Medical Device Reporting Variance E2020002

for

Essure (P020014)

Quarterly MDR Analysis Report

Medical Device Reports

Report Number: 2
Period: 01-SEP-2020 to 30-NOV-2020
Report Date: 31-DEC-2020
Version 1.0

Introduction

This quarterly report contains information related to medical device reports (MDRs) derived from social media received in litigation. MDRs have many notable limitations, and they cannot be used alone to establish or compare rates of event occurrence. Based on the limited information in the event descriptions for the reports and the nature of the information, it is difficult to identify duplicate reports within this report, as well as duplicate reports previously submitted to the FDA. The limited information prevents the ability to draw any conclusions as to whether the device, or its removal, caused or contributed to any of the events described in this report.

Table of Contents

Background and Scope

On 24-APR-2020 the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) approved Bayer's request for variance, E2020002, under 21 CFR 803.19(b) from certain medical device reporting requirements prescribed in 21 CFR Part 803 for the Essure System ("Essure"), approved under Premarket Approval (PMA) Application P020014, on November 4, 2002.

This variance is limited to MDR-reports for Essure that Bayer becomes aware of from information received November 2016 through November 2020 in connection with litigation regarding Essure and that is derived from the following two sources:

a. publicly available social media information regarding certain Essure plaintiffs identified by Bayer's outside legal counsel; and
b. social media documents produced by plaintiffs' lawyers to Bayer's outside legal counsel.

The conditions of the variance include submission of this quarterly MDR analysis report after the close of a three-month period. The scope of this quarterly analysis report is MDR-reportable events submitted to the FDA as part of the variance for reports processed within the respective three-month period. This analysis will capture all of the requirements outlined in the FDA variance letter dated April 24, 2020.

Although MDRs are a valuable source of information, this passive surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely, unverified, or biased data. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to under-reporting of events, inaccuracies in reports, lack of verification that the device caused the reported event, and lack of information about frequency of device use. Because of this, MDRs comprise only one of the FDA's several important post-market surveillance data sources.

- MDR data alone cannot be used to establish rates of events, evaluate a change in event rates over time or compare event rates between devices. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with devices.
- Confirming whether a device actually caused a specific event can be difficult based solely on information provided in a given report. Establishing a cause-and-effect relationship is especially difficult if circumstances surrounding the event have not been verified or if the device in question has not been directly evaluated.
- MAUDE data does not represent all known safety information for a reported medical device and should be interpreted in the context of other available information when making device-related or treatment decisions.
- Submission of a medical device report and the FDA's release of that information is not necessarily an admission that a product, user facility, importer, distributor, manufacturer, or medical personnel caused or contributed to the event.[1]

[1] https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/search.cfm#fn1

Analysis

Data Source

Data sourced for the provision of this quarterly MDR analysis report includes the reported line-item tabular data spreadsheets[2] for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) submitted as part of the Medical Device Reporting Variance Request for Essure (E2020002).

Reports processed and submitted by Bayer as part of this variance do not necessarily represent unique reports, but rather events identified in comment threads from social media posts, sometimes by the same individual. The time period in which the reports were processed also do not represent the time period in which the events occurred. Based on the limited information in the event descriptions for the reports and the nature of the information, it is difficult to identify duplicate reports within the spreadsheet of events, as well as duplicate reports previously submitted to the FDA. The limited information prevents the ability to draw any conclusions as to whether the device, or its removal, caused or contributed to any of the reported deaths or other events in the reports.[3]

In order to contextualize the received reports, data from the variance MDRs submitted between 01-SEP-2020 to 30-NOV-2020 will be compared with:

1. Variance MDRs from the first Quarterly MDR Analysis Report[4] submitted by Bayer covering the time period between 01-JUN-2020 and 31-AUG-2020. These reports will be classified as 'Report 1 Variance'.
2. MDRs initially reported to the FDA by the company during the cumulative timeframe of the variance. These reports, which will be classified as 'non-variance other sources', include all Essure MDRs originating from different sources (e.g. spontaneous reports, medical literature) and submitted to the FDA as initial MDRs (outside of the variance) during cumulative timeframe of the variance (between 01-JUN-2020 and 30-NOV-2020).

[2] Spreadsheets: https://www.fda.gov/medical-devices/essure-permanent-birth-control/problems-reported-essure#reports
[3] https://www.fda.gov/medical-devices/essure-permanent-birth-control/problems-reported-essure
[4] Report 1: https://www.bayer.com/en/us/essure-information

Comprehensive analysis

A comprehensive analysis of reports submitted to the FDA for the respective period has been performed and is provided below.

Total number of events by report type and patient or device problem code

Figure 1. Total number of variance MDRs by month submitted (Jun-Nov 2020)

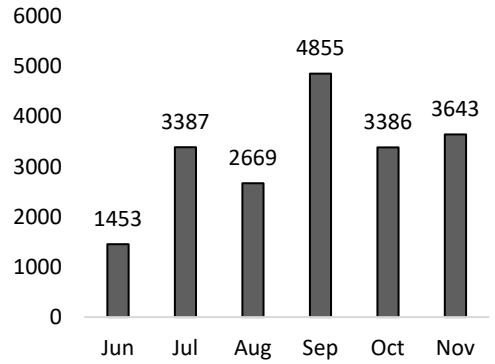


Figure 2. Total number of serious injury variance MDRs by month submitted (Jun-Nov 2020)

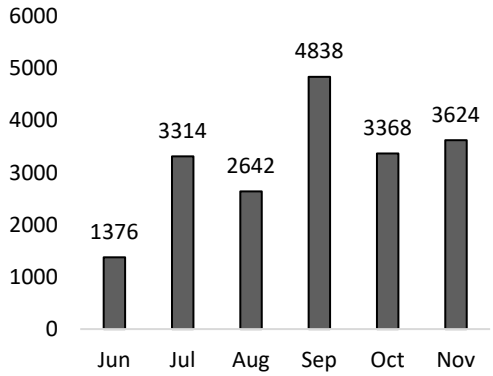


Figure 3. Total number of malfunction variance MDRs by month submitted (Jun-Nov 2020)

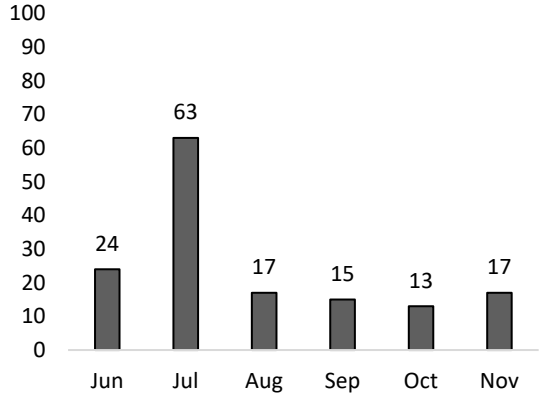
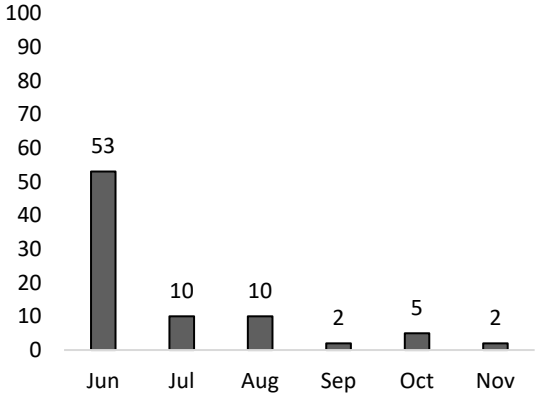


Figure 4. Total number of death variance MDRs by month submitted (Jun-Nov 2020)



For variance reports submitted, the time in which reports were processed does not necessarily represent the time in which the events reportedly occurred or when the patient made the information publicly available.

Table 1. Variance MDRs by posting year and type of reportable event (Jun-Nov 2020) [5]

Year of Posting	Serious Injury	Malfunction	Death	Total
≤ 2010	3356	14	0	3370
2011	302	0	0	302
2012	354	6	0	360
2013	797	16	16	829
2014	1622	16	5	1643
2015	2267	20	17	2304
2016	1258	5	2	1265
2017	616	1	1	618
2018	499	2	0	501
≥ 2019	408	3	1	412
Total	**11479**	**83**	**42**	**11604**

Year of posting is intended to refer to the date in which the information appeared on social media. Due to the unreliable nature of social media information and the process by which the date of posting was determined, there may exist dates which are not precise. Table 1 reflects this known limitation. The majority of the information from social media was posted between 04-JAN-2011 and 08-FEB-2020. Information about date of posting does not impact the known or labeled risks for the Essure device.

Table 2. Variance MDRs by event year and type of reportable event (Jun-Nov 2020) [5]

Year of Event	Serious Injury	Malfunction	Death	Total
≤ 2010	221	8	0	229
2011	72	6	0	78
2012	99	2	1	102
2013	149	6	0	155
2014	153	7	0	160
2015	154	3	0	157
2016	78	1	0	79
2017	40	2	0	42
2018	22	0	0	22
≥ 2019	7	0	0	7
Total	**995**	**35**	**1**	**1031**

Year of event is intended to refer to the date in which the event described by the information happened according to the report. Given the unreliable nature of social media information and the challenges of determining the accuracy of any reported event date, there may exist dates which are not precise. Table 2 reflects this known limitation. The majority of the reported event dates in the information from social media were between 01-JAN-2011 and 09-OCT-2019. Information about date of event does not impact the known or labeled risks for the Essure device.

[5] The table reflects information for variance MDRs only when it was made available to Bayer.

Table 3. Patient problem codes[6] for variance MDRs (Jun-Nov 2020)

Patient Problem Code	Report 1	Report 2	Total
1994: Pain	1354	4321	5675
3191: No Code Available	3218	3792	7010
2687: Foreign Body In Patient	638	1037	1675
2121: Uterine Perforation	919	1012	1931
3193: Pregnancy	425	787	1212
3165: Device Fragments In Patient	455	658	1113
2666: Heavier Menses	142	462	604
1888: Hemorrhage	124	337	461
1907: Hypersensitivity	112	297	409
1685: Pain, Abdominal	119	269	388
All other Patient Problem Codes	1052	1004	2057

Table 4. Patient problem codes for serious injury variance MDRs (Jun-Nov 2020)

Patient Problem Code	Report 1	Report 2	Total
1994: Pain	1354	4321	5675
3191: No Code Available	3218	3792	7010
2687: Foreign Body In Patient	626	1027	1653
2121: Uterine Perforation	907	1007	1914
3193: Pregnancy	417	783	1200
3165: Device Fragments In Patient	360	614	974
2666: Heavier Menses	142	462	604
1888: Hemorrhage	122	337	459
1907: Hypersensitivity	112	297	409
1685: Pain, Abdominal	119	269	388
All other Patient Problem Codes	960	986	1947

Table 5. Patient problem codes for malfunction variance MDRs (Jun-Nov 2020)

Patient Problem Code	Report 1	Report 2	Total
3165: Device Fragments In Patient	95	44	139
2687: Foreign Body In Patient	12	9	21
3193: Pregnancy	4	4	8
2121: Uterine Perforation	11	4	15
1946: Laceration(s)	0	1	1
2001: Perforation	1	1	2
1987: Organ(s), Perforation Of	1	0	1
2067: Sepsis	1	0	1
2668: Bowel Perforation	2	0	2

[6] It is possible for more than one Patient Problem Code to be selected per report. Therefore, the sum of the Patient Problem Codes is not expected to equal the total number of MDRs submitted during the period reviewed.

Table 6. Patient problem codes for death variance MDRs (Jun-Nov 2020)

Patient Problem Code	Report 1	Report 2	Total
1802: Death	72	9	81
2465: Labor, Premature	3	5	8
2121: Uterine Perforation	1	1	2
1930: Infection	0	1	1
2687: Foreign Body In Patient	0	1	1
2022: Pulmonary Insufficiency	0	1	1
3193: Pregnancy	4	0	4
1971: Necrosis	3	0	3
1855: Death, Intrauterine Fetal	2	0	2
2068: Shock, Septic	1	0	1
All other Patient Problem Codes	8	0	8

Table 7. Device problem codes for variance MDRs (Jun-Nov 2020)

Device Problem Code	Report 1	Report 2	Total
2993: No Known Device Problem	7061	11228	18289
1069: Break	447	656	1103
4003: Migration	1	0	1

Review of the figures and tables above provides a synopsis of the information provided in the H10 section 4th, 5th, and 6th variance submissions[7] [8] [9] as well as the variance submissions associated with Report 1 (01-JUN-2020 to 31-AUG-2020). Although limited, based on the information provided, reports are consistent with the known and labeled safety, quality and performance of the Essure device. No additional conclusions can be drawn as to whether the device, or its removal, caused or contributed to any of the reported deaths or other events in the reports.

Averages of patient demographics

Review of variance MDRs processed by Bayer over the variance time period of 01-JUN-2020 and 30-NOV-2020 indicates that the following measures related to patient age and weight.

Table 8. Table of patient demographics for age and weight (Jun-Nov 2020)

Measure	Age (years)		Weight (lbs.)	
	Report 1	Report 2	Report 1	Report 2
Sample size (n)*	913	2790	8	28
Minimum	20	18	101	88
Median	34	34	165	167
Average	34	35	166	164
Maximum	58	60	229	238

* Excludes child / fetal reports (only ≥ 18y)

Based on the information reviewed, no further investigation into patient age as it relates to variance MDRs is required.

[7] Submission 4: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=10819440&pc=HHS
[8] Submission 5: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=10875268&pc=HHS
[9] Submission 6: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/detail.cfm?mdrfoi__id=11036092&pc=HHS

Report Source

The reports processed by Bayer as part of the variance periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) are from the two sources of social media information in connection with Essure litigation as described in the variance letter. As the variance letter outlines, the two sources are:

- Publicly available social media information regarding certain Essure plaintiffs identified by Bayer's outside legal counsel and;
- Social media documents produced by the plaintiffs' lawyers to Bayer's outside legal counsel.

Entities Submitting Reports

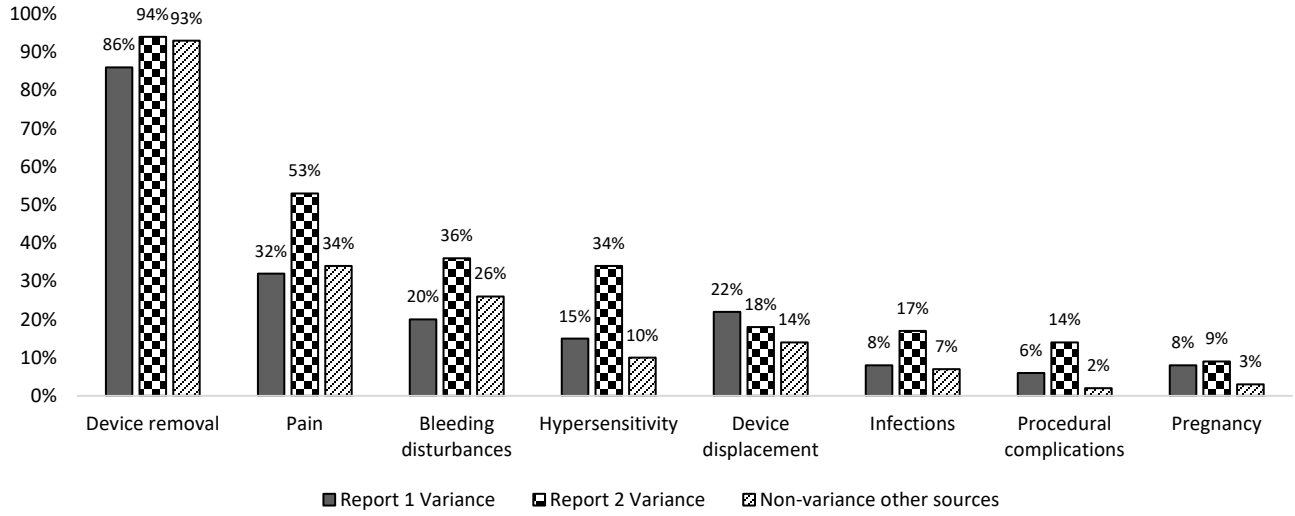
All variance MDRs for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) have been submitted to the FDA by Bayer Pharma AG.

Devices Involved

All reports processed by Bayer as part of the variance for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) are related to the Essure System, model numbers ESS205 and ESS305.

Synopsis of the nature of reports for the period

Figure 5. Distribution of initial MDR submissions by event grouping[10] (Jun-Nov 2020)



(N=7509) Report 1 Variance; (N=11884) Report 2 Variance; (N=7419) Non-variance other sources

[10] It is possible for more than one event grouping to be selected per report. Therefore, the sum of the event groupings is not expected to equal the total number (%) of MDRs submitted during the period reviewed.

The representative event groupings for Essure variance MDRs seems to be consistent with the non-variance other source reports processed during the same period which may reflect duplication of events in variance and non-variance sources. Information received as part of litigation accounts for 100% of variance reports and approximately 94% of non-variance other source reports. Device removal is the most frequently reported event in Report 1 Variance, Report 2 Variance, and non-variance other source reports with 86%, 94% and 93% respectively. Pain is the second most frequent in both variance and non-variance other source reports with 32% for Report 1 Variance, 53% for Report 2 Variance and 34% for non-variance other source reports.

Bleeding disturbances comes in third for Report 2 Variance and non-variances sources with 36% and 26% respectively.

Analysis of Additional Information

The following additional pieces of information were requested by FDA and prescribed within the variance letter.[11]

1. The variance MDRs processed by Bayer in the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) have all been reported via the two sources of social media information in connection with Essure litigation as described in the variance letter.

2. The variance MDRs processed by Bayer for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) are consistent with expected outcomes.

3. Considering that variance MDRs processed by Bayer for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) are consistent with expected outcomes, there have been no investigations opened related to these reports.

4. No corrective actions have been opened, are in-process, or implemented as a result of Variance MDRs processed by Bayer for the periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) as there were no events reported which indicate a new technical failure mode for the device.

No additional actions were required to address the reports summarized in this analysis.

[11] Variance Letter: https://www.fda.gov/media/137316/download

Number of returned devices

An evaluation on device returns was requested as part of the variance letter. An evaluation of device returns related to variance MDRs processed for the respective periods 01-JUN-2020 to 31-AUG-2020 (Report 1) and 01-SEP-2020 to 30-NOV-2020 (Report 2) indicates that there have been no devices returned to Bayer. Hence, as mentioned previously, no corrective actions have been opened or are in-process as a result of any variance MDRs processed in the same time period.

Presentation of report trends

An analysis of report trends in a comparative graphical display has been performed and is provided below. As stated previously, in order to contextualize the received reports, data from the variance MDRs submitted between 01-SEP-2020 to 30-NOV-2020 will be compared with:

1. Variance MDRs from the first Quarterly MDR Analysis Report submitted by Bayer covering the time period between 01-JUN-2020 and 31-AUG-2020. These reports will be classified as 'Report 1 Variance'.
2. MDRs initially reported to the FDA by the company during the cumulative timeframe of the variance. These reports, which will be classified as 'non-variance other sources', include all Essure MDRs originating from different sources (e.g. spontaneous reports, medical literature) and submitted to the FDA as initial MDRs (outside of the variance) during cumulative timeframe of the variance (between 01-JUN-2020 and 30-NOV-2020).

Figure 6. Total number of variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)

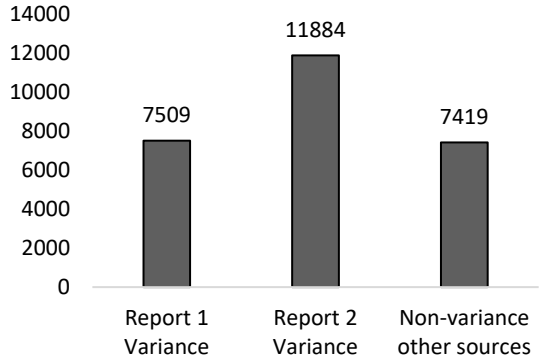


Figure 7. Variance MDRs vs. MDRs from non-variance other sources for serious injuries (Jun-Nov 2020)

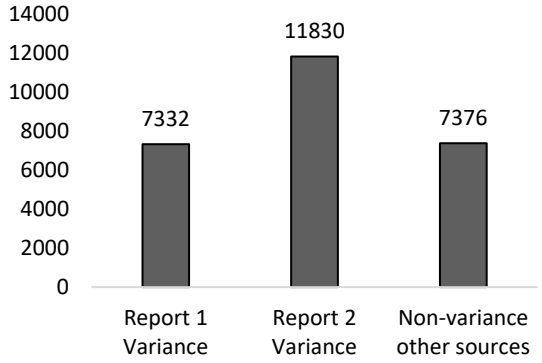


Figure 8. Variance MDRs vs. MDRs from non-variance other sources for malfunctions (Jun-Nov 2020)

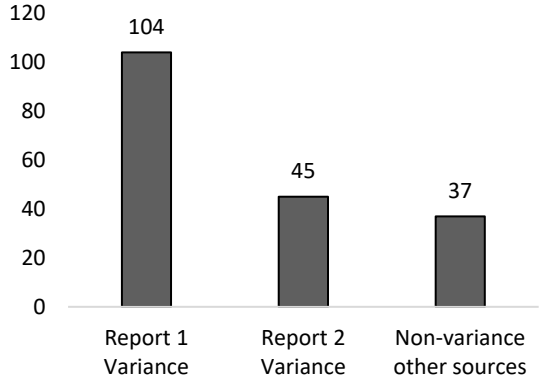


Figure 9. Variance MDRs vs. MDRs from non-variance other sources for deaths (Jun-Nov 2020)

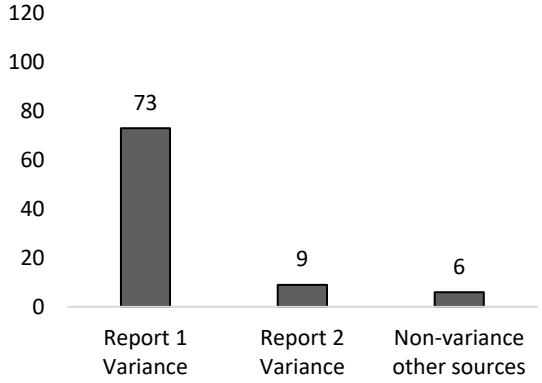


Figure 10. Top 10 patient problem codes[12] for variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)

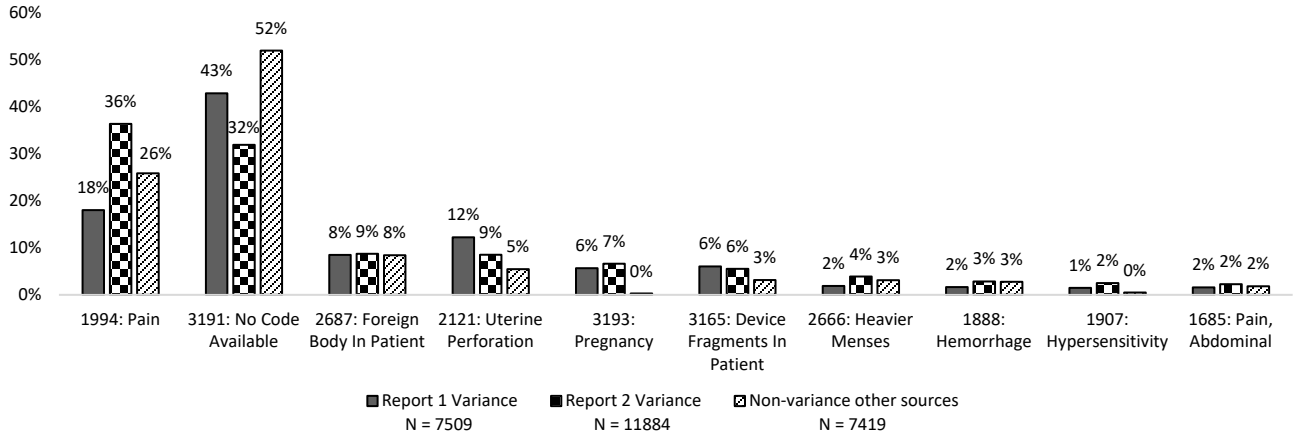
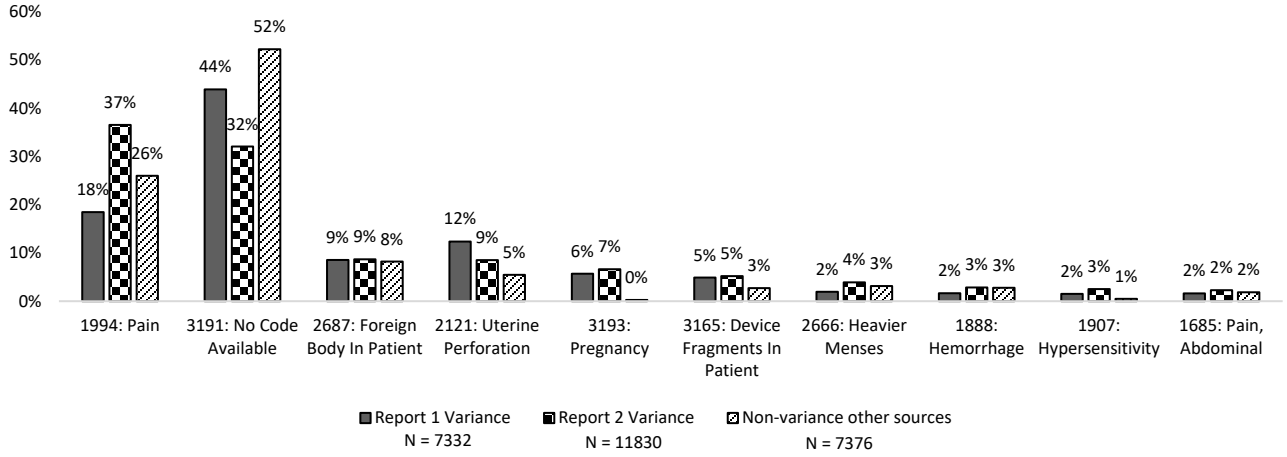


Figure 11. Top 10 patient problem codes for serious injury variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)



[12] It is possible for more than one Patient Problem Code to be selected per report. Therefore, the sum of the Patient Problem Codes is not expected to equal the total number of MDRs submitted during the period reviewed.

Figure 12. Patient problem codes for malfunction variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)

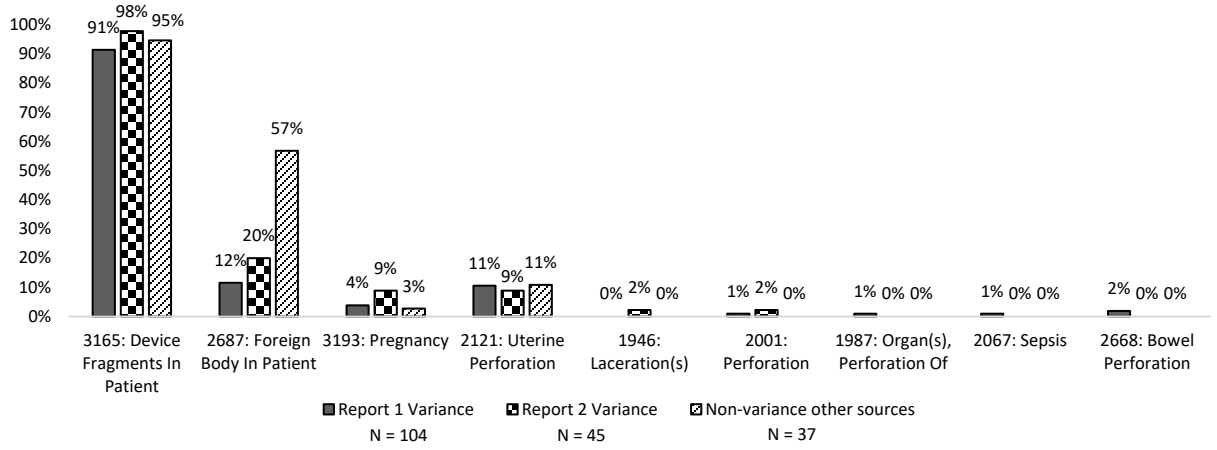


Figure 13. Top 10 patient problem codes for death variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)

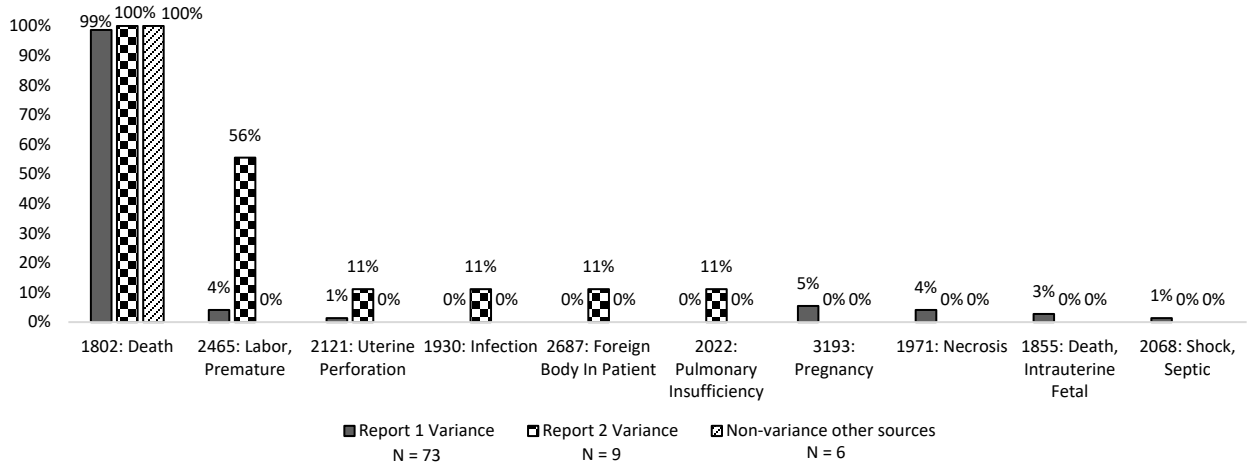
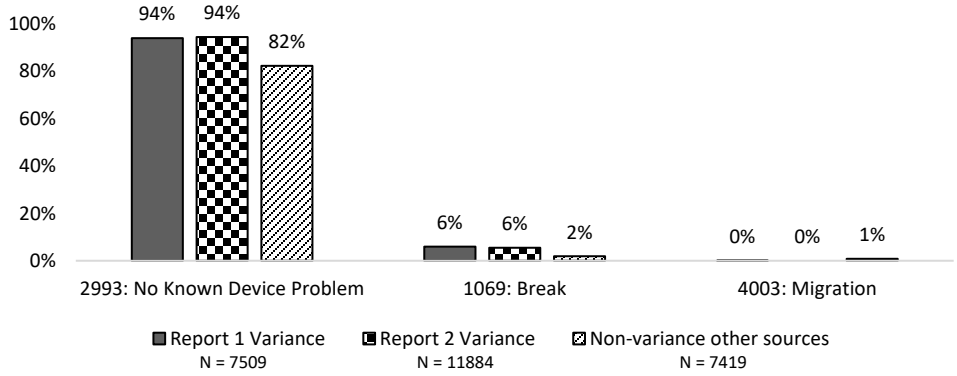


Figure 14. All Device problem codes for variance MDRs vs. MDRs from non-variance other sources[13] (Jun-Nov 2020)



[13] For the purposes of comparison, only Device Problem Codes captured within variance reports are displayed.

Review of the comparative graphical displays indicates that the distribution of Patient Problem Codes is similar. One observation of note is the increased frequency of PPC '1994: Pain' and the decreased frequency of 'PPC 3191: No Code Available' when comparing Report 2 Variance to Report 1 Variance. This variation in frequency is due to more descriptive social media postings, although still limited, contained in the associated source documents for reports processed between 01-SEP-2020 and 30-NOV-2020.

When delineating the data based on the Type of Reportable Event of Malfunction and Death in Figure 12 and 13, respectively, it appears as though the distribution of Patient Problem Codes does differ between Report 1 Variance, Report 2 Variance, and non-variance other sources. Based on the limited nature of social media information and the relatively small sample sizes for malfunction (Figure 12) and death variance MDRs (Figure 13) compared to all variance MDRs (Figure 10), no trends or conclusions related to safety, quality, or performance can be drawn.

Comparative Analysis of Patient Demographics

Table 9. Table of patient demographics for age and weight for variance MDRs vs. MDRs from non-variance other sources (Jun-Nov 2020)

Measure	Age (years)		Weight (lbs.)	
	All Variance	Non-variance other sources	All Variance	Non-variance other sources
Sample Size (n)*	3703	1267	36	182
Minimum	18	19	88	90
Median	34	38	166	165
Average	34	38	164	179
Maximum	60	65	238	441

* Excludes child / fetal reports (only ≥ 18y)

The average age in the variance is a slightly lower than reports from non-variance other sources. Considering the variance represents social media posting and the internet use decreases in older populations, this could justify the difference. Information about patient age was available in 19.1% of variance reports and 17.1% non-variance other source reports.

No statistically significant conclusions on weight differences can be drawn as the sample size is extremely small (0.2% in the variance and 2.5% in non-variance other source reports).

Conclusions

The information analyzed within the variance cohort represents a source of passive surveillance information with limitations given the nature of the report data received from legally derived social media sources. Therefore, the incidence or prevalence of these MDR events cannot be determined from this cohort alone. As a result, conclusions cannot be drawn regarding a change in the quality, safety and performance of the Essure product.[14]

[14] https://www.fda.gov/medical-devices/essure-permanent-birth-control/problems-reported-essure

When comparing the most recent variance quarter to the previous variance quarter and to non-variance other sources of equal time periods the observed trends assessed remain as expected and do not influence known or observed safety recommendations.

Bayer will continue to process and submit MDR reports for Essure under the conditions of the variance letter.