



Modular Program Report

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	
<u>Request Description</u>	FDA requested use of Modular Program #3 (MP3), version 2, to investigate anaphylaxis events (ICD-9-CM codes 995.0 and 999.4) following incident exposure to several vaccinations among members with a pre-existing condition of milk allergy (ICD-9-CM code 558.3) or anaphylaxis due to milk products (ICD-9-CM code 995.67). The vaccines of interest were Dtap (CPT 90700), Dtap-HepB-IPV (CPT 90723), Dtap-HIB (CPT 90721), Dtap-HIB-IPV (CPT 90698), Dtap-IPV (CPT 90696), and Tdap (CPT 90715). The query was run against the Mini-Sentinel Distributed Database (MSDD) for the time period of January 1, 2000 to December 31, 2010. The package was distributed to 4 Data Partners on April 30, 2012.
	Results presented in this report provide counts of members with an incident vaccination, vaccinations, events, days at risk, eligible members, and member days. A vaccination was considered incident if a member had not had a prior vaccination of interest in the previous one day. Because a multiple incidence type was used, multiple vaccinations and treatment episodes per member were captured. Procedures such as vaccinations are given a one day supply and an episode extension period of one day was used to capture events on the same day and day after vaccination. Anaphylaxis events were reported for three care setting categories: Emergency Department only, Outpatient only, and Emergent, Outpatient, and Inpatient combined. Please see the Specifications for details into the exact parameters used in this request.
<u>Request ID</u>	MSY3_MPR14_V1

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<u>Notes:</u>	Please contact the Mini-Sentinel Operations Center (MSOC_Requests@harvardpilgrim.org) for questions and to provide comments/suggestions for future enhancements to this document.

Modular Program Specifications for Query ID MSY3_MPR14_v1

FFDA requested use of Modular Program #3 (MP3), version 2, to investigate incident vaccination of members with a pre-existing diagnosis of milk allergy or anaphylaxis due to milk products and anaphylaxis events following these vaccinations. The query period was from January 1, 2000 to December 31, 2010. The enrollment gap was set to 45 days. The episode gap was set to 0 days, the episode extension period was set to 1 day, and both minimum episode duration and minimum days supplied were set to 0 days. There were no principal diagnosis requirements and the blackout period was set to 0. Age groups were split as follows: 0-<2, 2-<8, and 8-<17 years. In total, 3 different scenarios were examined in this report with differing event care settings. See below for a description of each of these scenarios.

Scenario	Drug/Exposure		Pre-Existing Condition						Event/Outcome				
	Incident exposure	Incident w/ respect to:	Washout (days)	Incidence Type	Pre-Existing Condition	Code Type	Lookback Period (days)	Lookback Type	Care Setting	Event/Outcome	Washout (days)	Incidence Type	Care Setting
1	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	1	Multiple	Milk Allergy, Milk Anaphylaxis	Diagnosis	1,000	Fixed	All	Anaphylactic Shock	1	Multiple	Emergency Department
2	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	1	Multiple	Milk Allergy, Milk Anaphylaxis	Diagnosis	1,000	Fixed	All	Anaphylactic Shock	1	Multiple	Outpatient
3	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap	1	Multiple	Milk Allergy, Milk Anaphylaxis	Diagnosis	1,000	Fixed	All	Anaphylactic Shock	1	Multiple	Emergency Department, Outpatient, or Inpatient

Glossary of Terms in Modular Program 3*

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).

Days at Risk - number of days supplied plus any episode gaps and exposure extension periods.

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.

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

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode.

Incidence Type (drug/exposure)- *Minimum incidence type* will consider the first treatment episode in the query period as long as it is the first treatment episode in the user's entire available history. *Single* and *Multiple incidence types* will use the washout period to establish incidence, however *Single* will only consider the first treatment episode whereas *Multiple* will consider all qualifying incident treatment episodes.

Incidence Type (event/outcome)- *Minimum incidence type* considers the first event in a valid episode as long as it is the first event in the user's entire available history. *Multiple incidence type* uses the washout period to establish incidence and considers all qualifying incident treatment episodes. The program will only consider one event per episode, but the *Multiple incidence type* will consider more than one event per user if a user has more than one incident episode.

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

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

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.

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

New Users (Members Vaccinated) - number of members with incident 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.

Principal Diagnosis - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. YES will only consider diagnoses flagged as Principal.

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

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

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.

*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 Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap Vaccinations and Anaphylaxis Events for Individuals with a Pre-Existing Condition of Milk Allergy or Milk Anaphylaxis in the MSDD between January 1, 2000 and December 31, 2010, by Event Care Setting.

Event Caresetting	Members		Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	Members	Vaccinations/	Anaphylaxis
	Vaccinated	Vaccinations*					Vaccinated/ 1K	Member	Events/100k
Emergency Department, Outpatient, or Inpatient	9,659	18,649	37,246	2	28,154	14,216,636	343.1	1.9	5.4
Emergency Department	9,659	18,649	37,247	0	28,154	14,217,245	343.1	1.9	0.0
Outpatient	9,659	18,649	37,246	2	28,154	14,217,228	343.1	1.9	5.4

*Procedures such as vaccinations are automatically given a one day supply. Therefore, number of vaccinations = number of days supplied

Table 2. Summary of Incident Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap Vaccinations and Anaphylaxis Events for Individuals with a Pre-Existing Condition of Milk Allergy or Milk Anyphylaxis in the MSDD between January 1, 2000 to December 31, 2010, by Event Care Setting and Age Group.

	Members		Days at	New Anaphylaxis	Eligible		Members	Vaccinations/	Anaphylaxis
	Vaccinated	Vaccinations*	Risk	Events	Members	Member-Days	Vaccinated/ 1K	Member	Events/100k
							Eligible Members	Vaccinated	Days at Risk
Emergency Department, Outpatient, or Inpatient									
0 - < 2 Years	7,846	16,544	33,042	2	10,840	3,641,131	723.8	2.1	6.1
2 - < 8 Years	1,283	1,323	2,646	0	8,725	3,599,359	147.0	1.0	0.0
8 - < 17 Years	746	782	1,558	0	13,636	6,906,189	54.7	1.0	0.0
Emergency Department									
0 - < 2 Years	7,846	16,544	33,043	0	10,840	3,641,251	723.8	2.1	0.0
2 - < 8 Years	1,283	1,323	2,646	0	8,725	3,599,564	147.0	1.0	0.0
8 - < 17 Years	746	782	1,558	0	13,636	6,906,471	54.7	1.0	0.0
Outpatient									
0 - < 2 Years	7,846	16,544	33,042	2	10,840	3,641,247	723.8	2.1	6.1
2 - < 8 Years	1,283	1,323	2,646	0	8,725	3,599,560	147.0	1.0	0.0
8 - < 17 Years	746	782	1,558	0	13,636	6,906,462	54.7	1.0	0.0

*Procedures such as vaccinations are automatically given a one day supply. Therefore, number of vaccinations = number of days supplied

Table 3. Summary of Incident Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap Vaccinations and Anaphylaxis Events for Individuals with a Pre-Existing Condition of Milk Allergy or Milk Anaphylaxis in the MSDD between January 1, 2000 to December 31, 2010, by Event Care Setting and Sex.

	Members Vaccinated	Vaccinations*	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	Members Vaccinated/ 1K Eligible Members	Vaccinations/ Member Vaccinated	Anaphylaxis Events/100k Days at Risk
Emergency Department, Outpatient, or Inpatient									
Female	4,312	8,326	16,637	0	14,488	7,218,514	297.6	1.9	0.0
Male	5,324	10,283	20,529	2	13,604	6,965,564	391.4	1.9	9.7
Unknown	23	40	80	0	62	32,558	371.0	1.7	0.0
Emergency Department									
Female	4,312	8,326	16,637	0	14,488	7,218,795	297.6	1.9	0.0
Male	5,324	10,283	20,530	0	13,604	6,965,892	391.4	1.9	0.0
Unknown	23	40	80	0	62	32,558	371.0	1.7	0.0
Outpatient									
Female	4,312	8,326	16,637	0	14,488	7,218,788	297.6	1.9	0.0
Male	5,324	10,283	20,529	2	13,604	6,965,882	391.4	1.9	9.7
Unknown	23	40	80	0	62	32,558	371.0	1.7	0.0

*Procedures such as vaccinations are automatically given a one day supply. Therefore, number of vaccinations = number of days supplied

Table 4. Summary of Incident Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap Vaccinations and Anaphylaxis Events for Individuals with a Pre-Existing Condition of Milk Allergy or Milk Anaphylaxis in the MSDD between January 1, 2000 to December 31, 2010, by Event Care Setting and Year.

	Members Vaccinated	Vaccinations*	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	Members Vaccinated/ 1K Eligible Members	Vaccinations/ Member Vaccinated	Anaphylaxis Events/100k Days at Risk
Emergency Department, Outpatient, or Inpatient									
2000	1	1	2	0	7	489	142.9	1.0	0.0
2001	31	54	108	0	148	27,314	209.5	1.7	0.0
2002	63	88	176	0	337	83,007	186.9	1.4	0.0
2003	58	75	148	0	495	127,183	117.2	1.3	0.0
2004	468	712	1,421	0	2,442	468,588	191.6	1.5	0.0
2005	792	1,150	2,299	0	4,044	969,163	195.8	1.5	0.0
2006	1,109	1,578	3,153	0	5,694	1,424,694	194.8	1.4	0.0
2007	1,503	2,154	4,302	0	7,537	1,790,442	199.4	1.4	0.0
2008	1,880	2,676	5,349	1	8,873	2,168,201	211.9	1.4	18.7
2009	3,129	4,673	9,329	0	13,604	3,119,567	230.0	1.5	0.0
2010	3,826	5,488	10,959	1	16,540	4,037,988	231.3	1.4	9.1
Emergency Department									
2000	1	1	2	0	7	489	142.9	1.0	0.0
2001	31	54	108	0	148	27,314	209.5	1.7	0.0
2002	63	88	176	0	337	83,007	186.9	1.4	0.0
2003	58	75	148	0	495	127,183	117.2	1.3	0.0
2004	468	712	1,421	0	2,442	468,611	191.6	1.5	0.0
2005	792	1,150	2,299	0	4,044	969,201	195.8	1.5	0.0
2006	1,109	1,578	3,153	0	5,694	1,424,733	194.8	1.4	0.0
2007	1,503	2,154	4,302	0	7,537	1,790,527	199.4	1.4	0.0
2008	1,880	2,676	5,349	0	8,873	2,168,284	211.9	1.4	0.0
2009	3,129	4,673	9,329	0	13,604	3,119,724	230.0	1.5	0.0
2010	3,826	5,488	10,960	0	16,540	4,038,172	231.3	1.4	0.0

Table 4. Summary of Incident Dtap, Dtap-HepB-IPV, Dtap-HIB, Dtap-HIB-IPV, Dtap-IPV, Tdap Vaccinations and Anaphylaxis Events for Individuals with a Pre-Existing Condition of Milk Allergy or Milk Anaphylaxis in the MSDD between January 1, 2000 to December 31, 2010, by Event Care Setting and Year.

	Members Vaccinated	Vaccinations*	Days at Risk	New Anaphylaxis Events	Eligible Members	Member-Days	Members Vaccinated/ 1K Eligible Members	Vaccinations/ Member Vaccinated	Anaphylaxis Events/100k Days at Risk
Outpatient									
2000	1	1	2	0	7	489	142.9	1.0	0.0
2001	31	54	108	0	148	27,314	209.5	1.7	0.0
2002	63	88	176	0	337	83,007	186.9	1.4	0.0
2003	58	75	148	0	495	127,183	117.2	1.3	0.0
2004	468	712	1,421	0	2,442	468,611	191.6	1.5	0.0
2005	792	1,150	2,299	0	4,044	969,201	195.8	1.5	0.0
2006	1,109	1,578	3,153	0	5,694	1,424,732	194.8	1.4	0.0
2007	1,503	2,154	4,302	0	7,537	1,790,525	199.4	1.4	0.0
2008	1,880	2,676	5,349	1	8,873	2,168,283	211.9	1.4	18.7
2009	3,129	4,673	9,329	0	13,604	3,119,714	230.0	1.5	0.0
2010	3,826	5,488	10,959	1	16,540	4,038,169	231.3	1.4	9.1

*Procedures such as vaccinations are automatically given a one day supply. Therefore, number of vaccinations = number of days supplied