Disclaimer

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

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

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

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

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Request ID: sbirth_mpl1r_wp003_nsdp_v01

Request Description: We designed this request to estimate the number of stillbirth cases available for potential health outcome of interest (HOI) validation in the Sentinel Distributed Database (SDD). This request was conducted in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) era only.

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis module, version 7.0.1

Data Source: We distributed this request to 13 Sentinel Data Partners on November 15, 2018. The study period included data from July 1, 2016 through June 30, 2018. Please see Appendix A for a list of dates of available data for each Data Partner.

Study Design: We examined the number of stillbirth cases occurring in inpatient hospital stays, emergency department encounters, ambulatory visits, or other ambulatory visits during the ICD-10-CM era in the United States. Results were stratified by Data Partner, calendar year, and age group.

Event of Interest: We defind the event of interest (index) as: 1) stillbirth diagnosis, or 2) intrauterine death or papyraceous fetus diagnosis with a code for ≥ 20-week gestational within the prior 28 days. We defined all events using ICD-10-CM diagnosis codes. Please see Appendix B for a list of specific codes used to define index events in this request.

Cohort Eligibility Criteria: We included a member's first qualifying event that occurred during the query period. Cohort re-entry was not allowed. Members included in the cohorts were required to be enrolled in plans with medical and drug coverage for 270 days prior to the index event date, during which gaps in coverage up to 45 days were allowed. In addition, event incidence was assessed in the 183 days preceding the index date. We included the following age groups in the cohort: 12-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-55 years.

Please refer to Appendices C, D, and E for detailed specifications of parameters and design diagram used in the analyses for this request.

Limitations: Algorithms used to define events are imperfect; thus, it is possible that there may be misclassification. Therefore, data should be interpreted with this limitation in mind.

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

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

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

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

   Ambulatory Visit (AV) - includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.

   Emergency Department (ED) - includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.

   Inpatient Hospital Stay (IP) - includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.

   Non-Acute Institutional Stay (IS) - includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.

   Other Ambulatory Visit (OA) - includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

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

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

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

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

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

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

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

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

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

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

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

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

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

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

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

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

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

*not all terms may be used in this report

Table 1. Distribution of Baseline Characteristics among Identified Stillbirth Cases in the Sentinel Distributed Database (SDD) from July 1, 2016 to June 30, 2018

Characteristic	Number	
Overall Number of Patients	2,495	-
Demographics	**Mean**	**Standard Deviation**
Mean age (years)	31.6	5.7
Age (years)	**Number**	**Percent**
12-19	94	3.8%
20-24	275	11.0%
25-29	572	22.9%
30-34	807	32.3%
35-39	572	22.9%
40-44	165	6.6%
45-55	10	0.4%
Year		
2016	963	38.6%
2017	1,402	56.2%
2018	130	5.2%
Index Code Distributions	**Number**	**Percent**
Stillbirth	2,054	82.3%
Not Stillbirth	441	17.7%
Combination (Intrauterine Death (IUD) or Papyraceous Fetus (PF) Diagnosis with a ≥ 20-Week Gestational Age (GA) Code 28 Days Prior to Index)	1,380	55.3%
Same-Day Stillbirth and Combination (IUD or PF + GA)	939	37.6%
Care Setting Distributions	**Number**	**Percent**
Inpatient (IP)	1,879	75.3%
Outpatient (OP) (Ambulatory Visits or Other Ambulatory Visits)	578	23.2%
Emergency Department (ED)	49	2.0%
Same-Day IP and OP	0	0.0%
Same-Day IP and ED	0	0.0%
Same-Day OP and ED	11	0.4%

Table 2. Summary of Stillbirth Cases in the Sentinel Distributed Database (SDD) from July 1, 2016 to June 30, 2018, Overall

	Members with Diagnoses	Eligible Members	Members with Diagnoses per 10,000 Eligible Members	Eligible Member-Years	Members with Diagnoses per 10,000 Eligible Member-Years	Diagnosis Codes
Overall	2,495	9,006,426	2.77	8,137,336	3.07	3,899

Table 3. Summary of Stillbirth Cases in the Sentinel Distributed Database (SDD) from July 1, 2016 to June 30, 2018, by Data Partner (DP)

Masked DP ID	Members with Diagnoses	Eligible Members	Members with Diagnoses per 10,000 Eligible Members	Eligible Member-Years	Members with Diagnoses per 10,000 Eligible Members-Years	Diagnosis Codes
DP01	458	1,302,682	3.52	1,534,959	2.98	895
DP02	52	201,052	2.59	275,114	1.89	82
DP03	378	1,521,788	2.48	1,310,372	2.88	515
DP04	169	423,988	3.99	505,556	3.34	237
DP05	42	259,500	1.62	194,066	2.16	73
DP06	407	1,771,080	2.30	1,120,115	3.63	620
DP07	64	143,582	4.46	162,101	3.95	95
DP08	28	80,477	3.48	104,008	2.69	41
DP09	78	248,622	3.14	311,707	2.50	113
DP10	178	518,238	3.43	243,040	7.32	241
DP11	168	573,403	2.93	538,939	3.12	327
DP12	38	224,661	1.69	230,810	1.65	57
DP13	435	1,737,353	2.50	1,606,548	2.71	603

Table 4. Summary of Stillbirth Cases in the Sentinel Distributed Database (SDD) from July 1, 2016 to June 30, 2018, by Calendar Year

Calendar Year	Members with Diagnoses	Eligible Members	Members with Diagnoses per 10,000 Eligible Members	Eligible Member-Years	Members with Diagnoses per 10,000 Eligible Member-Years	Diagnosis Codes
2016	963	6,878,830	1.40	2,882,266	3.34	1,476
2017	1,402	6,903,593	2.03	4,738,386	2.96	2,235
2018	130	2,582,849	0.50	516,684	2.52	188

Table 5. Summary of Stillbirth Cases in the Sentinel Distributed Database (SDD) from July 1, 2016 to June 30, 2018, by Age Group

Age Group	Members with Diagnoses	Eligible Members	Members with Diagnoses per 10,000 Eligible Members	Eligible Member-Years	Members with Diagnoses per 10,000 Eligible Member-Years	Diagnosis Codes
12-19	94	1,449,475	0.65	1,245,168	0.75	159
20-24	275	1,150,533	2.39	853,398	3.22	435
25-29	572	1,271,989	4.50	836,953	6.83	905
30-34	807	1,251,535	6.45	925,580	8.72	1,231
35-39	572	1,214,146	4.71	951,231	6.01	898
40-44	165	1,151,130	1.43	922,049	1.79	258
45-55	10	2,621,636	0.04	2,402,957	0.04	13

Appendix A. Dates of Available Data for Each Data Partner (DP) as of Request Distribution Date (November 15, 2018)

Masked DP ID	DP Start Date[1]	DP End Date[1]
DP01	01/01/2000	12/31/2017
DP02	01/01/2000	6/30/2018
DP03	01/01/2008	3/31/2018
DP04	01/01/2000	3/31/2018
DP05	01/01/2000	6/30/2017
DP06	01/01/2008	9/30/2017
DP07	01/01/2005	12/17/2017
DP08	01/01/2000	3/31/2018
DP09	01/01/2004	5/31/2018
DP10	01/01/2000	12/31/2016
DP11	06/01/2007	1/31/2018
DP12	01/01/2000	10/31/2017
DP13	01/01/2006	12/31/2017

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

Appendix B. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Index Events in this Request

Code	Code Type	Description
Stillbirth (Single-Event Index)		
Z37.1	ICD-10-CM	Single stillbirth
Z37.3	ICD-10-CM	Twins, one liveborn and one stillborn
Z37.4	ICD-10-CM	Twins, both stillborn
Z37.60	ICD-10-CM	Multiple births, unspecified, some liveborn
Z37.61	ICD-10-CM	Triplets, some liveborn
Z37.62	ICD-10-CM	Quadruplets, some liveborn
Z37.63	ICD-10-CM	Quintuplets, some liveborn
Z37.64	ICD-10-CM	Sextuplets, some liveborn
Z37.69	ICD-10-CM	Other multiple births, some liveborn
Z37.7	ICD-10-CM	Other multiple births, all stillborn
P95	ICD-10-CM	Stillbirth
Intrauterine Death or Papyraceous Fetus (Combination-Event Index)		
O31.00X0	ICD-10-CM	Papyraceous fetus, unspecified trimester, not applicable or unspecified
O31.00X1	ICD-10-CM	Papyraceous fetus, unspecified trimester, fetus 1
O31.00X2	ICD-10-CM	Papyraceous fetus, unspecified trimester, fetus 2
O31.00X3	ICD-10-CM	Papyraceous fetus, unspecified trimester, fetus 3
O31.00X4	ICD-10-CM	Papyraceous fetus, unspecified trimester, fetus 4
O31.00X5	ICD-10-CM	Papyraceous fetus, unspecified trimester, fetus 5
O31.00X9	ICD-10-CM	Papyraceous fetus, unspecified trimester, other fetus
O31.02X0	ICD-10-CM	Papyraceous fetus, second trimester, not applicable or unspecified
O31.02X1	ICD-10-CM	Papyraceous fetus, second trimester, fetus 1
O31.02X2	ICD-10-CM	Papyraceous fetus, second trimester, fetus 2
O31.02X3	ICD-10-CM	Papyraceous fetus, second trimester, fetus 3
O31.02X4	ICD-10-CM	Papyraceous fetus, second trimester, fetus 4
O31.02X5	ICD-10-CM	Papyraceous fetus, second trimester, fetus 5
O31.02X9	ICD-10-CM	Papyraceous fetus, second trimester, other fetus
O31.03X0	ICD-10-CM	Papyraceous fetus, third trimester, not applicable or unspecified
O31.03X1	ICD-10-CM	Papyraceous fetus, third trimester, fetus 1
O31.03X2	ICD-10-CM	Papyraceous fetus, third trimester, fetus 2
O31.03X3	ICD-10-CM	Papyraceous fetus, third trimester, fetus 3
O31.03X4	ICD-10-CM	Papyraceous fetus, third trimester, fetus 4
O31.03X5	ICD-10-CM	Papyraceous fetus, third trimester, fetus 5
O31.03X9	ICD-10-CM	Papyraceous fetus, third trimester, other fetus
O36.4XX0	ICD-10-CM	Maternal care for intrauterine death, not applicable or unspecified
O36.4XX1	ICD-10-CM	Maternal care for intrauterine death, fetus 1
O36.4XX2	ICD-10-CM	Maternal care for intrauterine death, fetus 2
O36.4XX3	ICD-10-CM	Maternal care for intrauterine death, fetus 3
O36.4XX4	ICD-10-CM	Maternal care for intrauterine death, fetus 4
O36.4XX5	ICD-10-CM	Maternal care for intrauterine death, fetus 5
O36.4XX9	ICD-10-CM	Maternal care for intrauterine death, other fetus
O36.4	ICD-10-CM	Maternal care for intrauterine death
>=20 Weeks Gestational Pregnancy (Combination Event)		
Z3A.20	ICD-10-CM	20 weeks gestation of pregnancy
Z3A.21	ICD-10-CM	21 weeks gestation of pregnancy

Appendix B. List of International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes Used to Define Index Events in this Request

Code	Code Type	Description
Z3A.22	ICD-10-CM	22 weeks gestation of pregnancy
Z3A.23	ICD-10-CM	23 weeks gestation of pregnancy
Z3A.24	ICD-10-CM	24 weeks gestation of pregnancy
Z3A.25	ICD-10-CM	25 weeks gestation of pregnancy
Z3A.26	ICD-10-CM	26 weeks gestation of pregnancy
Z3A.27	ICD-10-CM	27 weeks gestation of pregnancy
Z3A.28	ICD-10-CM	28 weeks gestation of pregnancy
Z3A.29	ICD-10-CM	29 weeks gestation of pregnancy
Z3A.30	ICD-10-CM	30 weeks gestation of pregnancy
Z3A.31	ICD-10-CM	31 weeks gestation of pregnancy
Z3A.32	ICD-10-CM	32 weeks gestation of pregnancy
Z3A.33	ICD-10-CM	33 weeks gestation of pregnancy
Z3A.34	ICD-10-CM	34 weeks gestation of pregnancy
Z3A.35	ICD-10-CM	35 weeks gestation of pregnancy
Z3A.36	ICD-10-CM	36 weeks gestation of pregnancy
Z3A.37	ICD-10-CM	37 weeks gestation of pregnancy
Z3A.38	ICD-10-CM	38 weeks gestation of pregnancy
Z3A.39	ICD-10-CM	39 weeks gestation of pregnancy
Z3A.40	ICD-10-CM	40 weeks gestation of pregnancy
Z3A.41	ICD-10-CM	41 weeks gestation of pregnancy
Z3A.42	ICD-10-CM	42 weeks gestation of pregnancy
Z3A.49	ICD-10-CM	Greater than 42 weeks gestation of pregnancy

Appendix C. Specifications Defining Parameters in this Request

In this request we used the Cohort Identification and Descriptive Analysis module, version 7.0.1 to estimate the number of stillbirth cases available for potential health outcome of interest (HOI) validation in the Sentinel Distributed Database (SDD). This request was conducted in the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) era only.

Query period:	July 1, 2016 - June 30, 2018
Coverage requirement:	Medical and Drug Coverage
Pre-index enrollment requirement:	270
Enrollment gap:	45
Age groups:	12-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-55 years
Sex:	Female
Stratifications:	Age Group, Calendar Year, Care Setting
Envelope macro:	Run envelope macro. Reclassify ambulatory visits, emergency department encounters, and other ambulatory encounters that occur during an inpatient stay as inpatient encounters
Freeze data:	Yes
Medical charts:	Yes
Baseline table:	Yes

Stillbirth Event

Scenario	Group	Index Event	Incident with respect to:	Cohort Definition	Washout Period	Care Settings	Censor Enrollment at Evidence of:
1	Index	Stillbirth or (Intrauterine Death/Papyraceous Fetus and ≥ 20-Week Gestation)	Stillbirth or (Intrauterine Death/Papyraceous Fetus and ≥ 20-Week Gestation)	First valid index dates during query period	183 days	Inpatient hospital stays; Emergency department encounters; Ambulatory visits; or Other ambulatory visits	Death

ICD-9, ICD-10, HCPCS, and CPT codes are provided by Optum360.

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

Appendix D. Specifications Defining Combo Tool Parameters in this Request

			Combo		
Combination Description	**Evaluation Period Start**	**Evaluation Period End**	**Combination Date**	**Encounter Type for Intrauterine Death Code**	**Encounter Type for ≥ 20-Week Gestation DX Code**
Inpatient Intrauterine Death/Papyraceous Fetus and ≥ 20-Week Gestational Age Code 28 Days Prior	-28	0	Inpatient Intrauterine Death/Papyraceous Fetus Code	Inpatient Hospital Stays (IP)	Any Care Setting
Outpatient Intrauterine Death/Papyraceous Fetus and ≥ 20-Week Gestational Age Code 28 Days Prior	-28	0	Outpatient Intrauterine Death/Papyraceous Fetus Code	Outpatient Visits (Ambulatory Visits, Other Ambulatory Visits)	Any Care Setting
Outpatient Intrauterine Death/Papyraceous Fetus and ≥ 20-Week Gestational Age Code 28 Days Prior	-28	0	Emergency Department Intrauterine Death/Papyraceous Fetus Code	Emergency Department Encounters (ED)	Any Care Setting

Appendix E. Design Diagram for this Request