Disclaimer

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

Data obtained through Mini-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 the Mini-Sentinel pilot in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Mini-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 to16_cap_mpl1r_wp031_nsdp_v01, Report 3 of 3

Request ID: to16_cap_mpl1r_wp031_nsdp_v01, Report 3 of 3

Request Description: This request investigated the use of enoxaparin, by manufacturer (Sanofi, Sandoz, or Amphastar) in the Mini-Sentinel Distributed Database (MSDD). Bleeding events and venous thromboembolism (VTE) events were used to define incidence.

Mini-Sentinel Modular Program Tool Used: Cohort Identification and Descriptive Analysis (CIDA) tool, version 2.0.5

Data Source: This package was distributed to 15 Data Partners in the MSDD on April 29, 2015. The query period for this request was August 1, 2010 - December 31, 2013. Please see Appendix A for dates of available data.

Study Design: Hospitalized bleeding in this report was defined as a definite bleeding event (hospital discharge diagnosis code in the primary position) with no trauma code within the same inpatient stay. Hospitalized bleeding was also defined as a possible bleeding code (flagged as a primary diagnosis), supported by a definite bleeding code (flagged as a secondary diagnosis), without a corresponding trauma code. All codes were required to be within the same inpatient stay. Major bleeding events included hospitalized bleeding events with the inclusion of a critical site code or a transfusion code within the same inpatient encounter. VTE events included either (1) an inpatient VTE code, or (2) an outpatient VTE code with a warfarin dispensing within 30 days after a deep vein thrombosis (DVT) diagnosis

Cohort of Interest: For the scenarios where we examined bleeding events among enoxaparin users, we created enoxaparin treatment episodes, with a 0-day episode extension period and a one-day episode gap, during which we identified bleeding events. For the scenarios where we examined VTE events among enoxaparin users, an intent-to-treat analysis was conducted. New users were followed for 42 days following enoxaparin initiation, during which we identified VTE events. Patients had to be enrolled for 180 days and were allowed an enrollment gap of up to 45 days.

Exposure of Interest: The exposures of interest were defined using National Drug Codes (NDCs). Please see Appendix B for generic names used in this request.

Outcomes of Interest: The outcome of interests were defined using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), Current Procedural Terminology, Fourth Edition (CPT-4), and Healthcare Common Procedure Coding System (HCPCS) codes. Please see Appendices C and D for specific codes used in this request.

Cohort Eligibility Criteria: We required eligible members to be enrolled in health plans with medical and drug coverage for at least 180 days prior to exposure; gaps in coverage of up to 45 days were allowed. The following age groups were included in the cohort: <20, 20-44, 45-64, 65-74, 75-84, 85+ years.

Limitations: The exposure and inclusion and exclusion criteria may have been misclassified due to imperfect algorithms used to identify them. Therefore, data should be interpreted with this limitation in mind.

Notes: Counts of members cannot be aggregated across years or procedure codes. Doing so will result in double-counting of members. For example, members with a specific procedure in 2007 may also have the same procedure in 2008. Adding those years would double-count that person. Also, a member with procedure X in 2007 may also have had procedure Y in 2007. Adding across those two procedure codes would double-count that person.

When interpreting changes in raw counts of patients over time, it is important to understand the way in which the MSDD population is constructed. For example, one large Data Partner has data beginning in 2004, while a second large Data Partner has data beginning in 2007. Increases in the raw numbers of diagnosis/procedure patients or drug product users in these years are likely due to the introduction of these Data Partners. Thus, year-to-year changes should not be interpreted as trends in diagnoses, procedures, or drug products.

A second important consideration is that the MSDD population is continually changing. Therefore, a query conducted in July 2011 will investigate a different MSDD population than a query conducted in July 2012.

Please contact the Sentinel Operations Center (info@sentinelsystem.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

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),

Censor Episodes at Evidence of Death - indicates whether treatment episodes are truncated based on death date. A member has a death date if he or she has an encounter with a discharge status of "expired" in the Encounter Table, or if he or she has a death date

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.

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

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled"

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

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

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time." (For Intent to Treat analyses

Lookback Period (pre-existing condition) - number of days wherein a member is required to have evidence of pre-existing condition

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.

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

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

Table 1. Summary of Incident Enoxaparin Use in the Mini-Sentinel Distributed Database (MSDD) between August 1, 2010 and December 31, 2013, by Manufacturer

New Users	Dispensings	Days Supplied	Amount Supplied	Years at Risk	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
Amphastar										
2,155	2,666	34,732	21,111	89.3	66,545,029	114,485,508.6	0.03	16.12	1.24	13.03
Sandoz										
86,291	104,456	1,455,437	845,766	3,754.0	66,545,029	114,411,806.1	1.30	16.87	1.21	13.93
Sanofi										
48,600	57,817	832,741	496,122	2,149.3	66,545,029	114,436,337.9	0.73	17.13	1.19	14.40

Table 2. Summary of Incident Enoxaparin Use in the Mini-Sentinel Distributed Database (MSDD) between August 1, 2010 and December 31, 2013, by Manufacturer and Age Group

	New Users	Dispensings	Days Supplied	Amount Supplied	Years at Risk	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
Amphastar											
Age (Years)											
0-19	18	31	420	210	1.1	17,358,098	27,824,458.1	0.00	23.33	1.72	13.55
20-44	375	489	10,036	5,242	26.5	27,126,075	39,188,545.9	0.01	26.76	1.30	20.52
45-64	741	855	11,334	7,955	29.0	19,744,889	34,469,989.5	0.04	15.30	1.15	13.26
65-74	440	549	6,010	3,901	15.3	4,580,152	7,757,320.9	0.10	13.66	1.25	10.95
75-84	381	477	4,734	2,748	12.0	2,076,319	3,815,056.8	0.18	12.43	1.25	9.92
85+	200	265	2,198	1,055	5.5	795,376	1,430,137.6	0.25	10.99	1.33	8.29
Sandoz											
Age (Years)											
0-19	1,057	1,373	22,714	15,084	59.4	17,358,098	27,823,853.9	0.06	21.49	1.30	16.54
20-44	19,049	27,330	528,851	285,636	1,397.7	27,125,768	39,174,875.5	0.70	27.76	1.43	19.35
45-64	39,158	43,756	552,027	339,915	1,405.7	19,743,585	34,436,168.9	1.98	14.10	1.12	12.62
65-74	15,907	18,090	211,373	126,438	535.9	4,577,895	7,742,307.7	3.47	13.29	1.14	11.68
75-84	8,023	9,663	101,270	59,502	256.0	2,074,541	3,806,870.2	3.87	12.62	1.20	10.48
85+	3,097	4,244	39,202	19,191	99.3	794,764	1,427,730.0	3.90	12.66	1.37	9.24
Sanofi											
Age (Years)											
0-19	797	1,144	21,495	13,775	56.7	17,358,098	27,823,908.0	0.05	26.97	1.44	18.79
20-44	8,369	12,264	235,464	139,222	622.6	27,125,880	39,181,857.2	0.31	28.14	1.47	19.20
45-64	20,822	23,137	303,961	182,112	775.8	19,744,218	34,449,661.9	1.05	14.60	1.11	13.14
65-74	10,784	12,201	161,306	100,250	412.5	4,578,150	7,745,147.4	2.36	14.96	1.13	13.22
75-84	5,927	6,749	83,362	46,791	212.3	2,074,957	3,807,864.6	2.86	14.06	1.14	12.35
85+	1,901	2,322	27,153	13,971	69.3	794,811	1,427,898.8	2.39	14.28	1.22	11.69

Table 3. Summary of Incident Enoxaparin Use in the Mini-Sentinel Distributed Database (MSDD) between August 1, 2010 and December 31, 2013, by Manufacturer and Sex

	New Users	Dispensings	Days Supplied	Amount Supplied	Years at Risk	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
Amphastar											
Female	1,347	1,682	23,121	12,381	59.7	33,885,012	58,807,965.1	0.04	17.16	1.25	13.75
Male	808	984	11,611	8,730	29.6	32,657,349	55,673,791.0	0.02	14.37	1.22	11.80
Unknown	0	0	0	0	0.0	2,668	3,752.4	0.00	---	---	---
Sandoz											
Female	54,111	67,491	1,006,317	553,626	2,610.7	33,885,012	58,761,552.1	1.60	18.60	1.25	14.91
Male	32,174	36,958	449,047	292,093	1,143.1	32,657,349	55,646,507.9	0.99	13.96	1.15	12.15
Unknown	6	7	73	47	0.2	2,668	3,746.1	2.25	12.17	1.17	10.43
Sanofi											
Female	29,967	36,625	554,047	319,508	1,436.5	33,885,012	58,777,603.4	0.88	18.49	1.22	15.13
Male	18,631	21,190	278,675	176,605	712.7	32,657,349	55,654,984.0	0.57	14.96	1.14	13.15
Unknown	2	2	19	9	0.0	2,668	3,750.6	0.75	9.50	1.00	9.50

Table 4. Summary of Incident Enoxaparin Use in the Mini-Sentinel Distributed Database (MSDD) between August 1, 2010 and December 31, 2013, by Manufacturer and Year

	New Users	Dispensings	Days Supplied	Amount Supplied	Years at Risk	Eligible Members	Member-Years	New Users per 1,000 Eligible Members	Days Supplied per User	Dispensings per User	Days Supplied per Dispensing
Amphastar											
Year											
2010	0	0	0	0	0.0	39,367,119	14,906,679.6	0.00	---	---	---
2011	15	15	218	150	0.6	42,937,947	34,024,455.0	0.00	14.53	1.00	14.53
2012	750	929	11,249	6,834	28.8	42,041,578	33,390,451.4	0.02	15.00	1.24	12.11
2013	1,390	1,722	23,265	14,128	60.0	40,831,527	32,163,922.6	0.03	16.74	1.24	13.51
Sandoz											
Year											
2010	11,822	14,179	196,328	112,941	505.8	39,367,119	14,906,679.6	0.30	16.61	1.20	13.85
2011	38,708	47,294	665,324	378,606	1,717.9	42,929,352	34,017,020.3	0.90	17.19	1.22	14.07
2012	22,241	26,577	368,039	217,348	948.1	42,006,022	33,361,786.4	0.53	16.55	1.19	13.85
2013	13,520	16,406	225,746	136,871	582.1	40,787,571	32,126,319.8	0.33	16.70	1.21	13.76
Sanofi											
Year											
2010	12,191	14,510	199,764	115,328	514.3	39,367,119	14,906,679.6	0.31	16.39	1.19	13.77
2011	17,230	20,565	289,842	167,316	747.2	42,928,613	34,017,361.9	0.40	16.82	1.19	14.09
2012	10,473	12,510	186,763	115,081	483.1	42,019,525	33,371,717.1	0.25	17.83	1.19	14.93
2013	8,706	10,232	156,372	98,396	404.7	40,805,200	32,140,579.3	0.21	17.96	1.18	15.28

Appendix A. Dates of Available Data in the Mini-Sentinel Distributed Database (MSDD) for Each Data Partner (DP) as of Request Send Date (April 29, 2015)

DP ID	Start Date	End Date
DP001	8/1/2010	12/31/2013
DP002	8/1/2010	12/31/2013
DP003	8/1/2010	12/31/2013
DP004	8/1/2010	12/31/2013
DP005	8/1/2010	12/31/2013
DP006	8/1/2010	12/31/2013
DP007	8/1/2010	12/31/2013
DP008	8/1/2010	12/31/2013
DP009	8/1/2010	12/31/2013
DP010	8/1/2010	12/31/2013
DP011	8/1/2010	12/31/2013
DP012	8/1/2010	12/31/2013
DP013	8/1/2010	12/31/2013
DP014	8/1/2010	12/31/2013
DP015	8/1/2010	12/31/2013

Appendix B. List of Generic Names to Define Incidence Criteria in this Request

Anticoagulants

Generic Name
enoxaparin
apixaban
argatroban
argatroban in 0.9 % sodium chloride
argatroban in sodium chloride, iso-osmotic
dabigatran etexilate mesylate
dalteparin sodium, porcine
fondaparinux sodium
heparin sodium, beef
heparin sodium, porcine
heparin sodium, porcine in 0.45 % sodium chloride
heparin sodium, porcine in 0.9 % sodium chloride
heparin sodium, porcine in 0.9 % sodium chloride
heparin sodium, porcine in 0.9 % sodium chloride/pf
heparin sodium, porcine/dextrose 5 % in water
heparin sodium, porcine/dextrose 5 % in water/pf
heparin sodium, porcine/pf
lepirudin, recombinant
rivaroxaban
tinzaparin sodium, porcine
warfarin sodium

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Hospitalized Bleeding
A bleeding event is defined as a definite bleeding code (primary) without a trauma code, or a possible bleeding code (primary) supported by a definite bleeding code (secondary); without a corresponding trauma - ***codes are required to be within the same inpatient stay***

Definite Bleeding Codes		
Code	**Code Type**	**Care Setting[1]**
531.0*	ICD-9-CM Diagnosis	
531.2*	ICD-9-CM Diagnosis	
531.4*	ICD-9-CM Diagnosis	
531.6*	ICD-9-CM Diagnosis	
532.0*	ICD-9-CM Diagnosis	
532.2*	ICD-9-CM Diagnosis	
532.4*	ICD-9-CM Diagnosis	
532.6*	ICD-9-CM Diagnosis	
533.0*	ICD-9-CM Diagnosis	
533.2*	ICD-9-CM Diagnosis	
533.4*	ICD-9-CM Diagnosis	
533.6*	ICD-9-CM Diagnosis	
534.0*	ICD-9-CM Diagnosis	
534.2*	ICD-9-CM Diagnosis	
534.6*	ICD-9-CM Diagnosis	
535.01	ICD-9-CM Diagnosis	
535.11	ICD-9-CM Diagnosis	
535.21	ICD-9-CM Diagnosis	
535.31	ICD-9-CM Diagnosis	
535.41	ICD-9-CM Diagnosis	
535.51	ICD-9-CM Diagnosis	
535.61	ICD-9-CM Diagnosis	
537.83	ICD-9-CM Diagnosis	
456.0	ICD-9-CM Diagnosis	
456.20	ICD-9-CM Diagnosis	
530.7	ICD-9-CM Diagnosis	
530.82	ICD-9-CM Diagnosis	
578.0	ICD-9-CM Diagnosis	
455.2	ICD-9-CM Diagnosis	
455.5	ICD-9-CM Diagnosis	
455.8	ICD-9-CM Diagnosis	
562.02	ICD-9-CM Diagnosis	
562.03	ICD-9-CM Diagnosis	
562.12	ICD-9-CM Diagnosis	
562.13	ICD-9-CM Diagnosis	
568.81	ICD-9-CM Diagnosis	
569.3	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
569.85	ICD-9-CM Diagnosis	
578.1	ICD-9-CM Diagnosis	
578.9	ICD-9-CM Diagnosis	
593.81	ICD-9-CM Diagnosis	
599.7	ICD-9-CM Diagnosis	
623.8	ICD-9-CM Diagnosis	
626.2	ICD-9-CM Diagnosis	
626.6	ICD-9-CM Diagnosis	
430	ICD-9-CM Diagnosis	
431	ICD-9-CM Diagnosis	
432	ICD-9-CM Diagnosis	
432.0	ICD-9-CM Diagnosis	
432.1	ICD-9-CM Diagnosis	
432.9	ICD-9-CM Diagnosis	
852.0	ICD-9-CM Diagnosis	
852.2	ICD-9-CM Diagnosis	
852.4	ICD-9-CM Diagnosis	
853.0	ICD-9-CM Diagnosis	
423.0	ICD-9-CM Diagnosis	
459.0	ICD-9-CM Diagnosis	
568.81	ICD-9-CM Diagnosis	
719.1x	ICD-9-CM Diagnosis	
784.7	ICD-9-CM Diagnosis	
784.8	ICD-9-CM Diagnosis	
786.3	ICD-9-CM Diagnosis	
Possible Bleeding Codes		
531.1	ICD-9-CM Diagnosis	
531.3	ICD-9-CM Diagnosis	
531.5	ICD-9-CM Diagnosis	
531.7	ICD-9-CM Diagnosis	
531.9	ICD-9-CM Diagnosis	
532.1	ICD-9-CM Diagnosis	
532.3	ICD-9-CM Diagnosis	
532.5	ICD-9-CM Diagnosis	
532.7	ICD-9-CM Diagnosis	
532.9	ICD-9-CM Diagnosis	
533.1	ICD-9-CM Diagnosis	
533.3	ICD-9-CM Diagnosis	
533.5	ICD-9-CM Diagnosis	
533.7	ICD-9-CM Diagnosis	
533.9	ICD-9-CM Diagnosis	
534.1	ICD-9-CM Diagnosis	
534.3	ICD-9-CM Diagnosis	
534.5	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
534.7	ICD-9-CM Diagnosis	
534.9	ICD-9-CM Diagnosis	
535.00	ICD-9-CM Diagnosis	
535.10	ICD-9-CM Diagnosis	
535.20	ICD-9-CM Diagnosis	
535.30	ICD-9-CM Diagnosis	
535.40	ICD-9-CM Diagnosis	
535.50	ICD-9-CM Diagnosis	
535.60	ICD-9-CM Diagnosis	
455*	ICD-9-CM Diagnosis	
562.00	ICD-9-CM Diagnosis	
562.01	ICD-9-CM Diagnosis	
562.10	ICD-9-CM Diagnosis	
562.11	ICD-9-CM Diagnosis	
530.1	ICD-9-CM Diagnosis	
280.0	ICD-9-CM Diagnosis	
285.1	ICD-9-CM Diagnosis	
285.9	ICD-9-CM Diagnosis	
790.92	ICD-9-CM Diagnosis	
Major Bleeding		
Major bleeding is defined as a bleeding event with a critical site code or a transfusion code		
Critical Site Code		
430	ICD-9-CM Diagnosis	
431	ICD-9-CM Diagnosis	
432	ICD-9-CM Diagnosis	
852.0	ICD-9-CM Diagnosis	
852.2	ICD-9-CM Diagnosis	
852.4	ICD-9-CM Diagnosis	
853.0	ICD-9-CM Diagnosis	
336.1	ICD-9-CM Diagnosis	
363.6	ICD-9-CM Diagnosis	
372.72	ICD-9-CM Diagnosis	
376.32	ICD-9-CM Diagnosis	
377.42	ICD-9-CM Diagnosis	
379.23	ICD-9-CM Diagnosis	
719.1	ICD-9-CM Diagnosis	
729.92	ICD-9-CM Diagnosis	
729.97	ICD-9-CM Diagnosis	
423.0	ICD-9-CM Diagnosis	
593.81	ICD-9-CM Diagnosis	
772.5	ICD-9-CM Diagnosis	
866.01	ICD-9-CM Diagnosis	
866.02	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
866.11	ICD-9-CM Diagnosis	
866.12	ICD-9-CM Diagnosis	
Transfusion Code		
9903	ICD-9-CM Procedure	
9904	ICD-9-CM Procedure	
9905	ICD-9-CM Procedure	
9906	ICD-9-CM Procedure	
9907	ICD-9-CM Procedure	
9909	ICD-9-CM Procedure	
P9010	HCPCS Procedure	
P9011	HCPCS Procedure	
P9016	HCPCS Procedure	
P9017	HCPCS Procedure	
P9019	HCPCS Procedure	
P9020	HCPCS Procedure	
P9021	HCPCS Procedure	
P9022	HCPCS Procedure	
P9023	HCPCS Procedure	
P9031	HCPCS Procedure	
P9032	HCPCS Procedure	
P9033	HCPCS Procedure	
P9034	HCPCS Procedure	
P9035	HCPCS Procedure	
P9036	HCPCS Procedure	
P9037	HCPCS Procedure	
P9038	HCPCS Procedure	
P9039	HCPCS Procedure	
P9040	HCPCS Procedure	
P9044	HCPCS Procedure	
P9051	HCPCS Procedure	
P9052	HCPCS Procedure	
P9053	HCPCS Procedure	
P9054	HCPCS Procedure	
P9055	HCPCS Procedure	
P9056	HCPCS Procedure	
P9057	HCPCS Procedure	
P9058	HCPCS Procedure	
P9059	HCPCS Procedure	
P9060	HCPCS Procedure	
0380	Revenue Center Procedure	
0381	Revenue Center Procedure	
0382	Revenue Center Procedure	
0383	Revenue Center Procedure	
0384	Revenue Center Procedure	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
0385	Revenue Center Procedure	
0386	Revenue Center Procedure	
0387	Revenue Center Procedure	
0388	Revenue Center Procedure	
0389	Revenue Center Procedure	
0390	Revenue Center Procedure	
0391	Revenue Center Procedure	
0392	Revenue Center Procedure	
0399	Revenue Center Procedure	
Venous Thromboembolism (VTE)		
Hospitalized PE/DVT OR Outpatient DVT		
415.1	ICD-9-CM Diagnosis	IP*
415.1*	ICD-9-CM Diagnosis	IP*
451	ICD-9-CM Diagnosis	IP*
451.*	ICD-9-CM Diagnosis	IP*
451.**	ICD-9-CM Diagnosis	IP*
453	ICD-9-CM Diagnosis	IP*
453.*	ICD-9-CM Diagnosis	IP*
453.**	ICD-9-CM Diagnosis	IP*
OR		
451.*	ICD-9-CM Diagnosis	AV, ED, OA
451.**	ICD-9-CM Diagnosis	AV, ED, OA
453	ICD-9-CM Diagnosis	AV, ED, OA
453.*	ICD-9-CM Diagnosis	AV, ED, OA
453.**	ICD-9-CM Diagnosis	AV, ED, OA
AND		
Warfarin prescription within 30 days after the DVT diagnosis		
AMI		
410*	ICD-9-CM Diagnosis	IP*
410**	ICD-9-CM Diagnosis	IP*
Ischemic Stroke		
433.*1	ICD-9-CM Diagnosis	IPP
434.*	ICD-9-CM Diagnosis	IPP
434.01	ICD-9-CM Diagnosis	IPP
434.11	ICD-9-CM Diagnosis	IPP
434.91	ICD-9-CM Diagnosis	IPP
Trauma Exclusions:		
62000	CPT-4	
62005	CPT-4	
62010	CPT-4	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
800	ICD-9-CM Diagnosis	
800*	ICD-9-CM Diagnosis	
801	ICD-9-CM Diagnosis	
801*	ICD-9-CM Diagnosis	
802	ICD-9-CM Diagnosis	
802*	ICD-9-CM Diagnosis	
803	ICD-9-CM Diagnosis	
803*	ICD-9-CM Diagnosis	
804	ICD-9-CM Diagnosis	
804*	ICD-9-CM Diagnosis	
805	ICD-9-CM Diagnosis	
805*	ICD-9-CM Diagnosis	
806	ICD-9-CM Diagnosis	
806*	ICD-9-CM Diagnosis	
8060*	ICD-9-CM Diagnosis	
8062*	ICD-9-CM Diagnosis	
807	ICD-9-CM Diagnosis	
8074	ICD-9-CM Diagnosis	
8074*	ICD-9-CM Diagnosis	
808	ICD-9-CM Diagnosis	
808*	ICD-9-CM Diagnosis	
809	ICD-9-CM Diagnosis	
809*	ICD-9-CM Diagnosis	
810	ICD-9-CM Diagnosis	
810*	ICD-9-CM Diagnosis	
811	ICD-9-CM Diagnosis	
811*	ICD-9-CM Diagnosis	
812	ICD-9-CM Diagnosis	
812*	ICD-9-CM Diagnosis	
813	ICD-9-CM Diagnosis	
813*	ICD-9-CM Diagnosis	
818	ICD-9-CM Diagnosis	
818*	ICD-9-CM Diagnosis	
819*	ICD-9-CM Diagnosis	
820*	ICD-9-CM Diagnosis	
821*	ICD-9-CM Diagnosis	
822*	ICD-9-CM Diagnosis	
823*	ICD-9-CM Diagnosis	
824*	ICD-9-CM Diagnosis	
825*	ICD-9-CM Diagnosis	
826*	ICD-9-CM Diagnosis	
827*	ICD-9-CM Diagnosis	
828*	ICD-9-CM Diagnosis	
829*	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
819	ICD-9-CM Diagnosis	
820	ICD-9-CM Diagnosis	
821	ICD-9-CM Diagnosis	
822	ICD-9-CM Diagnosis	
823	ICD-9-CM Diagnosis	
824	ICD-9-CM Diagnosis	
827	ICD-9-CM Diagnosis	
828	ICD-9-CM Diagnosis	
829	ICD-9-CM Diagnosis	
860*	ICD-9-CM Diagnosis	
860	ICD-9-CM Diagnosis	
8620	ICD-9-CM Diagnosis	
8620*	ICD-9-CM Diagnosis	
8621*	ICD-9-CM Diagnosis	
8621	ICD-9-CM Diagnosis	
8628*	ICD-9-CM Diagnosis	
8628	ICD-9-CM Diagnosis	
8629*	ICD-9-CM Diagnosis	
8629	ICD-9-CM Diagnosis	
8630*	ICD-9-CM Diagnosis	
8630	ICD-9-CM Diagnosis	
8631*	ICD-9-CM Diagnosis	
8631	ICD-9-CM Diagnosis	
8632*	ICD-9-CM Diagnosis	
8632	ICD-9-CM Diagnosis	
8633	ICD-9-CM Diagnosis	
8633*	ICD-9-CM Diagnosis	
8634*	ICD-9-CM Diagnosis	
8635*	ICD-9-CM Diagnosis	
8634	ICD-9-CM Diagnosis	
8635	ICD-9-CM Diagnosis	
8638*	ICD-9-CM Diagnosis	
8639*	ICD-9-CM Diagnosis	
8641*	ICD-9-CM Diagnosis	
8651*	ICD-9-CM Diagnosis	
8638	ICD-9-CM Diagnosis	
8639	ICD-9-CM Diagnosis	
8641	ICD-9-CM Diagnosis	
8651	ICD-9-CM Diagnosis	
866*	ICD-9-CM Diagnosis	
867*	ICD-9-CM Diagnosis	
8730*	ICD-9-CM Diagnosis	
8731*	ICD-9-CM Diagnosis	
8750*	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
8751*	ICD-9-CM Diagnosis	
9024*	ICD-9-CM Diagnosis	
866	ICD-9-CM Diagnosis	
867	ICD-9-CM Diagnosis	
8730	ICD-9-CM Diagnosis	
8731	ICD-9-CM Diagnosis	
8750	ICD-9-CM Diagnosis	
8751	ICD-9-CM Diagnosis	
9024	ICD-9-CM Diagnosis	
90255	ICD-9-CM Diagnosis	
90256	ICD-9-CM Diagnosis	
90281	ICD-9-CM Diagnosis	
90282	ICD-9-CM Diagnosis	
925*	ICD-9-CM Diagnosis	
926*	ICD-9-CM Diagnosis	
9268*	ICD-9-CM Diagnosis	
927*	ICD-9-CM Diagnosis	
928*	ICD-9-CM Diagnosis	
929*	ICD-9-CM Diagnosis	
9584*	ICD-9-CM Diagnosis	
9585*	ICD-9-CM Diagnosis	
9587*	ICD-9-CM Diagnosis	
9967*	ICD-9-CM Diagnosis	
925	ICD-9-CM Diagnosis	
926	ICD-9-CM Diagnosis	
9268	ICD-9-CM Diagnosis	
927	ICD-9-CM Diagnosis	
928	ICD-9-CM Diagnosis	
929	ICD-9-CM Diagnosis	
9584	ICD-9-CM Diagnosis	
9585	ICD-9-CM Diagnosis	
9587	ICD-9-CM Diagnosis	
9967	ICD-9-CM Diagnosis	
99811	ICD-9-CM Diagnosis	
99812	ICD-9-CM Diagnosis	
9982*	ICD-9-CM Diagnosis	
9982	ICD-9-CM Diagnosis	
E805	ICD-9-CM Diagnosis	
E870	ICD-9-CM Diagnosis	
E881	ICD-9-CM Diagnosis	
E882	ICD-9-CM Diagnosis	
E883	ICD-9-CM Diagnosis	
E922	ICD-9-CM Diagnosis	
E923	ICD-9-CM Diagnosis	

Appendix C. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Healthcare Common Procedure Coding Systems (HCPCS) Codes and Algorithms to Define Outcomes in this Request

Code	Code Type	Care Setting
E955	ICD-9-CM Diagnosis	
E960	ICD-9-CM Diagnosis	
E965	ICD-9-CM Diagnosis	
E970	ICD-9-CM Diagnosis	
E805*	ICD-9-CM Diagnosis	
E870*	ICD-9-CM Diagnosis	
E881*	ICD-9-CM Diagnosis	
E882*	ICD-9-CM Diagnosis	
E883*	ICD-9-CM Diagnosis	
E922*	ICD-9-CM Diagnosis	
E923*	ICD-9-CM Diagnosis	
E955*	ICD-9-CM Diagnosis	
E960*	ICD-9-CM Diagnosis	
E965*	ICD-9-CM Diagnosis	
E970*	ICD-9-CM Diagnosis	

[1]Inpatient (IP)

Ambulatory Visit (AV)

Emergency Department (ED)

Other Ambulatory (OA)

Appendix D. List of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) and Current Procedural Terminology, Fourth Edition (CPT-4) Codes to define Inclusion/Exclusion Criteria in this Request

Kidney Transplant	
Code	**Code Type**
V42.0	ICD-9-CM Diagnosis
996.81	ICD-9-CM Diagnosis
55.6*	ICD-9-CM Procedure
50360	CPT-4
50365	CPT-4
50340	CPT-4
50370	CPT-4
50380	CPT-4

Dialysis	
Code	**Code Type**
39.95	ICD-9-CM Procedure
54.98	ICD-9-CM Procedure
792.5*	ICD-9-CM Diagnosis
V56.2*	ICD-9-CM Diagnosis
90935	CPT-4
90937	CPT-4
90945	CPT-4
90947	CPT-4
99512	CPT-4
99601	CPT-4
99602	CPT-4

Appendix E. Specifications Defining Parameters in this Request

The Cohort Identification and Descriptive Analysis (CIDA) tool was executed to investigate use of enoxaparin, by manufacturer (Sanofi, Sandoz, or Amphastar) in the Mini-Sentinel Distributed Database (MSDD). Bleeding events and Venous Thromboembolism (VTE) events were used to define incidence.

Hospitalized bleeding in this report was defined as a definite bleeding event (hospital discharge diagnosis code in the primary position) with no trauma code within the same inpatient stay. Hospitalized bleeding was also defined as a possible bleeding code (flagged as a primary diagnosis), supported by a definite bleeding code (flagged as a secondary diagnosis), without a corresponding trauma code. All codes were required to be within the same inpatient stay. Major bleeding events included hospitalized bleeding events with the inclusion of a critical site code or a transfusion code within the same inpatient encounter. VTE events included either (1) an inpatient VTE code, or (2) an outpatient VTE code with a warfarin dispensing within 30 days after a deep vein thrombosis (DVT) diagnosis

Coverage Requirement	Drug and Medical Coverage
Query Period	August 1, 2010- December 31, 2013
Enrollment Gap	45 Days
Enrollment Days	180
Age Stratifications	<20; 20-44; 45-64, 65-74, 75-84; 85+ Years
Minimum Days Supplied and Minimum Episode Duration	0 Days

	Drug/Exposure								Inclusion/Exclusion				
Scenario	**Incident exposure***	**Incident w/ respect to:**	**Episode Gap**	**Episode Extension Period**	**Washout (days)**	**Cohort Definition**	**Episode truncation by additional criteria**	**Episode truncation by Death**	**Inclusion/ Exclusion**	**Inclusion / Exclusion**	**Lookback Start**	**Lookback End**	**Care Setting**
Number of Enoxaparin Users by Manufacturer													
1	Sanofi	All Enoxaparin, Anticoagulants	1	0	180	01	Yes- initiation of other anticoagulants, occurrence of primary or secondary event, initiation of dialysis, or kidney transplant, prescription for a comparator drug (switching)	No	Kidney transplant Dialysis	Exclude Exclude	-180 -180	0 0	Any

Appendix E. Specifications Defining Parameters in this Request

	Drug/Exposure								Inclusion/Exclusion				
Scenario	Incident exposure*	Incident w/ respect to:	Episode Gap	Episode Extension Period	Washout (days)	Cohort Definition	Episode truncation by additional criteria	Episode truncation by Death	Inclusion/ Exclusion	Inclusion / Exclusion	Lookback Start	Lookback End	Care Setting
2	Sandoz	All Enoxaparin, Anticoagulants	1	0	180	01	Yes- initiation of other anticoagulants, occurrence of primary or secondary event, initiation of dialysis, or kidney transplant, prescription for a comparator drug (switching)	No	Kidney transplant Dialysis	Exclude Exclude	-180 -180	0 0	Any
3	Amphastar	All Enoxaparin, Anticoagulants	1	0	180	01	Yes- initiation of other anticoagulants, occurrence of primary or secondary event, initiation of dialysis, or kidney transplant, prescription for a comparator drug (switching)	No	Kidney transplant Dialysis	Exclude Exclude	-180 -180	0 0	Any

Appendix E. Specifications Defining Parameters in this Request

	Event/Outcome					
Scenario	**Event/ Outcome**	**Care Setting**	**Incident w/ respect to:**	**Incident Care Setting**	**Washout (days)**	**Blackout Period**
1	DUMMY	Any	Any Bleeding ** VTE	IP, AV, ED, OA	30	1
2	DUMMY	Any	Any Bleeding VTE	IP, AV, ED, OA	30	1
3	DUMMY	Any	Any Bleeding VTE	IP, AV, ED, OA	30	1

All exposure, event, and pre-existing condition codes provided by FDA requester.

* 25% overlap rule to account for early refills

**Any bleeding refers to Hospitalized Bleeding or Major bleeding