# Medical Device Reporting Variance E2020002

# for

# Essure (P020014)

## Quarterly MDR Analysis Report

## Medical Device Reports


**Report Number: 1**
**Period: 01-JUN-2020 to 31-AUG-2020**
**Report Date: 01-OCT-2020**
**Final 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.

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# 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 first quarterly analysis report is MDR-reportable events submitted to the FDA as part of the variance for cases 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] [3] [4] for the respective period 01-JUN-2020 to 31-AUG-2020 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 cases, 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.[5]

In order to contextualize the received reports, data from the variance MDRs will be compared with MDRs initially reported to the FDA by the company during the same quarterly period. These cases, 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 the same period (between 01-JUN-2020 and 31-AUG-2020).

## 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 2. Total number of variance MDRs by month submitted*

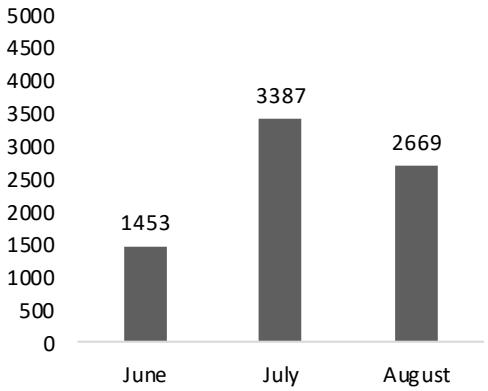
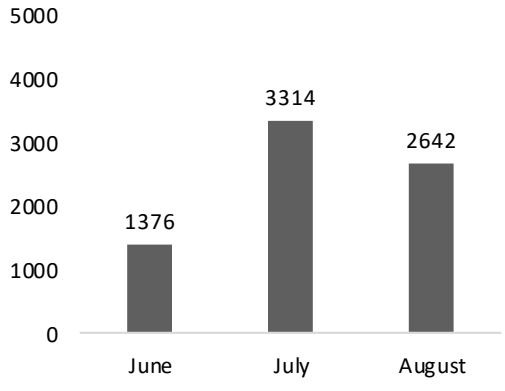



*Figure 1. Total number of serious injury variance MDRs by month submitted*




[2] Spreadsheet 1: https://www.fda.gov/media/141024/download
[3] Spreadsheet 2: https://www.fda.gov/media/142129/download
[4] Spreadsheet 3: https://www.fda.gov/media/142965/download
[5] https://www.fda.gov/medical-devices/essure-permanent-birth-control/problems-reported-essure

*Figure 3. Total number of malfunction variance MDRs by month submitted*

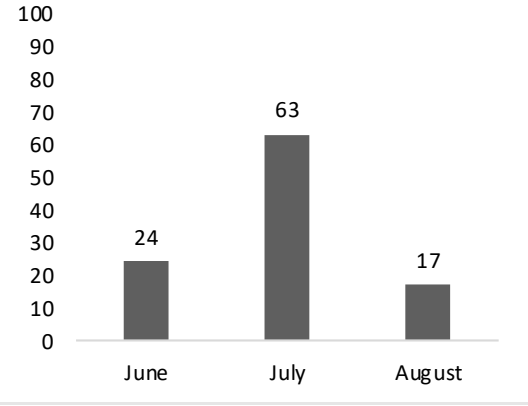
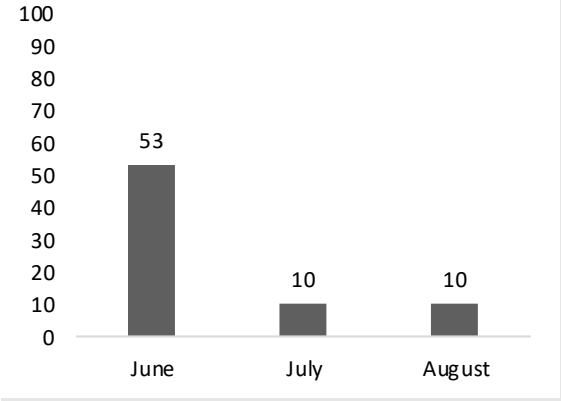



*Figure 4. Total number of death variance MDRs by month submitted*




For variance reports submitted in the time period, 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-Aug 2020)* [6]

| Year of Posting | Serious Injury | Malfunction | Death | Total |
|---|---|---|---|---|
| ≤ 2010 | 967 | 8 | 0 | 975 |
| 2011 | 107 | 0 | 0 | 107 |
| 2012 | 118 | 4 | 0 | 122 |
| 2013 | 288 | 9 | 15 | 312 |
| 2014 | 450 | 10 | 3 | 463 |
| 2015 | 667 | 13 | 16 | 696 |
| 2016 | 473 | 4 | 2 | 479 |
| 2017 | 309 | 1 | 1 | 311 |
| 2018 | 208 | 0 | 0 | 208 |
| ≥ 2019 | 259 | 3 | 1 | 263 |
| **Total** | 3846 | 52 | 38 | 3936 |

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.

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

*Table 2. Variance MDRs by event year and type of reportable event (Jun-Aug 2020)* [7]

| Year of Event | Serious Injury | Malfunction | Death | Total |
|---|---|---|---|---|
| ≤ 2010 | 199 | 8 | 0 | 207 |
| 2011 | 62 | 6 | 0 | 68 |
| 2012 | 91 | 2 | 1 | 94 |
| 2013 | 136 | 6 | 0 | 142 |
| 2014 | 125 | 7 | 0 | 132 |
| 2015 | 111 | 3 | 0 | 114 |
| 2016 | 56 | 1 | 0 | 57 |
| 2017 | 34 | 2 | 0 | 36 |
| 2018 | 8 | 0 | 0 | 8 |
| ≥ 2019 | 4 | 0 | 0 | 4 |
| **Total** | 826 | 35 | 1 | 862 |

Year of event is intended to refer to the reported date in which the event described by the information happened. Due to 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 26-SEP-2019. Information about date of event does not impact the known or labeled risks for the Essure device.

*Table 3. Patient problem codes[7] for variance MDRs*

| Patient Problem Code | Report 1 |
|---|---|
| 3191: No Code Available | 3218 |
| 1994: Pain | 1354 |
| 2121: Uterine Perforation | 919 |
| 2687: Foreign Body In Patient | 638 |
| 3165: Device Fragments In Patient | 455 |
| 3193: Pregnancy | 425 |
| 2666: Heavier Menses | 142 |
| 1819: Pregnancy, Ectopic | 135 |
| 1888: Hemorrhage | 124 |
| 1685: Pain, Abdominal | 119 |
| All other Patient Problem Codes | 1029 |

*Table 4. Patient problem codes for serious injury variance MDRs*

| Patient Problem Code | Report 1 |
|---|---|
| 3191: No Code Available | 3218 |
| 1994: Pain | 1354 |
| 2121: Uterine Perforation | 907 |
| 2687: Foreign Body In Patient | 626 |
| 3193: Pregnancy | 417 |
| 3165: Device Fragments In Patient | 360 |
| 2666: Heavier Menses | 142 |
| 1819: Pregnancy, Ectopic | 135 |
| 1888: Hemorrhage | 122 |
| 1685: Pain, Abdominal | 119 |
| All other Patient Problem Codes | 937 |

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

*Table 5. Patient problem codes for malfunction variance MDRs*

| Patient Problem Code | Report 1 |
|---|---|
| 3165: Device Fragments In Patient | 95 |
| 2687: Foreign Body In Patient | 12 |
| 2121: Uterine Perforation | 11 |
| 3193: Pregnancy | 4 |
| 2668: Bowel Perforation | 2 |
| 2067: Sepsis | 1 |
| 1987: Organ(s), Perforation Of | 1 |
| 2001: Perforation | 1 |

*Table 6. Patient problem codes for death variance MDRs*

| Patient Problem Code | Report 1 |
|---|---|
| 1802: Death | 72 |
| 3193: Pregnancy | 4 |
| 2465: Labor, Premature | 3 |
| 1971: Necrosis | 3 |
| 2000: Pelvic Inflammatory Disease | 3 |
| 1855: Death, Intrauterine Fetal | 2 |
| 1888: Hemorrhage | 2 |
| 2108: Toxic Shock Syndrome | 2 |
| 2072: Shock | 1 |
| 2121: Uterine Perforation | 1 |
| 2068: Shock, Septic | 1 |

*Table 7. Device problem codes for variance MDRs*

| Device Problem Code | Report 1 |
|---|---|
| 2993: No Known Device Problem | 7061 |
| 1069: Break | 447 |
| 4003: Migration | 1 |

Review of the figures and tables above provides a synopsis of the information provided in the H10 section of the first three (3) variance submissions[8] [9] [10]. 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.

[8] Submission 1: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=10260064&pc=HHS
[9] Submission 2: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=10464545&pc=HHS
[10] Submission 3: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/detail.cfm?mdrfoi__id=10592806&pc=HHS

## Averages of patient demographics

Review of variance MDRs processed by Bayer between 01-JUN-2020 and 31-AUG-2020 indicates that the following measures related to patient age and weight.

*Table 8. Table of patient demographics for age and weight*

| Measure | Age (years) | Weight (lbs.) |
|---|---|---|
| Sample size (n) | 913* | 8 |
| Minimum | 20 | 101 |
| Median | 34 | 165 |
| Average | 34 | 166 |
| Maximum | 58 | 229 |

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

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

## Report Source

The reports processed by Bayer as part of the variance between 01-JUN-2020 and 31-AUG-2020 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

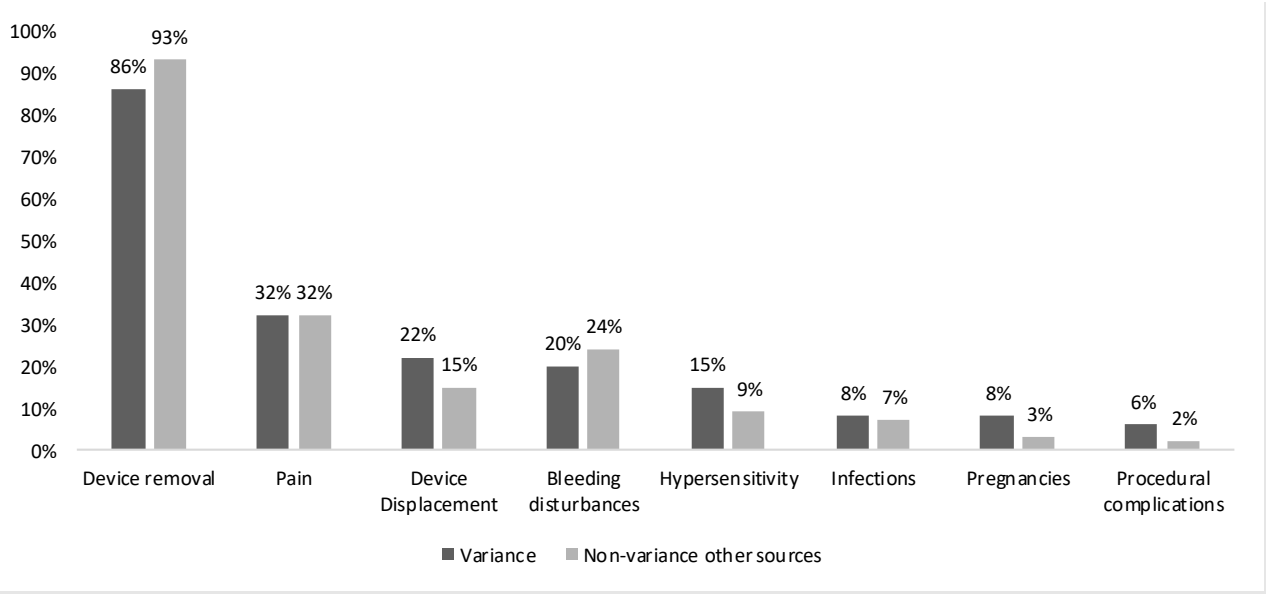
All variance MDRs submitted to the FDA have been submitted by Bayer Pharma AG.

## Devices Involved

All reports processed by Bayer between 01-JUN-2020 and 31-AUG-2020 as part of the variance 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[11] (Jun-Aug 2020)*




(N=7509) Variance; (N=5271) Non-variance other sources

The representative event groupings for Essure MDRs variance seems to be consistent with the non-variance other source cases processed during the same period. Information received as part of litigation accounts for 100% of variance reports and approximately 95% of non-variance other sources. Device removal is the most frequently reported event in both variance and non-variance other source cases with 86% and 93% respectively. Pain is the second most frequent in both variance and non-variance other source cases with the same 32% for both.

In the variance cases, Device displacement and Bleeding disturbances follow with 22% and 20% respectively.

In non-variance other source cases, Bleeding disturbances comes in third with 24%, followed by Device displacement with 15%.

The remainder of the events: Hypersensitivity, Infections, Pregnancies and procedural complications followed the same position.

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

## Analysis of Additional Information

The following additional pieces of information were requested by FDA and prescribed within the variance letter.[12]

1. The variance MDRs processed by Bayer in the reviewed time period 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 between 01-JUN-2020 and 31-AUG-2020 are consistent with expected outcomes.

3. Considering that variance MDRs processed by Bayer between 01-JUN-2020 and 31-AUG-2020 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 period as there was there were no events reported which indicates a new technical failure mode for the device.

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

## 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 between 01-JUN-2020 and 31-AUG-2020 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 will be compared with non-variance other source MDRs initially reported to the FDA received by the company during the same quarterly period. These cases, 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 the same period (between 01-JUN-2020 and 31-AUG-2020).

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

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

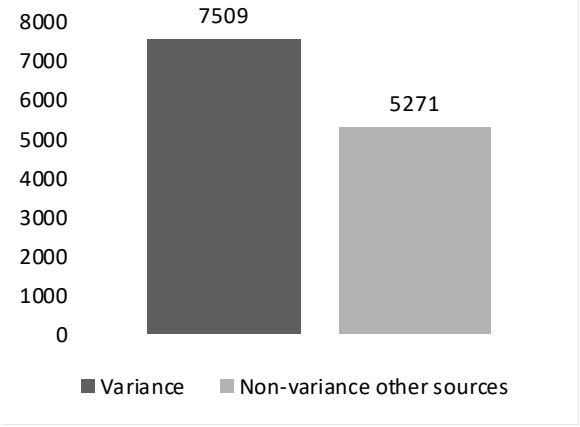



*Figure 7. Variance MDRs vs. MDRs from non-variance other sources for serious injuries (Jun-Aug 2020)*

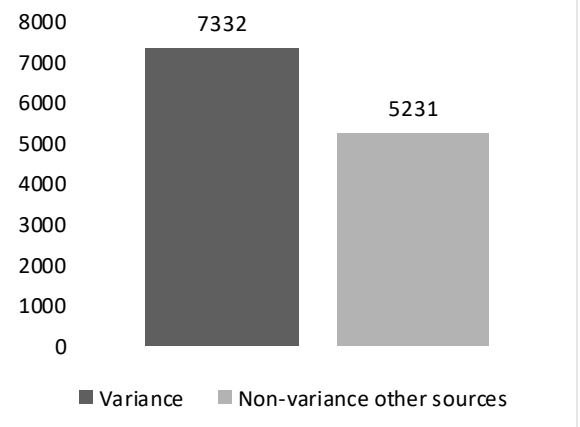



*Figure 8. Variance MDRs vs. MDRs from non-variance other sources for malfunctions (Jun-Aug 2020)*

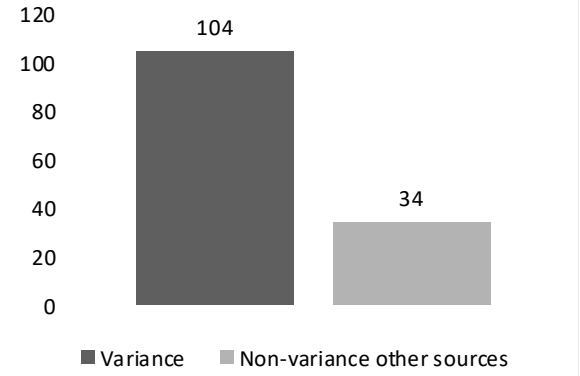



*Figure 9. Variance MDRs vs. MDRs from non-variance other sources for deaths (Jun-Aug 2020)*

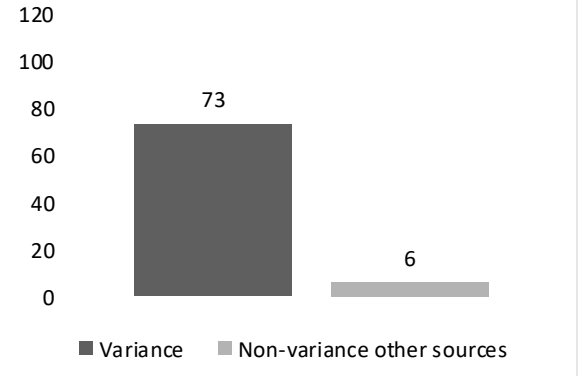
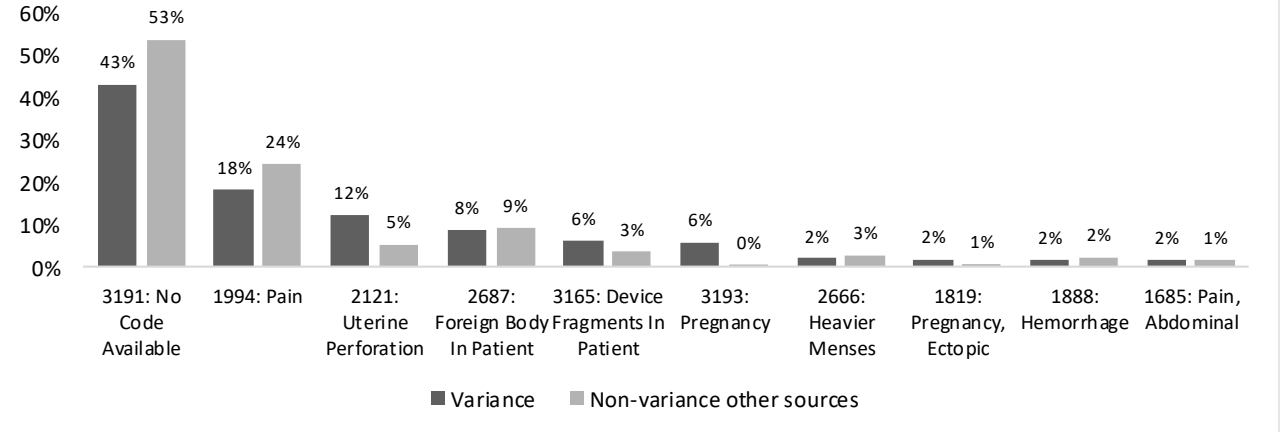



*Figure 10. Top 10 patient problem codes[13] for variance MDRs vs. MDRs from non-variance other sources (Jun-Aug 2020)*




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

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

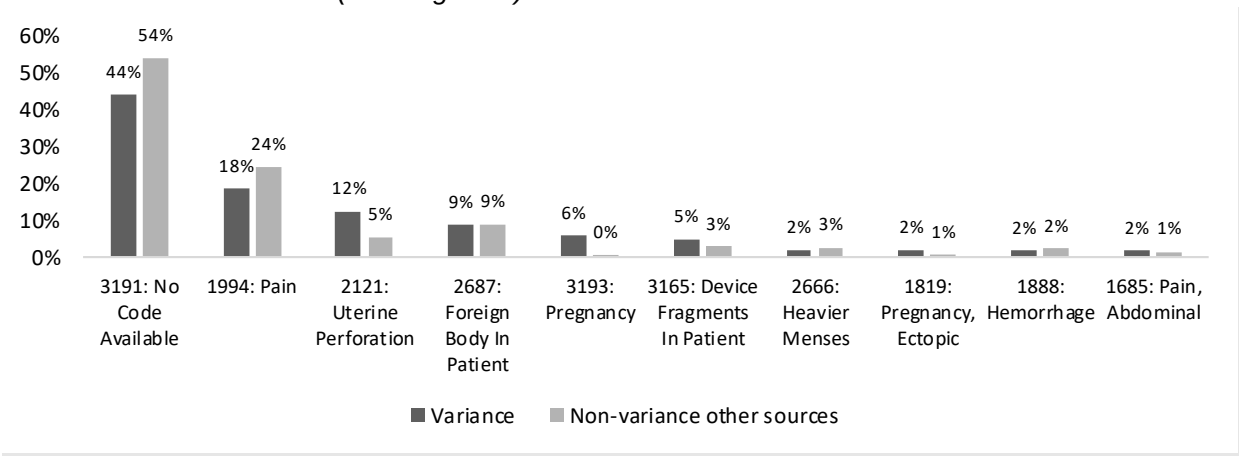



*Figure 12. All patient problem codes for malfunction variance MDRs vs. MDRs from non-variance other sources (Jun-Aug 2020)*

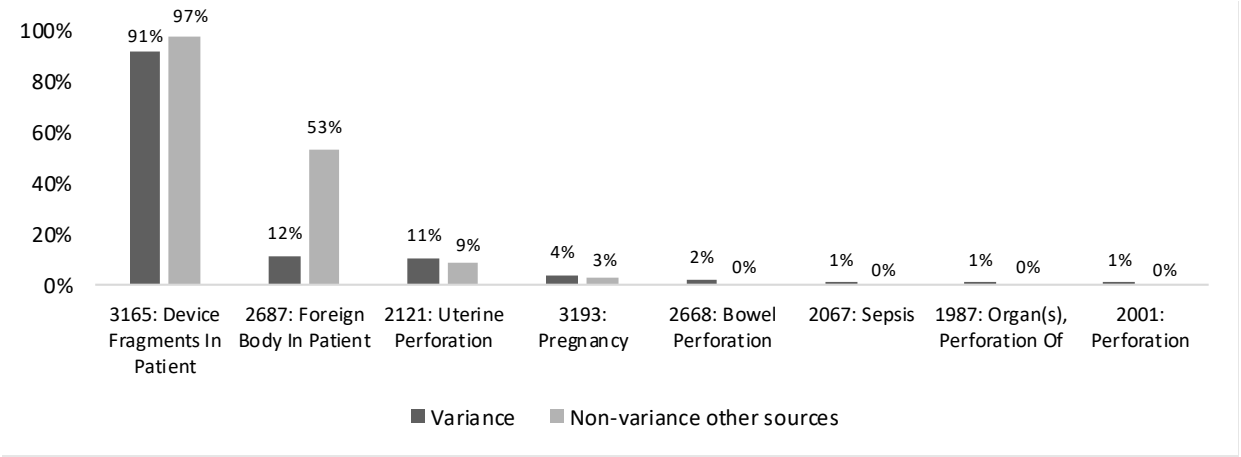



*Figure 13. All patient problem codes for death variance MDRs vs. MDRs from non-variance other sources (Jun-Aug 2020)*

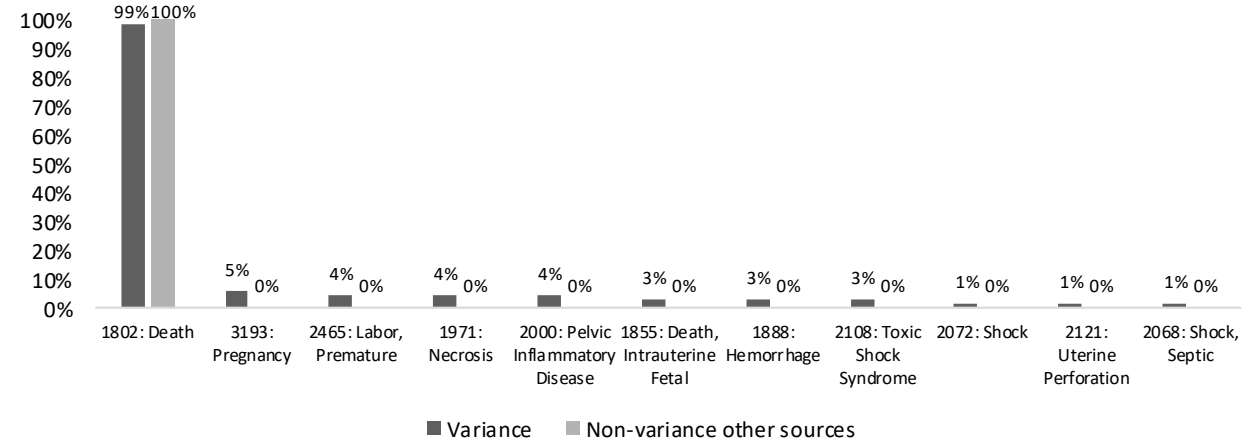
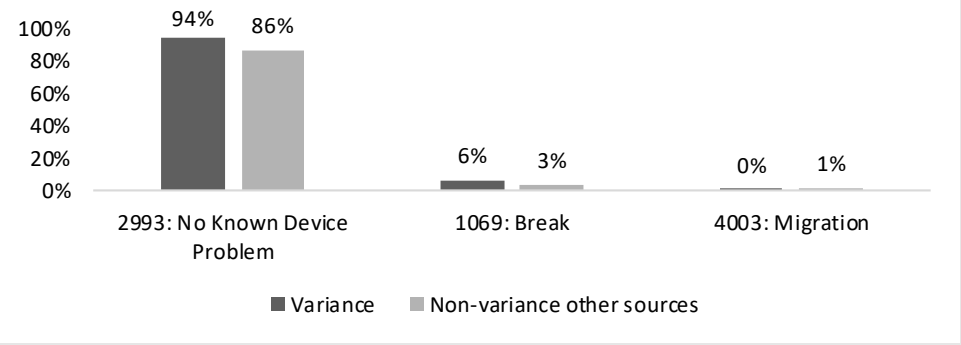


*Figure 14. Device problem codes for variance MDRs vs. MDRs from non-variance other sources (Jun-Aug 2020)*[14]




Review of the comparative graphical displays of variance MDRs vs. MDRs from non-variance other sources reported for Essure submitted between 01-JUN-2020 and 31-AUG-2020 indicates that the distribution of Patient Problem Codes is similar.

When delineating the data based on the Type of Reportable Event (i.e. Serious Injury, Death, Malfunction) it appears as though the PPCs of '1802: Death', for Death reports, and the PPC of '3165: Device Fragments in Patient', for Malfunction reports, occur more often within the variance. This can be explained by the limited information provided and the fact that it is difficult to identify duplicate reports for reports under the variance. Hence, it is possible that duplicate reports exist within the variance itself and/or reports previously submitted to the FDA are also captured within the variance.

**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-Aug 2020)*

| Measure | Age (years) | | Weight (lbs.) | |
|---|---|---|---|---|
| | Variance | Non-variance other sources | Variance | Non-variance other sources |
| Sample Size (n) | 913* | 3267* | 8 | 115 |
| Minimum | 20 | 19 | 101 | 109 |
| Median | 34 | 40 | 165 | 161 |
| Average | 34 | 40 | 166 | 175 |
| Maximum | 58 | 65 | 229 | 376 |

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

The average age in the variance is lower than cases 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. Also, consistent with the limited information in the variance, only 12.2% of the cases contained information about age vs 62.0% of non-variance other source cases.

The table cannot draw any conclusions on weight differences since the sample size is extremely small (0.1% in the variance and 2.2% in non-variance other source cases).

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

# Conclusions

The information analyzed within the variance cohort represents a source of passive surveillance information with limitations given the nature of the case 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.[15]

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

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