0	0	0%	7	6	86%	1	1	100%	5	5	100%	-	-	0%
	Nov 2010	0	0	0%	2	2	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2010	0	0	0%	1	1	100%	-	-	0%	4	2	50%	-	-	0%
	Jan 2011	0	0	0%	3	1	33%	-	-	0%	5	3	60%	1	1	100%
	Feb 2011	1	1	100%	2	1	50%	-	-	0%	3	1	33%	-	-	0%
	Mar 2011	0	0	0%	3	2	67%	-	-	0%	4	1	25%	-	-	0%
	Apr 2011	0	0	0%	5	3	60%	-	-	0%	7	5	71%	-	-	0%
	May 2011	0	0	0%	5	3	60%	-	-	0%	4	2	50%	-	-	0%
	Jun 2011	0	0	0%	2	1	50%	-	-	0%	-	-	0%	-	-	0%
	Jul 2011	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%
	Aug 2011	0	0	0%	1	1	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2011	0	0	0%	4	2	50%	1	-	0%	5	4	80%	1	1	100%
	Oct 2011	0	0	0%	2	2	100%	-	-	0%	1	-	0%	-	-	0%
	Nov 2011	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Dec 2011	0	0	0%	4	2	50%	-	-	0%	2	2	100%	-	-	0%
	Jan 2012	0	0	0%	3	2	67%	-	-	0%	3	2	67%	-	-	0%
	Feb 2012	0	0	0%	2	2	100%	-	-	0%	6	4	67%	-	-	0%
	Mar 2012	0	0	0%	3	3	100%	-	-	0%	2	2	100%	-	-	0%
	Apr 2012	1	1	100%	5	5	100%	-	-	0%	6	5	83%	-	-	0%
	May 2012	0	0	0%	4	1	25%	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	0	0	0%	2	2	100%	-	-	0%	6	1	17%	-	-	0%
	Jul 2012	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	0	0	0%	4	4	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2012	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2012	0	0	0%	4	3	75%	-	-	0%	2	2	100%	-	-	0%
	Nov 2012	0	0	0%	2	2	100%	-	-	0%	5	3	60%	-	-	0%
	Dec 2012	0	0	0%	3	1	33%	-	-	0%	1	-	0%	-	-	0%
	Jan 2013	0	0	0%	4	-	0%	-	-	0%	4	1	25%	-	-	0%
	Feb 2013	1	1	100%	3	2	67%	-	-	0%	-	-	0%	-	-	0%
	Mar 2013	0	0	0%	2	1	50%	-	-	0%	3	1	33%	-	-	0%
	Apr 2013	0	0	0%	-	-	0%	-	-	0%	5	3	60%	-	-	0%
	May 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%
	Jun 2013	0	0	0%	-	-	0%	-	-	0%	5	2	40%	-	-	0%
	Jul 2013	0	0	0%	2	2	100%	-	-	0%	3	3	100%	-	-	0%
	Aug 2013	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Sep 2013	0	0	0%	1	-	0%	-	-	0%	3	1	33%	-	-	0%
	Oct 2013	0	0	0%	3	1	33%	-	-	0%	1	1	100%	-	-	0%
	Nov 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2013	0	0	0%	1	-	0%	-	-	0%	3	2	67%	-	-	0%

Table 2b: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Secondary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Secondary Tolerance Definition (≥30 mg per day for seven days in the 30 days prior)										
	Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	52	30	58%	5	3	60%	4	1	25%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	1	1	100%	-	-	0%	-	-	0%
	18 - 24 years	3	3	100%	-	-	0%	-	-	0%
	25 - 34 years	3	2	67%	-	-	0%	1	1	100%
	35 - 44 years	7	4	57%	3	2	67%	1	-	0%
	45 - 54 years	17	10	59%	2	1	50%	-	-	0%
	55 - 64 years	21	10	48%	-	-	0%	2	-	0%
Gender	Male	17	12	71%	5	3	60%	2	1	50%
	Female	35	18	51%	-	-	0%	2	-	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	2	1	50%	-	-	0%	-	-	0%
	Feb 2009	2	1	50%	-	-	0%	-	-	0%
	Mar 2009	2	2	100%	1	-	0%	1	-	0%
	Apr 2009	4	4	100%	1	1	100%	-	-	0%
	May 2009	1	1	100%	-	-	0%	-	-	0%
	Jun 2009	1	-	0%	-	-	0%	-	-	0%
	Jul 2009	2	2	100%	-	-	0%	1	1	100%
	Aug 2009	-	-	0%	-	-	0%	-	-	0%
	Sep 2009	2	2	100%	-	-	0%	-	-	0%
	Oct 2009	-	-	0%	-	-	0%	-	-	0%
	Nov 2009	1	1	100%	-	-	0%	-	-	0%
	Dec 2009	-	-	0%	-	-	0%	-	-	0%
	Jan 2010	-	-	0%	-	-	0%	-	-	0%
	Feb 2010	-	-	0%	-	-	0%	-	-	0%
	Mar 2010	1	1	100%	1	1	100%	-	-	0%
	Apr 2010	-	-	0%	-	-	0%	-	-	0%
	May 2010	1	-	0%	-	-	0%	-	-	0%
	Jun 2010	1	-	0%	-	-	0%	-	-	0%
	Jul 2010	-	-	0%	-	-	0%	-	-	0%
	Aug 2010	2	2	100%	-	-	0%	1	-	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%
	Oct 2010	1	1	100%	-	-	0%	-	-	0%
	Nov 2010	-	-	0%	-	-	0%	-	-	0%
	Dec 2010	1	1	100%	-	-	0%	-	-	0%
	Jan 2011	1	-	0%	-	-	0%	-	-	0%
	Feb 2011	2	1	50%	-	-	0%	-	-	0%
	Mar 2011	2	1	50%	-	-	0%	-	-	0%
	Apr 2011	2	-	0%	-	-	0%	-	-	0%
	May 2011	-	-	0%	-	-	0%	-	-	0%
	Jun 2011	2	1	50%	-	-	0%	-	-	0%
	Jul 2011	-	-	0%	-	-	0%	-	-	0%
	Aug 2011	1	-	0%	-	-	0%	-	-	0%
	Sep 2011	3	2	67%	-	-	0%	-	-	0%
	Oct 2011	2	-	0%	-	-	0%	-	-	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%
	Dec 2011	-	-	0%	-	-	0%	-	-	0%
	Jan 2012	-	-	0%	-	-	0%	-	-	0%
	Feb 2012	-	-	0%	-	-	0%	-	-	0%
	Mar 2012	1	-	0%	-	-	0%	-	-	0%
	Apr 2012	2	1	50%	-	-	0%	-	-	0%
	May 2012	1	1	100%	-	-	0%	-	-	0%
	Jun 2012	1	-	0%	-	-	0%	-	-	0%
	Jul 2012	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	-	-	0%	-	-	0%	-	-	0%
	Sep 2012	-	-	0%	-	-	0%	-	-	0%
	Oct 2012	-	-	0%	-	-	0%	-	-	0%
	Nov 2012	1	-	0%	-	-	0%	1	-	0%
	Dec 2012	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	-	-	0%	-	-	0%	-	-	0%
	Feb 2013	1	-	0%	-	-	0%	-	-	0%
	Mar 2013	1	1	100%	-	-	0%	-	-	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%
	May 2013	1	1	100%	-	-	0%	-	-	0%
	Jun 2013	1	-	0%	2	1	50%	-	-	0%
	Jul 2013	-	-	0%	-	-	0%	-	-	0%
	Aug 2013	-	-	0%	-	-	0%	-	-	0%
	Sep 2013	1	1	100%	-	-	0%	-	-	0%
	Oct 2013	1	-	0%	-	-	0%	-	-	0%
	Nov 2013	-	-	0%	-	-	0%	-	-	0%
	Dec 2013	1	1	100%	-	-	0%	-	-	0%

Table 2c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			Dose 37 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Total	17,812	8,739	49.1%	3	2	67%	49,148	26,155	53.2%	1	0	0%	339	200	59%	
Age (years)																
0 - 11 years	34	7	20.6%	-	0	0%	25	6	24.0%	0	0	0%	1	0	0%	
12 - 17 years	81	25	30.9%	-	0	0%	85	31	36.5%	0	0	0%	2	0	0%	
18 - 24 years	412	181	43.9%	-	0	0%	925	470	50.8%	0	0	0%	9	4	44%	
25 - 34 years	1,605	945	58.9%	-	0	0%	4,297	2,619	60.9%	1	0	0%	27	18	67%	
35 - 44 years	3,153	1,732	54.9%	2	2	100%	8,915	5,098	57.2%	0	0	0%	71	39	55%	
45 - 54 years	5,672	2,807	49.5%	-	0	0%	16,409	8,870	54.1%	0	0	0%	99	60	61%	
55 - 64 years	6,855	3,042	44.4%	1	0	0%	18,492	9,061	49.0%	0	0	0%	130	79	61%	
Gender																
Male	5,595	2,805	50.1%	1	1	100%	20,233	10,836	53.6%	0	0	0%	145	91	63%	
Female	12,217	5,934	48.6%	2	1	50%	28,915	15,319	53.0%	1	0	0%	194	109	56%	
Ambiguous	-	-	0.0%	-	0	0%	-	-	0.0%	0	0	0%	0	0	0%	
Unknown	0	0	0	0	0	0%	-	0	0	0	0	0%	0	0	0%	
Month and Year of Episode Start Date																
Jan 2009	238	124	52.1%	-	0	0%	1,070	536	50.1%	0	0	0%	6	3	50%	
Feb 2009	227	102	44.9%	-	0	0%	992	484	48.8%	0	0	0%	9	4	44%	
Mar 2009	284	126	44.4%	-	0	0%	1,072	545	50.8%	0	0	0%	5	3	60%	
Apr 2009	251	117	46.6%	-	0	0%	1,147	589	51.4%	1	0	0%	4	2	50%	
May 2009	283	137	48.4%	-	0	0%	1,039	566	54.5%	0	0	0%	6	5	83%	
Jun 2009	300	130	43.3%	-	0	0%	1,080	525	48.6%	0	0	0%	8	7	88%	
Jul 2009	267	133	49.8%	-	0	0%	966	497	51.4%	0	0	0%	8	4	50%	
Aug 2009	284	128	45.1%	-	0	0%	946	458	48.4%	0	0	0%	3	2	67%	
Sep 2009	318	153	48.1%	-	0	0%	1,007	516	51.2%	0	0	0%	5	5	100%	
Oct 2009	278	125	45.0%	-	0	0%	948	473	49.9%	0	0	0%	1	1	100%	
Nov 2009	244	113	46.3%	-	0	0%	898	444	49.4%	0	0	0%	8	4	50%	
Dec 2009	261	120	46.0%	-	0	0%	970	533	54.9%	0	0	0%	8	4	50%	
Jan 2010	245	114	46.5%	-	0	0%	881	444	50.4%	0	0	0%	6	0	0%	
Feb 2010	254	135	53.1%	-	0	0%	790	414	52.4%	0	0	0%	9	9	100%	
Mar 2010	283	137	48.4%	-	0	0%	853	448	52.5%	0	0	0%	8	5	63%	
Apr 2010	289	130	45.0%	-	0	0%	958	486	50.7%	0	0	0%	4	2	50%	
May 2010	261	137	52.5%	-	0	0%	845	463	54.8%	0	0	0%	6	2	33%	
Jun 2010	285	139	48.8%	-	0	0%	884	470	53.2%	0	0	0%	7	3	43%	
Jul 2010	239	115	48.1%	-	0	0%	837	462	55.2%	0	0	0%	5	3	60%	
Aug 2010	270	135	50.0%	-	0	0%	871	457	52.5%	0	0	0%	3	2	67%	
Sep 2010	320	144	45.0%	-	0	0%	908	502	55.3%	0	0	0%	2	2	100%	
Oct 2010	313	145	46.3%	-	0	0%	843	438	52.0%	0	0	0%	5	3	60%	
Nov 2010	306	147	48.0%	-	0	0%	889	455	51.2%	0	0	0%	8	5	63%	
Dec 2010	307	142	46.3%	-	0	0%	796	435	54.6%	0	0	0%	3	1	33%	
Jan 2011	264	120	45.5%	-	0	0%	774	397	51.3%	0	0	0%	1	1	100%	
Feb 2011	279	130	46.6%	-	0	0%	674	344	51.0%	0	0	0%	3	2	67%	
Mar 2011	292	154	52.7%	-	0	0%	845	459	54.3%	0	0	0%	9	5	56%	
Apr 2011	307	156	50.8%	-	0	0%	812	439	54.1%	0	0	0%	10	9	90%	
May 2011	299	135	45.2%	-	0	0%	795	419	52.7%	0	0	0%	4	3	75%	
Jun 2011	316	145	45.9%	-	0	0%	777	433	55.7%	0	0	0%	4	2	50%	
Jul 2011	294	148	50.3%	-	0	0%	728	375	51.5%	0	0	0%	4	2	50%	
Aug 2011	328	171	52.1%	-	0	0%	820	418	51.0%	0	0	0%	5	2	40%	
Sep 2011	307	144	46.9%	-	0	0%	795	419	52.7%	0	0	0%	6	4	67%	
Oct 2011	279	143	51.3%	-	0	0%	768	435	56.6%	0	0	0%	3	2	67%	
Nov 2011	306	155	50.7%	-	0	0%	718	409	57.0%	0	0	0%	7	2	29%	
Dec 2011	323	151	46.7%	-	0	0%	747	388	51.9%	0	0	0%	5	4	80%	
Jan 2012	298	134	45.0%	-	0	0%	776	423	54.5%	0	0	0%	3	2	67%	
Feb 2012	269	131	48.7%	-	0	0%	696	373	53.6%	0	0	0%	7	5	71%	
Mar 2012	307	152	49.5%	-	0	0%	738	383	51.9%	0	0	0%	7	5	71%	
Apr 2012	316	155	49.1%	-	0	0%	803	436	54.3%	0	0	0%	7	3	43%	
May 2012	389	190	48.8%	-	0	0%	786	432	55.0%	0	0	0%	8	6	75%	
Jun 2012	293	151	51.5%	-	0	0%	683	374	54.8%	0	0	0%	4	2	50%	
Jul 2012	315	158	50.2%	-	0	0%	672	373	55.5%	0	0	0%	5	2	40%	
Aug 2012	324	176	54.3%	-	0	0%	857	469	54.7%	0	0	0%	2	1	50%	
Sep 2012	290	135	46.6%	-	0	0%	705	370	52.5%	0	0	0%	5	4	80%	
Oct 2012	330	173	52.4%	-	0	0%	754	453	60.1%	0	0	0%	3	2	67%	
Nov 2012	332	170	51.2%	-	0	0%	775	397	51.2%	0	0	0%	6	4	67%	
Dec 2012	316	154	48.7%	-	0	0%	666	363	54.5%	0	0	0%	9	3	33%	
Jan 2013	296	151	51.0%	-	0	0%	650	354	54.5%	0	0	0%	5	3	60%	
Feb 2013	275	139	50.5%	-	0	0%	675	394	58.4%	0	0	0%	3	3	100%	
Mar 2013	274	148	54.0%	-	0	0%	632	368	58.2%	0	0	0%	4	3	75%	
Apr 2013	327	180	55.0%	-	0	0%	724	410	56.6%	0	0	0%	11	5	45%	
May 2013	293	148	50.5%	-	0	0%	754	436	57.8%	0	0	0%	9	6	67%	
Jun 2013	306	168	54.9%	1	1	100%	701	390	55.6%	0	0	0%	5	3	60%	
Jul 2013	345	168	48.7%	-	0	0%	719	412	57.3%	0	0	0%	9	7	78%	
Aug 2013	358	171	47.8%	-	0	0%	780	428	54.9%	0	0	0%	7	2	29%	
Sep 2013	323	161	49.8%	-	0	0%	687	373	54.3%	0	0	0%	5	4	80%	
Oct 2013	366	186	50.8%	1	1	100%	784	426	54.3%	0	0	0%	4	1	25%	
Nov 2013	344	188	54.7%	1	0	0%	702	381	54.3%	0	0	0%	7	1	14%	
Dec 2013	325	172	52.9%	0	0	0%	686	362	52.8%	0	0	0%	6	4	67%	

Table 2c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			Dose 100 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	21,245	12,517	59%	26	7	27%	6,215	3,644	59%	14	4	29%	4,524	2,600	57%
	0 - 11 years	8	3	38%	1	0	0%	3	-	0%	0	0	0%	6	-	0%
	12 - 17 years	37	13	35%	0	0	0%	14	4	29%	0	0	0%	9	3	33%
	18 - 24 years	423	229	54%	2	0	0%	121	64	53%	0	0	0%	91	46	51%
	25 - 34 years	1,911	1,240	65%	2	0	0%	614	392	64%	2	2	100%	375	239	64%
	35 - 44 years	4,031	2,563	64%	6	2	33%	1,229	728	59%	1	0	0%	870	520	60%
	45 - 54 years	7,320	4,328	59%	11	3	27%	2,201	1,312	60%	6	2	33%	1,644	956	58%
	55 - 64 years	7,515	4,141	55%	4	2	50%	2,033	1,144	56%	5	0	0%	1,529	836	55%
Gender	Male	9,916	6,031	61%	13	6	46%	2,974	1,824	61%	6	2	33%	2,316	1,413	61%
	Female	11,329	6,486	57%	13	1	8%	3,241	1,820	56%	8	2	25%	2,208	1,187	54%
	Ambiguous	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
	Unknown	-	-	0%	0	0	0%	-	-	0%	0	0	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	490	264	54%	2	2	100%	189	97	51%	1	0	0%	131	62	47%
	Feb 2009	484	288	60%	0	0	0%	152	79	52%	0	0	0%	132	76	58%
	Mar 2009	492	298	61%	0	0	0%	140	81	58%	0	0	0%	101	52	51%
	Apr 2009	532	323	61%	0	0	0%	147	89	61%	0	0	0%	120	73	61%
	May 2009	470	264	56%	0	0	0%	146	73	50%	0	0	0%	122	63	52%
	Jun 2009	496	278	56%	0	0	0%	138	69	50%	1	0	0%	107	73	68%
	Jul 2009	440	248	56%	2	0	0%	112	62	55%	1	1	100%	114	68	60%
	Aug 2009	398	240	60%	0	0	0%	129	74	57%	0	0	0%	98	51	52%
	Sep 2009	457	267	58%	0	0	0%	108	75	69%	2	0	0%	89	45	51%
	Oct 2009	486	270	56%	1	0	0%	123	72	59%	0	0	0%	108	62	57%
	Nov 2009	402	233	58%	1	1	100%	108	68	63%	0	0	0%	93	54	58%
	Dec 2009	429	244	57%	0	0	0%	135	75	56%	1	0	0%	96	56	58%
	Jan 2010	406	223	55%	0	0	0%	120	65	54%	0	0	0%	115	68	59%
	Feb 2010	362	197	54%	1	0	0%	100	52	52%	1	0	0%	74	40	54%
	Mar 2010	354	208	59%	0	0	0%	132	75	57%	0	0	0%	71	40	56%
	Apr 2010	368	210	57%	0	0	0%	122	77	63%	0	0	0%	98	68	69%
	May 2010	388	218	56%	0	0	0%	109	60	55%	1	0	0%	75	46	61%
	Jun 2010	402	240	60%	1	0	0%	103	58	56%	0	0	0%	71	49	69%
	Jul 2010	371	237	64%	0	0	0%	98	52	53%	0	0	0%	66	43	65%
	Aug 2010	363	210	58%	0	0	0%	116	66	57%	0	0	0%	86	55	64%
	Sep 2010	373	219	59%	1	1	100%	105	69	66%	0	0	0%	84	47	56%
	Oct 2010	383	243	63%	0	0	0%	115	72	63%	0	0	0%	75	55	73%
	Nov 2010	353	223	63%	0	0	0%	102	69	68%	1	0	0%	70	42	60%
	Dec 2010	404	228	56%	0	0	0%	90	54	60%	0	0	0%	77	36	47%
	Jan 2011	346	186	54%	1	1	100%	138	72	52%	0	0	0%	115	61	53%
	Feb 2011	305	191	63%	0	0	0%	109	69	63%	0	0	0%	77	48	62%
	Mar 2011	371	230	62%	0	0	0%	103	69	67%	0	0	0%	101	59	58%
	Apr 2011	386	211	55%	0	0	0%	124	81	65%	0	0	0%	70	36	51%
	May 2011	346	195	56%	0	0	0%	98	60	61%	0	0	0%	69	41	59%
	Jun 2011	344	187	54%	1	0	0%	96	64	67%	1	0	0%	59	35	59%
	Jul 2011	350	216	62%	0	0	0%	80	55	69%	0	0	0%	53	30	57%
	Aug 2011	342	195	57%	0	0	0%	94	49	52%	0	0	0%	52	36	69%
	Sep 2011	337	199	59%	0	0	0%	87	53	61%	0	0	0%	55	34	62%
	Oct 2011	306	176	58%	2	0	0%	86	61	71%	0	0	0%	68	38	56%
	Nov 2011	300	181	60%	0	0	0%	85	50	59%	0	0	0%	62	31	50%
	Dec 2011	312	181	58%	0	0	0%	88	48	55%	0	0	0%	73	43	59%
	Jan 2012	310	182	59%	0	0	0%	108	66	61%	0	0	0%	69	36	52%
	Feb 2012	300	190	63%	1	0	0%	86	56	65%	0	0	0%	60	39	65%
	Mar 2012	314	198	63%	0	0	0%	84	52	62%	0	0	0%	61	41	67%
	Apr 2012	359	226	63%	1	0	0%	118	67	57%	1	1	100%	74	41	55%
	May 2012	363	232	64%	1	0	0%	98	61	62%	0	0	0%	77	50	65%
	Jun 2012	299	180	60%	1	0	0%	82	51	62%	0	0	0%	64	40	63%
	Jul 2012	331	207	63%	0	0	0%	103	57	55%	0	0	0%	52	23	44%
	Aug 2012	297	176	59%	1	0	0%	102	64	63%	0	0	0%	61	40	66%
	Sep 2012	283	169	60%	1	0	0%	89	54	61%	1	1	100%	48	28	58%
	Oct 2012	285	166	58%	0	0	0%	83	53	64%	0	0	0%	60	25	42%
	Nov 2012	336	188	56%	0	0	0%	105	57	54%	2	1	50%	77	40	52%
	Dec 2012	286	187	65%	0	0	0%	64	30	47%	0	0	0%	54	24	44%
	Jan 2013	302	178	59%	2	1	50%	103	51	50%	0	0	0%	64	32	50%
	Feb 2013	246	149	61%	2	0	0%	64	38	59%	0	0	0%	52	30	58%
	Mar 2013	248	153	62%	0	0	0%	80	47	59%	0	0	0%	40	21	53%
	Apr 2013	280	162	58%	0	0	0%	93	51	55%	0	0	0%	59	34	58%
	May 2013	307	188	61%	1	1	100%	83	51	61%	0	0	0%	54	34	63%
	Jun 2013	288	162	56%	0	0	0%	89	57	64%	0	0	0%	55	30	55%
	Jul 2013	272	161	59%	0	0	0%	88	53	60%	0	0	0%	60	27	45%
	Aug 2013	300	186	62%	0	0	0%	75	33	44%	0	0	0%	39	19	49%
	Sep 2013	276	168	61%	1	0	0%	75	42	56%	0	0	0%	52	28	54%
	Oct 2013	274	169	62%	0	0	0%	78	48	62%	0	0	0%	56	35	63%
	Nov 2013	265	156	59%	0	0	0%	71	46	65%	0	0	0%	57	33	58%
	Dec 2013	276	163	59%	1	0	0%	67	45	67%	0	0	0%	52	34	65%

Table 2c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)																
	Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr			Dose 162 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	5	4	80%	179	93	52%	2	1	50%	233	121	52%	2	1	50%
	0 - 11 years	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	0	0	0%	1	-	0%	-	-	0%	2	-	0%	-	-	0%
	18 - 24 years	0	0	0%	2	2	100%	-	-	0%	5	4	80%	1	-	0%
	25 - 34 years	0	0	0%	10	8	80%	-	-	0%	13	6	46%	-	-	0%
	35 - 44 years	1	1	100%	30	15	50%	-	-	0%	37	22	59%	-	-	0%
	45 - 54 years	1	1	100%	72	35	49%	1	-	0%	88	46	52%	-	-	0%
	55 - 64 years	3	2	67%	64	33	52%	1	1	100%	88	43	49%	1	1	100%
Gender	Male	2	2	100%	83	45	54%	-	-	0%	125	71	57%	2	1	50%
	Female	3	2	67%	96	48	50%	2	1	50%	108	50	46%	-	-	0%
	Ambiguous	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	0	0	0%	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	1	1	100%	5	3	60%	-	-	0%	7	3	43%	-	-	0%
	Feb 2009	0	0	0%	5	1	20%	-	-	0%	3	2	67%	-	-	0%
	Mar 2009	0	0	0%	4	2	50%	-	-	0%	2	1	50%	-	-	0%
	Apr 2009	0	0	0%	5	3	60%	-	-	0%	7	3	43%	-	-	0%
	May 2009	0	0	0%	4	3	75%	-	-	0%	8	5	63%	-	-	0%
	Jun 2009	0	0	0%	4	3	75%	-	-	0%	9	6	67%	-	-	0%
	Jul 2009	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%
	Aug 2009	0	0	0%	3	2	67%	-	-	0%	5	-	0%	-	-	0%
	Sep 2009	0	0	0%	1	-	0%	-	-	0%	5	3	60%	-	-	0%
	Oct 2009	0	0	0%	2	-	0%	-	-	0%	6	2	33%	-	-	0%
	Nov 2009	0	0	0%	3	2	67%	-	-	0%	7	5	71%	-	-	0%
	Dec 2009	0	0	0%	5	2	40%	-	-	0%	7	5	71%	-	-	0%
	Jan 2010	0	0	0%	10	2	20%	-	-	0%	7	3	43%	-	-	0%
	Feb 2010	0	0	0%	6	1	17%	-	-	0%	5	3	60%	-	-	0%
	Mar 2010	0	0	0%	3	-	0%	-	-	0%	5	3	60%	-	-	0%
	Apr 2010	0	0	0%	3	1	33%	-	-	0%	6	5	83%	-	-	0%
	May 2010	0	0	0%	2	1	50%	-	-	0%	5	3	60%	-	-	0%
	Jun 2010	0	0	0%	6	3	50%	-	-	0%	5	2	40%	-	-	0%
	Jul 2010	0	0	0%	4	3	75%	-	-	0%	6	4	67%	-	-	0%
	Aug 2010	1	0	0%	3	1	33%	-	-	0%	3	1	33%	-	-	0%
	Sep 2010	0	0	0%	1	-	0%	-	-	0%	3	-	0%	-	-	0%
	Oct 2010	0	0	0%	7	6	86%	1	1	100%	5	4	80%	-	-	0%
	Nov 2010	0	0	0%	2	2	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2010	0	0	0%	1	1	100%	-	-	0%	4	2	50%	-	-	0%
	Jan 2011	0	0	0%	3	1	33%	-	-	0%	5	2	40%	1	-	0%
	Feb 2011	1	1	100%	2	1	50%	-	-	0%	3	1	33%	-	-	0%
	Mar 2011	0	0	0%	3	1	33%	-	-	0%	4	1	25%	-	-	0%
	Apr 2011	0	0	0%	5	3	60%	-	-	0%	7	4	57%	-	-	0%
	May 2011	0	0	0%	5	1	20%	-	-	0%	4	1	25%	-	-	0%
	Jun 2011	0	0	0%	2	1	50%	-	-	0%	-	-	0%	-	-	0%
	Jul 2011	0	0	0%	2	-	0%	-	-	0%	4	4	100%	-	-	0%
	Aug 2011	0	0	0%	1	1	100%	-	-	0%	1	1	100%	-	-	0%
	Sep 2011	0	0	0%	4	3	75%	1	-	0%	5	4	80%	1	1	100%
	Oct 2011	0	0	0%	2	2	100%	-	-	0%	1	-	0%	-	-	0%
	Nov 2011	0	0	0%	1	1	100%	-	-	0%	2	1	50%	-	-	0%
	Dec 2011	0	0	0%	4	2	50%	-	-	0%	2	2	100%	-	-	0%
	Jan 2012	0	0	0%	3	2	67%	-	-	0%	3	2	67%	-	-	0%
	Feb 2012	0	0	0%	2	1	50%	-	-	0%	6	4	67%	-	-	0%
	Mar 2012	0	0	0%	3	3	100%	-	-	0%	2	1	50%	-	-	0%
	Apr 2012	1	1	100%	5	5	100%	-	-	0%	6	3	50%	-	-	0%
	May 2012	0	0	0%	4	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jun 2012	0	0	0%	2	2	100%	-	-	0%	6	1	17%	-	-	0%
	Jul 2012	0	0	0%	1	1	100%	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	0	0	0%	4	3	75%	-	-	0%	1	1	100%	-	-	0%
	Sep 2012	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Oct 2012	0	0	0%	4	2	50%	-	-	0%	2	2	100%	-	-	0%
	Nov 2012	0	0	0%	2	2	100%	-	-	0%	5	3	60%	-	-	0%
	Dec 2012	0	0	0%	3	1	33%	-	-	0%	1	-	0%	-	-	0%
	Jan 2013	0	0	0%	4	-	0%	-	-	0%	4	-	0%	-	-	0%
	Feb 2013	1	1	100%	3	1	33%	-	-	0%	-	-	0%	-	-	0%
	Mar 2013	0	0	0%	2	1	50%	-	-	0%	3	1	33%	-	-	0%
	Apr 2013	0	0	0%	-	-	0%	-	-	0%	5	2	40%	-	-	0%
	May 2013	0	0	0%	1	1	100%	-	-	0%	3	1	33%	-	-	0%
	Jun 2013	0	0	0%	-	-	0%	-	-	0%	5	1	20%	-	-	0%
	Jul 2013	0	0	0%	2	2	100%	-	-	0%	3	2	67%	-	-	0%
	Aug 2013	0	0	0%	2	2	100%	-	-	0%	2	1	50%	-	-	0%
	Sep 2013	0	0	0%	1	-	0%	-	-	0%	3	1	33%	-	-	0%
	Oct 2013	0	0	0%	3	1	33%	-	-	0%	1	1	100%	-	-	0%
	Nov 2013	0	0	0%	1	1	100%	-	-	0%	3	2	67%	-	-	0%
	Dec 2013	0	0	0%	1	-	0%	-	-	0%	3	2	67%	-	-	0%

Table 2c: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Tertiary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Tertiary Tolerance Definition (>0 mg per day in the prior 7 consecutive days)										
	Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	52	26	50%	5	3	60%	4	-	0%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	1	1	100%	-	-	0%	-	-	0%
	18 - 24 years	3	3	100%	-	-	0%	-	-	0%
	25 - 34 years	3	2	67%	-	-	0%	1	-	0%
	35 - 44 years	7	5	71%	3	2	67%	1	-	0%
	45 - 54 years	17	7	41%	2	1	50%	-	-	0%
	55 - 64 years	21	8	38%	-	-	0%	2	-	0%
Gender	Male	17	11	65%	5	3	60%	2	-	0%
	Female	35	15	43%	-	-	0%	2	-	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	2	-	0%	-	-	0%	-	-	0%
	Feb 2009	2	1	50%	-	-	0%	-	-	0%
	Mar 2009	2	2	100%	1	-	0%	1	-	0%
	Apr 2009	4	4	100%	1	1	100%	-	-	0%
	May 2009	1	1	100%	-	-	0%	-	-	0%
	Jun 2009	1	1	100%	-	-	0%	-	-	0%
	Jul 2009	2	-	0%	-	-	0%	1	-	0%
	Aug 2009	-	-	0%	-	-	0%	-	-	0%
	Sep 2009	2	1	50%	-	-	0%	-	-	0%
	Oct 2009	-	-	0%	-	-	0%	-	-	0%
	Nov 2009	1	1	100%	-	-	0%	-	-	0%
	Dec 2009	-	-	0%	-	-	0%	-	-	0%
	Jan 2010	-	-	0%	-	-	0%	-	-	0%
	Feb 2010	-	-	0%	-	-	0%	-	-	0%
	Mar 2010	1	1	100%	1	1	100%	-	-	0%
	Apr 2010	-	-	0%	-	-	0%	-	-	0%
	May 2010	1	-	0%	-	-	0%	-	-	0%
	Jun 2010	1	-	0%	-	-	0%	-	-	0%
	Jul 2010	-	-	0%	-	-	0%	-	-	0%
	Aug 2010	2	2	100%	-	-	0%	1	-	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%
	Oct 2010	1	1	100%	-	-	0%	-	-	0%
	Nov 2010	-	-	0%	-	-	0%	-	-	0%
	Dec 2010	1	1	100%	-	-	0%	-	-	0%
	Jan 2011	1	-	0%	-	-	0%	-	-	0%
	Feb 2011	2	1	50%	-	-	0%	-	-	0%
	Mar 2011	2	1	50%	-	-	0%	-	-	0%
	Apr 2011	2	-	0%	-	-	0%	-	-	0%
	May 2011	-	-	0%	-	-	0%	-	-	0%
	Jun 2011	2	1	50%	-	-	0%	-	-	0%
	Jul 2011	-	-	0%	-	-	0%	-	-	0%
	Aug 2011	1	-	0%	-	-	0%	-	-	0%
	Sep 2011	3	1	33%	-	-	0%	-	-	0%
	Oct 2011	2	-	0%	-	-	0%	-	-	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%
	Dec 2011	-	-	0%	-	-	0%	-	-	0%
	Jan 2012	-	-	0%	-	-	0%	-	-	0%
	Feb 2012	-	-	0%	-	-	0%	-	-	0%
	Mar 2012	1	-	0%	-	-	0%	-	-	0%
	Apr 2012	2	1	50%	-	-	0%	-	-	0%
	May 2012	1	1	100%	-	-	0%	-	-	0%
	Jun 2012	1	-	0%	-	-	0%	-	-	0%
	Jul 2012	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	-	-	0%	-	-	0%	-	-	0%
	Sep 2012	-	-	0%	-	-	0%	-	-	0%
	Oct 2012	-	-	0%	-	-	0%	-	-	0%
	Nov 2012	1	-	0%	-	-	0%	1	-	0%
	Dec 2012	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	-	-	0%	-	-	0%	-	-	0%
	Feb 2013	1	-	0%	-	-	0%	-	-	0%
	Mar 2013	1	1	100%	-	-	0%	-	-	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%
	May 2013	1	1	100%	-	-	0%	-	-	0%
	Jun 2013	1	-	0%	2	1	50%	-	-	0%
	Jul 2013	-	-	0%	-	-	0%	-	-	0%
	Aug 2013	-	-	0%	-	-	0%	-	-	0%
	Sep 2013	1	1	100%	-	-	0%	-	-	0%
	Oct 2013	1	-	0%	-	-	0%	-	-	0%
	Nov 2013	-	-	0%	-	-	0%	-	-	0%
	Dec 2013	1	1	100%	-	-	0%	-	-	0%

Table 2d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg per day for seven days in the 30 days prior)													
	Dose 12 mcg/hr			Dose 24 mcg/hr			Dose 25 mcg/hr			Dose 36 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	17,812	12,713	71.4%	3	3	100%	49,148	37,514	76.3%	1	0	0%
	0 - 11 years	34	14	41.2%	-	0	0%	25	9	36.0%	0	0	0%
	12 - 17 years	81	38	46.9%	-	0	0%	85	39	45.9%	0	0	0%
	18 - 24 years	412	266	64.6%	-	0	0%	925	639	69.1%	0	0	0%
	25 - 34 years	1,605	1,259	78.4%	-	0	0%	4,297	3,482	81.0%	1	0	0%
	35 - 44 years	3,153	2,377	75.4%	2	2	100%	8,915	7,040	79.0%	0	0	0%
	45 - 54 years	5,672	4,072	71.8%	-	0	0%	16,409	12,569	76.6%	0	0	0%
	55 - 64 years	6,855	4,687	68.4%	1	1	100%	18,492	13,736	74.3%	0	0	0%
Gender	Male	5,595	4,067	72.7%	1	1	100%	20,233	15,573	77.0%	0	0	0%
	Female	12,217	8,646	70.8%	2	2	100%	28,915	21,941	75.9%	1	0	0%
	Ambiguous	-	-	0.0%	-	0	0%	-	-	0.0%	0	0	0%
	Unknown	0	0	0	0	0	0%	-	0	0	0	0	0%
Month and Year of Episode Start Date	Jan 2009	238	176	73.9%	-	0	0%	1,070	794	74.2%	0	0	0%
	Feb 2009	227	154	67.8%	-	0	0%	992	740	74.6%	0	0	0%
	Mar 2009	284	186	65.5%	-	0	0%	1,072	803	74.9%	0	0	0%
	Apr 2009	251	177	70.5%	-	0	0%	1,147	851	74.2%	1	0	0%
	May 2009	283	207	73.1%	-	0	0%	1,039	806	77.6%	0	0	0%
	Jun 2009	300	195	65.0%	-	0	0%	1,080	816	75.6%	0	0	0%
	Jul 2009	267	189	70.8%	-	0	0%	966	717	74.2%	0	0	0%
	Aug 2009	284	200	70.4%	-	0	0%	946	683	72.2%	0	0	0%
	Sep 2009	318	231	72.6%	-	0	0%	1,007	764	75.9%	0	0	0%
	Oct 2009	278	184	66.2%	-	0	0%	948	699	73.7%	0	0	0%
	Nov 2009	244	163	66.8%	-	0	0%	898	642	71.5%	0	0	0%
	Dec 2009	261	179	68.6%	-	0	0%	970	737	76.0%	0	0	0%
	Jan 2010	245	165	67.3%	-	0	0%	881	649	73.7%	0	0	0%
	Feb 2010	254	180	70.9%	-	0	0%	790	588	74.4%	0	0	0%
	Mar 2010	283	196	69.3%	-	0	0%	853	651	76.3%	0	0	0%
	Apr 2010	289	199	68.9%	-	0	0%	958	716	74.7%	0	0	0%
	May 2010	261	204	78.2%	-	0	0%	845	670	79.3%	0	0	0%
	Jun 2010	285	198	69.5%	-	0	0%	884	654	74.0%	0	0	0%
	Jul 2010	239	170	71.1%	-	0	0%	837	645	77.1%	0	0	0%
	Aug 2010	270	194	71.9%	-	0	0%	871	673	77.3%	0	0	0%
	Sep 2010	320	225	70.3%	-	0	0%	908	701	77.2%	0	0	0%
	Oct 2010	313	213	68.1%	-	0	0%	843	625	74.1%	0	0	0%
	Nov 2010	306	221	72.2%	-	0	0%	889	669	75.3%	0	0	0%
	Dec 2010	307	217	70.7%	-	0	0%	796	617	77.5%	0	0	0%
	Jan 2011	264	176	66.7%	-	0	0%	774	585	75.6%	0	0	0%
	Feb 2011	279	187	67.0%	-	0	0%	674	518	76.9%	0	0	0%
	Mar 2011	292	203	69.5%	-	0	0%	845	659	78.0%	0	0	0%
	Apr 2011	307	227	73.9%	-	0	0%	812	624	76.8%	0	0	0%
	May 2011	299	210	70.2%	-	0	0%	795	599	75.3%	0	0	0%
	Jun 2011	316	221	69.9%	-	0	0%	777	600	77.2%	0	0	0%
	Jul 2011	294	197	67.0%	-	0	0%	728	548	75.3%	0	0	0%
	Aug 2011	328	248	75.6%	-	0	0%	820	606	73.9%	0	0	0%
	Sep 2011	307	219	71.3%	-	0	0%	795	611	76.9%	0	0	0%
	Oct 2011	279	206	73.8%	-	0	0%	768	600	78.1%	0	0	0%
	Nov 2011	306	215	70.3%	-	0	0%	718	569	79.2%	0	0	0%
	Dec 2011	323	225	69.7%	-	0	0%	747	560	75.0%	0	0	0%
	Jan 2012	298	205	68.8%	-	0	0%	776	609	78.5%	0	0	0%
	Feb 2012	269	198	73.6%	-	0	0%	696	538	77.3%	0	0	0%
	Mar 2012	307	228	74.3%	-	0	0%	738	575	77.9%	0	0	0%
	Apr 2012	316	225	71.2%	-	0	0%	803	607	75.6%	0	0	0%
	May 2012	389	275	70.7%	-	0	0%	786	605	77.0%	0	0	0%
	Jun 2012	293	218	74.4%	-	0	0%	683	535	78.3%	0	0	0%
	Jul 2012	315	240	76.2%	-	0	0%	672	506	75.3%	0	0	0%
	Aug 2012	324	244	75.3%	-	0	0%	857	672	78.4%	0	0	0%
	Sep 2012	290	206	71.0%	-	0	0%	705	544	77.2%	0	0	0%
	Oct 2012	330	240	72.7%	-	0	0%	754	603	80.0%	0	0	0%
	Nov 2012	332	244	73.5%	-	0	0%	775	597	77.0%	0	0	0%
	Dec 2012	316	233	73.7%	-	0	0%	666	501	75.2%	0	0	0%
	Jan 2013	296	212	71.6%	-	0	0%	650	495	76.2%	0	0	0%
	Feb 2013	275	195	70.9%	-	0	0%	675	547	81.0%	0	0	0%
	Mar 2013	274	200	73.0%	-	0	0%	632	506	80.1%	0	0	0%
	Apr 2013	327	248	75.8%	-	0	0%	724	568	78.5%	0	0	0%
	May 2013	293	206	70.3%	-	0	0%	754	590	78.2%	0	0	0%
	Jun 2013	306	226	73.9%	1	1	100%	701	553	78.9%	0	0	0%
	Jul 2013	345	250	72.5%	-	0	0%	719	566	78.7%	0	0	0%
	Aug 2013	358	256	71.5%	-	0	0%	780	618	79.2%	0	0	0%
	Sep 2013	323	237	73.4%	-	0	0%	687	521	75.8%	0	0	0%
	Oct 2013	366	270	73.8%	1	1	100%	784	604	77.0%	0	0	0%
	Nov 2013	344	262	76.2%	1	1	100%	702	541	77.1%	0	0	0%
	Dec 2013	325	238	73.2%	0	0	0%	686	524	76.4%	0	0	0%

Table 2d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg per day for seven days in the 30 days)																
	Dose 37 mcg/hr			Dose 50 mcg/hr			Dose 62 mcg/hr			Dose 75 mcg/hr			Dose 87 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	339	253	75%	21,245	16,661	78%	26	9	35%	6,215	4,682	75%	14	7	50%
	0 - 11 years	1	0	0%	8	4	50%	1	0	0%	3	1	33%	0	0	0%
	12 - 17 years	2	0	0%	37	20	54%	0	0	0%	14	5	36%	0	0	0%
	18 - 24 years	9	6	67%	423	306	72%	2	0	0%	121	83	69%	0	0	0%
	25 - 34 years	27	22	81%	1,911	1,557	81%	2	0	0%	614	480	78%	2	2	100%
	35 - 44 years	71	47	66%	4,031	3,293	82%	6	3	50%	1,229	928	76%	1	0	0%
	45 - 54 years	99	76	77%	7,320	5,753	79%	11	4	36%	2,201	1,668	76%	6	4	67%
	55 - 64 years	130	102	78%	7,515	5,728	76%	4	2	50%	2,033	1,517	75%	5	1	20%
Gender	Male	145	114	79%	9,916	7,893	80%	13	7	54%	2,974	2,284	77%	6	4	67%
	Female	194	139	72%	11,329	8,768	77%	13	2	15%	3,241	2,398	74%	8	3	38%
	Ambiguous	0	0	0%	-	-	0%	0	0	0%	-	-	0%	0	0	0%
	Unknown	0	0	0%	-	-	0%	0	0	0%	-	-	0%	0	0	0%
Month and Year of Episode Start Date	Jan 2009	6	6	100%	490	364	74%	2	2	100%	189	128	68%	1	0	0%
	Feb 2009	9	5	56%	484	394	81%	0	0	0%	152	108	71%	0	0	0%
	Mar 2009	5	5	100%	492	396	80%	0	0	0%	140	98	70%	0	0	0%
	Apr 2009	4	2	50%	532	413	78%	0	0	0%	147	116	79%	0	0	0%
	May 2009	6	6	100%	470	342	73%	0	0	0%	146	102	70%	0	0	0%
	Jun 2009	8	7	88%	496	377	76%	0	0	0%	138	101	73%	1	0	0%
	Jul 2009	8	6	75%	440	342	78%	2	0	0%	112	80	71%	1	1	100%
	Aug 2009	3	2	67%	398	321	81%	0	0	0%	129	99	77%	0	0	0%
	Sep 2009	5	5	100%	457	359	79%	0	0	0%	108	90	83%	2	1	50%
	Oct 2009	1	1	100%	486	359	74%	1	0	0%	123	95	77%	0	0	0%
	Nov 2009	8	5	63%	402	312	78%	1	1	100%	108	89	82%	0	0	0%
	Dec 2009	8	6	75%	429	334	78%	0	0	0%	135	97	72%	1	0	0%
	Jan 2010	6	0	0%	406	300	74%	0	0	0%	120	80	67%	0	0	0%
	Feb 2010	9	9	100%	362	268	74%	1	0	0%	100	71	71%	1	1	100%
	Mar 2010	8	6	75%	354	278	79%	0	0	0%	132	99	75%	0	0	0%
	Apr 2010	4	2	50%	368	288	78%	0	0	0%	122	99	81%	0	0	0%
	May 2010	6	2	33%	388	293	76%	0	0	0%	109	78	72%	1	0	0%
	Jun 2010	7	4	57%	402	318	79%	1	0	0%	103	83	81%	0	0	0%
	Jul 2010	5	4	80%	371	300	81%	0	0	0%	98	71	72%	0	0	0%
	Aug 2010	3	2	67%	363	287	79%	0	0	0%	116	81	70%	0	0	0%
	Sep 2010	2	2	100%	373	291	78%	1	1	100%	105	88	84%	0	0	0%
	Oct 2010	5	5	100%	383	313	82%	0	0	0%	115	88	77%	0	0	0%
	Nov 2010	8	6	75%	353	287	81%	0	0	0%	102	85	83%	1	0	0%
	Dec 2010	3	2	67%	404	315	78%	0	0	0%	90	71	79%	0	0	0%
	Jan 2011	1	1	100%	346	260	75%	1	1	100%	138	97	70%	0	0	0%
	Feb 2011	3	3	100%	305	242	79%	0	0	0%	109	83	76%	0	0	0%
	Mar 2011	9	6	67%	371	294	79%	0	0	0%	103	85	83%	0	0	0%
	Apr 2011	10	10	100%	386	292	76%	0	0	0%	124	94	76%	0	0	0%
	May 2011	4	3	75%	346	261	75%	0	0	0%	98	73	74%	0	0	0%
	Jun 2011	4	3	75%	344	263	76%	1	0	0%	96	79	82%	1	1	100%
	Jul 2011	4	2	50%	350	279	80%	0	0	0%	80	69	86%	0	0	0%
	Aug 2011	5	3	60%	342	270	79%	0	0	0%	94	67	71%	0	0	0%
	Sep 2011	6	5	83%	337	271	80%	0	0	0%	87	70	80%	0	0	0%
	Oct 2011	3	2	67%	306	240	78%	2	0	0%	86	70	81%	0	0	0%
	Nov 2011	7	4	57%	300	238	79%	0	0	0%	85	64	75%	0	0	0%
	Dec 2011	5	5	100%	312	255	82%	0	0	0%	88	61	69%	0	0	0%
	Jan 2012	3	2	67%	310	246	79%	0	0	0%	108	85	79%	0	0	0%
	Feb 2012	7	6	86%	300	245	82%	1	0	0%	86	65	76%	0	0	0%
	Mar 2012	7	6	86%	314	260	83%	0	0	0%	84	68	81%	0	0	0%
	Apr 2012	7	5	71%	359	284	79%	1	0	0%	118	87	74%	1	1	100%
	May 2012	8	7	88%	363	284	78%	1	0	0%	98	77	79%	0	0	0%
	Jun 2012	4	3	75%	299	243	81%	1	0	0%	82	65	79%	0	0	0%
	Jul 2012	5	4	80%	331	266	80%	0	0	0%	103	76	74%	0	0	0%
	Aug 2012	2	2	100%	297	233	78%	1	1	100%	102	77	75%	0	0	0%
	Sep 2012	5	5	100%	283	229	81%	1	0	0%	89	67	75%	1	1	100%
	Oct 2012	3	2	67%	285	229	80%	0	0	0%	83	65	78%	0	0	0%
	Nov 2012	6	4	67%	336	241	72%	0	0	0%	105	72	69%	2	1	50%
	Dec 2012	9	5	56%	286	226	79%	0	0	0%	64	41	64%	0	0	0%
	Jan 2013	5	3	60%	302	235	78%	2	1	50%	103	72	70%	0	0	0%
	Feb 2013	3	3	100%	246	201	82%	2	0	0%	64	52	81%	0	0	0%
	Mar 2013	4	4	100%	248	194	78%	0	0	0%	80	57	71%	0	0	0%
	Apr 2013	11	8	73%	280	225	80%	0	0	0%	93	71	76%	0	0	0%
	May 2013	9	7	78%	307	241	79%	1	1	100%	83	67	81%	0	0	0%
	Jun 2013	5	4	80%	288	232	81%	0	0	0%	89	67	75%	0	0	0%
	Jul 2013	9	7	78%	272	219	81%	0	0	0%	88	73	83%	0	0	0%
	Aug 2013	7	5	71%	300	249	83%	0	0	0%	75	48	64%	0	0	0%
	Sep 2013	5	4	80%	276	225	82%	1	0	0%	75	54	72%	0	0	0%
	Oct 2013	4	2	50%	274	218	80%	0	0	0%	78	58	74%	0	0	0%
	Nov 2013	7	3	43%	265	207	78%	0	0	0%	71	56	79%	0	0	0%
	Dec 2013	6	5	83%	276	213	77%	1	1	100%	67	53	79%	0	0	0%

Table 2d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013

Quaternary Tolerance Definition (>0 mg per day for seven days in the 30 days prior)																
		Dose 100 mcg/hr			Dose 112 mcg/hr			Dose 125 mcg/hr			Dose 137 mcg/hr			Dose 150 mcg/hr		
		Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance
Age (years)	Total	4,524	3,253	72%	5	4	80%	179	121	68%	2	1	50%	233	152	65%
	0 - 11 years	6	1	17%	0	0	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	9	4	44%	0	0	0%	1	1	100%	-	-	0%	2	-	0%
	18 - 24 years	91	56	62%	0	0	0%	2	2	100%	-	-	0%	5	4	80%
	25 - 34 years	375	297	79%	0	0	0%	10	8	80%	-	-	0%	13	9	69%
	35 - 44 years	870	640	74%	1	1	100%	30	24	80%	-	-	0%	37	27	73%
	45 - 54 years	1,644	1,189	72%	1	1	100%	72	43	60%	1	-	0%	88	57	65%
	55 - 64 years	1,529	1,066	70%	3	2	67%	64	43	67%	1	1	100%	88	55	63%
Gender	Male	2,316	1,730	75%	2	2	100%	83	57	69%	-	-	0%	125	90	72%
	Female	2,208	1,523	69%	3	2	67%	96	64	67%	2	1	50%	108	62	57%
	Ambiguous	-	-	0%	0	0	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	0	0	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	131	88	67%	1	1	100%	5	4	80%	-	-	0%	7	3	43%
	Feb 2009	132	100	76%	0	0	0%	5	2	40%	-	-	0%	3	3	100%
	Mar 2009	101	68	67%	0	0	0%	4	2	50%	-	-	0%	2	1	50%
	Apr 2009	120	92	77%	0	0	0%	5	3	60%	-	-	0%	7	5	71%
	May 2009	122	83	68%	0	0	0%	4	3	75%	-	-	0%	8	5	63%
	Jun 2009	107	84	79%	0	0	0%	4	3	75%	-	-	0%	9	7	78%
	Jul 2009	114	80	70%	0	0	0%	1	1	100%	-	-	0%	3	1	33%
	Aug 2009	98	64	65%	0	0	0%	3	2	67%	-	-	0%	5	1	20%
	Sep 2009	89	58	65%	0	0	0%	1	-	0%	-	-	0%	5	4	80%
	Oct 2009	108	77	71%	0	0	0%	2	1	50%	-	-	0%	6	2	33%
	Nov 2009	93	67	72%	0	0	0%	3	2	67%	-	-	0%	7	5	71%
	Dec 2009	96	72	75%	0	0	0%	5	4	80%	-	-	0%	7	6	86%
	Jan 2010	115	80	70%	0	0	0%	10	4	40%	-	-	0%	7	4	57%
	Feb 2010	74	50	68%	0	0	0%	6	3	50%	-	-	0%	5	4	80%
	Mar 2010	71	48	68%	0	0	0%	3	-	0%	-	-	0%	5	4	80%
	Apr 2010	98	78	80%	0	0	0%	3	2	67%	-	-	0%	6	5	83%
	May 2010	75	56	75%	0	0	0%	2	1	50%	-	-	0%	5	4	80%
	Jun 2010	71	56	79%	0	0	0%	6	5	83%	-	-	0%	5	3	60%
	Jul 2010	66	53	80%	0	0	0%	4	4	100%	-	-	0%	6	4	67%
	Aug 2010	86	65	76%	1	0	0%	3	2	67%	-	-	0%	3	2	67%
	Sep 2010	84	63	75%	0	0	0%	1	-	0%	-	-	0%	3	1	33%
	Oct 2010	75	63	84%	0	0	0%	7	6	86%	1	1	100%	5	5	100%
	Nov 2010	70	53	76%	0	0	0%	2	2	100%	-	-	0%	3	2	67%
	Dec 2010	77	45	58%	0	0	0%	1	1	100%	-	-	0%	4	2	50%
	Jan 2011	115	82	71%	0	0	0%	3	1	33%	-	-	0%	5	3	60%
	Feb 2011	77	57	74%	1	1	100%	2	2	100%	-	-	0%	3	2	67%
	Mar 2011	101	73	72%	0	0	0%	3	2	67%	-	-	0%	4	2	50%
	Apr 2011	70	49	70%	0	0	0%	5	4	80%	-	-	0%	7	5	71%
	May 2011	69	46	67%	0	0	0%	5	3	60%	-	-	0%	4	2	50%
	Jun 2011	59	44	75%	0	0	0%	2	2	100%	-	-	0%	-	-	0%
	Jul 2011	53	41	77%	0	0	0%	2	-	0%	-	-	0%	4	4	100%
	Aug 2011	52	45	87%	0	0	0%	1	1	100%	-	-	0%	1	1	100%
	Sep 2011	55	41	75%	0	0	0%	4	3	75%	1	-	0%	5	4	80%
	Oct 2011	68	47	69%	0	0	0%	2	2	100%	-	-	0%	1	-	0%
	Nov 2011	62	43	69%	0	0	0%	1	1	100%	-	-	0%	2	1	50%
	Dec 2011	73	54	74%	0	0	0%	4	2	50%	-	-	0%	2	2	100%
	Jan 2012	69	45	65%	0	0	0%	3	2	67%	-	-	0%	3	2	67%
	Feb 2012	60	50	83%	0	0	0%	2	2	100%	-	-	0%	6	4	67%
	Mar 2012	61	52	85%	0	0	0%	3	3	100%	-	-	0%	2	2	100%
	Apr 2012	74	52	70%	1	1	100%	5	5	100%	-	-	0%	6	5	83%
	May 2012	77	57	74%	0	0	0%	4	2	50%	-	-	0%	-	-	0%
	Jun 2012	64	49	77%	0	0	0%	2	2	100%	-	-	0%	6	1	17%
	Jul 2012	52	31	60%	0	0	0%	1	1	100%	-	-	0%	-	-	0%
	Aug 2012	61	46	75%	0	0	0%	4	4	100%	-	-	0%	1	1	100%
	Sep 2012	48	39	81%	0	0	0%	2	2	100%	-	-	0%	2	1	50%
	Oct 2012	60	40	67%	0	0	0%	4	3	75%	-	-	0%	2	2	100%
	Nov 2012	77	51	66%	0	0	0%	2	2	100%	-	-	0%	5	4	80%
	Dec 2012	54	37	69%	0	0	0%	3	1	33%	-	-	0%	1	-	0%
	Jan 2013	64	39	61%	0	0	0%	4	-	0%	-	-	0%	4	1	25%
	Feb 2013	52	40	77%	1	1	100%	3	2	67%	-	-	0%	-	-	0%
	Mar 2013	40	30	75%	0	0	0%	2	2	100%	-	-	0%	3	1	33%
	Apr 2013	59	41	69%	0	0	0%	-	-	0%	-	-	0%	5	3	60%
	May 2013	54	35	65%	0	0	0%	1	1	100%	-	-	0%	3	2	67%
	Jun 2013	55	38	69%	0	0	0%	-	-	0%	-	-	0%	5	4	80%
	Jul 2013	60	39	65%	0	0	0%	2	2	100%	-	-	0%	3	3	100%
	Aug 2013	39	23	59%	0	0	0%	2	2	100%	-	-	0%	2	1	50%
	Sep 2013	52	37	71%	0	0	0%	1	1	100%	-	-	0%	3	1	33%
	Oct 2013	56	38	68%	0	0	0%	3	1	33%	-	-	0%	1	1	100%
	Nov 2013	57	39	68%	0	0	0%	1	1	100%	-	-	0%	3	2	67%
	Dec 2013	52	40	77%	0	0	0%	1	-	0%	-	-	0%	3	2	67%

Table 2d: Counts of Transdermal Fentanyl Episodes and Proportions of Transdermal Fentanyl Episodes with Prior Tolerance with a 91-day Washout Period and a Quaternary Definition in the Mini-Sentinel Distributed Database (MSDD) from January 1, 2009 to December 31, 2013													
Quaternary Tolerance Definition (>0 mg per day for seven days in the 30 days prior)													
	Dose 162 mcg/hr			Dose 175 mcg/hr			Dose 200 mcg/hr			Dose 225 mcg/hr			
	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	Total N of Transdermal Fentanyl Episodes	N with Prior Tolerance	% with Prior Tolerance	
Age (years)	Total	2	2	100%	52	33	63%	5	3	60%	4	1	25%
	0 - 11 years	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	12 - 17 years	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	18 - 24 years	1	1	100%	3	3	100%	-	-	0%	-	-	0%
	25 - 34 years	-	-	0%	3	2	67%	-	-	0%	1	1	100%
	35 - 44 years	-	-	0%	7	6	86%	3	2	67%	1	-	0%
	45 - 54 years	-	-	0%	17	10	59%	2	1	50%	-	-	0%
	55 - 64 years	1	1	100%	21	11	52%	-	-	0%	2	-	0%
Gender	Male	2	2	100%	17	12	71%	5	3	60%	2	1	50%
	Female	-	-	0%	35	21	60%	-	-	0%	2	-	0%
	Ambiguous	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Unknown	-	-	0%	-	-	0%	-	-	0%	-	-	0%
Month and Year of Episode Start Date	Jan 2009	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	Feb 2009	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	Mar 2009	-	-	0%	2	2	100%	1	-	0%	1	-	0%
	Apr 2009	-	-	0%	4	4	100%	1	1	100%	-	-	0%
	May 2009	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jun 2009	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jul 2009	-	-	0%	2	2	100%	-	-	0%	1	1	100%
	Aug 2009	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Sep 2009	-	-	0%	2	2	100%	-	-	0%	-	-	0%
	Oct 2009	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Nov 2009	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Dec 2009	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jan 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Feb 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Mar 2010	-	-	0%	1	1	100%	1	1	100%	-	-	0%
	Apr 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	May 2010	-	-	0%	1	-	0%	-	-	0%	-	-	0%
	Jun 2010	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jul 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Aug 2010	-	-	0%	2	2	100%	-	-	0%	1	-	0%
	Sep 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Oct 2010	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Nov 2010	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Dec 2010	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jan 2011	1	1	100%	1	-	0%	-	-	0%	-	-	0%
	Feb 2011	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	Mar 2011	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	Apr 2011	-	-	0%	2	-	0%	-	-	0%	-	-	0%
	May 2011	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jun 2011	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	Jul 2011	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Aug 2011	-	-	0%	1	-	0%	-	-	0%	-	-	0%
	Sep 2011	1	1	100%	3	2	67%	-	-	0%	-	-	0%
	Oct 2011	-	-	0%	2	-	0%	-	-	0%	-	-	0%
	Nov 2011	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Dec 2011	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jan 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Feb 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Mar 2012	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Apr 2012	-	-	0%	2	1	50%	-	-	0%	-	-	0%
	May 2012	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jun 2012	-	-	0%	1	-	0%	-	-	0%	-	-	0%
	Jul 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Aug 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Sep 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Oct 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Nov 2012	-	-	0%	1	-	0%	-	-	0%	1	-	0%
	Dec 2012	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Jan 2013	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Feb 2013	-	-	0%	1	-	0%	-	-	0%	-	-	0%
	Mar 2013	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Apr 2013	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	May 2013	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Jun 2013	-	-	0%	1	-	0%	2	1	50%	-	-	0%
	Jul 2013	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Aug 2013	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Sep 2013	-	-	0%	1	1	100%	-	-	0%	-	-	0%
	Oct 2013	-	-	0%	1	-	0%	-	-	0%	-	-	0%
	Nov 2013	-	-	0%	-	-	0%	-	-	0%	-	-	0%
	Dec 2013	-	-	0%	1	1	100%	-	-	0%	-	-	0%

Appendix A: Latest Date of Available Data for Each Data Partner up to Request Send Date (April 20, 2016)

DP ID	Start Date	End Date
DP0001	1/1/2009	12/31/2013
DP0002	1/1/2009	12/31/2013
DP0003	1/1/2009	12/31/2013
DP0004	1/1/2009	12/31/2013
DP0005	1/1/2009	12/31/2013
DP0006	1/1/2009	6/30/2012
DP0007	1/1/2009	12/31/2013
DP0008	1/1/2009	12/31/2013
DP0009	1/1/2009	12/31/2013
DP0010	1/1/2009	12/31/2013
DP0011	1/1/2009	12/31/2013
DP0012	1/1/2009	12/31/2013
DP0013	1/1/2009	12/31/2013
DP0014	1/1/2009	12/31/2013
DP0015	1/1/2009	12/31/2013

Appendix B: List of Drugs Used to Define Exposures in this Request

Generic Name	Form	Route	Strength	Unit
Fentanyl Patch				
FENTANYL	PATCH 72 HOUR	TRANSDERMAL	25	MCG/HR
FENTANYL	PATCH 72 HOUR	TRANSDERMAL	50	MCG/HR
FENTANYL	PATCH 72 HOUR	TRANSDERMAL	75	MCG/HR
FENTANYL	PATCH 72 HOUR	TRANSDERMAL	100	MCG/HR
FENTANYL	PATCH 72 HOUR	TRANSDERMAL	12	MCG/HR

Appendix C: List of International Classification of Diseases, Ninth Edition, Clinical Modification (ICD-9-CM) Codes Used to Define Exclusion Criteria in this Request

Opioid Poisoning	Description	Code Type
965.0	Poisoning by opiates and related narcotics	ICD-9-CM Diagnosis Code
965.00	Poisoning by opium (alkaloids), unspecified	ICD-9-CM Diagnosis Code
965.01	Poisoning by heroin	ICD-9-CM Diagnosis Code
965.02	Poisoning by methadone	ICD-9-CM Diagnosis Code
965.09	Poisoning by other opiates and related narcotics	ICD-9-CM Diagnosis Code