Improving Adverse Event Report Processing at the U.S. Food and Drug Administration

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Submitted to:

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Abstract

Adverse drug events, or unintended and dangerous drug effects, impact millions of people in the United States each year. Our goal was to increase the efficiency of adverse event case report processing at the United States Food and Drug Administration using business process improvement methods. Information was collected from shadowing and surveying staff, conducting interviews, and participating in meetings and presentations. Our recommendations focused on improving consumer education resources, enhancing the data entry user interface, utilizing new and existing metrics, and ultimately decreasing total report processing time and cost while considering the needs of the system's stakeholders.

Executive Summary

Project Background and Goals

Adverse drug reactions (ADRs), or unintended and dangerous effects that a drug may cause, pose a significant threat to public health, causing thousands of cases of illness, injury, and death each year. These reactions account for 3-7% of hospitalizations (Smith Marsh, 2016) and approximately 100,000 deaths annually in the United States (Ferner, 2016). As the country's regulatory authority for human drugs, the United States Food and Drug Administration (FDA)'s mission includes monitoring these products for adverse events (AE), or potential ADRs. The FDA collects adverse event case reports through phone, mail, fax, and online submissions in order to monitor drugs for suspected adverse reactions. The overall number of adverse event reports that the FDA receives has quadrupled in the past ten years, reflecting an increase in reporting as well as increased drug approvals and usage. The FDA expects to receive over 1.8 million reports in 2016, up from 470,261 in 2006 (USFDA, 2015, November 24), as shown in Figure 1 below.

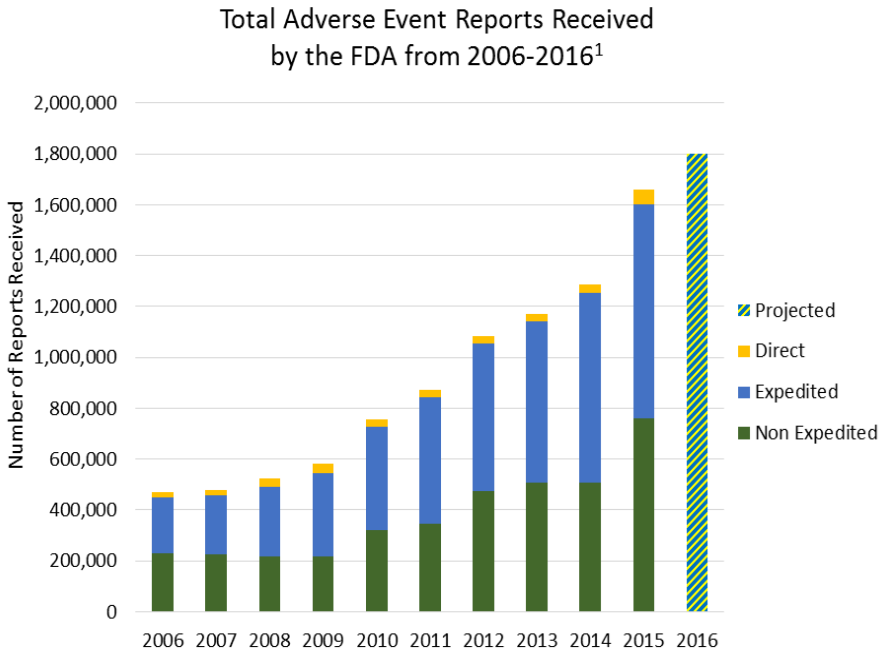

Figure 1: The number of adverse event reports received by the FDA from 2006-2016

The FDA collects information about adverse events using the FDA Adverse Event Reporting System, or FAERS. FAERS involves collecting and processing reports from drug manufacturers electronically (mandatory reports) or from consumers and healthcare professionals (voluntary reports) through MedWatch forms. Safety Evaluators, typically licensed pharmacists, use the FAERS database to detect adverse drug reactions and propose regulatory action, such as labeling changes. While 96% of reports are submitted to FAERS electronically by manufacturers and do not require any processing, the FDA sends the rest—over 100,000 in fiscal year 2016—to a group of contractors, called the FAERS Data Management Program (FAERS-DMP), for triage, data entry, medical coding, and quality control.

This project was intended to assist the FDA Center for Drug Evaluation and Research (CDER)'s Office of Surveillance and Epidemiology (OSE) to monitor and assess marketed drug safety by improving the processing of adverse event case reports. Components of existing business process improvement (BPI) methods were applied to the system to identify and address delays and inefficiencies.

Methodology

The four main objectives we established for the project were:

1. *To understand and map the current process for submitting and recording MedWatch reports into the FAERS database.*
2. *To understand the stakeholders' needs and goals for improvement.*
3. *To compare the current system for processing AE case reports with case report processing systems used by other FDA centers.*
4. *To develop recommendations for increasing the overall efficiency of AE data processing utilizing BPI methods.*

We began by researching both the process of submitting an adverse event report as well as what happens after it has been submitted through the MedWatch program. We conducted interviews with project leaders and shadowed data entry staff to fully understand how the system works from start to finish. We also attended meetings and presentations so that we could meet the people behind the process and collect important statistics and data. More information was needed in order to understand the intricacies of the process, especially from a data entry point of view, so we developed a survey to determine how satisfied the data entry staff were with the software systems they work with and what improvements they thought would make their jobs easier. Their responses were coded to find common factors in the data. Afterwards we visited the FDA's Center for Devices and Radiological Health (CDRH) and the FDA's Center for Tobacco Products (CTP) so that their report processing systems could be compared to FAERS-DMP. Once we had gathered all of our information, we performed a strengths, weaknesses, opportunities, and threats (SWOT) analysis on each step of the process to determine inefficiencies and identify where we could make recommendations.

Results

From the information collected through various conversations, interviews, and job shadowing, we created a process map, shown in Figure 2 below. This shows the current steps a voluntary report goes through to get from a consumer or healthcare professional to the FAERS Business Intelligence Solution (FBIS), the interface that Safety Evaluators use to view reports. The process map shows the steps that occur in each of the two software systems used, FLARe (First Look at Reports) and FAERS. Initial data entry and triage of reports takes place in FLARe, while full data entry, quality control, and medical coding are done using FAERS.

Analysis of the survey, interview data, and observations revealed five major issues the data entry staff experienced: difficulties with the optical character recognition (OCR) software, field placement problems in the FAERS software, inconsistent field size and fonts in the FAERS software, resolution of report images, and difficulty reading handwriting on paper and fax reports. Comparison of the CDRH and CTP programs to FAERS-DMP provided information about typical FDA report processing systems. Each center's program consisted of the same basic steps of triage, data entry, quality control, and database submission, despite using different software and having very different contractual requirements and forms to process. SWOT analyses were performed on the MedWatch forms, the FLARe system, and the FAERS system, combining our data collected from survey responses, research, interviews, and job shadowing.

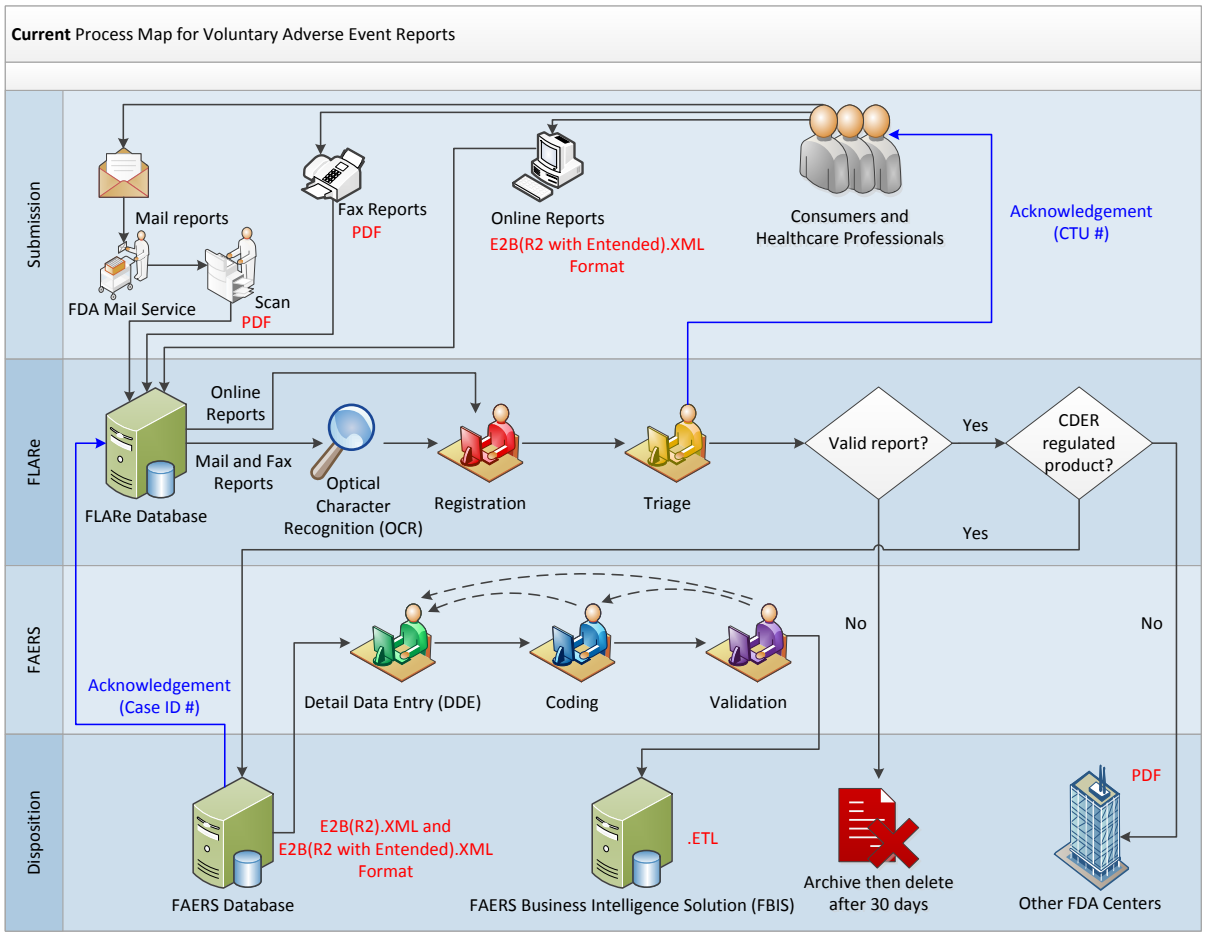

Figure 2: Current Process Map for Voluntary Adverse Event Reports

Recommendations

We recommend that the FLARe and FAERS user interfaces be updated based on data entry staff feedback.

Based on the feedback from data entry staff, we compiled a list of user interface recommendations to be implemented into the FLARe and FAERS systems. Making the FLARe and FAERS software more user-friendly and conducive to data entry and other FAERS-DMP tasks, as detailed in this report, would decrease processing time. Reducing the amount of scrolling and tab switching performed by DDE, for example, by just 30 seconds for each report, would save over 400 hours per year.

We recommend combining the FLARe and FAERS software into one system.

Currently the data entry process is done in both the FLARe and FAERS software with the total disposition process from FLARe to FAERS taking 84 minutes, shown in Figure 3 below. Performing all data entry tasks in one system would eliminate the need for this step. Also, since all the tasks would be in one system, only the Case ID Number would need to be used to track reports and an acknowledgement step would be eliminated between Detail Data Entry (DDE) and Triage. Reports would also be easily sent back to FLARe from FAERS for corrections.

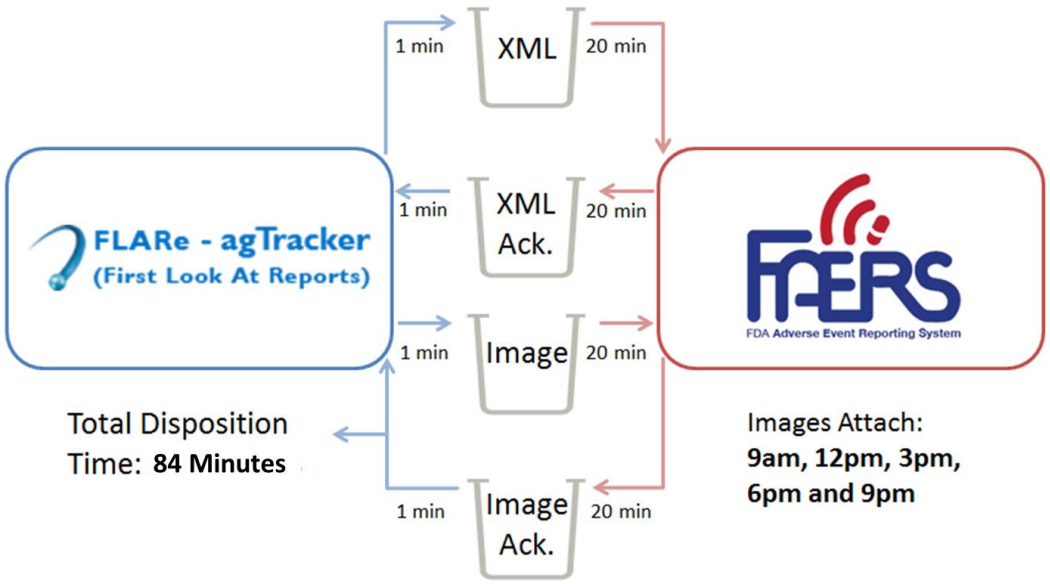

Figure 3: The process for transferring forms from FLARe to FAERS

We recommend that the FLARe optical character recognition (OCR) software be replaced.

Every Registration and Triage staff member that responded to the open response questions of our survey had issues with the OCR software and either wanted OCR to be removed or disabled entirely for a particular report. Registration staff also reported that using OCR sometimes requires more time per report to correct mistakes and incorrect data fields than if OCR weren't used at all. In order to increase the efficiency of staff and lower the amount of time spent per report, the FDA might consider replacing the OCR software or allowing staff to choose whether or not OCR is used on an individual report or on specific fields.

We recommend that detailed data entry (DDE) staff be moved from FAERS to FLARe

The FAERS software fields are currently in a different order than information is presented on MedWatch forms. This requires staff to scroll through forms and jump between tabs in FAERS to input and validate data, which is inefficient. Having the fields in the same order as the forms present would allow staff to work faster. Unlike FAERS, the FLARe data fields are set up to align with MedWatch reports. If DDE was moved to this software, staff would not have to spend as much time switching between fields and tabs, so they could get reports done seconds or minutes faster. When multiplied by the number of reports received per year, even one minute saved per report becomes a significant processing time decrease. This recommendation is a short-term alternative to combining FLARe and FAERS, which would be designed with a field layout matching the MedWatch forms.

We recommend that the FDA provide consumers with a more easily accessible FAQ on how to fill out MedWatch forms.

Data entry staff have indicated that consumers commonly fill out forms incorrectly due to misinterpreting instructions or not understanding a question, requiring staff to correct consumer mistakes. One potential solution to this problem would be to have an easily accessible FAQ online or on paper for consumers to use. Additionally, more detailed instructions could be placed directly on the MedWatch forms next to each question, giving the user more information without requiring them to go through the FAQ, saving them time and increasing the likelihood of them filling out a form accurately.

We recommend user-end system monitoring.

Currently, FAERS-DMP managers are unable to monitor the status of the FAERS servers. Since the vast majority of mandatory reports come in through electronic submission, and all reports are processed electronically, knowing immediately if the server is encountering an issue may mean hours of saved time in the event of a crash and prevention of a case backlog being created.

We recommend using existing metrics to benchmark future performance.

Existing statistics—such as average processing time per report for each department, total processing time of one report, cost per report type (mail, fax, or online) per department, total operation costs, number of reports received daily, and the number of reports completed daily— can be used in the future to provide useful benchmarks and evaluation of system changes.

We recommend surveying employees routinely to use the collected data to help guide future system improvements.

Surveys resembling the one we conducted would provide useful information on potential system improvements and employee satisfaction. Comparing survey data before and after a large system update could provide insight on how successful the changes are.

Conclusions

This project was able to produce several recommendations for increasing the efficiency of adverse event report processing through the FDA's FAERS Data Management Program. Increased efficiency will allow the program to better respond to the expected increase in the number of reports. Most importantly, faster processing of reports could allow potentially dangerous adverse events to be reviewed by Safety Evaluators sooner. Our recommendations focused on improving consumer education resources, enhancing the data entry user interface, utilizing new and existing metrics, and ultimately decreasing total report processing time and cost while considering the needs of the system's stakeholders. The main recommendation of using a combined software solution would reduce processing steps, thereby reducing the time and cost needed per report. Software recommendations were designed with the goal of making employee's jobs easier and more efficient. In addition to implementing our recommendations, OSE may implement continuous improvement, a step often included in BPI, to develop more recommendations for FAERS-DMP in the future. This can be aided by the use of staff surveys, as we found this method of data collection to be beneficial for developing potential system improvements. Lastly, a more in-depth study of CDRH, CTP, other FDA centers, and possibly other agencies' case processing systems could further identify best practices in report processing.

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1. Introduction

Adverse drug reactions, or unintended and dangerous effects that a drug may cause, pose a significant threat to public health, causing thousands of cases of illness, injury, and death each year. These reactions account for 3-7% of hospitalizations (Smith Marsh, 2016) and approximately 100,000 deaths annually in the United States (Ferner, 2016). They also injure about 1.5 million people per year at a cost of nearly $3.5 billion (Craigle, 2007). As the country's regulatory authority for human drugs, part of the United States Food and Drug Administration (FDA)'s mission is to monitor drug products for the adverse drug reactions that have a large impact on our nation's health and healthcare system.

Within the FDA, the Office of Surveillance and Epidemiology (OSE) is tasked with performing pharmacovigilance, the detection, assessment, understanding, and prevention of adverse drug reactions (Sakaeda, Tamon, Kadoyama, & Okuno, 2013). OSE detects these reactions by having licensed pharmacists, called Safety Evaluators, monitor MedWatch forms entered into the FDA Adverse Event Reporting System (FAERS). MedWatch is the system through which adverse event (AE) reports are submitted by patients, healthcare professionals, pharmaceutical companies, and manufacturers. MedWatch forms are processed by the FAERS Data Management Program (FAERS-DMP) before they can be viewed by Safety Evaluators, who review the reports when scientifically determining whether an adverse event is truly caused by a drug, requiring regulatory action such as a labeling update. FAERS processed about 1.7 million reports last year (De & Sahoo, 2016) and is expected to receive over 1.8 million reports in 2016 (Eley, 2016, Oct. 25). In order to be accessible and convenient, MedWatch accepts reports by postal mail, phone, and fax in addition to an online form. Accepting these various types of submissions requires staff to manually process the reports.

While 96% of reports are submitted electronically by manufacturers and do not require any processing, the FDA sends the rest—over 100,000 in fiscal year 2016—to a group of contractors for triage, data entry, medical coding, and quality control. It currently takes about 6-7 days for paper reports to become available to FDA Safety Evaluators (Eley, 2016, Nov. 30). This processing time represents almost a week where other patients could be experiencing the same adverse event without warning, as an FDA business rule states that a Safety Evaluator cannot review a report until it is fully entered into FAERS. In order to get the reports in the hands of Safety Evaluators promptly, the process must be as efficient as possible, especially considering that about 20% of reports involve a death (Quinn, pers. comm.). Manual report processing also incurs a large cost to the FDA, at an estimated $26 per paper or fax report and $16 for an electronic report requiring corrections, compared to just $1-2 per electronic submission (Eley, 2016, Nov. 30).

Many studies have been performed analyzing the reporting rates of adverse events and reasons for underreporting, analysis of the report database for duplicate reports, and the effectiveness of various data mining algorithms for analysis of adverse event data. Hazell and Shakir (2006) conducted a systematic review of studies mentioning underreporting and estimated the rate of underreporting of adverse events in several European countries to be around 90%. Underreporting was also found to be a concern in Gavaza et al.'s 2011 survey of Texas pharmacists. Multiple studies have compared different data mining algorithms for their accuracy and quality in detecting suspected problems with a drug. (Evans, Waller, & Davis, 2001, Harpaz, et al., 2013) Duplication of reports has also been assessed in several papers (Hauben, Reich, Demicco, & Kim, 2007, Wong, Ho, Saini, Hibbs, & Fois, 2015). The existing literature contains information about the beginning and end of the adverse drug reaction identification process, report submission and data analysis, respectively.

Despite all these studies, none have focused on the intermediate portion of the process: how information gets from a MedWatch form into FAERS and to Safety Evaluators, because this is an FDA internal process. However, OSE has expressed a desire to reduce the time, cost, and resources that this step consumes, as well as to reduce sources of error, improve the metrics collected about the system, and compare the processing time of fax, mail, and electronic reports. Developing recommendations for meeting these goals required an in-depth study of current performance and methods used.

This project was implemented to assist the FDA's Office of Surveillance and Epidemiology to monitor and assess marketed drug safety by improving the triage, coding, quality control, and data entry of adverse event case reports by the FDA's contractors. We identified problems that occur during report processing by analyzing the current system, and developed recommended solutions by applying business process improvement methods. One of the components of the 2013-2017 strategy for the FDA's Center for Drug Evaluation and Research (CDER), which the OSE is under, is business modernization (USFDA, 2014). Improving the entry of MedWatch forms into FAERS falls under this objective because process improvement methods include automation, metrics, communication, and optimization.

2. Background

The following chapter addresses adverse drug reactions and their powerful effect on public health, pharmacovigilance and FAERS, and business process improvement and its applications to safety reporting. A robust event reporting system is critical so that the FDA can identify adverse drug reactions and take regulatory action. A review of similar reporting systems in use at the FDA and elsewhere provided insight on the current state of safety report processing in the US and the EU. Understanding business process improvement tactics allowed us to identify methods for developing recommendations for improving the system.

2.1. The Importance of Reporting Adverse Drug Reactions

Adverse drug reactions (ADRs) refer to any unintended, unsafe, or uncomfortable effects that a drug may cause, including side effects and adverse events. Adverse events differ from side effects, or secondary, undesirable drug effects that occur within the drug's therapeutic range, because side effects are known at the time a drug is approved and brought to market, while adverse events are not (Smith Marsh, 2016). Adverse events also refer to any instances of harm to a patient while taking a drug, even if the event was not caused specifically by the drug (Ferner, 2016). If an adverse event is found not to be caused by a drug, then it is not an adverse drug reaction. All possible ADRs are not usually found in clinical trials because these trials are small relative to the population that may begin taking the drug once it is marketed and are primarily designed to determine a drug's efficacy and obtain regulatory approval (Ferner, 2016). Clinical trials also exclude many patient populations that are at an increased risk for ADRs, such as the elderly, children, pregnant women, and those taking multiple medications at a time.

Adverse drug reactions can be classified as dose-related, allergic, or idiosyncratic. Dose-related adverse reactions can be caused by improper dosing or interactions between multiple drugs and are especially a concern for drugs with a narrow therapeutic range. Allergic reactions occur when a drug triggers an allergic response after the initial dose. Idiosyncratic ADRs are the category given to all other events which are not dose-related or allergic reactions (Smith Marsh, 2016), such as long-term effects from a therapeutic dose that were not discovered in clinical trials. For example, Infliximab, a biologic drug that has potent anti-inflammatory potential and is used to treat rheumatoid arthritis and Crohn's disease, was found to have serious effects after coming onto the market. While most of the effects caused by Infliximab are relatively mild, the drug was found to cause fatal or severe instances of autoimmune hepatitis and other similar liver issues in some cases (Tobon, Cañas, Jaller, Restrepo, &

Anaya, 2007). ADRs can also be labeled as collateral effects, reactions that occur at standard therapeutic doses, or hypersusceptibility reactions, those that occur below the standard dose (Ferner, 2016). The most common drug types that result in a serious hospitalized adverse event are pictured below in Figure 1.

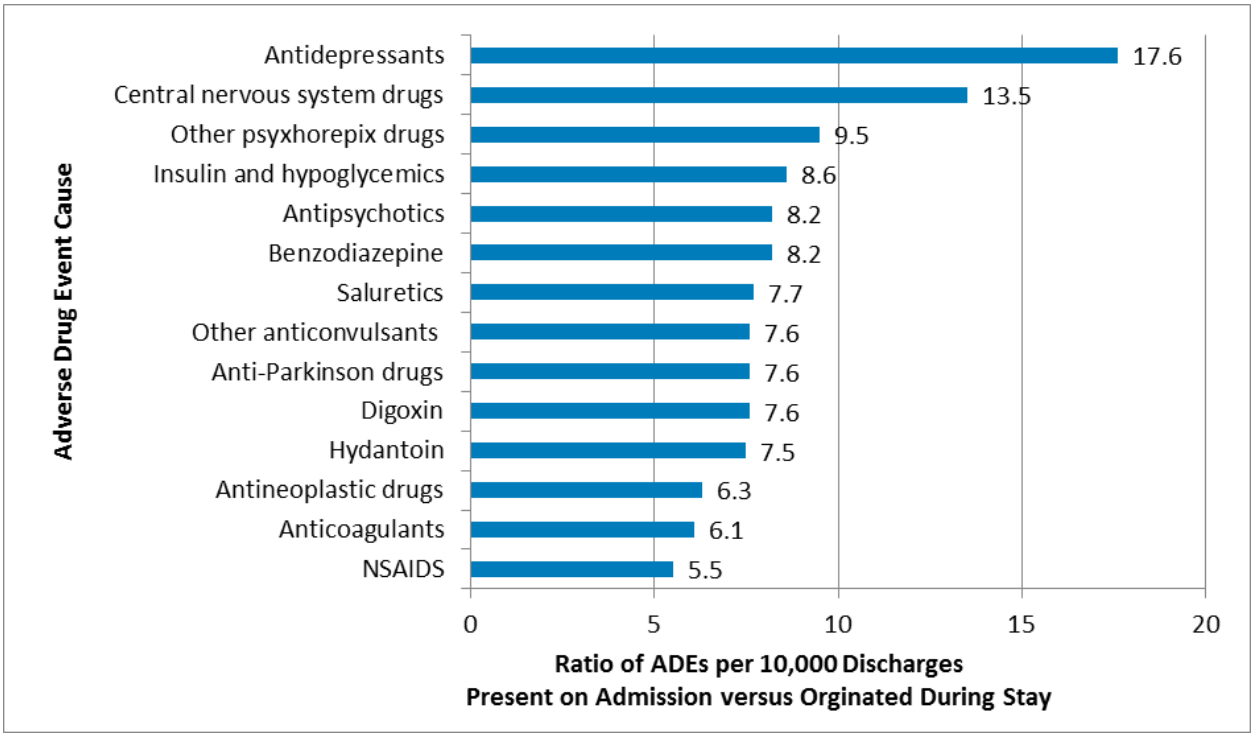


Figure 1: The most common drugs causing ADERs resulting in admission to the hospital. (Weiss, Elixhauser, Bae, 2013)

ADR underreporting is a widespread issue among drug regulatory agencies, both in the U.S. and abroad. A study by Hazell & Shakir (2006) estimated that the underreporting rate by healthcare practitioners in the United Kingdom, Germany, France, and Spain for adverse drug events was likely around 90%, with the highest reporting rate occurring in the two-year period following a drug's initial approval. The authors found that common reasons cited for not reporting an event are being too busy, trouble finding reporting forms, and being unsure of whether the event was related to the drug (Hazell & Shakir, 2006). Events that occur soon after the first dose are the easiest to diagnose, while ADRs from chronic drug use can be difficult for doctors to associate with a drug (Smith Marsh, 2016). A systematic review of 45 papers conducted by Lopez-Gonazlez, Herdeiro, and Figueiras (2009) found that 95% of the studies listed lack of knowledge on the ADR reporting system as a primary reason for underreporting.

According to the authors, many medical professionals assume incorrectly that only severe ADRs should be reported; however all ADRs for a drug should be reported for the drug's safety profile, according to Lopez-Gonazlez et al (2009). In addition, 47% of papers cited underreporting due to complacency with the safety of drugs on the market. The presumption that only safe drugs are available on the market is dangerous as it can lead to further ADRs (Lopez-Gonazlez, Herdeiro, & Figueiras, 2009).

Potential associations between an adverse event and a specific drug are identified from report databases using signal detection algorithms (Harpaz et al., 2013); however, this is an inexact science that relies on multiple data types, complex reporting, and analysis. Signal generation refers to analyzing adverse event data for potential threats, which involves calculation within a report database to identify a signal, which is a statistical correlation between an event and a drug. If the FDA or a drug company confirms this relationship after further study, they can take action in order to inform the public and minimize drug risks. The amount of adverse event reports that constitute a signal can be ambiguous, but the amount and quality of case reports, the type of adverse reaction, the type of drug, and the prescription amount can all be used to determine the number of reports needed for generation (Evans, Waller, & Davis, 2001). In addition to the ambiguity in report quantity, signal detection algorithms have a tradeoff between sensitivity, the lack of false positives, and selectivity, the lack of false negatives, when making calculations (Harpaz et al., 2013).

According to Evans, Waller, & Davis (2001), there are two tactics to determining a signal. The first approach uses allocated prescriptions, sales of medication, and the reporting rate of ADRs for signal calculation. This approach can be biased in that it does not compensate for increased reporting rates for new drugs and drug publicity. The second approach for determining a signal uses the total amount of reports for a drug and calculates the proportion of any reaction that is of interest. This proportional tactic is useful in that external data is not needed, and the biases related to variable reporting present in the first approach do not apply. The result of this second tactic is called a proportional reporting ratio (PRR). A PRR of one or less is often related to background noise; however, a PRR of three to five could indicate that a signal needs to be investigated (Evans et al., 2001).

If ADRs were reported more frequently, it would take less time for signal generation to occur, and medical professionals and the public could be informed of potentially serious ADRs faster (Evans et al., 2001). An important example of this is discontinuation syndrome, an ADR associated with specific antidepressants called selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs). Discontinuation syndrome is a combination of withdrawal symptoms that can occur when patients stop taking antidepressant medications. The symptoms include headaches, loss

of concentration, focus issues, and even electric shock feelings in the brain. A review performed in Canada by Hosenbocus & Chahal (2011) analyzed the effect of discontinuation syndrome on children and adolescents and found that oftentimes, patients and physicians are not made aware of some of the adverse effects caused by drugs they are taking and prescribing. Due to the high rate of side effects, younger patients are more likely to abruptly discontinue antidepressant medication, and for many SSRIs, any sudden discontinuation of the drug can cause considerable duress and possibly even impairment in day-to-day functioning. If physicians were more informed of the potential adverse events related to discontinuation syndrome, they would have been more likely to advise tapering the drug out of the patient's system before discontinuing or switching to a different drug (Hosenbocus & Chahal, 2011). In order to prevent patient and prescriber ignorance, spontaneous ADR reporting needs to be taken seriously.

2.2. Pharmacovigilance and the FDA's Adverse Event Reporting System

Pharmacovigilance is the detection, assessment, understanding, and prevention of adverse events or other drug related problems (Sakaeda, 2013). One important component of pharmacovigilance is detecting and controlling the unknown effects of a medication while the product is on the market. This is done through spontaneous reporting to regulatory agencies from healthcare practitioners and patients, mandatory reporting from manufacturers, and post-marketing studies (Ferner, 2016). The FDA monitors drugs after they are approved through their MedWatch and FAERS programs.

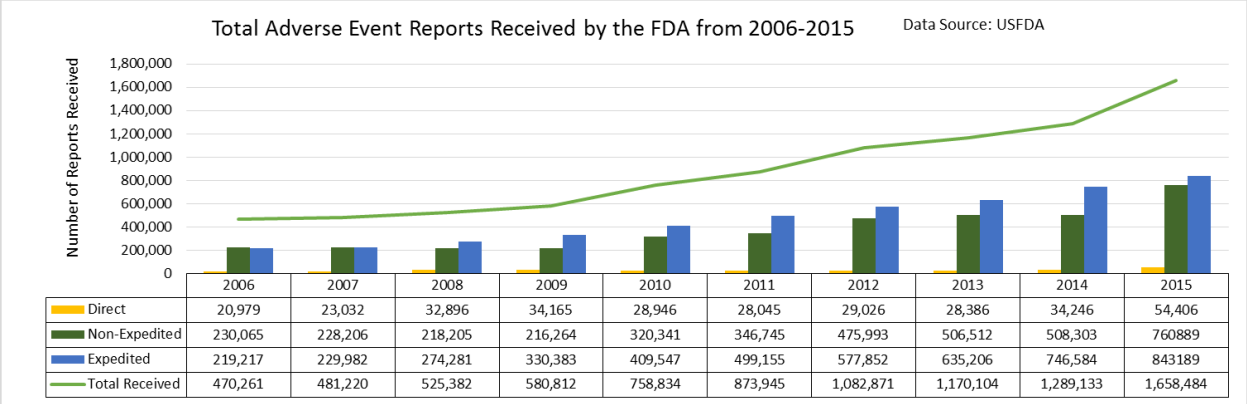
Voluntary adverse event reports are reports made by consumers and healthcare professionals to the FDA through the MedWatch program or to a drug's manufacturer. FAERS-DMP is the FDA's contracted system used to process such reports, which can be sent electronically or by phone, mail, or fax, and enter them into the FAERS database. Since voluntary reports are not required, the FDA cannot mandate that consumers and healthcare professionals submit their forms electronically; therefore, they continue to accept these reports in all formats to ensure convenience. If a report is sent from a consumer or healthcare provider to a manufacturer, the company is required to forward the information to the FDA, so it is then considered a mandatory report. MedWatch has separate forms for each type of reporter: Form 3500 (Appendix A) for healthcare professionals, 3500A (Appendix B) for manufacturers' mandatory reports, and 3500B (Appendix C) for consumers.

Mandatory reports are 15-day, quarterly, or annual reports from manufacturers required by the FDA which, as of September 2015, must be electronically submitted directly into FAERS. Case reports

submitted this way do not use the 3500A form. Instead, they submit the information required to meet the International Conference on Harmonization's Data Elements for Transmission of Individual Case Safety Reports, or E2B, standard. Only noncompliant paper mandatory reports still use the 3500A form. Expedited mandatory reports are required after a company receives notice of a serious and unexpected adverse event, after which they must report it to the FDA within 15 days. Quarterly and annual, or periodic, reports describe adverse events already contained in product labeling and are also called non-expedited. While 95% of adverse event reports the FDA receives are mandatory reports submitted directly into the database, (De & Sahoo, 2016), the remaining 5% that are voluntary, as well as a small amount of mandatory reports that require corrections (totaling about 108,000 reports in fiscal year 2016) must be processed manually by FAERS-DMP.

The FDA's Divisions of Pharmacovigilance I and II work within OSE to monitor the FAERS database and determine if any drugs should be relabeled, fixed, or pulled from shelves. When a potential safety concern is detected by the signal generation algorithm, the FDA's post-marketing Safety Evaluators, typically clinical pharmacists, review the associated reports. Safety Evaluators also closely monitor cases involving a Designated Medical Event, a particularly serious adverse event—such as a death or a heart attack. If the evaluators think that a case needs to be examined further, they will look for other similar cases in medical literature, FAERS, and other countries' FDA equivalents to determine a causal relationship between the drug and the event. Next, the FDA works with investigators to search through multiple large databases that gather patient information from hospitals and insurance companies through the Sentinel initiative. The FDA can also contact foreign agencies and the World Health Organization's Uppsala Monitoring Center, which runs its own database on adverse drug events with data from over 60 countries, to determine whether the adverse drug reaction has occurred elsewhere in the world. If the FDA determines that the adverse event report is firmly associated with the drug, FDA officials can have the manufacturer correct production problems or change the warning labels and side effect information. The FDA can also issue a public health advisory, contact prescribing doctors, restrict distribution of the medication, issue recalls, or revoke drug approval (Ahmad, 2003).

On August 28, 2012, the FDA switched their database from the Adverse Event Reporting System (AERS) to FAERS (USFDA, 2015, November 24). This database contains data on adverse event reports from 1969 to the present. The number of adverse event reports that the FDA received has significantly increased in the past few years. In 2015, the FDA received 1,658,484 total reports, up from 470,261 in 2006 (USFDA, 2015, November 24). Figure 2 shows the total number of adverse event reports received by the FDA during that period.



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Direct	20,979	23,032	32,896	34,165	28,946	28,045	29,026	28,386	34,246	54,406
Non-Expedited	230,065	228,206	218,205	216,264	320,341	346,745	475,993	506,512	508,303	760889
Expedited	219,217	229,982	274,281	330,383	409,547	499,155	577,852	635,206	746,584	843189
Total Received	470,261	481,220	525,382	580,812	758,834	873,945	1,082,871	1,170,104	1,289,133	1,658,484

Figure 2: The number of adverse event reports received by the FDA from 2006-2014 (USFDA, 2015)

The increase in reports received can be attributed to a number of factors, but the FDA suspects that it is partly due to improved reporting (USFDA, 2016) and an increased amount of drugs being approved. FDA enforcement actions and media coverage can also lead to increased reporting. There is typically an increase in reports when the FDA releases new safety alerts (Weiss-Smith, Deshpande, Chung, & Gogolak, 2011). It is also unclear whether the increase in adverse event reports is due to an actual increase in adverse drug reactions, an increased amount of adverse events that are not associated with a drug (Weiss-Smith et al., 2011), or an increased reporting rate.

In September 2016, mandatory reports submitted electronically made up 95.7% of total reports, and reports from consumers (Form 3500B) made up 30% of the voluntary reports. Most voluntary reports (52%) were faxes, 98% of which were submitted by healthcare professionals (Form 3500). Thirty-five percent of voluntary reports were submitted through MedWatch Online, and 13% were received by mail (Eley, 2016, Oct. 26).

2.3. Review of Similar Event Reporting Systems

The FDA and other government agencies, in the U.S. and internationally, use reporting systems similar to FAERS to process consumer and manufacturer-submitted health and safety incident reports. Reporting systems for different products in the United States are created when Congress enacts a law that requires an agency to conduct surveillance. Each system has its own unique legal requirements, funding source, software, and contractors (Quinn, pers. comm.). This means that other systems cannot be directly compared to FAERS since they all serve different purposes. However, a study of the methods used for report processing in each system may still identify more efficient business practices, such as a better way to manage mail or data entry that could be implemented by the FAERS contractors.

In addition to running FAERS, the FDA co-sponsors two other reporting systems with other U.S. agencies. The FDA and the Centers for Disease Control and Prevention (CDC) co-sponsor the Vaccine Adverse Event Reporting System (VAERS), which maintains and utilizes a database of vaccine-related adverse events. Voluntary reports can be submitted to VAERS by postal mail, fax, or online form, and vaccine manufacturers can submit mandatory reports electronically directly into the system ("Report an Adverse Event", 2016). VAERS receives about 30,000 reports annually ("About the VAERS Program", 2016), 73% of which come from manufacturers or health care providers ("Frequently Asked Questions", 2016). When a VAERS online form is submitted, the sender automatically receives a confirmation number. If a report is filed by mail or fax, however, the confirmation number will be sent by mail within a few days ("Frequently Asked Questions", 2016), suggesting that data entry of paper reports typically begins around that timeframe.

The FDA and the National Institutes of Health (NIH) co-sponsor the FDA-NIH Safety Reporting Portal (SRP). This portal accepts online reports for various human and animal products regulated by the FDA or NIH that are not covered by MedWatch or VAERS, such as human and animal food, beverages, and tobacco. The site includes a Safety Report Directory to guide users to the correct reporting system for their issue ("Safety Reporting Portal", 2013). Users can create an account to save a draft of their report, view previous reports, and add follow-up submissions. Creating an account also allows users to enter their basic information once, after which it is automatically added to future reports for faster completion. Users can also form groups that allow members of the same organization to view, edit, submit, or follow-up with other group members' reports ("Safety Reporting Portal", 2013).

The Consumer Product Safety Commission (CPSC) oversees all consumer products that do not fall under the jurisdiction of other U.S. agencies. They administer the SaferProducts.gov system, where consumers can submit product safety reports by online form, phone, fax, or postal mail. Like the FDA-NIH portal, users can register for an account, allowing consumers to save their report to complete later within 30 days and to receive email updates on their report's status ("Reports", 2016). Once a report has been submitted, the CPSC has five business days to process and review it before they are required to forward it to the product's manufacturer. The manufacturer then has ten business days to add a comment to the report, after which it is added to the SaferProducts.gov database ("Reports", 2016).

The European Union's European Medicines Agency (EMA) manages a pharmacovigilance system called the European Union Drug Regulating Authorities Pharmacovigilance, or EudraVigilance. Unlike the U.S. reporting systems, EudraVigilance only accepts online submission and does not accept reports directly from consumers or health care providers. They only accept reports from manufacturers, clinical

trial sponsors, and the national drug regulatory authorities of EU member countries ("EudraVigilance", 2016). Also unlike the U.S. systems, EudraVigilance requires that organizations and individual users within them register for an account before using the system. In addition, to improve security and data quality ("EudraVigilance system overview, 2016), each organization must have one designated individual complete an online course about proper use of the system and pass an evaluation ("EudraVigilance: How to register", 2016). Since EudraVigilance is not meant for use by consumers, the program includes a separate web database where the public can search adverse event reports, called Adrreports.eu ("EudraVigilance system overview, 2016).

2.4. Business Process Improvement Methods

Business process improvement (BPI) is a strategy commonly used in the private sector to analyze and modify processes to ensure maximum efficiency and quality, typically for manufacturing or customer service applications. Although BPI was developed by private companies, its goals of creating effectiveness, efficiency, and adaptability (Page, 2010, p. 7) are all relevant to government agencies like the FDA who wish to streamline their systems. The author of a report on the Louisiana Department of Health and Hospitals (DHH)'s process improvement program found that it "consistently demonstrated that process improvement strategies used in the private sector can be used in government benefit programs with measurable results" (Grant, 2010, p. 5).

BPI can be applied in virtually any type of company or organization that manages complex, time-constrained processes. In the field of manufacturing, Toyota applied its BPI plan to a General Motors (GM) Factory located in Fremont, California. The plant was said to have the worst workforce in car manufacturing in the United States (Siegel, 2010), and GM closed it down in 1982 due to it producing poor quality, defective cars. In 1984, Toyota reopened the plant with most of the same workforce and applied its Toyota Production System model. The plant went on to have the one of the smallest numbers of defective cars produced in the U.S. (Siegel, 2010).

The Louisiana DHH implemented a process improvement program for their Medicaid and Children's Health Insurance Program (CHIP) eligibility process in 2006. The program utilized the Toyota Production System approach, particularly their well-known Plan-Do-Check-Act cycle model for testing and modifying proposed changes on a small scale before officially implementing them (Grant, 2010, p. 23). The initiative reduced the state's average application processing time down to 7% of the federally required maximum time for children's cases, and 30% of the maximum time for elderly and disabled applicants (Grant, 2010, p. 8).

For this report, five methods for business process improvement were compared (see Appendix D), those from Brewer (1996), Harrington (1991), Page (2010), Robson (1991), and Liker (2004). Liker's book describes Toyota's BPI method (Figure 3). While unique, each system studied contains a similar order of steps. All five methods studied have either organization or process definition as their first step. Organization includes logistical tasks such as assembling a team, setting the project start and end dates, and gathering necessary materials that will be needed for BPI (Brewer, 1996 and Harrington, 1991). During process definition, a thorough description of the current process is documented. The information gathered should include a list of internal and external stakeholders and a visualization of the process in the form of a flowchart (Wilson and Harsin, 1998), such as a fishbone diagram (Brewer, 1996) or a process map (Harrington, 1991 and Page, 2010).

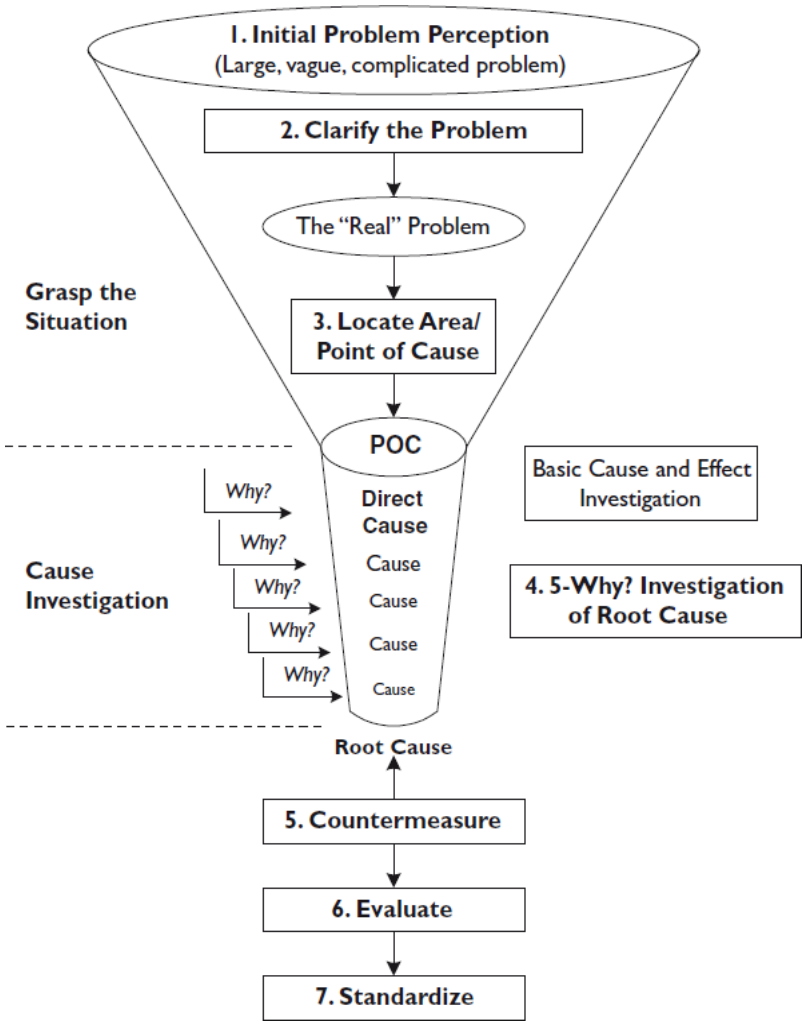


Figure 3: Toyota's BPI Method (Liker, 2004)

After the organization and process definition steps have been completed, Brewer (1996) recommends data collection and analysis, while Harrington (1991) and Page (2010) recommend streamlining and estimating time and cost, respectively. While these intermediate steps differ, all of the process improvement techniques include an evaluation or measurement step afterwards, followed by implementing the changes and monitoring the process for continuous improvement (Brewer, 1996, Harrington, 1991, Liker, 2004, Page, 2010, and Robson, 1991).

Two of the five methods, Toyota and Robson (1991), focus on addressing specific problems within a process rather than general improvement. Their steps are similar to the other BPI systems, but include a step after organization for determining the root cause of the problem (Liker, 2004 and Robson, 1991). Toyota's strategy for finding a root cause is called 5-Why, which proposes that once the question "Why?" has been asked five times, the root cause will have been revealed (Liker, 2004). Both of these methods list creating countermeasures or taking corrective action as their next steps. Toyota's method also includes standardization after evaluation. Standardization is important to Toyota because it allows for workers in different divisions to understand each other's work, and for improvements to be made at once across the company by updating the standards (Liker, 2004). Standardization is relevant to government agencies as well since their processes involve a significant amount of paperwork and they have a large number of employees working in different divisions and locations.

Lean Six Sigma, an additional business process improvement strategy, combines the methods of the Lean and Six Sigma systems. Lean is focused on speeding up processes by eliminating steps that do not add value, called "non-value-added" activities or "wastes" (George, 2013). Like the other BPI systems studied, it includes analysis of the process flow, determination of the root causes for problems, identification of sources of delays (bottlenecks), and establishing quantitative performance measures (George, 2013). One aspect of Lean that applies to report processing is switching from "push" systems to "pull" systems. In a push system, a worker is assigned new cases by a manager, whereas in a pull system, the workers take new cases from a pool when they are ready (George, 2013). This eliminates non-value-added work for managers and speeds up the process. In the Louisiana DHH case, the department switched from a push system to a pull system for distributing Medicaid and CHIP applications to evaluators for review (Grant, 2010). Six Sigma is meant to solve problems and reduce variation in business systems by utilizing the "DMAIC" methodology: Define, Measure, Analyze, Improve, and Control. Combining both Lean and Six Sigma is effective for service applications, such as government, because both speed and quality are improved (Grant, 2010).

2.5. Applications of BPI to Government Reporting Systems

Business process improvement has been successfully applied to both local and federal government reporting systems, as demonstrated by the BPI programs developed by the U.S. Department of Defense (DoD) and the city of Fort Wayne, Indiana. The DoD developed a BPI plan in fiscal year 2015 to fix problems in the reporting of intragovernmental transactions (IGTs) (Kemp, 2016). IGT's occur when two governmental organizations buy or sell to each other. "During fiscal year 2015, DoD recorded over $80 billion in unsupported journal vouchers (JV) in order to balance IGTs between internal buyers and sellers" (Kemp, 2016). The Government Accountability Office (GAO) cited failure to balance IGTs as an impediment for auditing in the federal government (Kemp, 2013). To address their significant problem with IGT reporting, the DoD Comptroller developed an IGT business process model. The model involved standardizing financial reporting and data exchange, 28 specific activities to track progress, and change management, or gaining commitment and support from employees to transition to the new system. Pilot programs for change management will begin in fiscal year 2016 (Kemp, 2016).

The city of Fort Wayne, Indiana applied Lean Six Sigma to various city government processes in 2000 (George, 2013). The mayor at the time, Graham Richard, had been successful using Six Sigma in the private sector before being elected mayor, and wanted to bring these techniques with him to help strengthen the city's economy, focus on service to citizens, and make the city safer (George, 2013). Mayor Richard established an executive council to oversee new process development, trained division managers and department leaders in Lean Six Sigma techniques, and created a full-time Quality Enhancement Manager position. After three years, the city had saved $3 million and launched 60 new projects (George, 2013). One specific improvement was in the processing of road pothole complaints. Before the Lean Six Sigma initiative, 77% of potholes were repaired within 24 hours of reporting, with some cases taking up to 80 hours. Afterwards, 98% of potholes were being repaired within 24 hours of reporting, with an average time of just 10 hours (George, 2013).

3. Methodology

This project was intended to assist the United States Food and Drug Administration's Office of Surveillance and Epidemiology to monitor and assess marketed drug safety by improving the processing of adverse event case reports. Components of existing business process improvement methods were applied to the system to identify and address delays and inefficiencies. The four main objectives established for the project were:

1. *To understand and map the current process for submitting and recording MedWatch reports into the FAERS database.*
2. *To understand the stakeholders' needs and goals for improvement.*
3. *To compare the current process with other FDA database collection methods.*
4. *To develop recommendations for increasing the overall efficiency of AE data processing utilizing BPI methods.*

We applied BPI strategies in all of our methods. In order to understand the impact BPI had on each objective, the intended BPI application must first be described. Our BPI strategy is outlined in Section 3.1, preceding the methods used to carry out our four objectives.

3.1. Adapted BPI Strategy

We applied the Lean Six Sigma business process improvement method to the FDA contractor's current system for processing MedWatch forms, FAERS-DMP. Lean and Six Sigma used together allowed us to create a set of recommendations for improving both the efficiency and accuracy of the FAERS-DMP report processing system. First we assessed the system to get a better understanding of it and to identify problem points. The Lean method identifies eight different types of wastes, or non-value added work, to look for in a process: defects, over-production, waiting, non-utilized skills, transportation, inventory, motion, and extra-processing. Recommendations were developed to eliminate as many of these wastes as possible. We also determined if the current method of assigning employees reports is a push system or a pull system. Once waste was removed from the process using Lean, the Six Sigma method was used to increase the efficiency of the process by identifying and solving problems. Many aspects of DMAIC, such as Define, Measure, and Analyze, had already been performed during Lean. However, they were performed in the context of reducing waste and processing time. DMAIC was also implemented in Six Sigma, but for the purpose of identifying problems and developing solutions. The

Measure and Analyze steps were aided by studying comparable reporting systems from other FDA centers. The methods used to carry out our adapted BPI approach can be seen below in Figure 4.

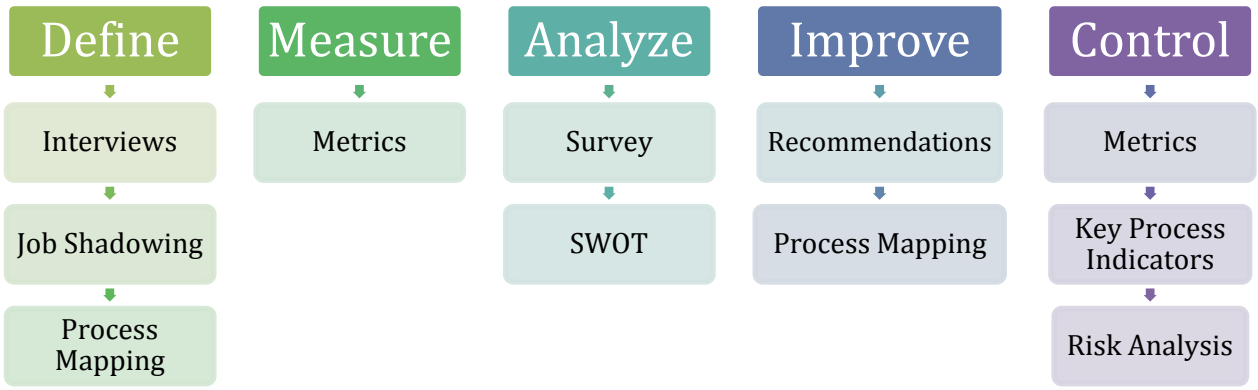


Figure 4: Business Process Improvement Approach

3.2. Objective 1: Evaluating the Existing System

To understand and map the current process for submitting and recording MedWatch reports into the FAERS database.

The goal of this objective was to create a process map of how reports move through the FAERS system and to gain a detailed understanding of the work each staff member does in the process. A summary of the techniques used to accomplish this goal is provided in Figure 5. Completion of this objective utilized the Six Sigma steps of Define and Measure, and the general BPI concepts of process and problem definition, process mapping or flowcharting, and applying evaluative measurements.

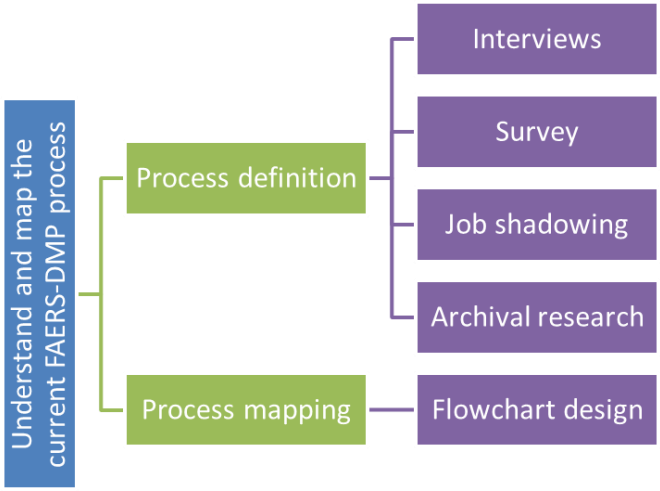


Figure 5: Techniques for evaluating the current FAERS-DMP system

Process definition was accomplished through interviews, a survey, observation, and archival research. Once the current process was well understood, a flowchart was created to visualize the system and track information flow. We shadowed the contractor's staff to observe the process and understand how MedWatch reports are entered into the FAERS database for each type of report submission and to determine if the current system for getting new reports to staff members is a push or a pull system. Conversations with managers and staff allowed us to get answers to any questions that arose during observation and added further details to our understanding of the process. After obtaining the necessary data, a flowchart, or process map, of the system was developed and reviewed by both FDA and contractor employees. The flowchart was made in swim lane style to show the software used during each step. An additional swim lane flowchart was made for mandatory report submission and processing, although this process is largely automated, so it was not a significant component of our project. Both diagrams can be seen in Section 4.2.

We surveyed the FAERS-DMP staff to inquire about their work (see Appendix E for survey questions). The first part of the survey asked the staff to describe their role in the system and how long it takes them to work with a report of each submission type. Their job descriptions helped to confirm and add to the information gained during job shadowing. The estimates for how long it takes them to work on a report allowed us to calculate the average time spent on a mailed, faxed, or online report in each department and to compare this data to the contractor's metrics.

Archival research was a large part of completing this objective. We studied the long-term and short-term statistics collected about FAERS-DMP, which allowed us to determine what measurements are currently being tracked. We were also given access to workflow documents, Standard Operating Procedures (SOPs), and the preproduction version of the software used for some of the report data entry and triage steps, which aided in our understanding of the program and the roles of different staff members. Another important topic we looked for in FDA records was how the report processing system has changed over time, why changes were made, and what effects they had. All of these archival research topics, together with the job shadowing and interviews with current staff, allowed us to create process maps and gain a complete and accurate understanding of the adverse event report processing system before moving on to further objectives that required analysis, comparison, and improvement of it.

3.3. Objective 2: Determining the Stakeholders' Needs

To understand the stakeholders' needs and goals for improvement.

A successful BPI plan rests on the ability to understand and meet the stakeholders' needs as best as possible throughout the duration of a project, so we aimed to fully understand the needs of our sponsor, the employees, and anyone else directly impacted by the MedWatch program. This information allowed us to later set goals for the improvement of MedWatch that maximized benefit and minimized harm for the stakeholders involved. Interviews were a key part of understanding the stakeholders' needs. We established our liaisons' concerns about the current system and their goals for improvement through semi-structured interviews and casual conversation at the beginning of our time at the FDA. We also spoke with contract managers in order to understand their priorities and needs for the system and their ideal vision for a newer, updated system. We spoke further with our liaisons in order to understand their ideas and goals for the project as it progressed. This input was critical to the direction of our project. Most of these interviews were casual discussions or during general body meetings and were semi-structured with some questions prepared to guide conversation.

In addition to their managers, the contractor's data-entry, triage, and medical coding employees were also stakeholders since they use the system daily, so their needs and concerns were identified in the aforementioned survey. While the first part of the survey supported our first objective, the second part of the survey supported our second objective by inquiring about the survey respondent's opinions and their desired changes to the system, including changes to each software program and to the MedWatch forms themselves. These suggestions were incorporated into our recommendations (see Chapter 5).

3.4. Objective 3: Comparing FAERS to Other FDA Reporting Systems

To compare the current process with other FDA database collection methods.

This objective consisted of analyzing various aspects of different FDA report processing and database entry systems and identifying common problems, comparing process flow, and determining how each system handles or has corrected any processing complications. Completion involved researching other systems, including observation via tours and presentations, and comparative criteria analysis. It is ineffective to compare the outcomes and purposes of other systems to FAERS because they are all strictly regulated government systems fulfilling different requirements. However, this research provided valuable insight on pain points common in reporting systems and typical processing methods. Comparisons were drawn to the current FAERS program and to two other systems used by the Center

for Devices and Radiological Health (CDRH) and the Center for Tobacco Products (CTP). The processes and functions of these systems were analyzed to determine what works well within each one's case processing and what drawbacks should be avoided when developing recommendations for FAERS. Throughout our study, it was important to consider the difference between various operating procedures, as what function wells for one center may not be valid or feasible for another.

The criteria compared among the three systems were the data entry process, staff functionality, type of data collected, case turnaround time, and process organization. While the same level of detail was not available for the CTP and CDRH programs as FAERS-DMP, comparing these systems to FAERS identified methods that we recommended to avoid or adopt, and allowed us to make more educated recommendations in the next objective.

3.5. Objective 4: Recommending Methods to Increase Efficiency and Productivity of Data Processing

To develop recommendations for increasing the overall efficiency of AE data processing utilizing BPI methods.

Our final goal was to analyze the FAERS-DMP system and provide recommendations for improvement after obtaining a thorough knowledge of the current process, identifying the needs of the FDA and other stakeholders, and then determining how the program performs in relation to other report processing systems. This step allowed us to develop a plan to adjust the current system so that it best fits the stakeholders' goals of reducing processing time, reducing cost to the FDA and contractors, minimizing potential risks, and collecting valuable metrics for use in both maintaining and improving overall efficiency. This objective incorporated the Lean strategy of identifying waste and the Six Sigma steps of Analyze, Improve, and Control. We utilized the mapping of the current system structure to break down and evaluate each step in order to see what it does, how much time it takes, and what feedback was given about it.

We then performed several strengths, weaknesses, opportunities, and threats, or SWOT, analyses in order to identify what issues were most pressing to solve and what steps needed the most improvements. The opportunities component of the SWOT analyses allowed us to determine what changes would be more feasible to implement into the system based on upcoming contract and software updates. A SWOT analysis was done for each step of the process map that was a part of FAERS-DMP in order to evaluate the present system. The analysis used the data and information collected in the previous objectives. The survey was also utilized here, because it asked employees to help

determine the strengths and weakness of the systems that they use and aimed to determine if the employees have any existing concerns about the process.

The survey responses were analyzed to systematically identify concerns in the FAERS-DMP process. The number of respondents with similar problems was identified through searches for complaints or suggestions involving a certain topic. The topics searched for were optical character recognition (OCR), the text field placement in the FAERS software, the size and font consistency in the FAERS software, the resolution or clarity of mail or fax report PDFs, and consumers' handwriting on MedWatch forms.

After all of these analyses, we suggested changes based on the sponsors' and stakeholders' feedback and our own ideas stemming from our research on business process improvement. We designed an ideal system that more efficiently moves electronic and paper forms from submission to evaluation without losing any methods of submitting forms or any critical data from the forms themselves. We then created a process map of the new system (see Section 5.1) and explained each change and the reasoning for its addition, modification or removal. We compared each step of the new system side by side with the map of the current system and our collected data in order to generate ideas and suggestions on how to best turn the current system into the ideal one. The new system structure and the methods and metrics used to design it, along with our recommendations, were presented to the FDA at the end of our project. CDER may either implement these changes into the current FAERS program or utilize similar methods in the future when developing new FAERS contracts and software in order to find newer, better solutions.

4. Results

In this chapter, we describe the information and data we acquired from implementing our methods as discussed in Chapter 3. We first established our sponsors' goals, the current state of the FDA's contract with Diamond Solutions, Inc. (DSI), as well as what metrics are currently collected on the FAERS-DMP program. The FAERS system was then mapped out, showing each individual step for easier identification of steps that could be improved upon. Then, we analyzed the results from the survey conducted of FAERS-DMP staff to determine what common complaints the employees have and what they would like to see improved in the systems they work with. We also compared the FAERS-DMP system to other reporting systems within the FDA used by CDRH and CTP to determine whether or not the other systems have any methods that could be implemented by CDER. Finally, once we gathered all of this data, we performed SWOT analyses of the FAERS-DMP process steps and related program components, as well as an analysis of Lean wastes, to provide us with the groundwork needed for creating recommendations for the system.

4.1. The FAERS-DMP Contract, Metrics, and Performance Goals

The FDA began collecting adverse event data in 1969 and processed reports internally before they began contracting out the program in 1997 (Eley, 2016, Oct. 25). Each contract lasts approximately five years (Quinn, pers. comm.), and the current contract provides for three companies to process MedWatch forms. The primary company is DSI, and there are two subcontractors, Zimmerman Associates, Inc. (ZAI), and HeiTech Services, Inc. (HeiTech). Two other companies are involved with the FAERS-DMP contract: ArisGlobal, LLC (ArisGlobal) and CNI Professional Services, LLC. (CNI). CNI is the primary contractor for the FAERS software, and ArisGlobal is a subcontractor that provides another software product called First Look at Reports, or FLARe, that is used for initial data entry and triaging of reports before they are sent to the FAERS database. DSI, ZAI, and HeiTech are located in Landover, MD, approximately 30 minutes away by car from the FDA headquarters located in Silver Spring, MD, where mail is initially received. This requires paper reports to be shipped between the two locations as well as CDER's central document room in Beltsville, MD.

FAERS-DMP (DSI, ZAI, and HeiTech) consists of 35 full-time employees. Two employees perform Registration in FLARe where initial entry of about 10% of MedWatch voluntary report data occurs. Two full-time equivalent (FTE) pharmacists perform Triage and, based on the product involved, they determine to which FDA center reports should be sent. Registration and Triage make up the Central

Triage Unit, or CTU. Seven FTEs perform Detail Data Entry (DDE), where the rest of data entry is completed, seven FTEs perform Coding, or data entry quality control, and nine FTEs perform Validation, or MedDRA coding of the medical events described in the report (Eley, pers. comm.). The specific tasks these employees perform on a report and their position relative to the overall process will be described in detail in Section 4.2.

The FAERS-DMP managers meet monthly with FDA representatives to discuss the previous month's performance (Eley, 2016, Oct. 26). A weekly email with similar metrics is sent to the same group of representatives (Sahoo, pers. comm.). The following metrics are reported (Eley, 2016, Oct. 26):

- Number of days that were needed to process direct, expedited, and non-expedited reports
- Number of reports processed per hour by Registration, Triage, DDE, Coding, and Validation
- Number of companies submitting electronic mandatory reports
- Monthly budget of the contract
- Number of paper mandatory reports received despite the electronic submission requirement
- Number of electronic 15-day and periodic mandatory reports received
- Number of mandatory electronic reports with errors that must go back to Coding to be corrected
- Total number of cases triaged by CTU and the number sent to the FAERS database and other centers
- Percentage of cases triaged by CTU received by mail, fax, and online and by form type (Form 3500 or Form 3500B)
- Number of reports by type sent to the FAERS database
- Overall volume of reports received

The program keeps six-month and yearly metrics as well, presented at biannual meetings. These metrics are less specific than the weekly and monthly ones. For example, they do not differentiate between mail and fax reports or voluntary and mandatory electronic reports, or break down the number of reports processed by each department. FAERS-DMP received 108,000 reports requiring manual processing in fiscal year 2016, consisting of 75,000 voluntary and mandatory paper reports and 33,000 electronic mandatory reports with errors.

FAERS-DMP has established hourly performance goals for their DDE, Coding, and Validation staff, shown in Table 1 below. According to the September 2016 monthly data, the staff in each of these three departments are meeting or exceeding these goals (Eley, 2016, Oct. 26).

Table 1: Hourly FAERS Performance Goals

Department	Expedited paper cases/hour	Expedited Electronic cases/hours	Periodic paper cases/hour	Periodic electronic cases/hour	Direct cases/hour
DDE	Initial reports: 4 Follow-up reports: 3	N/A	5	N/A	4
Coding	6-7	8	8-10	10	6-7
Validation	6-8	8-10	20	20	8-10

In addition to these specific goals set by the contractor, our FDA liaisons provided us with a set of three key performance indicators, or KPIs, to guide improvement of the current system. These KPIs, which are cost, time, and resources, provide a basic guideline of the areas the FDA most wants to see improved. Cost is a large factor, as the contract requires millions of dollars per year to maintain employee salaries and other expenses. (Eley, 2016, Oct. 26). The FDA would like costs to either go down or remain the same. Since reporting is expected to continue to increase, the cost per report would go down if the contractors can process these additional reports without raising their budget. The second KPI is time: voluntary reports take 6 business days to fully process (Eley, 2016, Nov. 30). This number has not changed despite the implementation of FLARe, indicating a need for other methods to reduce report processing time. Resources include people, tools, software, and any other assets available to the FDA to process each MedWatch form.

4.2. Process Mapping and Analysis

From the information collected through various conversations and interviews, we created process maps, or flowcharts (see Figures 9 and 10), tracking the process that voluntary and mandatory adverse event reports follow. All voluntary reports go through the FDA's MedWatch program. Forms that are sent in through mail are first scanned into the FLARe system. The FLARe user interface is shown in Figure 6. Next, the forms go through Optical Character Recognition (OCR) software. OCR software converts the text on the scanned document into electronic text characters. Forms that are received through fax are automatically sent to FLARe and also go through OCR software.

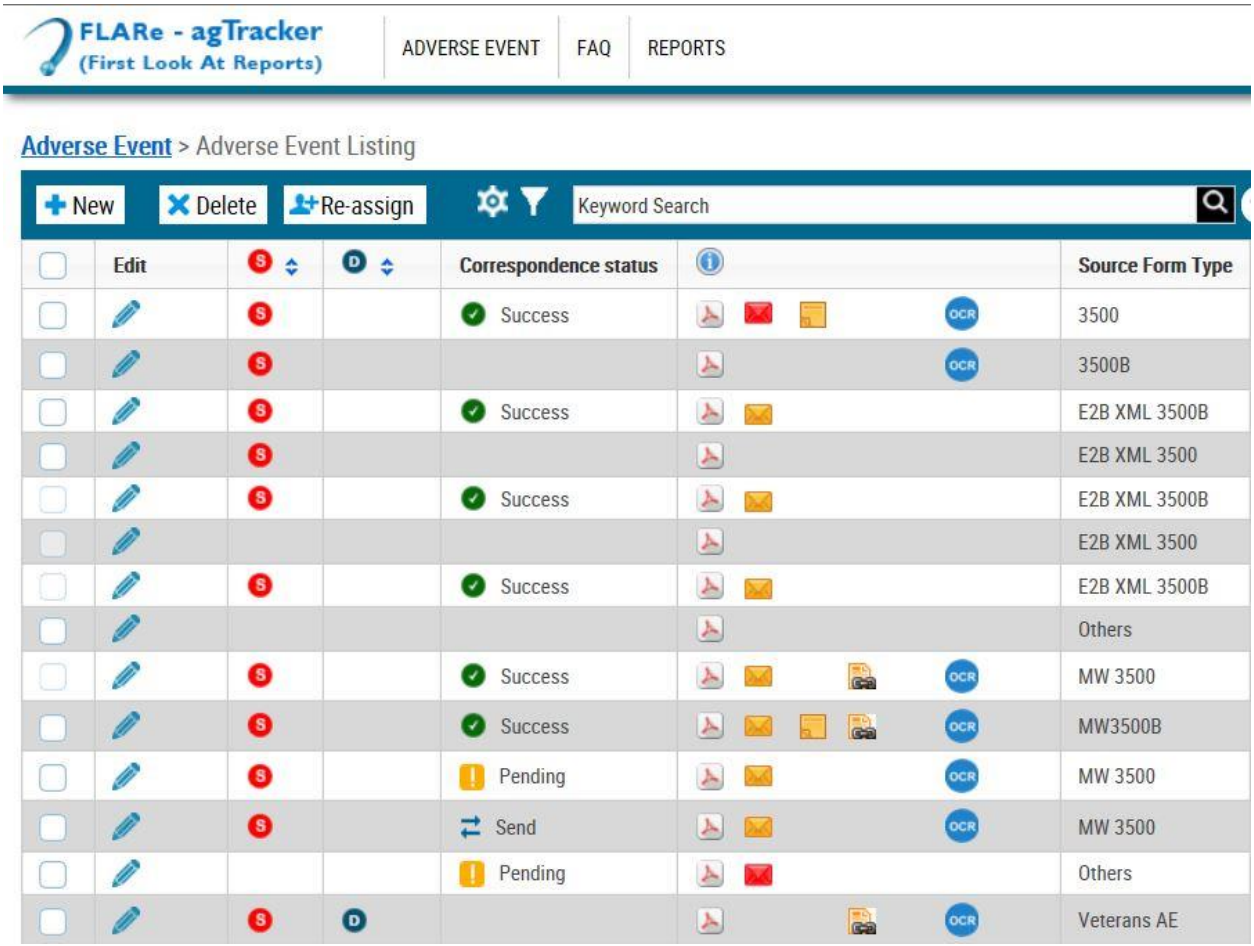


Figure 6: The FLARe User Interface

After OCR, both the fax and mail forms go to Registration. Since the online reports are already entered into FLARe in electronic text character, they go straight to Registration. During Registration, a staff member reviews or enters the reporter's information, the product's name, the date the report was received by the FDA, and the form type. The staff member also checks for duplicate reports and splits faxes containing multiple reports. FLARe automatically assigns each report a CTU number during this step. Registration employees have access to an inbox in FLARe with all of the un-registered reports, and they are free to choose a case to work on when they are finished with their previous case. This is the same for the rest of the steps as well, indicating that the system is a pull system. Next, all of the voluntary reports go to Triage. Here, a licensed pharmacist reads through the narrative to decide if an adverse event occurred and if the report belongs in the FAERS database. If a report does not belong in the FAERS database, the Triage employee decides which FDA center the report should be sent to. About 30% of reports are emailed as PDFs to other centers, and the remaining 70% go to the FAERS database.

He or she also checks for omitted information and misspelled drug names. For example, consumers sometimes submit cosmetic or dietary supplement adverse event reports through MedWatch. Those reports are not handled by CDER, so they are sent as a PDF by email to the Center for Food Safety and Applied Nutrition (CFSAN). The action of sending a report out of FLARe is referred to as disposition. If the adverse event report does involve a drug, the report is disposed from FLARe and sent to FAERS, after which an email is automatically sent to the reporter acknowledging that their report has been received.

A detailed map of the disposition process is shown in Figure 7 below. First, the XML version of the report is sent from FLARe to a bucket, taking 1 minute. The XML then takes 20 minutes to go from the bucket to FAERS. An acknowledgement that the XML has been received is sent back to FLARe, taking 20 minutes to get to the bucket, then 1 minute to go to FLARe. The same steps are repeated for the image, or PDF, of the original report, and the image acknowledgement, for a total of 84 minutes. Once the XML and image are in FAERS, the image is not available for viewing with the XML until a batch of images is sent in 3-hour intervals from 9:00 am to 9:00 pm. Once disposition is complete, it is marked as successful in FLARe. The files are archived in FLARe for seven days and then deleted, at which point they only remain in the FAERS database.

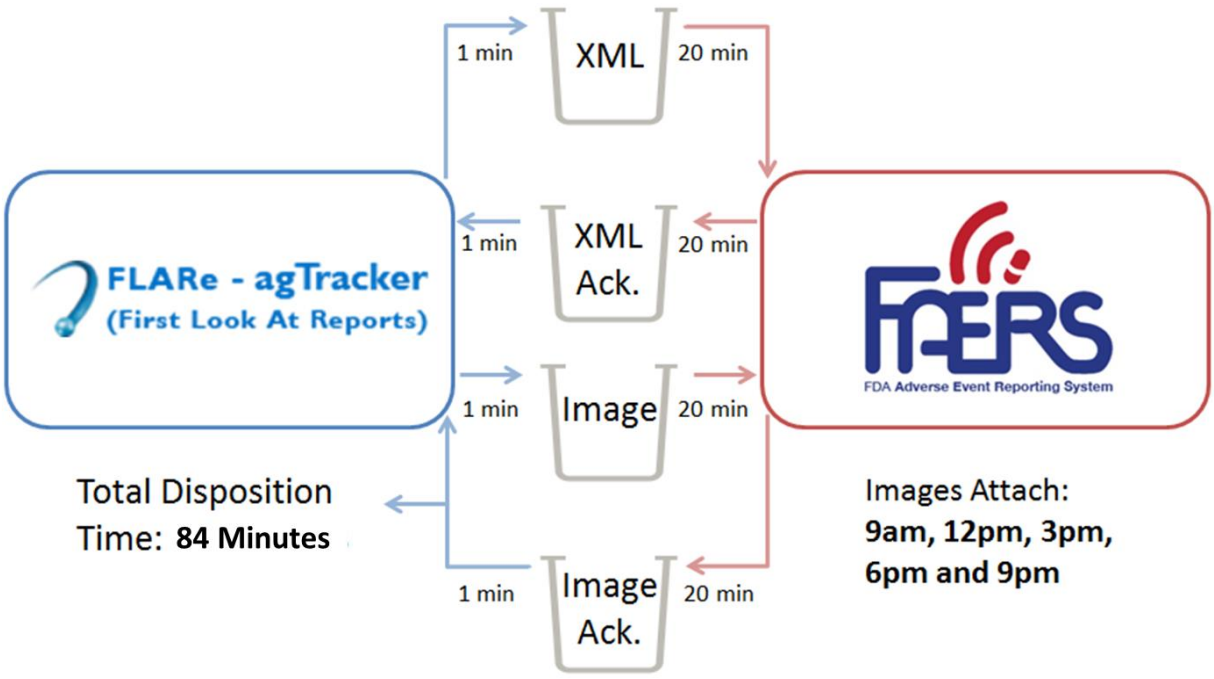


Figure 7: Disposing forms between FLARe and FAERS

Once in FAERS, the report goes to Detail Data Entry (DDE) where employees perform quality control on the information entered in Registration and enter the remaining information from the report into FAERS. The FAERS user interface for data entry is shown in Figure 8 below. Data entry is done verbatim, which means that the text is entered with no interpretation or correction. Next, the report is sent to Coding, which was formerly called Data Entry Quality Control (DEQC). The Coding team consists of people with scientific backgrounds who are familiar with medical terminology and products. The product's name is checked in the FAERS Product Dictionary (FPD) and the product manufacturer's name is checked in the FAERS Manufacturer Dictionary (FMD). Errors are also corrected in the verbatim data entry text. Afterwards the report goes to Validation. During Validation, Medical Dictionary for Regulatory Activities (MedDRA) coding is applied to the report. MedDRA coding is an international standard used by the pharmaceutical industry to classify adverse events. After MedDRA coding, a report is considered complete and is allowed to be seen by Safety Evaluators.

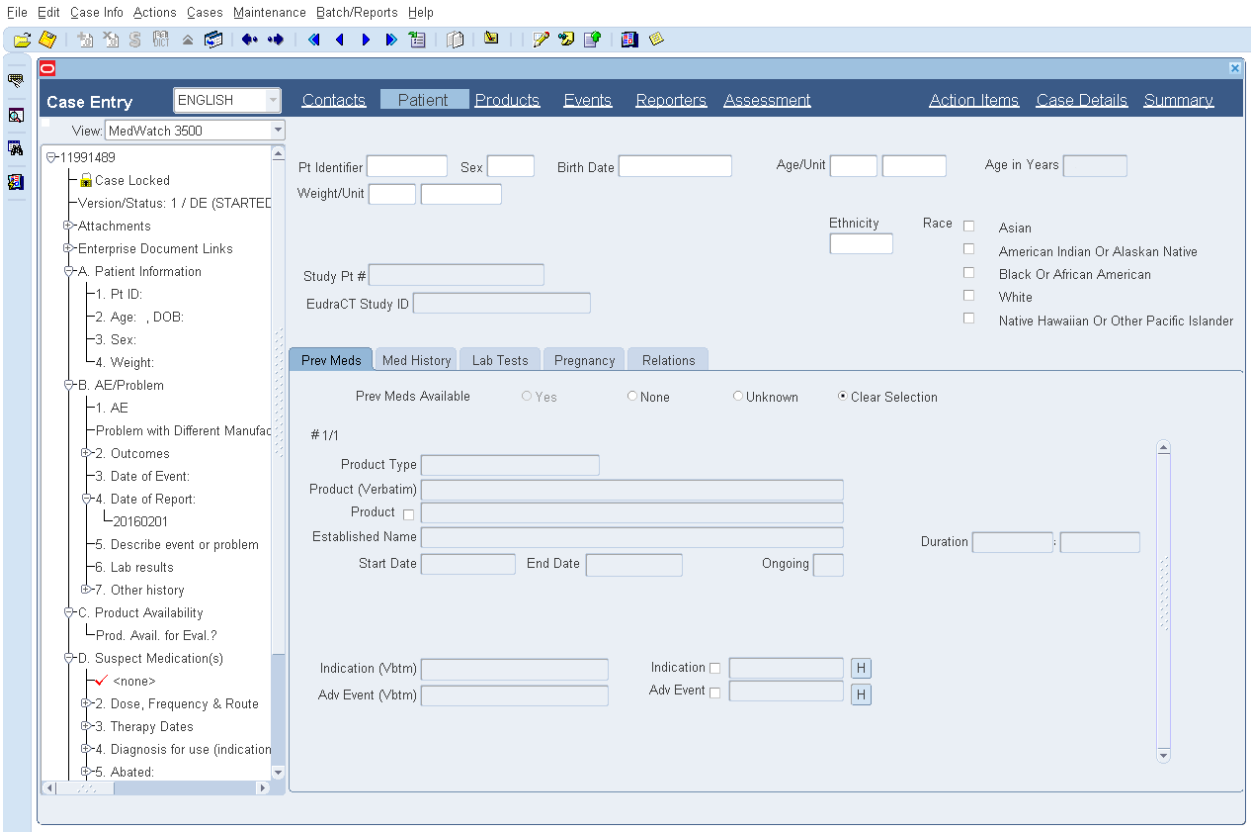


Figure 8: The FAERS User Interface

Although 95% of mandatory reports are received in electronic forms, the other 5% of reports are received in paper form. There are two different ways for mandatory reports to be submitted into FAERS but both methods require the use of E2B files. E2B is the international standard for individual case safety report submissions. If the company has the ability and software needed to create an E2B file themselves, the form is submitted using the Electronic Submissions Gateway (ESG). Otherwise, companies must use the Safety Reporting Portal (SRP), an online portal which turns forms into E2B format. Next, the file is automatically flagged if its product or manufacturer name does not match an entry in the FPD or FMP. If there is no dictionary error, the forms go directly into the FAERS database, with the exception of a small percentage of forms which undergo a quality control check to make sure the forms sent to the FAERS database are of good quality. A flagged form is sent to Coding where the error is corrected. If a term is not available in the FMD or FPD, the Coder must email the FDA to request it be added to the dictionary. Noncompliant mandatory paper reports are tracked using software called Automated Production Logs (APL) where the forms are batched and assigned unique bar codes as well as digitized. These reports then follow the same process as a voluntary form.

Once completed in the FAERS database, Safety Evaluators have access to the forms where they run queries and review forms using a user interface called FAERS Business Intelligence Solution, or FBIS. Further study and scientific evidence that an adverse event is caused by a drug can eventually lead to regulation. Reports in the FAERS database are also made available to the public in Quarterly Data Extracts (QDE) after Personally Identifiable Information (PII) is removed. The process as a whole, as described in detail above, is shown in Figures 9 and 10 below.

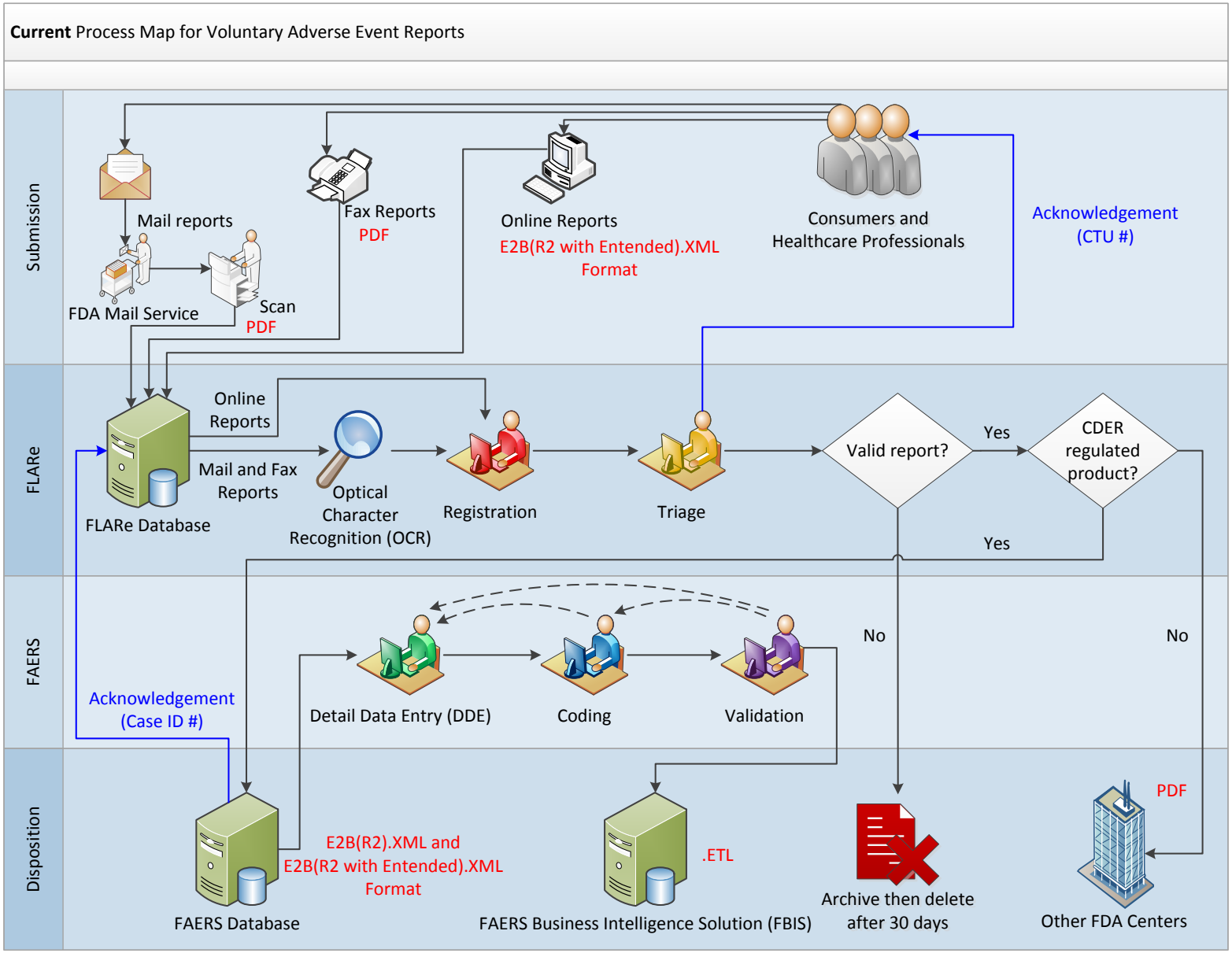


Figure 9: Current Process Map for Voluntary Adverse Event Reports

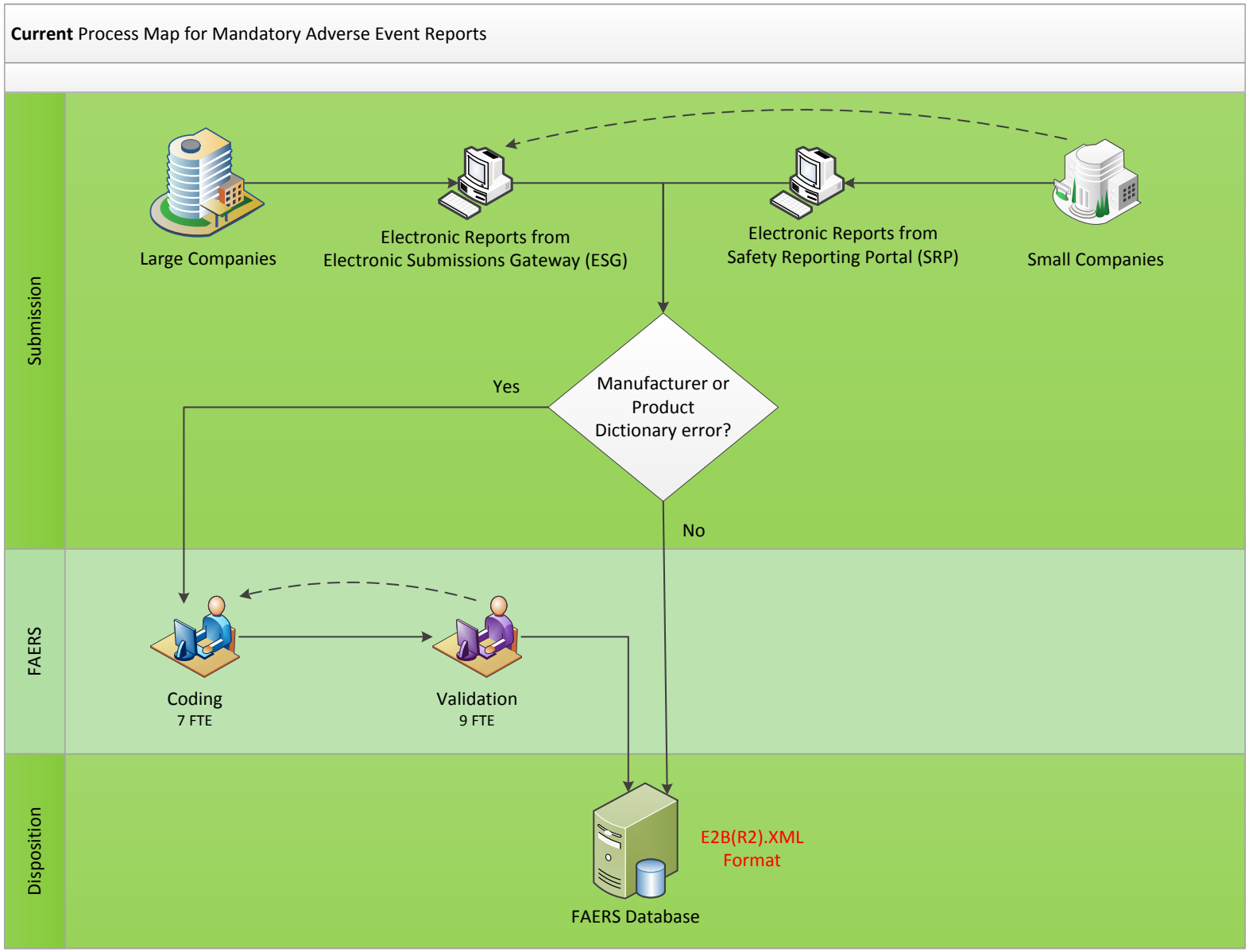


Figure 10: Current Process Map for Mandatory Adverse Event Reports

4.3. Survey Results and Analysis

A survey was designed and distributed to FAERS-DMP staff in order to gain information about their job responsibilities, the amount of time they spend on each report, and their opinions and suggestions about the program and its software. The survey was sent to all 35 employees, and we received 32 responses: a 91% response rate. The first part of the survey consisted of multiple choice and open ended questions to establish the employees' roles in the system, their opinions on FLARe, FAERS, and MedWatch forms, and estimates of how long it takes them to process a faxed, online, and mailed form. Multiple choice questions were used to ask employees what their job function is (Registration, CTU, DDE, Coding, or Validation) and how many years they have worked with FAERS-DMP. Open ended questions asked employees to provide a brief job description to see how they describe their work in their own words, and whether they have worked in other jobs in the FAERS-DMP system.

Of the 32 respondents, two stated that they work in Registration, two in CTU, ten in DDE, six in Coding, and nine in Validation. DDE staff made up the largest percentage of responses, 31%, as shown in Figure 11 below. The remaining three respondents did not provide an answer to this question because they do not work in one of the categories provided, but instead have management or support roles. These non-responses are included as "other" in Figure 11, which shows the results of the survey question that asked respondents to choose their position in FAERS-DMP.

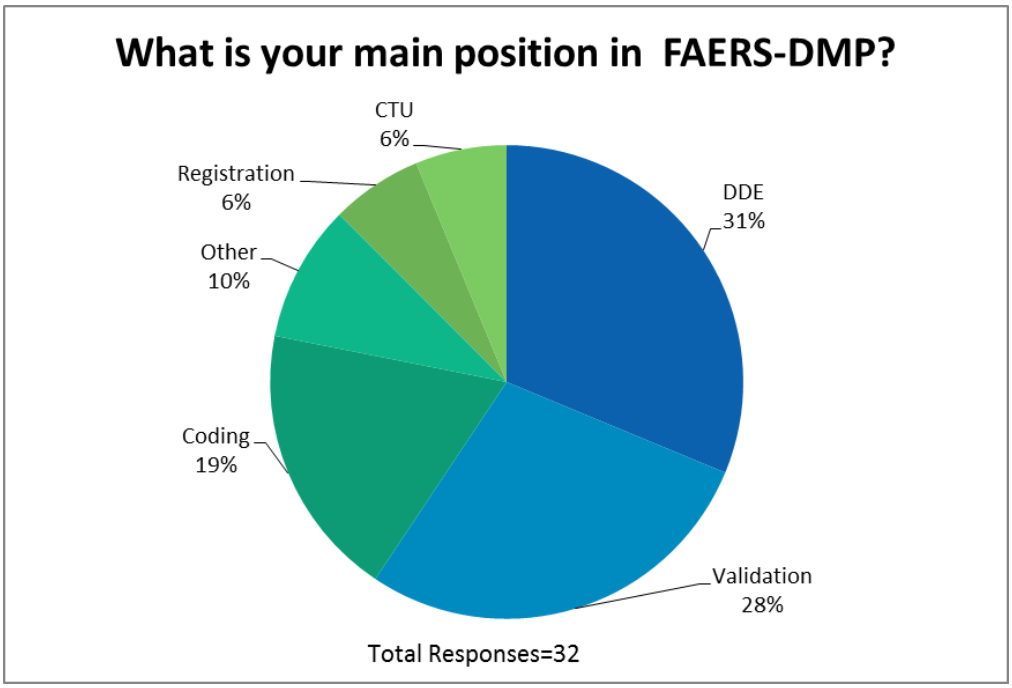


Figure 11: Employee positions within FAERS-DMP

The next survey questions asked the employees to describe their position and to indicate if they currently assist with or have previously worked in other positions in FAERS-DMP, respectively. The job descriptions provided us with confirmation of the information gained in interviews and job shadowing about what each type of employee does. Eighteen of the respondents indicated that they currently work in multiple roles or have previously worked in another role. The most common overlap was with Coding: four of the nine Validators and three of the ten DDE respondents wrote that they also perform Coding tasks.

The next survey question asked employees to select the number of years they have been working with FAERS-DMP in order to quantitatively gauge the experience of the staff and amount of employee turnover. The average length of time employees had worked on the program was 11.5 years, indicating high levels of employee retention and FAERS experience.

The last question in this section of the survey asked respondents to rank how much they agreed with the following statements:

- The FLARe software suits the needs of my position.
- FLARe is efficient for processing data.
- The FAERS software suits the needs of my position.
- FAERS is efficient for processing data.
- There are significant corrections that I need to make to adverse event reports that come from MedWatch forms.

The survey gave the options of Not Applicable, Strongly Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, and Strongly Agree for each statement. All three of the respondents with jobs that work most closely with FLARe selected Strongly Agree for "The FLARe software suits the needs of my position" and "FLARe is efficient for processing data." This included the two Registration employees as well as a CTU employee. The second CTU respondent indicated in their job description that they handle mail as part of CTU but do not work with either software. Four of the nine DDE respondents selected either Strongly or Somewhat Disagree for both of the FLARe statements. Of the employees who work most closely with FAERS (DDE, Coding, and Validation), 16 out of the 22 (73%) who provided an answer for "The FAERS software suits the needs of my position" chose Somewhat or Strongly Agree. No respondents selected Strongly Disagree for the statement "FAERS is efficient for processing data," and, as with the previous statement about FAERS, 73% of DDE, Coding, and Validation respondents chose Somewhat or Strongly Agree for this statement. On the last

statement, “There are significant corrections that I need to make to adverse event reports that come from MedWatch forms,” 44% of the total respondents somewhat or strongly agreed. This survey finding, as well as information from job shadowing, indicated that consumers often fill out MedWatch forms incorrectly and data entry staff must later take time to correct these mistakes.

The final multiple choice question on our survey asked respondents to estimate how much time it typically takes them to work on mail, fax, and online forms, in units of two minutes ranging from less than two minutes to greater than 30 minutes. Averages were calculated for each job type, shown in Figure 12 below, where n is the number of respondents from each job type who answered this set of questions in the survey.

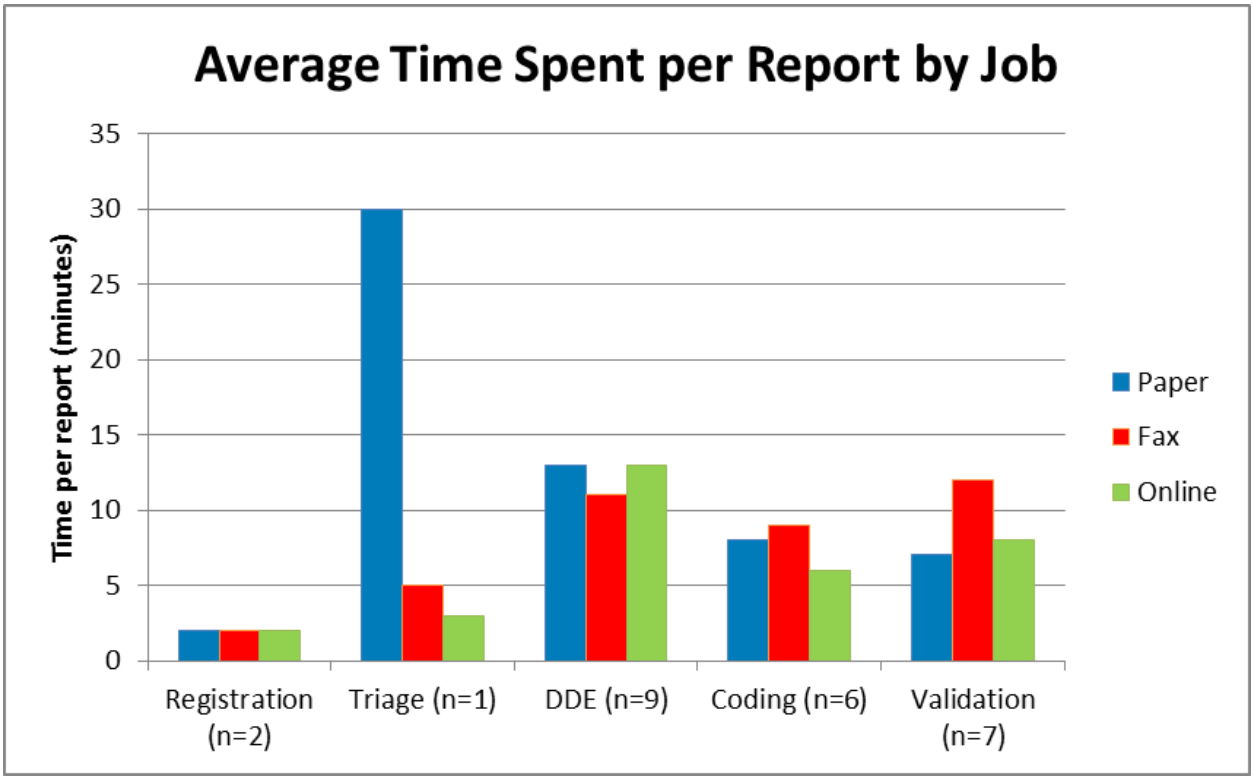


Figure 12: Average time spent per report by job type

Registration employees had an average of two minutes for all report types, the shortest of all the jobs. One CTU employee answered this question, and they indicated that paper reports take a significantly longer time to process than fax or online reports, about six times as long. DDE employees spend more time on paper and online cases than faxes, while Coding and Validation spend more time on faxes than on paper or online cases. Aside from paper reports processed by CTU, FAERS users (DDE,

Coding, and Validation) spent more time per report for each job type than FLARe users (Registration and CTU).

The second half of the survey was designed with open ended questions so the staff could provide us with more detailed responses than a multiple choice question would allow. Of the 32 staff who were surveyed, 25 completed the final open response questions: two from Registration, one from CTU, ten from DDE, four from Coding, six from Validation, and two other staff. Those working with the FAERS software accounted for 22 of the 25 responses, while the three other staff who responded work with the FLARe software.

After the survey responses were received, they were coded to find common factors in the data. After an initial review, five major issues were identified: difficulties with the OCR software, field placement problems in the FAERS software, field size and font consistency issues in the FAERS software, resolution of report images, and difficulty reading handwriting on handwritten reports. The first issue, the OCR software, was most frequently mentioned among all of the responses. A majority (60%) of the staff who are involved with the OCR software process, Registration, Triage, and DDE, encountered issues with it, oftentimes stating that the software made their job more difficult than it had to be. Most complaints involved OCR's lack of accuracy in recognizing characters, resulting in narratives that were either completely incorrect or producing small errors that are difficult to spot, such as the replacement of an 'I' with a '1'. When OCR software is not accurate, employees must retype the entire narrative or closely monitor the other fields to ensure the data is correct. This correction time is inefficient and wastes FDA resources and employee time.

The next most mentioned issues by data entry staff were general complaints about the FAERS-DMP system, including the lack of consistent field placement, field size, and font size in the software. The way the current system is configured, the data entry staff must constantly switch between windows to enter or perform quality control (QC) on the data as they go through the MedWatch reports. Figure 13 shows the order of fields in FAERS compared to a 3500 form. About one-third of the staff who work with the FAERS software voiced concerns about this system design. The same number of people also had a complaint about the size of fields and the text size in the system. Currently, many of the fields that data entry personnel are filling out are not large enough to read or view comfortably, and the text in the fields is too small. Data entry staff mentioned the desire to have these fields increased in size in addition to having larger text in order to make their job easier.

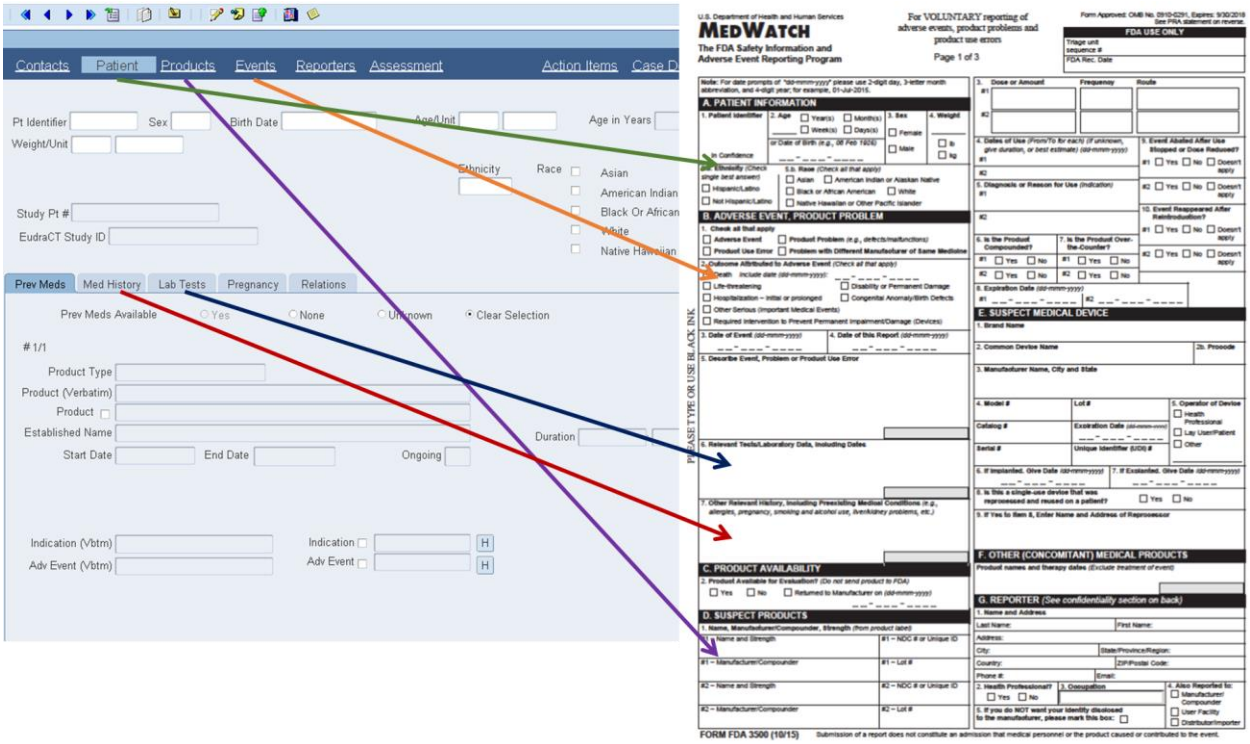


Figure 13: FAERS interface vs. MedWatch form field placement

The remaining issues experienced by the data entry staff are problems originating from consumers and other reporters. Difficulty reading handwriting on mailed paper voluntary forms was mentioned by seven respondents, and six mentioned poor resolution clarity of faxed reports received. In some cases, the handwriting cannot be deciphered at all. However, since these are not problems with the FAERS-DMP system, they cannot be improved upon as long as paper and fax reports are still accepted by the FDA.

4.4. Comparison of FAERS-DMP to Other Case Processing Systems

We were able to tour the Center for Devices and Radiological Health (CDRH) and the Center for Tobacco Products (CTP)'s document processing facilities to compare their methods to those used by FAERS-DMP to help analyze the FAERS-DMP case processing system. These centers utilize two contractors who are also on the FAERS contract, HeiTech and DSI. HeiTech is a subcontractor for FAERS and the primary contractor for CDRH's program called the Fully Integrated Records Facility, or FIRF. DSI is the primary contractor on both CDER's FAERS-DMP program and the CTP Office of Compliance and Enforcement's Retailer Response program. Both FIRF and the Retailer Response programs are much larger in scale than FAERS-DMP, since FAERS-DMP handles just one task order, processing adverse event

reports. FIRF and Retailer Response handle multiple task orders, or contractual obligations to perform specific functions for the agency. FIRF's task orders include processing device adverse event reports and premarket submissions for device approvals. Some of the Retailer Response program's task orders are processing Compliance Check Inspection (CCI) reports from Undercover Buys and Advertising and Labeling checks, and sending and receiving correspondence with tobacco retailers.

4.4.1. CDRH's Fully Integrated Records Facility (FIRF)

The FIRF program includes a mail room, server room, document tracking software, and staff who perform triage, data entry, quality control, MedDRA coding, and editing. Unlike FAERS-DMP, the FIRF mail room accepts mail directly, although they still receive some mail that goes through the FDA mail room. Documents are then triaged by task order. For document tracking, FIRF uses an internally-developed program, HeiQuality Automated Reporting and Tracking System (HeiQuality), rather than a third-party program under a separate contract, like FLARe and FAERS. After initial registration of reports, each task order uses different software for data entry.

After triage, premarket documents are sorted and processed by form type, which can be one of 30-40 different forms. Most premarket submissions are IDEs, Investigational Device Exemptions, 510Ks, applications for new uses for existing devices, and PMAs, or Premarket Applications. Companies submitting premarket documents must pay a filing fee and do not receive any acknowledgement of receipt like MedWatch reporters do. However, they can call FIRF, who will then locate the document in HeiQuality and inform the company of its status. All premarket submissions are processed on the same business day they are received, and 100% of them go through quality control, compared to a small sample of mandatory FAERS reports. FIRF processes about 150-200 premarket documents per day. Unlike FAERS, which accepts electronic reports directly into the database through the ESG or SRP, premarket documents submitted electronically are done so by mailing physical media, such as CDs or flash drives.

Postmarket adverse event reports involving medical devices are submitted to CDRH's Medical Device Reporting (MDR) program, which is much more similar to FAERS than FIRF's premarket document processing. MDR accepts voluntary reports using MedWatch forms, and mandatory reports are required to be electronically submitted as of August 2015. Mandatory reports are sent using either ESG or a web-based tool called WebTrader, analogous to SRP for FAERS mandatory reports. The software where forms are entered and stored is eMDR, FAERS's equivalent for medical devices, and the interface for users to view them is the Manufacturer and User Facility Device Experience (MAUDE), analogous to FBIS. Reports

are stored in on-site servers at FIRF, while FAERS reports are stored on a third-party server and FBIS contains only links to the files.

The data entry process for device voluntary adverse event reports has a similar workflow to FAERS-DMP. Scanning of paper reports is done at the mailroom and reports are entered into the HeiQuality tracking software. After triage, data entry employees type the reports into eMDR. After data entry, reports go to Analyst Coders for MedDRA coding, rather than to a QC step like Coding in FAERS-DMP. Analyst Coders perform the same role as Validators in FAERS-DMP. They code voluntary reports and correct MedDRA coding errors in mandatory electronic reports. For Analyst Coders, the eMDR software automatically queues stopped mandatory reports by priority. In FAERS, Coders must search for the highest priority cases to work on first. While there is no formal QC step, the MDR program has an additional step not performed in FAERS-DMP: editing. Unlike drug adverse event reports, all device reports are made publically available in MAUDE, so editors are needed to redact any PII or confidential medical information before the reports are published (McClintock, pers. comm.).

4.4.2. CTP's Retailer Response Program

The Retailer Response program managed by DSI for CTP is a national system that receives information from 50 state-level programs for Compliance Check Inspections (CCIs): Undercover Buys, when a minor attempts to purchase tobacco products from retailers, and Advertising and Labeling inspections, when retailers are checked to ensure they are advertising and displaying tobacco products in compliance with regulations. Each state issues their own contract for inspections, and CTP issues a contract for the Retailer Response program to compile the data from each state contractor. In addition to processing CCIs, the Retailer Response program generates Compliance Follow-Ups and reviews Grandfather and Substantial Equivalent requests. Compliance Follow-Ups are automatically generated for retailers that have had previous violations, and they consist of another Undercover Buy and an Advertising and Labeling check. Grandfather requests are voluntarily submitted by companies to prove that their product was commercially marketed before February 15, 2007, in which case the product would be exempt from new premarket requirements. Requests are reviewed by Retailer Response, who sends CTP a recommendation for approval or denial. The final decision is then made by CTP.

CCI reports come to the Retailer Response program from inspectors who work for the 50 state contractors through an iPhone application, and are entered into the Tobacco Inspection Management System (TIMS) database. Undercover Buy narratives from minors come in as paper mail and are also put into TIMS. Similar to how the number of MedWatch reports from consumers increases after media

coverage, Undercover Buy reports spike during public school breaks and the summer months, when more minors are available to work.

Retailer Response has 115 employees who put the information from reports into a template in TIMS, perform QC on data entry and send mail to retailers. Unlike FAERS-DMP, no employees work from home, and the software they use does not track their work, so they must enter their hours themselves in another program. Data processing specialists perform data entry as well as mailing and shipping of letters to retailers. Quality control specialists review data entry. QC is particularly important to CTP because the FDA uses inspection reports in court cases, so the information must be correct. A second unit of data processing specialists ensures that the name and address on correspondence letters is correct, prints shipping labels, and scans the barcodes. Letters for inspection results can be either a No Violation Observed letter, a Civil Money Penalty of up to $30,000, or a No Tobacco Sale Order, given when a retailer has five or more violations within 36 months. These letters are picked up by a courier daily, as are acknowledgement letters from FAERS (Padgett, pers. comm.).

4.4.3. Comparison to FAERS-DMP

Figure 14 shows the similarities and differences between FAERS-DMP, FIRF, and Retailer Response. The largest difference between FAERS and the other two systems was the scale of each program. Since FAERS works on a single task order, it is the smallest of the operations, with 35 employees compared to Retailer Response's 115 employees (Padgett, pers. comm.). FAERS was most similar to the adverse event report task order in FIRF. Both programs use MedWatch forms for reporting, ESG for mandatory electronic submission, and MedDRA coders to classify adverse events. The most notable difference is FIRF's inclusion of editors, which are not required in FAERS because reports are not made public until Quarterly Data Extracts or through Freedom of Information Act requests (McClintock, pers. comm.). Retailer Response processes inspection reports rather than event reports; however, all three programs use the same general steps for data entry. First, paper reports are scanned and entered into tracking software, and all reports are triaged by task order and/or form type. Data entry staff copy the information from a report, which is then checked by quality control. The last step in each process is the submission of completed reports into one of the FDA databases: FAERS, TIMS, and MAUDE.

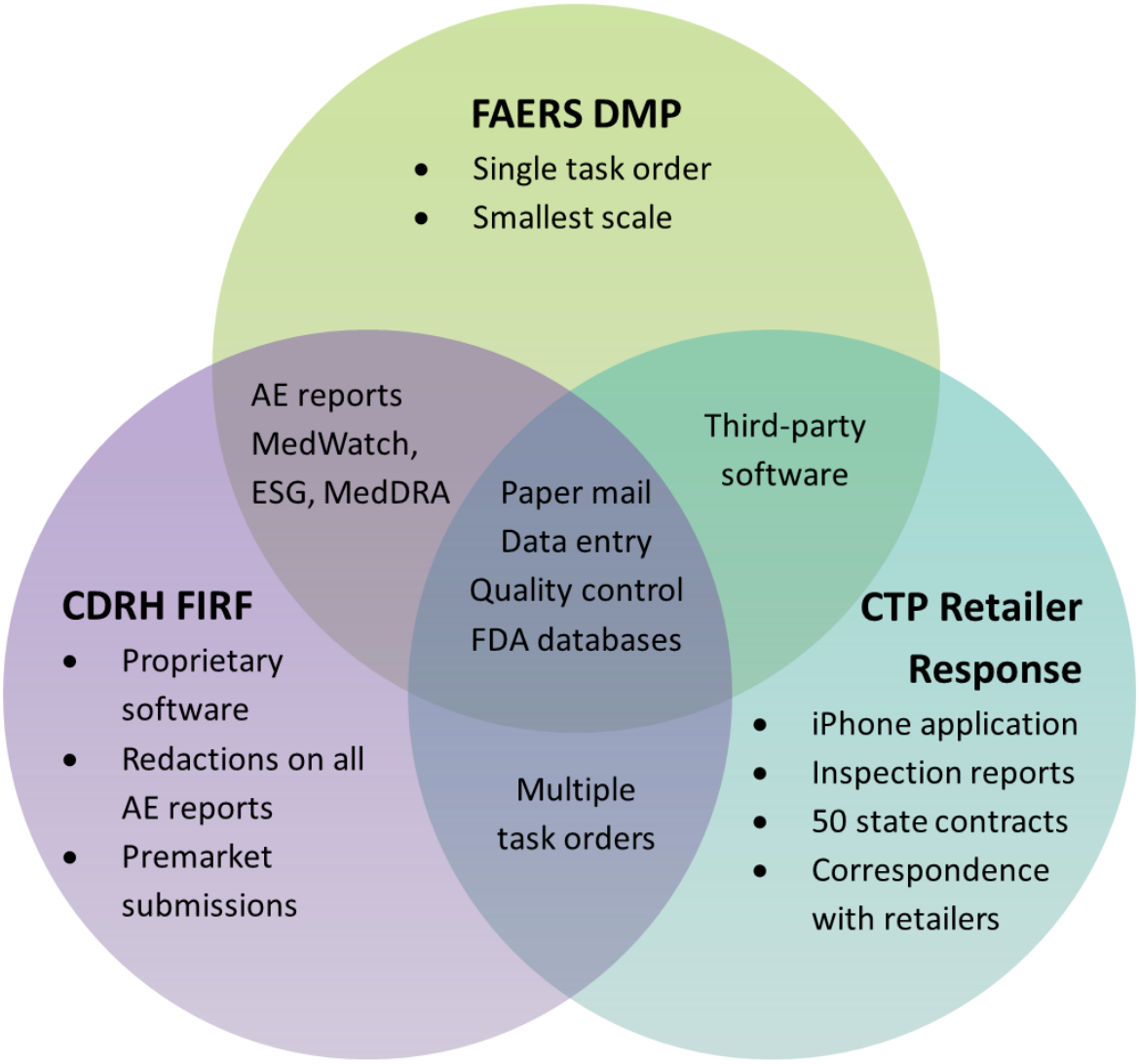


Figure 14: Venn diagram comparing FAERS-DMP, CDRH FIRF, and the CTP Retailer Response program

4.5. SWOT Analysis of FAERS-DMP Process Steps

A SWOT analysis was conducted on the MedWatch program, FAERS-DMP processing steps, and the software involved with FAERS-DMP. The analyses are shown in Tables 2, 3, 4, and 5 below.

Table 2: SWOT analysis of MedWatch forms and paper report handling

	Form 3500	Form 3500B	Paper report courier route
Strengths	Concise layout. Has a basic instructions section and additional instructions next to some fields.	Includes basic instructions about adverse event reporting and submitting a form.	Paper reports are shipped from several FDA facilities to Landover daily.
Weaknesses	Reporter info section puts last name before first name, leading to errors.	Patient info section puts last name before first name, leading to errors. Does not include an explanation of compounded products.	One extra day is needed to complete mailed reports, not including the days needed for the mail to reach the FDA from consumers.
Opportunities	Could potentially be restructured to make data entry more efficient.	Could potentially be restructured to make data entry more efficient.	When new contract is awarded, could look for a location closer to the MedWatch mailroom.
Threats	Registration only swaps first and last names if obvious, the rest will go uncorrected.	Registration only swaps first and last names if obvious, the rest will go uncorrected.	Mail may be delayed due to inclement weather.

Table 3: SWOT analysis of FLARe processes

	Registration	CTU	Disposition
Strengths	Survey indicated this step typically takes less than 2 minutes. Information from this step can be QC'ed by CTU and DDE.	Reports sent to CTU are usually triaged the same day.	Full reports go into FAERS in batches on a set schedule, so DDE knows when to expect them.
Weaknesses	Poor OCR and difficult PDF splitting in FLARe slows the process.	Survey indicated that paper reports take significantly longer to triage.	Sending a report from FLARe to FAERS takes 84 minutes. Retrieving reports accidentally disposed before they were ready is difficult and requires a manager.
Opportunities	A FLARe 2 system is in development.		
Threats		If reports are sent to the wrong centers, safety reviewers may not have all available data to analyze. The reports may also need to be triaged a second time at the other center, adding time.	Reports which fail disposition the first time must be corrected and sent again, so they may end up in a later batch.

Table 4: SWOT analysis of FAERS processes

	DDE	Coding	Validation
Strengths	According to survey results, the DDE staff is very experienced in data entry. Some DDE workers are also trained in Coding. Data entry from this step is QC'ed in Coding.		Performed by medical professionals. In addition to coding voluntary reports, Validation also does QA for a random sample of mandatory reports to ensure compliance.
Weaknesses	Difficulty reading handwritten reports or scans/faxes with poor resolution. If there is a concern, a report may be sent around to several employees to look at before it is completed.	Must email an FDA employee to add new entries to the manufacturer or product dictionaries, cannot make a request within the FAERS software.	
Opportunities	The appropriate fields exists in FLARe for DDE to move from FAERS to FLARe, so DDE will not have to wait for disposition.	In the next version of FAERS, a feature for dictionary requests could be added so Coding employees do not have to leave the application.	The old AERS software could automatically code, and the FDA is potentially interested in looking for another system to do it again.
Threats		This is the last QC step before submission to FAERS, so errors here will go into the database.	Only a very small percentage of mandatory reports are reviewed for correctness.

Table 5: SWOT analysis of FAERS-DMP software

	ESG and SRP	MedWatch Online	OCR	FLARe	FAERS
Strengths	Allows companies to submit directly to FAERS without any processing.	Allows consumers and medical professionals to submit online. Sent in XML format (if no devices are included), which has very little need for data entry.	When correct, reduces amount of data entry.	Internet-based, allowing users to work remotely. Eliminates paper report handling after initial scanning. Faxes upload as PDFs instead of printing out.	Internet-based, allowing users to work remotely.
Weaknesses	There is no automatic notification to the contractors if the ESG and/or SRP stop working.	Requires corrections when consumers misplace information or incorrectly classify a product. XMLs still require corrections to 11 fields.	Often incorrect, requiring correction or deletion of data entered.	Many aspects of the interface are not user-friendly. Employees are not notified if cases are assigned to them for review, and instead have to run a search.	The Oracle system is no longer being supported by the developers. The text fields do not match up with the MedWatch form layout, requiring switching pages often.
Opportunities		If perfected, online reports would only need triage, QC, and MedDRA coding.	If more accurate, it could reduce the amount of time needed in Registration and DDE.	A new version is in development.	A new version will begin development after a new contract is awarded.
Threats	If the programs stop working and this is not identified quickly, reports will not be collected.	FAQs can be vague, resulting in inaccurate entries by consumers.	Can make very subtle letter replacements, such as 'I' to '1,' that are difficult to identify and can be easily overlooked.		If a user is kicked out of the system while in a report, the user can be locked out of the report.

4.6. Analysis of Lean Wastes

Wastes within the FAERS-DMP process were identified through system analyses. The wastes we discovered are shown in Figure 15 below. We identified numerous defects resulting in increased processing time within the system, including poor quality handwritten reports, poor quality fax reports, and erroneous OCR software results. The data entry staff must spend more time per report when they have difficulty deciphering handwriting or must correct text entered by OCR. Another example of wasted time occurs when the data entry staff have to wait multiple seconds for the FLARe and FAERS software to respond. When these seconds are multiplied by the number of reports per year, hours of working time are wasted. Data entry must also wait when there is a server or website failure since they are not able to access reports within the online databases. A transportation waste occurs during the mail courier route for paper reports. A paper report travels over 50 miles during the courier route. Motion wastes identified include the disposition process from FLARe to FAERS, excess scrolling within the software, and excess clicking and mouse movements within the software. For example, in FLARe, the Registration staff has to enter data at the bottom of the webpage and then scroll all of the way back to the top to save the report. Additionally, in FAERS, it is not always possible to switch between fields using the tab key so data entry staff has to click between fields. Extra-processing wastes were identified as dictionary errors and human errors. Both these errors cause a report to return to DDE or Coding to be processed again and corrected. No examples of Over-production, Non-utilized skills, or Inventory wastes were identified within the system.

Defects	•Poor quality handwritten reports •Poor quality fax reports •Erroneous OCR software
Over-production	•N/A
Waiting	•Server/website failure •Slow software
Non-utilized skills	•N/A
Transportation	•Mail courier route
Inventory	•N/A
Motion	•Disposition from FLARe to FAERS •Excess scrolling within software •Excess clicking and mouse movements within software
Extra-processing	•Dictionary error •Human error

Figure 15: Analysis of Lean wastes

5. Recommendations

In this chapter, we use the results from Chapter 4 to create recommendations for our sponsor to improve report processing efficiency and assessment. First, we address recommendations related to combining the FLARe and FAERS systems. Currently, the FDA is intending to combine the two systems, so we provided a map of the possible process in Section 5.1. However, the combination of the systems could take a few years, so in Sections 5.2 and 5.3 we provide recommendations that could be implemented to the current FLARe and FAERS systems to increase efficiency. Recommendations from Sections 5.2 and 5.3 could also be considered for the future combined system, as many employee suggestions were taken into account. We also looked into potential changes to the MedWatch forms themselves and consumer education to enable consumers to fill the forms out more accurately. Finally, we make recommendations for potential metrics that the FDA can use to track how our potential changes might affect their systems.

5.1. Recommendation for a Combined Data Entry Software

We recommend combining the FLARe and FAERS software into one system.

Currently the data entry process is done in both the FLARe and FAERS software. Registration enters approximately 10% of a case's information in FLARe before a report is triaged. If the report belongs in the FAERS database, DDE completes the remaining 90% in the FAERS software. This requires sending a case's XML file and PDF image file from FLARe to FAERS after triage, as well as sending acknowledgements between the two. The total disposition process takes 84 minutes, and the PDF images of the original reports are attached to their XML versions in batches five times a day: 9:00 am, 12:00 pm, 3:00 pm, 6:00 pm, and 9:00 pm. Performing all data entry tasks in one system would eliminate the need for this step and would remove the need for a CTU number. Since all tasks would be in one system, only the Case ID Number would be needed to track reports, and an acknowledgement step would be eliminated between the FLARe and FAERS databases. In addition, cases that are accidentally sent to DDE would no longer require approval to be reopened in FLARe. Figure 16 shows a new process map incorporating this recommendation. The number of swim lanes has been reduced from four to three as there are now only swim lanes for submission, the combined software, and disposition. The number of acknowledgments would decrease from two to one.

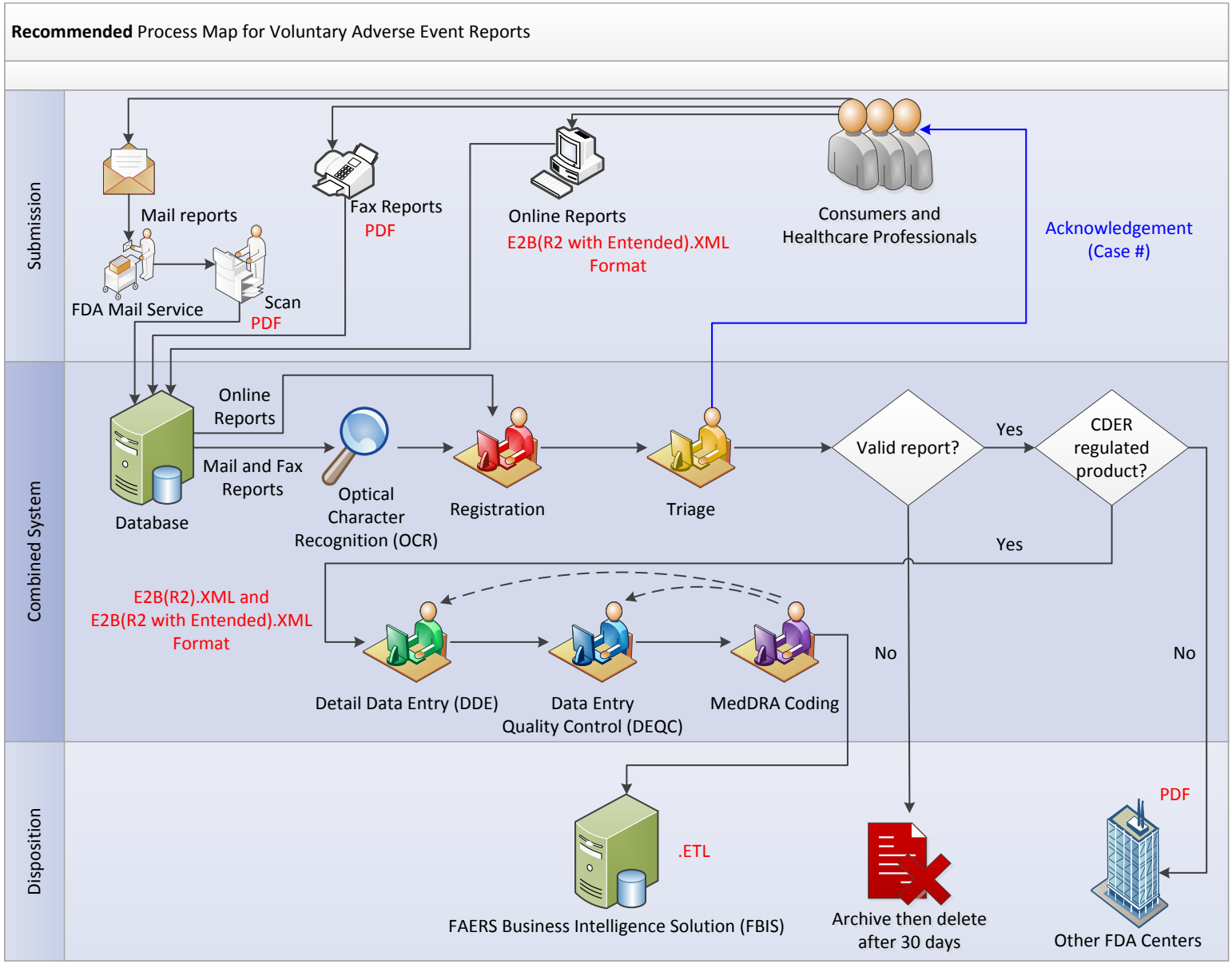


Figure 16: Recommended Process Map for Voluntary Adverse Event Reports

The development of a combined system also opens up an opportunity for a new or updated user interface. The FLARe software could be updated to include the FAERS tasks, or an entirely new software system could be developed. In either case, changes to the user interface could be incorporated at the same time the tasks are combined. Recommendations for making the software more user-friendly and conducive to efficient data entry are described in Sections 5.2.2 and 5.3.

5.2. Recommendations for the FLARe System

5.2.1. Recommendation for moving DDE into the FLARe system

We recommend that DDE be moved from FAERS to FLARe.

While the combined system that integrates all steps of FLARe and FAERS together was a more long term recommendation for how to improve case processing efficiency, the FDA wanted shorter term suggestions for how to improve processing time. One major change that could be implemented in the interim before the combined system is that DDE could be moved from FAERS to FLARe. One motivating factor behind this change is that, currently, the FAERS software is very inefficient for data entry. The data fields in FAERS do not line up with MedWatch forms at all, requiring data entry staff to switch between tabs and click into different fields instead of being able to easily tab through data entry. The comparison between the FAERS interface and a 3500 form was shown earlier in Figure 13.

FLARe's data fields are set up sequentially so the fields line up with the MedWatch reports, as seen in Figure 17. Data entry staff would spend much less time switching between fields and tabs, and they could get reports done minutes or seconds faster.

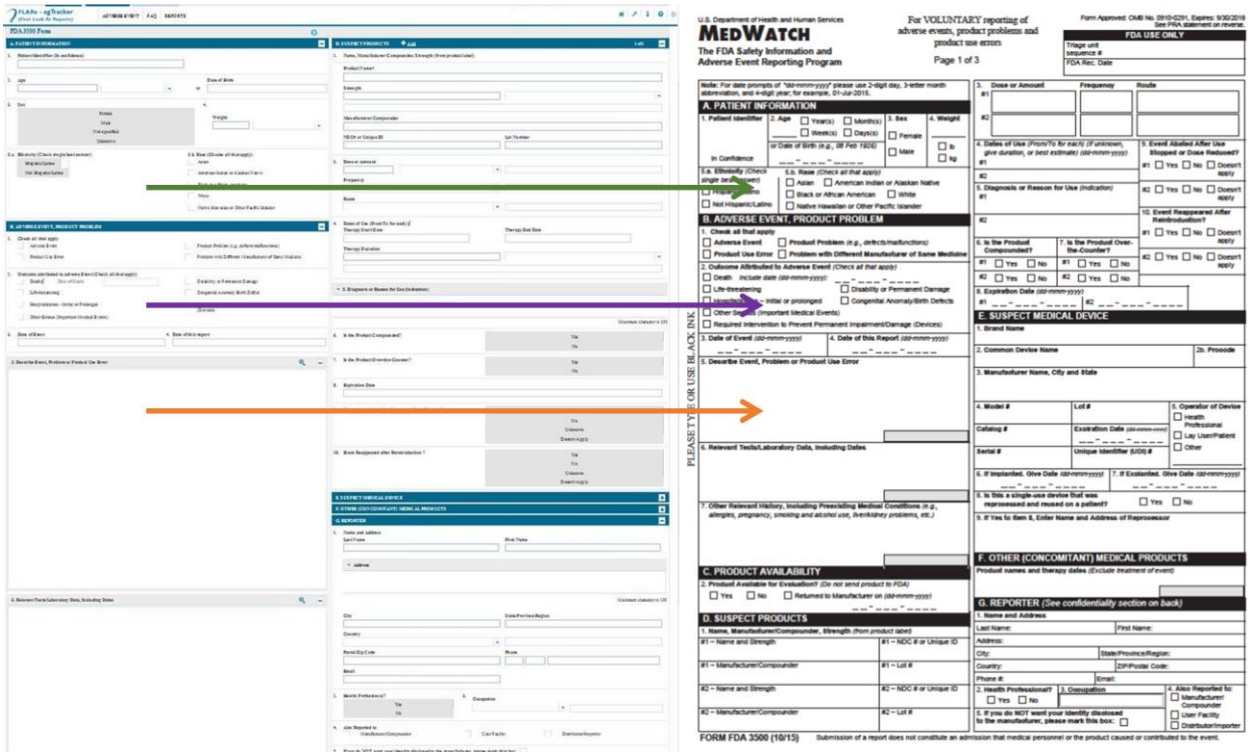


Figure 17: FLARe interface vs. MedWatch field placement

5.2.2. Recommendation for FLARe Software

We recommend that the FLARe OCR software be replaced.

Every Registration and CTU staff member that responded to the open response questions of our survey had issues with the OCR software and either wanted OCR to be removed or disabled entirely for a single report. Registration staff also reported that OCR required more time per report to correct mistakes and incorrect data fields. In order to increase the efficiency of staff and lower the amount of time spent per report, the FDA might consider replacing the OCR software or allowing staff to choose whether or not OCR is used on an individual report or individual fields. It also might be beneficial to include a feature that allows employees to clear individual fields in the form. Sometimes, only a few fields have erroneous data and clearing the entire form would delete both the good and bad data. If staff could delete fields of their choice, this could increase efficiency so they do not have to delete incorrect data and reenter correct data that was already present.

5.2.3. Recommendations for FLARe User Interface

We recommend that the main screen of the software have columns for file size and patient ID number.

A feature requested by Registration staff was the addition of columns for file sizes and patient ID number in the main screen of the software. This would allow staff to identify duplicate reports more easily, since a large file size would indicate that there are multiple reports in the same PDF that need to be split into separate cases.

We recommend that employees be able to customize the order of columns on the main screen of the program.

Another change that could be implemented is the ability for customization of the columns on the main page. Currently, FLARe has the ability to move around columns but the customization reverts back to the original set up after opening and closing one report. The ability for permanent customization would allow staff to see the most important columns for them first, decreasing the amount of time required for them to find the columns that have the information they need and increasing the amount of time employees can spend on registration and triaging.

We recommend that users be allowed to customize their search filter terms.

In a similar vein, users should also be allowed to customize their search filter terms so that the default search terms can be what a particular staff member wants them to be. For example, a Registration staff member will usually not need to look up reports that need to be triaged. Having an option to only display report that need to be registered decrease the amount of time they have to spend searching for reports.

We recommend that the report screen have a 'back to the top' button at the bottom of the report.

A 'back to the top' button should also be added to FLARe report screens. Currently, the Registration and CTU staff must scroll from the bottom of the report back to the top in order to save changes and move to the next report. A 'back to the top' button would prevent the staff from having to scroll back up and save time. Even if it is just a few seconds saved, that time difference multiplied by the number of reports received each year would add up to a significant time savings. Alternatively, a second save button could be added to the bottom of the screen. Ideally, these buttons would move as the user scrolls through the report, remaining at the bottom of the screen so they are able to jump back to the top or save at any time.

We recommend that the system alert users before they are allowed to dispose a report.

In the current FLARe system, any user who is accessing a report that is in the Triage stage can dispose a report with the click of a button. This can be inconvenient, as once a report is disposed to another agency or FAERS, it cannot be retrieved unless it is manually sent back by the receiver. This problem can be solved by having the system create an alert when the user clicks the button to dispose a report. That way, users who did not intend to dispose the report can ensure that it stays in the FLARe system.

We recommend that the system alert users about reports assigned to them.

Another change that could be implemented is to create notifications when a report is assigned to a specific staff member. For example, if Registration or CTU staff members are unsure about a form, they assign it to the head of CTU. Currently the head of CTU does not get a notification and needs to run a specific search to find out if any reports have been assigned to him or her. If a staff member received a notification, he or she could immediately work on the assigned report, instead of having the report sit in the system until the employee remembered to search for assigned reports.

We recommend that the amount of time required for a user to be timed out of the system be increased.

Users expressed an interest in having the timeout period of the system increase, as well as having the timer reset to zero when the user makes any keystroke or clicks the mouse. Currently just inputting one keystroke is not enough for the system to recognize that the user is still present.

We recommend that PDFs be able to be split as many times as necessary instead of having a maximum split number.

A current issue for Registration staff is that PDFs occasionally must be split, as multiple adverse event cases have been sent as one file. As of now, the capability for the software to split the PDFs has a maximum number of times one PDF can be split, somewhere between 40 and 50 times. If a report needs to be split 60 times, Registration staff must split the document in two separate batches instead of just one. If the system could have a larger maximum for the number of times a PDF could be split, it would save Registration staff's time and prevent them from having to split a document more than once.

We recommend implementing an easier way to split reports.

The Registration staff mentioned during our interview that it is difficult to split report images. They must open the PDF and type the first and last page numbers of each report in a single line text field, which is a time consuming process. One way to make this easier would be to have a visual representation of each page, allowing the user to drag and drop each page into individual cases. Another option would be to have the user state how many reports are in the file, then fill individual text boxes with the correct page numbers. The user would have the ability to quickly tab through these boxes and could easily see which pages are assigned to each case.

We recommend that the country field for addresses be left blank instead of having USA be the default.

As of now, the FLARe system automatically assigns USA as the default country when a report is registered. This can be problematic for staff because occasionally MedWatch receives international reports, and if an employee is not paying very close attention, they could forget to change the country of origin field to something other than USA. This makes more work for quality control further down the line. If there was no default, this would not be a problem.

We recommend that the location of automatically added date stamps be changed.

In the current FLARe system, automatic date stamps are added to every form so that they can be easily kept track of. However, sometimes, the stamps are placed in locations that cover up some text or information in the report. It would be best if the system added the date stamp in a location where no text would be entered, so Registration and other staff do not have to struggle to discern what is written under the date stamp.

5.3. Recommendations for the FAERS System

We recommend that the software that disposes reports from FLARe to FAERS be updated to make the disposition process faster.

As described in Section 4.2, the disposition of a report from FLARe to FAERS is currently a multistep process with information exchanged between the systems five times, taking about 84 minutes. Updating this process to reduce the disposition time and make PDF attachment an open-door system rather than a batch system would allow reports to enter FAERS as soon as they are finished or go back to FLARe if needed without making staff wait. The factor that adds the most time, over an hour, to the disposition process is that reports can go back and forth from FLARe to the bucket in one minute,

but take 20 minutes to go back and forth from the bucket and FAERS. This is intentionally set by the developers to avoid overloading the server. If this could be changed without updating the servers, we recommend allowing PDF images to attach to the XML files to avoid adding more time delay to the 84 minutes disposition.

The time needed for disposition would also be saved if FLARe and FAERS were combined in a single system so that disposition was unnecessary. This alternative change was discussed in Section 5.1.

We recommend that field and font size in FAERS are kept consistent.

The data entry staff that use FAERS have noted that some fields will not expand upon clicking and they do not allow the staff to view the entire field at a time. This can slow the process of quality control, when employees want to quickly scan through data to ensure there are no mistakes. It can also make data entry more difficult if staff cannot see where they are entering data. Ensuring that all fields can be expanded would get rid of this problem, and help employees do their jobs more efficiently. It would also be beneficial to have font on forms and the software be consistent. Currently, on some forms, the font size is too small and difficult to read, so it would be useful to make the font size and style standardized. These changes could ensure that the work done in FAERS run smoother.

We recommend that coding staff are not barred from editing any fields in the FAERS system.

One of the tasks Coding staff perform is quality control of the data entered into the software fields. When the Coders notice any incorrect data, they fix it. However, currently, the FAERS system bars the Coders from editing certain sections. This is inefficient because it forces Coders to send the report back to DDE to have data entry staff fix the mistake, and then the DDE staff send the report back to the Coders. This wastes time, as Coders could easily fix the mistake in the locked fields if they were able to access the information. If Coding staff were permitted to edit in any field, this would increase efficiency, as reports would move to validation quicker if they do not have to go back to DDE for correction.

We recommend that clicking on a field does not highlight the all of its contents.

FAERS has a feature that highlights the entire field when a user clicks on it. This feature can be frustrating, as an employee could accidentally delete the entire field's worth of data, requiring him or her to retype everything or send it back to DDE to be retyped. If the system did not have this feature, this mistake would be less likely. Additionally, an undo and redo button can be implemented in the software to recover deleted text.

We recommend that drop down menus have more options.

Some employees have requested that more options be added to drop down menus to enable them to enter data more accurately. For example, in order to provide more accurate data entry, additional medical dosage terms should be added to the drop down menu of dosage forms such as intravesical and pills. This would allow the data from the forms to be entered in the most verbatim way possible.

We recommend that locked cases be listed to users and allow users to reenter those cases more easily.

Currently, if a user times out of FAERS or closes a case, the case the user was working on becomes locked. This prevents anyone from editing the case, even the user that was working on it. This is a problem because if employees cannot get back into the report for an amount of time, that report is delayed until it can be unlocked. It would also be useful for locked cases to be listed in the main screen of FAERS if the users want to search for them.

We recommend that the autofill function should only activate when it does not recognize the input.

When inputting data to certain fields, an autofill feature gives suggestions to the user as to what it thinks they are trying to input. While it can be a useful feature, the system forces a user to choose an auto filled response instead of the field accepting what was written. This can cause a few seconds of delay while the data entry staff are forced pick from a list even if they have already finished typing. If this feature only activated when the field did not recognize the input, it would decrease the processing time of each report by a few seconds.

5.4. Recommendations for Consumer Education and MedWatch Forms

We recommend that the FDA provide consumers with a more easily accessible instructions on how to fill out MedWatch forms.

Data entry staff have identified that consumers commonly fill out forms incorrectly due to misinterpreting instructions or not understanding a question. This requires staff to make more corrections, which is very inefficient. One potential solution to this problem would be to have easily accessible instructions online or on paper for consumers to use. Currently there are instructions on the MedWatch website, but it is not easy to find, and is only for Form 3500. Instead of filling out incorrect information, consumers could easily look up questions they have about the form if the instructions were to be made more accessible and a second set of instructions was made for Form 3500B. Additionally,

more information could be placed directly on the MedWatch forms next to each question. There is a smaller chance of errors due to misunderstanding questions if the form walked the consumer through the process of filling it out, leading to more accurate information. Implementing these changes would lower the amount of errors staff are required to fix, allowing them to process forms faster.

The online submission website, MedWatch Online, could also be updated to provide more helpful information for users when filling out the form without needing to leave the website. For example, one section that is corrected often by Triage is the compounded product check box. Consumers often mistakenly select this option when their product was not compounded. This error could be reduced by providing an explanation of what compounded products are in MedWatch Online, similar to the help text for over-the-counter products, shown in Figure 18 below. The additional information window describes an over-the-counter product; however, the window for compounding, shown in Figure 19, suggests only that consumers contact a professional without giving any explanation as to what compounding is or how to tell if your drug is compounded. Users may not be willing to stop filling out the form to call their physician or lookup compounded products elsewhere, leading to errors which increase the time spent by CTU or the user getting frustrated and not filling out the forms at all. Fields may also be improved by including the information on the screen under the question instead of clicking on the additional information button, so users filling out the form quickly will see the information.

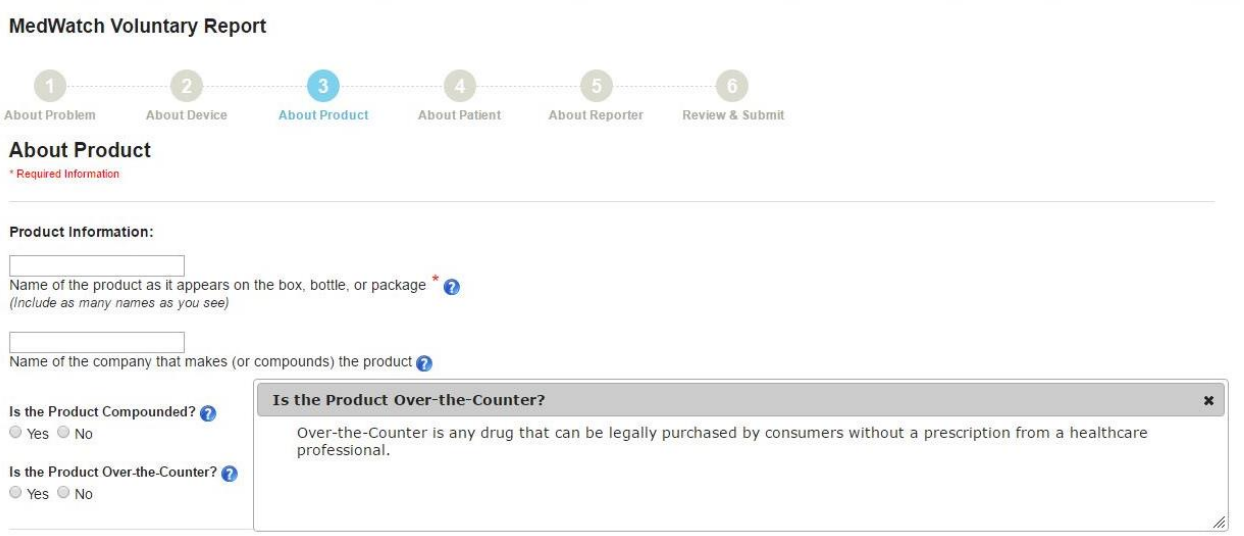


Figure 18: Over-the-Counter Product Description in MedWatch Online

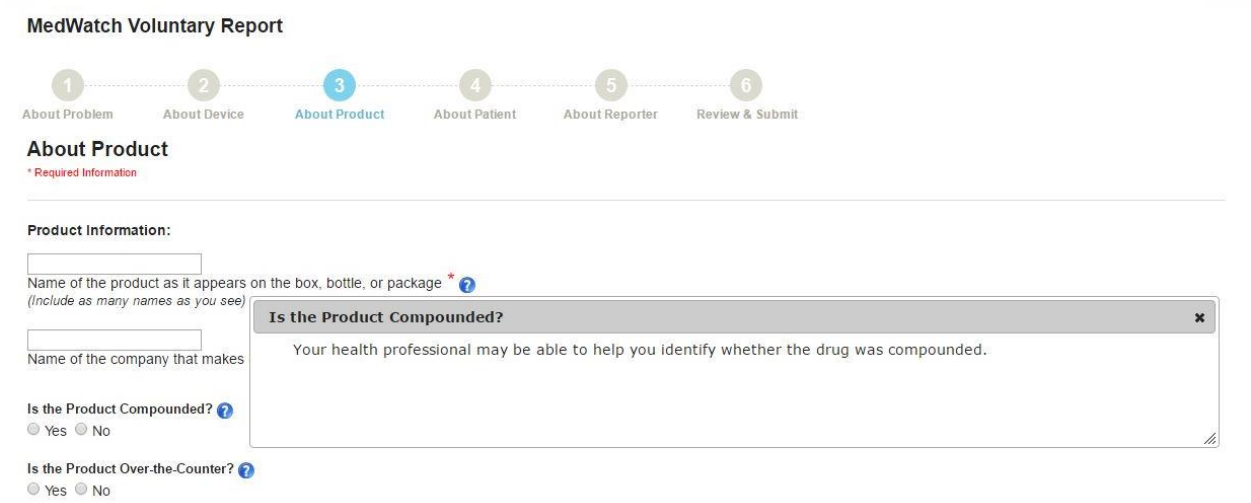


Figure 19: Compounded Product Description in MedWatch Online

An existing FAQ for Form 3500 is easily available online from the MedWatch reporting website that is shown in Figure 20. Currently when the 'Frequently Asked Questions' button is clicked, consumers are brought to a webpage that answers questions about browser compatibility and report submission. Only a small hyperlink within the FAQ links to the instructions with information on how to fill out report fields. An additional button could be added to the MedWatch reporting website that directly links to the form instructions, as shown in Figure 21.

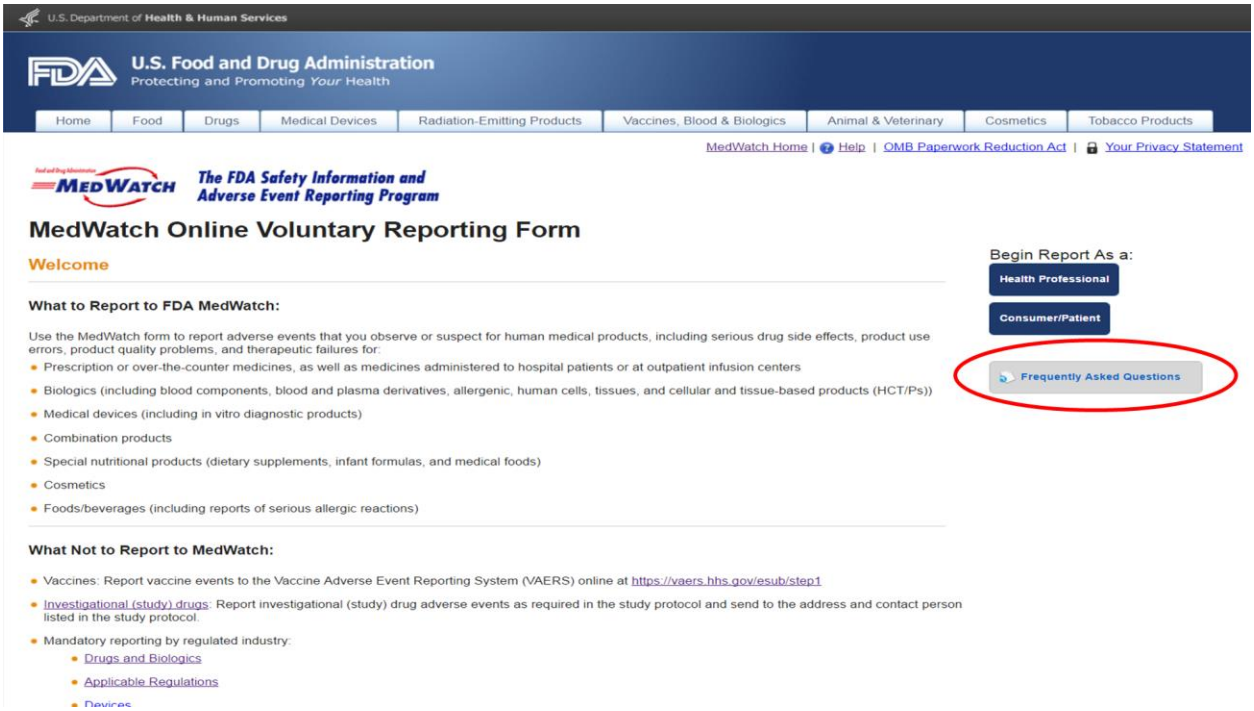


Figure 20: Current MedWatch online form instructions

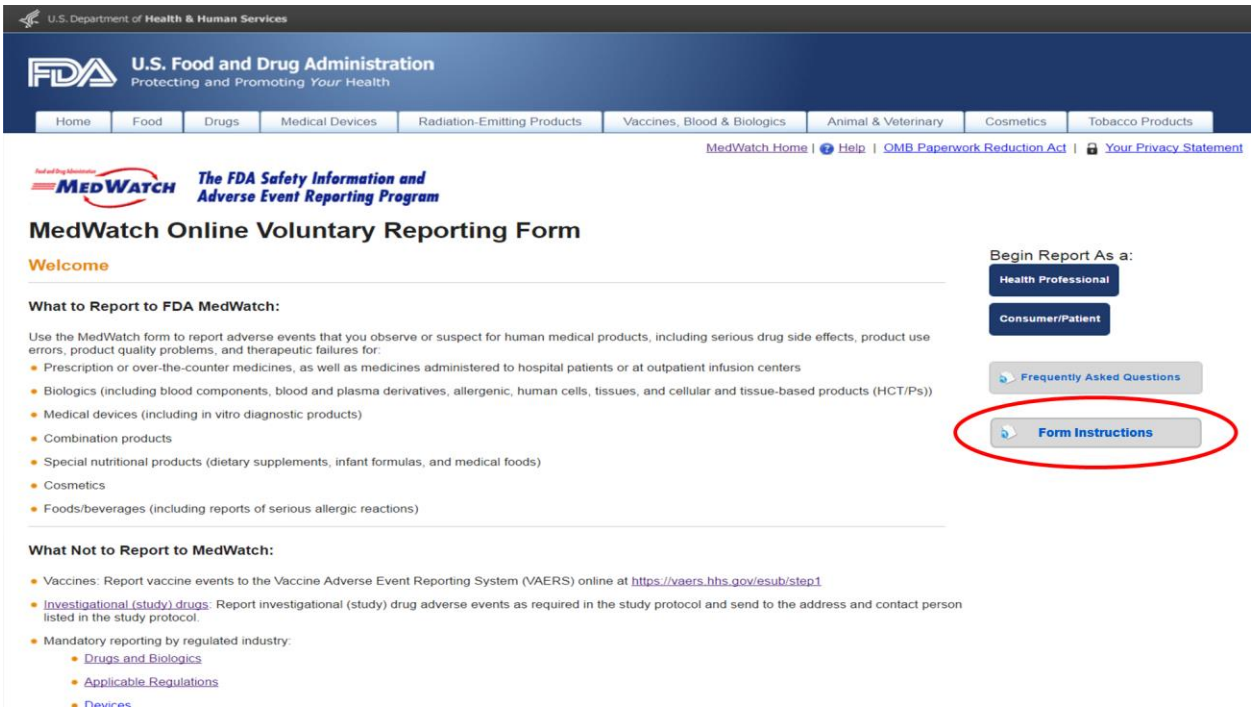


Figure 21: Recommended MedWatch online form instructions

5.5. Using New and Existing Metrics to Measure Performance

We recommend surveying employees routinely to use the collected data to help guide future system improvements.

The survey given to FAERS-DMP staff was a significant part of our project results. The employees' point of view is important to consider since these stakeholders work with FAERS on a daily basis. Their answers provided useful statistics and suggestions that were previously unexplored, such as how long reports take to process from the employee's perspective, how user friendly the system is, and where they can see improvements. The survey provided us with valuable information on how reports are processed and where problems may be occurring from a user standpoint.

We suggest giving surveys similar to ours in the future, particularly while new software is being developed and when significant software changes have been implemented. This may help the contractor and the FDA to ensure staff members are working to their full potential. These surveys could provide more opportunities for staff to suggest changes and provide consistent data for managers and the FDA to track employee satisfaction and software performance. Survey data, such as average report processing time, can also be compared to system data.

We recommend utilizing metrics specifically related to the FDA's software.

The following metrics could provide additional understanding as to how well the system is operating and identify areas for improvements to be made in the future.

Server Uptime:

When the FAERS server is down, reports cannot enter the system to be processed. During December 2016, the FAERS-DMP contractor had six hundred reports come in at once due to a server failure. Reports were held in a queue until the system could be restarted a few hours later. Currently, the only way to make sure the system is active is by logging in to FAERS and running a report on the number of cases that have been submitted in the past few hours. If this number is unusually low, it could indicate that the system has experienced a software glitch or crash. Our suggestion is to have the project managers receive alerts when the system is encountering an issue without allowing them access to the server's functions. This would quickly notify them if there was an issue so data entry staff could be alerted.

Transfer Rates and Processing Power:

The 20 minute time intervals that FAERS requires to submit XMLs and PDFs to and from the bucket between FLARe and FAERS may be due to either a buffer or a lack of processing power. A buffer would indicate that the server needs space between each report to process them, meaning a shorter time could potentially be used without the risk of overloading the server. On the other hand, if processing power is an issue, then the server could be strained under its current workload and crashing, leading to long queues and potentially lost reports. Obtaining this information from the company that maintains the server would aid in determining the feasibility of a change to a single system.

OCR Correctness:

The FDA could monitor the accuracy of the FLARe OCR software. This would allow for a way to evaluate each update from within FLARe without needing to rely solely on user feedback. One way OCR correctness could be measured is by tracking the number of times the 'Clear Field' button is used to delete the OCR text. Every time the button is pressed by a staff member, it most likely means that the OCR data in that field is unusable. FLARe could monitor the use of this button to show whether the OCR results are improving. Alternatively, the FDA might consider working with ArisGlobal to implement new

OCR software that is better tailored for analyzing MedWatch forms if the current one is found to be too inaccurate to use.

Consumer Errors:

Tracking common mistakes consumers make over time could determine whether MedWatch FAQ improvement were effective. This could be accomplished by having FLARe monitor changes made by staff to MedWatch submissions. The FDA could use this data to evaluate future FAQ and form improvements, making forms easier for consumers to complete and reducing the amount of corrections data entry staff need to make.

Corporate Errors:

Some corporations, such as pharmacies, hospitals, and insurance agencies, submit large amounts of voluntary reports. Often these reports have consistent errors such as incorrect reporter information, incorrect document size, and reports that do not contain an adverse event. While these reports are always accepted, the lack of MedWatch standardization can cause significant processing delays. Corporations may simply not know they are causing problems, and while the FDA cannot force them to send proper voluntary reports, the FDA might benefit from keeping track of and contacting these companies if the issue becomes persistent.

We recommend using existing metrics to benchmark future performance.

FLARe and FAERS provide metrics in regards to processing times, employee performance, and how many reports are being received. We suggest focusing on the following metrics to see the benefits of any changes implemented to improve the FAERS-DMP system:

- Average processing time per report for each department
- Total processing time of one report
- Cost per report type (mail, fax, or online) per department
- Total operation costs
- Number of reports received daily
- Number of reports completed daily

6. Conclusions

By implementing our adapted business process improvement plan, we were able to create several recommendations for increasing the efficiency of adverse event report processing at FAERS-DMP for the FDA. Reducing the time needed to process a report may allow the program to more easily cope with the expected increase of reports received in the future. A more efficient system utilizing some of our recommended changes would also reduce the technology resources and waiting time involved with file transfer between software. Improved instructions for MedWatch Form 3500B may reduce the number of errors made by consumers and the time data entry staff must spend to correct them.

The recommendations developed for FAERS-DMP were intended to meet this project's goal of increasing the efficiency of adverse event report processing while considering the needs of the system's stakeholders, primarily the FDA and the contractor's employees. The FDA expressed a desire to reduce the time, cost, and resources that report processing consumes, while the contractor's employees wanted the software they work with to be easier to use and for the program to become more efficient without cutting jobs. Our recommendations for improvements to the FLARe and FAERS user interfaces and MedWatch form instructions are intended to make data entry both faster and easier. The recommendation for a combined system encompassing FLARe and FAERS jobs would eliminate the disposition step and simplify the process without removing any positions. Due to the complications and requirements of government contracting that affect FAERS stakeholders, our recommendations include both short term and long term suggestions.

In addition to implementing our software and MedWatch related recommendations, OSE may consider continuous improvement, an important aspect of the cyclical Six Sigma method, to develop more recommendations for FAERS-DMP in the future. Existing system metrics can be used to assess changes. Additional surveys of the contractor's employees may be carried out before and after future software updates to ensure that the program is conducive to efficient data entry. Lastly, while our project included general comparisons between the FAERS-DMP, FIRF, and Retailer Response programs, a more detailed study of these programs, as well as analysis of programs from other centers and even other government agencies, would allow for the best practices in case report processing to be identified more systematically.

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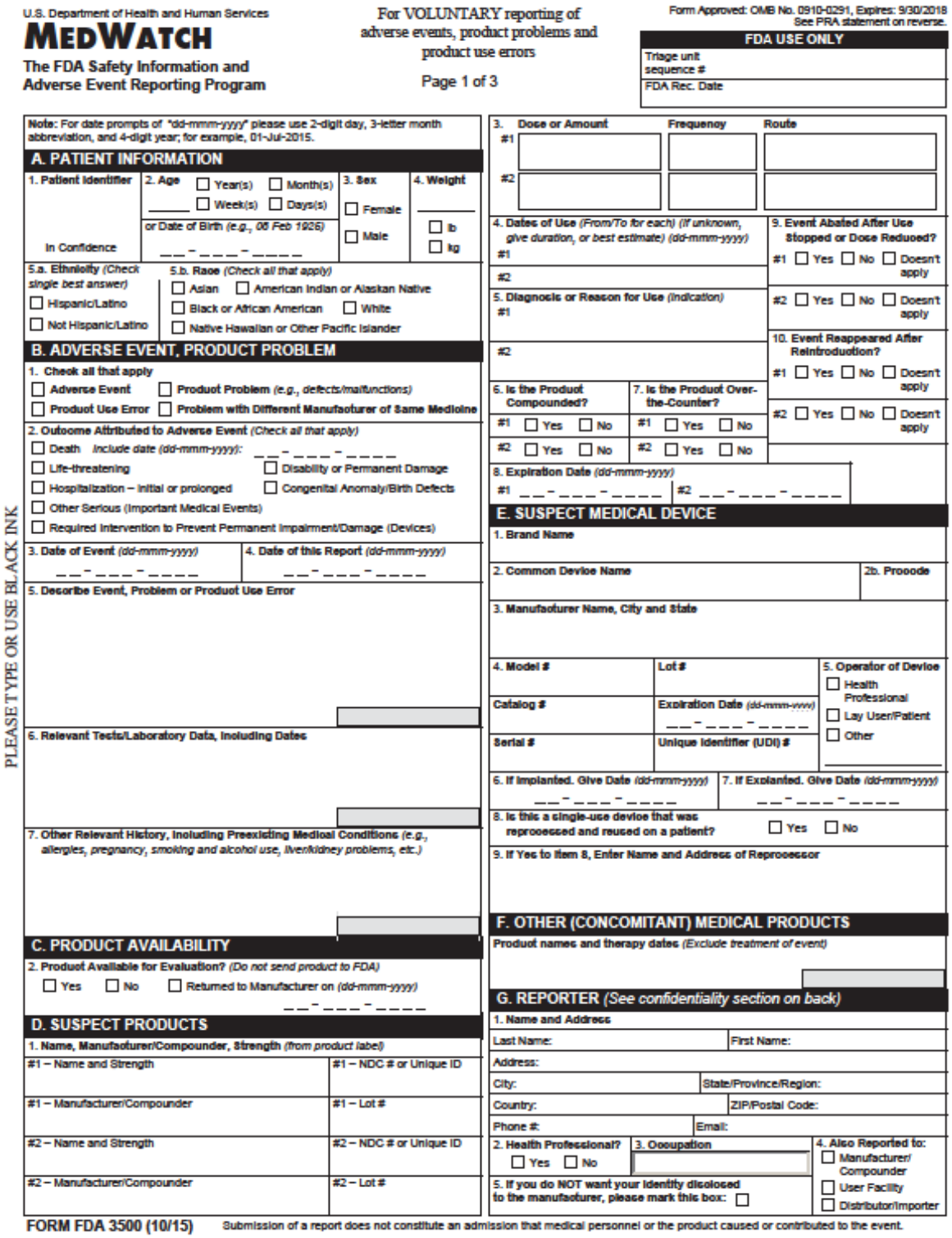
Appendix A: MedWatch Form FDA 3500- Voluntary Reporting



U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page 1 of 3

Form Approved: OMB No. 0910-0291, Expires: 9/30/2018
See PRA statement on reverse.

FDA USE ONLY

Triage unit sequence #

FDA Rec. Date

PLEASE TYPE OR USE BLACK INK

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2015.

A. PATIENT INFORMATION

1. Patient Identifier — In Confidence
2. Age ☐ Year(s) ☐ Month(s) ☐ Week(s) ☐ Days(s) — or Date of Birth (e.g., 06 Feb 1926) __-___-____
3. Sex ☐ Female ☐ Male
4. Weight ☐ lb ☐ kg
5.a. Ethnicity (Check single best answer) ☐ Hispanic/Latino ☐ Not Hispanic/Latino
5.b. Race (Check all that apply) ☐ Asian ☐ American Indian or Alaskan Native ☐ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT, PRODUCT PROBLEM

1. Check all that apply
☐ Adverse Event ☐ Product Problem (e.g., defects/malfunctions)
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcome Attributed to Adverse Event (Check all that apply)
☐ Death Include date (dd-mmm-yyyy): __-___-____
☐ Life-threatening ☐ Disability or Permanent Damage
☐ Hospitalization – initial or prolonged ☐ Congenital Anomaly/Birth Defects
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event (dd-mmm-yyyy) __-___-____
4. Date of this Report (dd-mmm-yyyy) __-___-____

5. Describe Event, Problem or Product Use Error

6. Relevant Tests/Laboratory Data, Including Dates

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)

C. PRODUCT AVAILABILITY

2. Product Available for Evaluation? (Do not send product to FDA)
☐ Yes ☐ No ☐ Returned to Manufacturer on (dd-mmm-yyyy) __-___-____

D. SUSPECT PRODUCTS

1. Name, Manufacturer/Compounder, Strength (from product label)

#1 – Name and Strength	#1 – NDC # or Unique ID
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
#2 – Manufacturer/Compounder	#2 – Lot #

3. Dose or Amount	Frequency	Route
#1		
#2		

4. Dates of Use (From/To for each) (If unknown, give duration, or best estimate) (dd-mmm-yyyy)
#1
#2

5. Diagnosis or Reason for Use (Indication)
#1
#2

6. Is the Product Compounded?	7. Is the Product Over-the-Counter?
#1 ☐ Yes ☐ No	#1 ☐ Yes ☐ No
#2 ☐ Yes ☐ No	#2 ☐ Yes ☐ No

8. Expiration Date (dd-mmm-yyyy)
#1 __-___-____ #2 __-___-____

9. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☐ Doesn't apply
#2 ☐ Yes ☐ No ☐ Doesn't apply

10. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☐ Doesn't apply
#2 ☐ Yes ☐ No ☐ Doesn't apply

E. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name
2b. Procode
3. Manufacturer Name, City and State
4. Model # | Lot # | Catalog # | Expiration Date (dd-mmm-yyyy) __-___-____ | Serial # | Unique Identifier (UDI) #
5. Operator of Device ☐ Health Professional ☐ Lay User/Patient ☐ Other
6. If Implanted, Give Date (dd-mmm-yyyy) __-___-____
7. If Explanted, Give Date (dd-mmm-yyyy) __-___-____
8. Is this a single-use device that was reprocessed and reused on a patient? ☐ Yes ☐ No
9. If Yes to Item 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates (Exclude treatment of event)

G. REPORTER *(See confidentiality section on back)*

1. Name and Address
Last Name: First Name:
Address:
City: State/Province/Region:
Country: ZIP/Postal Code:
Phone #: Email:
2. Health Professional? ☐ Yes ☐ No
3. Occupation
4. Also Reported to: ☐ Manufacturer/Compounder ☐ User Facility ☐ Distributor/Importer
5. If you do NOT want your identity disclosed to the manufacturer, please mark this box: ☐

FORM FDA 3500 (10/15) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: http://www.fda.gov/medwatch/report/consumer/instruct.htm

Report adverse events, product problems or product use errors with:

- Medications *(drugs or biologics)*
- Medical devices *(including in-vitro diagnostics)*
- Combination products *(medication & medical devices)*
- Human cells, tissues, and cellular and tissue-based products
- Special nutritional products *(dietary supplements, medical foods, infant formulas)*
- Cosmetics
- Food *(including beverages and ingredients added to foods)*

Report product problems - quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization - initial or prolonged
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage (devices)
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details

How to report:

- Just fill in the sections that apply to your report
- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer *(or both)*

Other methods of reporting:

- 1-800-FDA-0178 - To FAX report
- 1-800-FDA-1088 - To report by phone
- www.fda.gov/medwatch/report.htm - To report online

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

If your report involves a serious adverse event with a vaccine, call 1-800-822-7967 to report.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

-Fold Here-

-Fold Here-

The information in this box applies only to requirements of the Paperwork Reduction Act of 1995

The burden time for this collection of information has been estimated to average 40 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed, and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

Please DO NOT RETURN this form to the PRA Staff e-mail to the left.

OMB statement:
"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FORM FDA 3500 (10/15) (Back) **Please Use Address Provided Below -- Fold In Thirds, Tape and Mail**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Official Business
Penalty for Private Use $300

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES OR APO/FPO

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 946 ROCKVILLE MD

POSTAGE WILL BE PAID BY FOOD AND DRUG ADMINISTRATION

MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

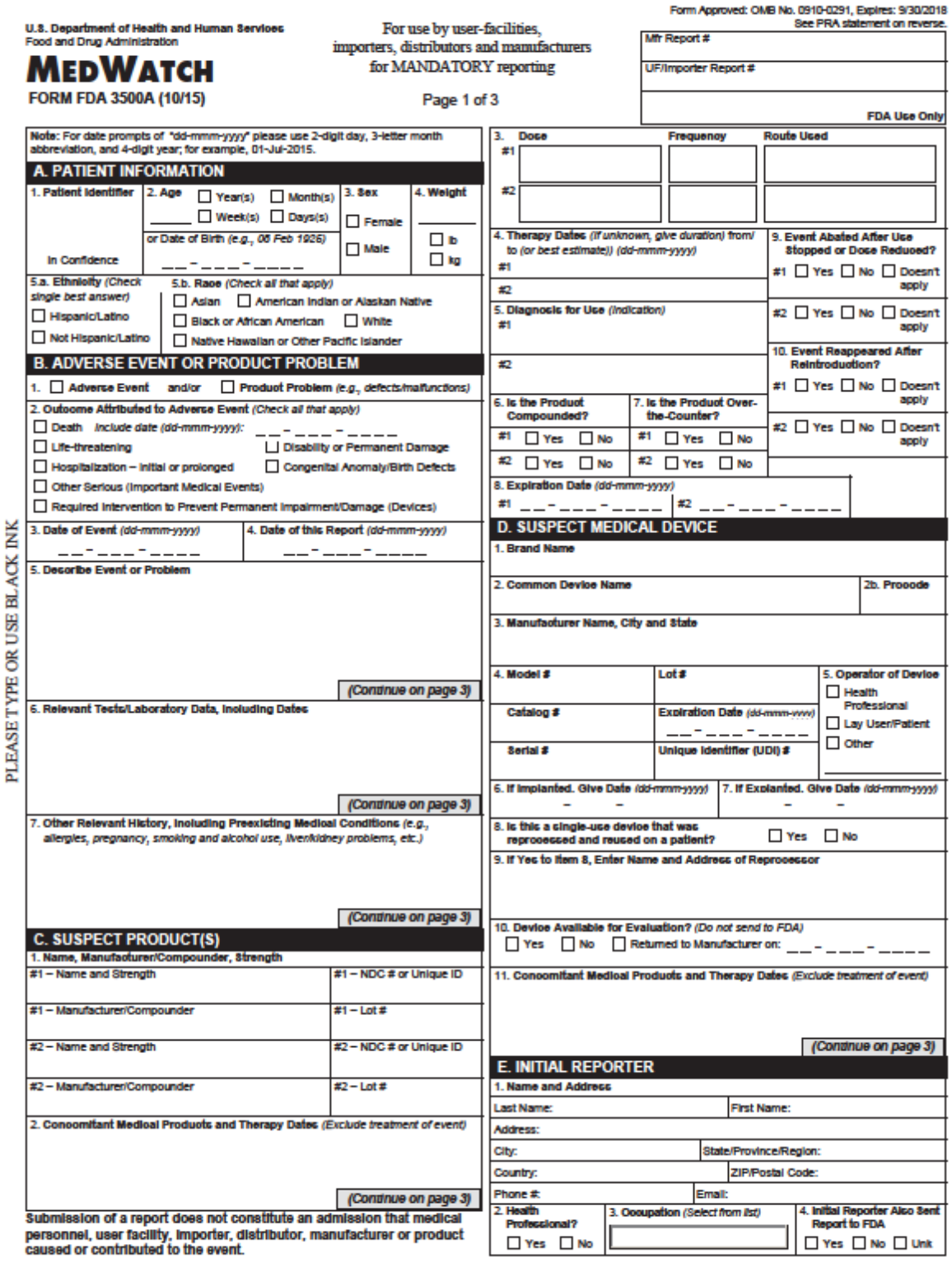
FORM FDA 3500 (10/15) *(continued)*

(CONTINUATION PAGE)

For VOLUNTARY reporting of adverse events and product problems

B.5. **Describe Event or Problem** *(continued)*
B.6. **Relevant Tests/Laboratory Data, Including Dates** *(continued)*
B.7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)* *(continued)*
F. **Concomitant Medical Products and Therapy Dates** *(Exclude treatment of event)* *(continued)*

Appendix B: MedWatch Form FDA 3500A-Mandatory Reporting



U.S. Department of Health and Human Services
Food and Drug Administration

MEDWATCH
FORM FDA 3500A (10/15)

For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting

Page 1 of 3

Form Approved: OMB No. 0910-0291, Expires: 9/30/2018
See PRA statement on reverse.

Mfr Report #
UF/Importer Report #
FDA Use Only

PLEASE TYPE OR USE BLACK INK

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2015.

A. PATIENT INFORMATION

1. Patient Identifier — In Confidence
2. Age ☐ Year(s) ☐ Month(s) ☐ Week(s) ☐ Days(s) — or Date of Birth (e.g., 05 Feb 1925) __ - ___ - ____
3. Sex ☐ Female ☐ Male
4. Weight ☐ lb ☐ kg
5.a. Ethnicity (Check single best answer) ☐ Hispanic/Latino ☐ Not Hispanic/Latino
5.b. Race (Check all that apply) ☐ Asian ☐ American Indian or Alaskan Native ☐ Black or African American ☐ White ☐ Native Hawaiian or Other Pacific Islander

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☐ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)
2. Outcome Attributed to Adverse Event (Check all that apply)
☐ Death Include date (dd-mmm-yyyy): __ - ___ - ____
☐ Life-threatening ☐ Disability or Permanent Damage
☐ Hospitalization – initial or prolonged ☐ Congenital Anomaly/Birth Defects
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)
3. Date of Event (dd-mmm-yyyy) __ - ___ - ____
4. Date of this Report (dd-mmm-yyyy) __ - ___ - ____
5. Describe Event or Problem
(Continue on page 3)
6. Relevant Tests/Laboratory Data, Including Dates
(Continue on page 3)
7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)
(Continue on page 3)

C. SUSPECT PRODUCT(S)

1. Name, Manufacturer/Compounder, Strength

#1 – Name and Strength	#1 – NDC # or Unique ID
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
#2 – Manufacturer/Compounder	#2 – Lot #

2. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
(Continue on page 3)

Submission of a report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event.

3. Dose / Frequency / Route Used
#1
#2
4. Therapy Dates (if unknown, give duration) from/to (or best estimate)) (dd-mmm-yyyy)
#1
#2
5. Diagnosis for Use (Indication)
#1
#2
6. Is the Product Compounded? #1 ☐ Yes ☐ No #2 ☐ Yes ☐ No
7. Is the Product Over-the-Counter? #1 ☐ Yes ☐ No #2 ☐ Yes ☐ No
8. Expiration Date (dd-mmm-yyyy) #1 __ - ___ - ____ #2 __ - ___ - ____
9. Event Abated After Use Stopped or Dose Reduced? #1 ☐ Yes ☐ No ☐ Doesn't apply #2 ☐ Yes ☐ No ☐ Doesn't apply
10. Event Reappeared After Reintroduction? #1 ☐ Yes ☐ No ☐ Doesn't apply #2 ☐ Yes ☐ No ☐ Doesn't apply

D. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name
2b. Procode
3. Manufacturer Name, City and State
4. Model # / Lot # / Catalog # / Expiration Date (dd-mmm-yyyy) / Serial # / Unique Identifier (UDI) #
5. Operator of Device ☐ Health Professional ☐ Lay User/Patient ☐ Other
6. If Implanted, Give Date (dd-mmm-yyyy) – –
7. If Explanted, Give Date (dd-mmm-yyyy) – –
8. Is this a single-use device that was reprocessed and reused on a patient? ☐ Yes ☐ No
9. If Yes to Item 8, Enter Name and Address of Reprocessor
10. Device Available for Evaluation? (Do not send to FDA) ☐ Yes ☐ No ☐ Returned to Manufacturer on: __ - ___ - ____
11. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
(Continue on page 3)

E. INITIAL REPORTER

1. Name and Address
Last Name: First Name:
Address:
City: State/Province/Region:
Country: ZIP/Postal Code:
Phone #: Email:
2. Health Professional? ☐ Yes ☐ No
3. Occupation (Select from list)
4. Initial Reporter Also Sent Report to FDA ☐ Yes ☐ No ☐ Unk

MEDWATCH

FORM FDA 3500A (10/15) *(continued)*

FDA USE ONLY

F. FOR USE BY USER FACILITY/IMPORTER *(Devices Only)*

1. Check One ☐ User Facility ☐ Importer
2. UF/Importer Report Number
3. User Facility or Importer Name/Address
4. Contact Person
5. Phone Number
6. Date User Facility or Importer Became Aware of Event *(dd-mmm-yyyy)* ___-___-____
7. Type of Report ☐ Initial ☐ Follow-up #____
8. Date of This Report *(dd-mmm-yyyy)* ___-___-____
9. Approximate Age of Device
10. Event Problem Codes *(Refer to coding manual)* Patient Code ___-___-___ Device Code ___-___-___
11. Report Sent to FDA? *(If Yes, enter date (dd-mmm-yyyy))* ☐ Yes ___-___-____ ☐ No
12. Location Where Event Occurred ☐ Hospital ☐ Home ☐ Nursing Home ☐ Outpatient Treatment Facility ☐ Outpatient Diagnostic Facility ☐ Ambulatory Surgical Facility ☐ Other:_____ *(Specify)*
13. Report Sent to Manufacturer? *(If Yes, enter date (dd-mmm-yyyy))* ☐ Yes ___-___-____ ☐ No
14. Manufacturer Name/Address

G. ALL MANUFACTURERS

1. Contact Office (and Manufacturing Site for Devices) Name / Address / Email Address
2. Phone Number
3. Report Source *(Check all that apply)* ☐ Foreign ☐ Study ☐ Literature ☐ Consumer ☐ Health Professional ☐ User Facility ☐ Company Representative ☐ Distributor ☐ Other:
Compounding Outsourcing Facility 503B? ☐ Yes
4. Date Received by Manufacturer *(dd-mmm-yyyy)* ___-___-____
5. NDA #_____ ANDA #_____ IND #_____ BLA #_____ PMA/ 510(k) #_____ Combination Product ☐ Yes Pre-1938 ☐ Yes OTC ☐ Yes
6. If IND, Give Protocol #
7. Type of Report *(Check all that apply)* ☐ 5-day ☐ 7-day ☐ 10-day ☐ 15-day ☐ 30-day ☐ Periodic ☐ Initial ☐ Follow-up #____
8. Adverse Event Term(s)
9. Manufacturer Report Number

H. DEVICE MANUFACTURERS ONLY

1. Type of Reportable Event ☐ Death ☐ Serious Injury ☐ Malfunction
2. If Follow-up, What Type? ☐ Correction ☐ Additional Information ☐ Response to FDA Request ☐ Device Evaluation
3. Device Evaluated by Manufacturer? ☐ Not Returned to Manufacturer ☐ Yes ☐ Evaluation Summary Attached ☐ No *(Attach page to explain why not)* or provide code:
4. Device Manufacture Date *(dd-mmm-yyyy)* ___-___-____
5. Labeled for Single Use? ☐ Yes ☐ No
6. Event Problem and Evaluation Codes *(Refer to coding manual)* Patient Code ___-___-___ Device Code ___-___-___ Method ___-___-___-___ Results ___-___-___-___ Conclusions ___-___-___-___
7. If Remedial Action Initiated, Check Type ☐ Recall ☐ Repair ☐ Replace ☐ Relabeling ☐ Notification ☐ Inspection ☐ Patient Monitoring ☐ Modification/ Adjustment ☐ Other:_____
8. Usage of Device ☐ Initial Use of Device ☐ Reuse ☐ Unknown
9. If action reported to FDA under 21 USC 360i(f), list correction/ removal reporting number:
10. ☐ Additional Manufacturer Narrative and / or 11. ☐ Corrected Data

MEDWATCH
FORM FDA 3500A (10/15) *(continued)*

B.5. Describe Event or Problem *(continued)*
B.6. Relevant Tests/Laboratory Data, Including Dates *(continued)*
B.7. Other Relevant History, Including Preexisting Medical Conditions *(e.g., allergies, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)* *(continued)*
Concomitant Medical Products and Therapy Dates *(Exclude treatment of event)* *(For continuation of C.2 and/or D.11; please distinguish)*
Other Remarks

Appendix C: MedWatch Form FDA 3500B- Voluntary Reporting for Consumers

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0291
Expiration Date: 9/30/2018
(See PRA Statement below)

MEDWATCH Consumer Voluntary Reporting (FORM FDA 3500B)

When do I use this form?

- You were hurt or had a bad side effect (including new or worsening symptoms) after taking a drug or using a medical device or product.
- You used a drug, product, or medical device incorrectly which could have or led to unsafe use.
- You noticed a problem with the quality of the drug, product or medical device.
- You had problems with how a drug worked after switching from one maker to another maker.

Don't use this form to report:

- Vaccines – report problems to the Vaccine Adverse Event Reporting System (VAERS).
- Investigational drugs or medical devices (those being studied) – report problems to your doctor or to the contact person listed in the clinical trial.

Will the information I report be kept private?

The FDA recognizes that privacy is an important concern, so you should know:

- We ask only for the name and contact information of the person filling out the form in case we need more information.
- Your name and contact information may be shared with the company that makes the product to help them better understand the problem you are reporting, unless you request otherwise (see Section E).

What types of products should I use this form for?

- Drugs, including prescription or over-the-counter medicines, and biologics, such as human cells and tissues used for transplantation (for example, tendons, ligaments, and bone) and gene therapies
- Medical devices, including any health-related kit, test, tool, or piece of equipment (such as breast implants, pacemakers, diabetes glucose-test kits, hearing aids, breast pumps, and many others)
- Nutrition products including vitamins and minerals, herbal remedies, infant formulas, medical foods, such as those labeled for people with a specific disease or condition
- Cosmetics such as moisturizers, makeup, shampoos and conditioners, face and body washes, deodorants, nail care products, hair dyes and relaxers, and tattoos
- Foods (including beverages and ingredients added to foods)

Are there specific instructions for filling out the form?

- Fill in as much information as possible and send in the report even if you do not have all the information.
- You can fill out this form yourself or have someone fill it out for you. If you need help, you may want to talk with your health professional.
- Feel free to include or attach an image of the product. Please do not send the products to the FDA.

How will I know the FDA has received my form?

- You will receive a reply from the FDA after we receive your report. We will personally contact you only if we need additional information.
- Your report will become part of a database so that it can be reviewed and compared to other reports by an FDA safety evaluator who will determine what steps to take.

How can I contact the FDA if I have questions?

Toll-free line: 1-800-332-1088
www.fda.gov/reportinghelp
To report online: www.fda.gov/medwatch/report.htm

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information is estimated to average 30 minutes per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the address to the right:

OMB Statement: "An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

DO NOT SEND YOUR COMPLETED FORM TO THIS PRA STAFF ADDRESS.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0291
Expiration Date: 9/30/2018
(See PRA Statement on preceding general information page)

MEDWATCH Consumer Voluntary Reporting (FORM FDA 3500B)

Note: For date prompts of "dd-mmm-yyyy" please use 2-digit day, 3-letter month abbreviation, and 4-digit year; for example, 01-Jul-2015.

Section A – About the Problem

What kind of problem was it? *(Check all that apply)*

- ☐ Were hurt or had a bad side effect *(including new or worsening symptoms)*
- ☐ Used a product incorrectly which could have or led to a problem
- ☐ Noticed a problem with the quality of the product
- ☐ Had problems after switching from one product maker to another maker

Did any of the following happen? *(Check all that apply)*

- ☐ Hospitalization – admitted or stayed longer
- ☐ Required help to prevent permanent harm *(for medical devices only)*
- ☐ Disability or health problem
- ☐ Birth defect
- ☐ Life-threatening
- ☐ Death *(include date)(dd-mmm-yyyy)*: __ - ___ - ____
- ☐ Other serious/important medical incident *(Please describe below)*

Date the problem occurred *(dd-mmm-yyyy)*

__ - ___ - ____

Tell us what happened and how it happened. *(Include as many details as possible)*

Continuation Page

List any relevant tests or laboratory data if you know them. *(Include dates)*

Continuation Page

For a problem with a product, including

- prescription or over-the-counter medicine
- biologics, such as human cells and tissues used for transplantation (for example, tendons, ligaments, and bone) and gene therapies
- nutrition products, such as vitamins and minerals, herbal remedies, infant formulas, and medical foods
- cosmetics or make-up products
- foods (including beverages and ingredients added to foods)

Go to Section B

For a problem with a medical device, including

- any health-related test, tool, or piece of equipment
- health-related kits, such as glucose monitoring kits or blood pressure cuffs
- implants, such as breast implants, pacemakers, or catheters
- other consumer health products, such as contact lenses, hearing aids, and breast pumps

Go to Section C (Skip Section B)

For more information, visit http://www.fda.gov/MedWatch

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Section B – About the Products

Name of the product as it appears on the box, bottle, or package *(Include as many names as you see)*

Name of the company that makes (or compounds) the product

Is the Product Compounded? *(Your health professional may be able to help you identify whether the drug was compounded.)*	☐ Yes ☐ No	Is the Product Over-the-Counter?	☐ Yes ☐ No

Expiration date *(dd-mmm-yyyy)*	Lot number	NDC number
__ - ___ - ____		

Strength *(for example, 250 mg per 500 mL or 1 g)*	Quantity *(for example, 2 pills, 2 puffs, or 1 teaspoon, etc.)*	Frequency *(for example, twice daily or at bedtime)*	How was it taken or used *(for example, by mouth, injection, or on the skin)*?

Date the person first started taking or using the product *(dd-mmm-yyyy)*: __ - ___ - ____

Date the person stopped taking or using the product *(dd-mmm-yyyy)*: __ - ___ - ____

Why was the person using the product? *(such as, what condition was it supposed to treat)*

Did the problem stop after the person reduced the dose or stopped taking or using the product? ☐ Yes ☐ No

Did the problem return if the person started taking or using the product again? ☐ Yes ☐ No ☐ Didn't restart

Do you still have the product in case we need to evaluate it? *(Do not send the product to FDA. We will contact you directly if we need it.)* ☐ Yes ☐ No

Go to Section D (Skip Section C)

Section C – About the Medical Device

Name of medical device

Name of the company that makes the medical device

Other identifying information *(The model, catalog, lot, serial, or UDI number, and the expiration date, if you can locate them)*

Was someone operating the medical device when the problem occurred?

☐ Yes
☐ No

If yes, who was using it?

☐ The person who had the problem
☐ A health professional *(such as a doctor, nurse, or aide)*
☐ Someone else *(Please explain who)*

For implanted medical devices ONLY *(such as pacemakers, breast implants, etc.)*

Date the implant was put in *(dd-mmm-yyyy)*	Date the implant was taken out *(If relevant) (dd-mmm-yyyy)*
__ - ___ - ____	__ - ___ - ____

Go to Section D

Section D – About the Person Who Had the Problem

Person's Initials	Sex	Age *(specify unit of time for age)*	Date of Birth *(dd-mmm-yyyy)*	Weight *(Specify lbs or kg)*
	☐ Female ☐ Male	_____ ☐ Year(s) ☐ Month(s) ☐ Week(s) ☐ Day(s)	__ - ___ - ____	_____ ☐ lb ☐ kg

Race/ Ethnicity	Ethnicity *(Choose only one)*	Race *(Choose all that apply)*		
	☐ Hispanic/Latino ☐ Not Hispanic/Latino	☐ American Indian or Alaskan Native ☐ Native Hawaiian or Other Pacific Islander	☐ Asian ☐ White	☐ Black or African American

List known medical conditions. *(Such as diabetes, high blood pressure, cancer, heart disease, or others)*

Please list all allergies *(such as to drugs, foods, pollen or others)*

List any other important information about the person *(such as smoking, pregnancy, alcohol use, etc.)*

List all current prescription medications and medical devices being used.

Continuation Page

List all over-the-counter medications and any vitamins, minerals, supplements, and herbal remedies being used.

Continuation Page

Go to Section E

Section E – About the Person Filling Out This Form

We will contact you only if we need additional information.

Last name	First name
Number/Street	City and State/Province
Country	ZIP or Postal code

Telephone number	Email address	Today's date *(dd-mmm-yyyy)*

Did you report this problem to the company that makes the product (the manufacturer/compounder)? ☐ Yes ☐ No

If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

Send This Report by Mail or Fax

Keep the product in case the FDA wants to contact you for more information. Please do not send products to the FDA.
Mail or fax the form to: MedWatch, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20852; FAX: 800-332-0178 (toll-free).

Thank you for helping us protect the public health.

For more information, visit *http://www.fda.gov/MedWatch*	**Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.**

Continued Entries
CONTINUED ENTRY FOR: Tell us what happened and how it happened. *(Include as many details as possible)* Back to Form
CONTINUED ENTRY FOR: List any relevant tests or laboratory data if you know them. *(Include dates)* Back to Form
CONTINUED ENTRY FOR: List all current prescription medications and medical devices being used. Back to Form
CONTINUED ENTRY FOR: List all over-the-counter medications and any vitamins, minerals, and herbal remedies being used. Back to Form

Appendix D: Comparison of Business Process Improvement Methods

Brewer, 1996	Harrington, 1991	Liker, 2004 (Toyota)	Page, 2010	Robson, 1991
Organization	Organizing for Improvement	Initial Problem Perception	Develop Process Inventory	State the Problem
Project Selection	Understanding the Process	Clarify the Problem	Establish Foundation	Test the Statement
Problem Solving	Streamlining	Locate Area/Point of Cause	Draw Process Map	Search for Root Causes
Data Collection	Measurements and Controls	5-Why? (Investigation of Root Cause)	Estimate Time and Cost	Establish and Eliminate Root Causes
Data Analysis	Continuous Improvement	Counter-measure	Verify Process Map	Implement Corrective Action
Evaluation		Evaluate	Apply Improvement Techniques	Install Appropriate Measurements
Process Improvements		Standardize	Apply Internal Controls, Tools, and Metrics	Change Operating Practices
			Test and Rework	
			Implement the Change	
			Drive Continuous Improvement	

Appendix E: Survey for FAERS-DMP Staff

Hello! Thank you for taking the time to complete this survey about FAERS-DMP. We are students from Worcester Polytechnic Institute (WPI) working on a 7 week student research project to study FAERS-DMP and develop recommendations for improvements. A report about our research will be published by our university and will be made publicly available, pending FDA approval. By completing this survey, you agree that we can use your responses in our report without using your name or other identifiable information.

This survey is voluntary and anonymous. You may skip any questions that you do not want to answer. This survey should take approximately 10 minutes to complete.

What is your main position in the FAERS-DMP system?

- ❍ Registration
- ❍ CTU
- ❍ DDE
- ❍ Coding
- ❍ Validation

Briefly describe your current position and responsibilities in regards to the system.

Do you ever work in other positions? If yes, please explain.

How long have you worked with FAERS-DMP?

- ❍ Less than 6 months
- ❍ 6 months-less than 1 year
- ❍ 1 year
- ❍ 2 years
- ❍ 3 years
- ❍ 4 years
- ❍ 5 years
- ❍ 6 years
- ❍ 7 years
- ❍ 8 years
- ❍ 9 years
- ❍ 10 years
- ❍ 11 years
- ❍ 12 years
- ❍ 13 years
- ❍ 14 years
- ❍ 15 years
- ❍ 16 years
- ❍ 17 years
- ❍ 18 years
- ❍ 19 years
- ❍ 20 years
- ❍ Greater than 20 years

Rate the following statements:

	Strongly agree	Somewhat agree	Neither agree nor disagree	Somewhat disagree	Strongly disagree	Not applicable
The FLARe software suits the needs of my position	❍	❍	❍	❍	❍	❍
FLARe is efficient for processing data	❍	❍	❍	❍	❍	❍
The FAERS software suits the needs of my position	❍	❍	❍	❍	❍	❍
FAERS is efficient for processing data	❍	❍	❍	❍	❍	❍
There are significant corrections that I need to make to adverse event reports that come from MedWatch forms	❍	❍	❍	❍	❍	❍

On average, how long do you think it takes you to process one of each of the following forms?

	Less than 2 minutes	2-4 minutes	4-6 minutes	6-8 minutes	8-10 minutes	10-12 minutes	12-14 minutes	14-16 minutes
Paper	❍	❍	❍	❍	❍	❍	❍	❍
Fax	❍	❍	❍	❍	❍	❍	❍	❍
Online	❍	❍	❍	❍	❍	❍	❍	❍
	16-18 minutes	18-20 minutes	20-22 minutes	22-24 minutes	24-26 minutes	26-28 minutes	28-30 minutes	Greater than 30 minutes
Paper	❍	❍	❍	❍	❍	❍	❍	❍
Fax	❍	❍	❍	❍	❍	❍	❍	❍
Online	❍	❍	❍	❍	❍	❍	❍	❍

What factors slow the process of processing a form? How would you resolve them?

What change(s) would you like to see in the software to make your job easier?

Could any other changes be made to make your job easier?

Could changes be made to the MedWatch forms themselves to make data processing easier?

Comments?

Appendix F: Additional Survey Graphs

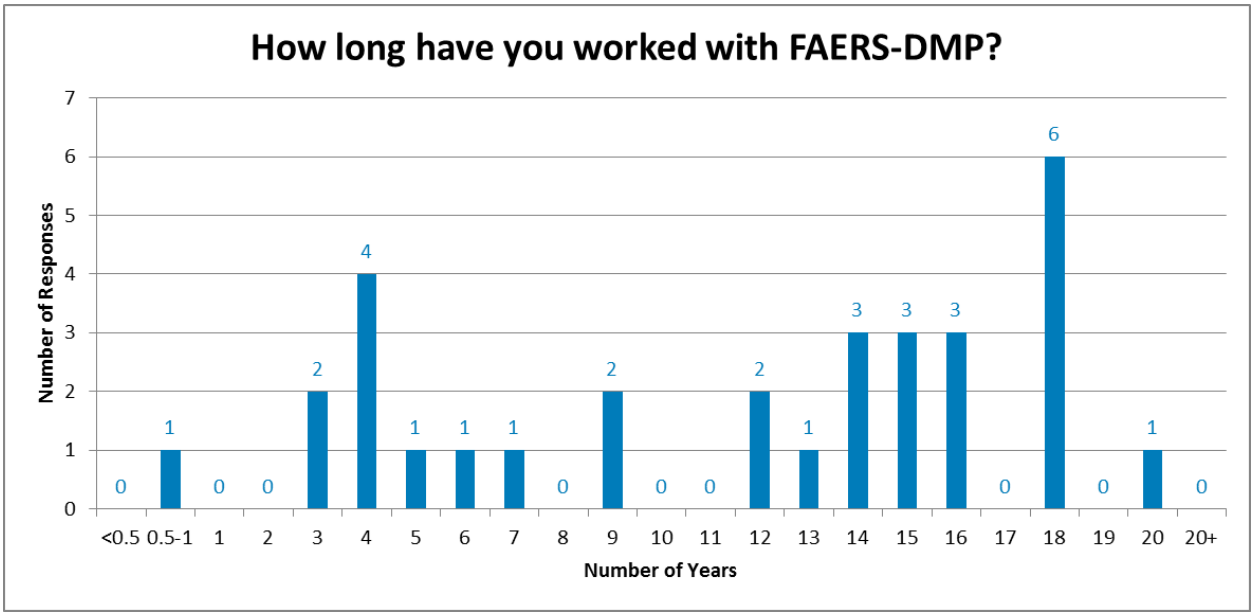


Figure 22: Number of years employees worked for the FAERS-DMP System

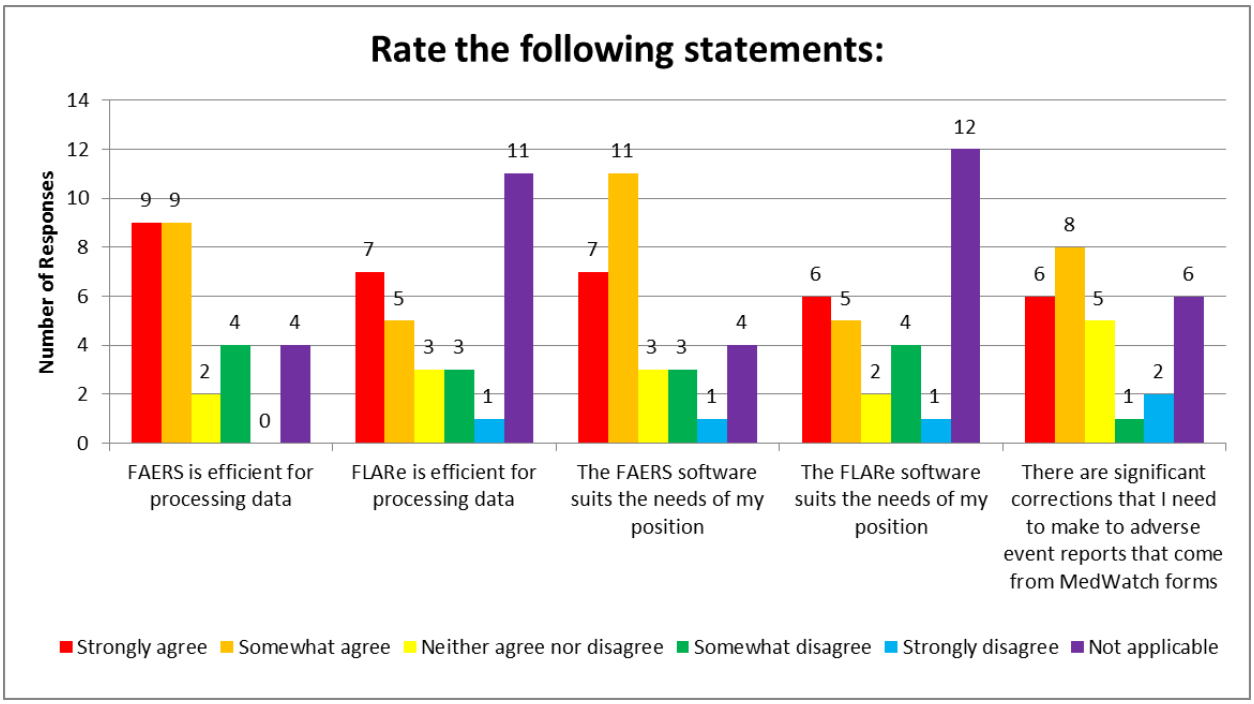


Figure 23: Employee rankings of the suitability and efficiency of FLARe and FAERS

On average, how long do you think it takes you to process one of each of the following forms?

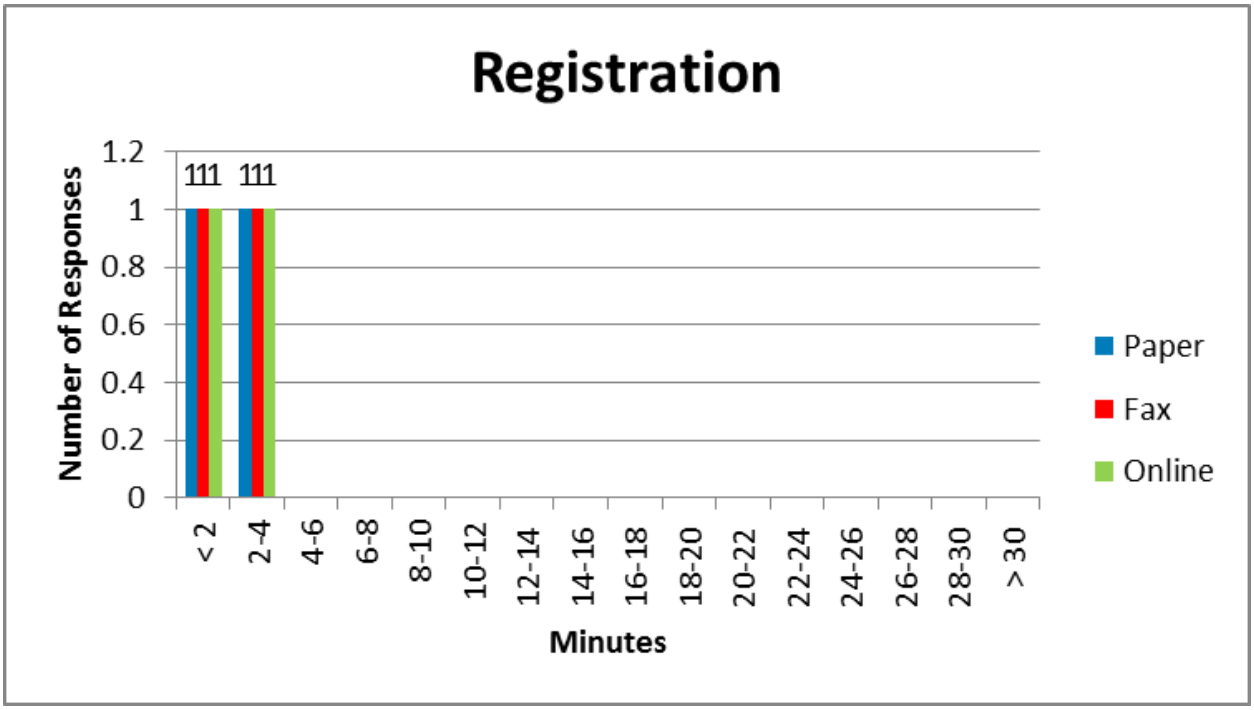


Figure 24: Processing time of adverse event reports for Registration staff

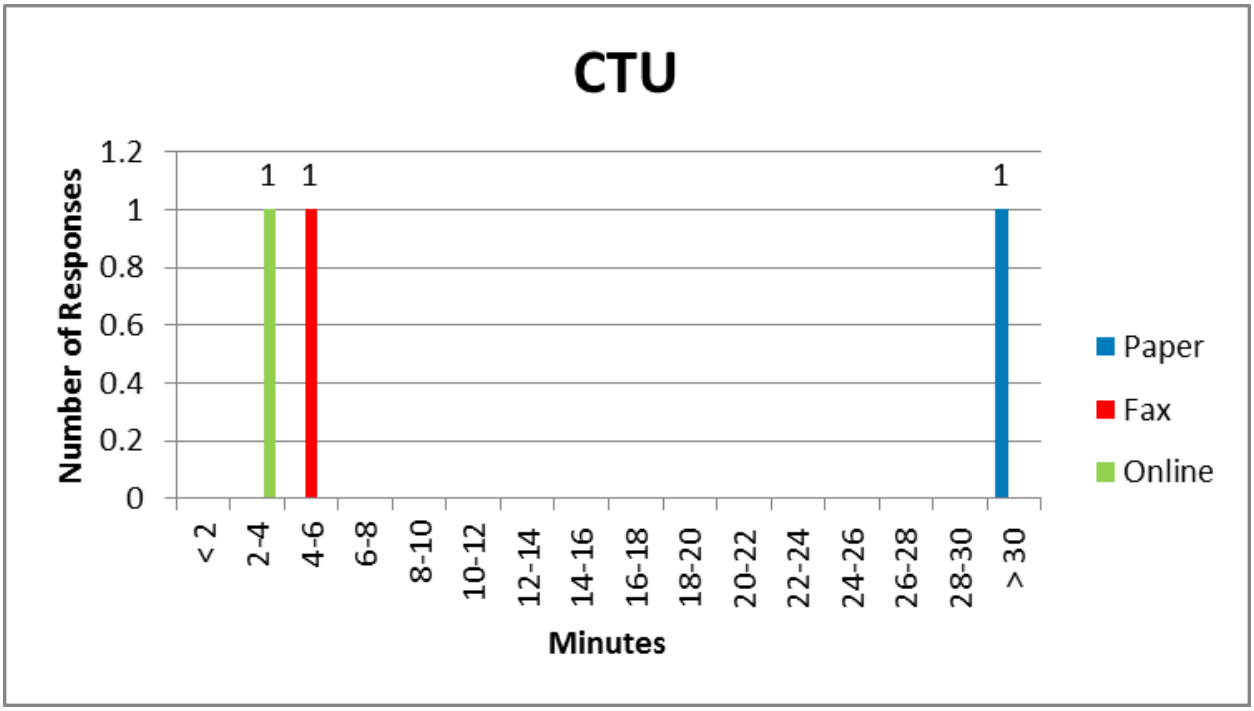


Figure 25: Processing time of adverse event reports for Triage staff

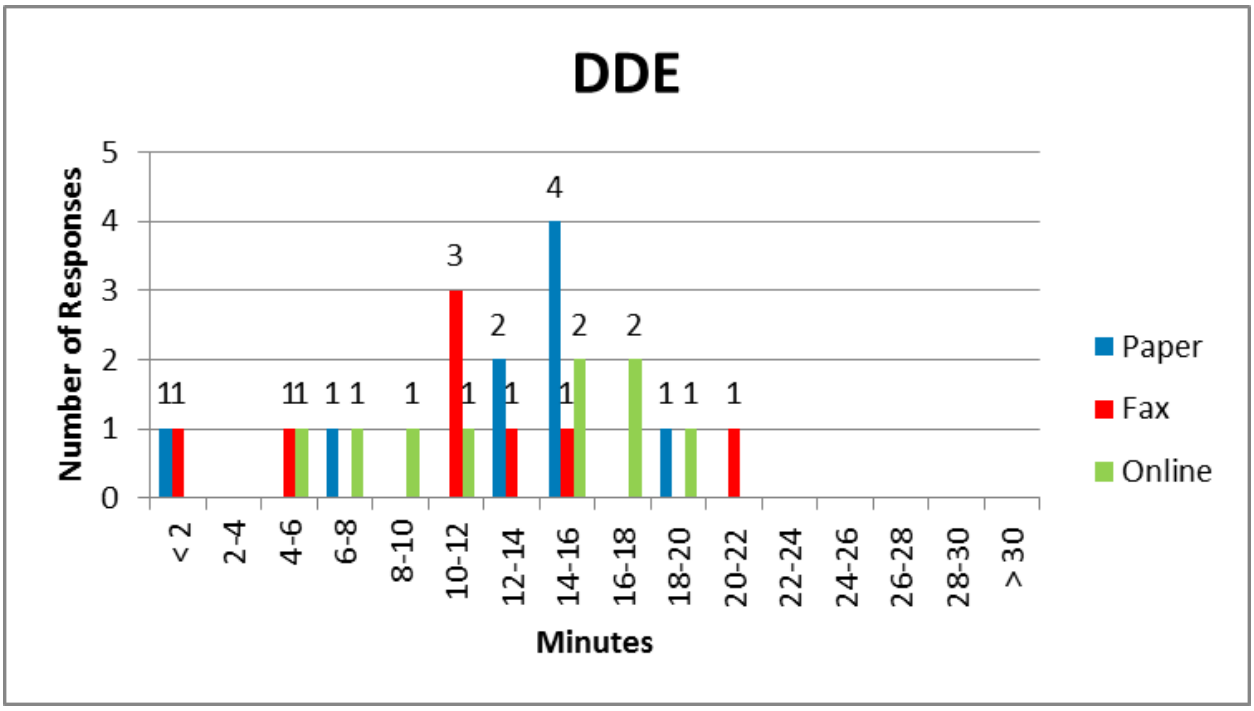


Figure 26: Processing time of adverse event reports for DDE staff

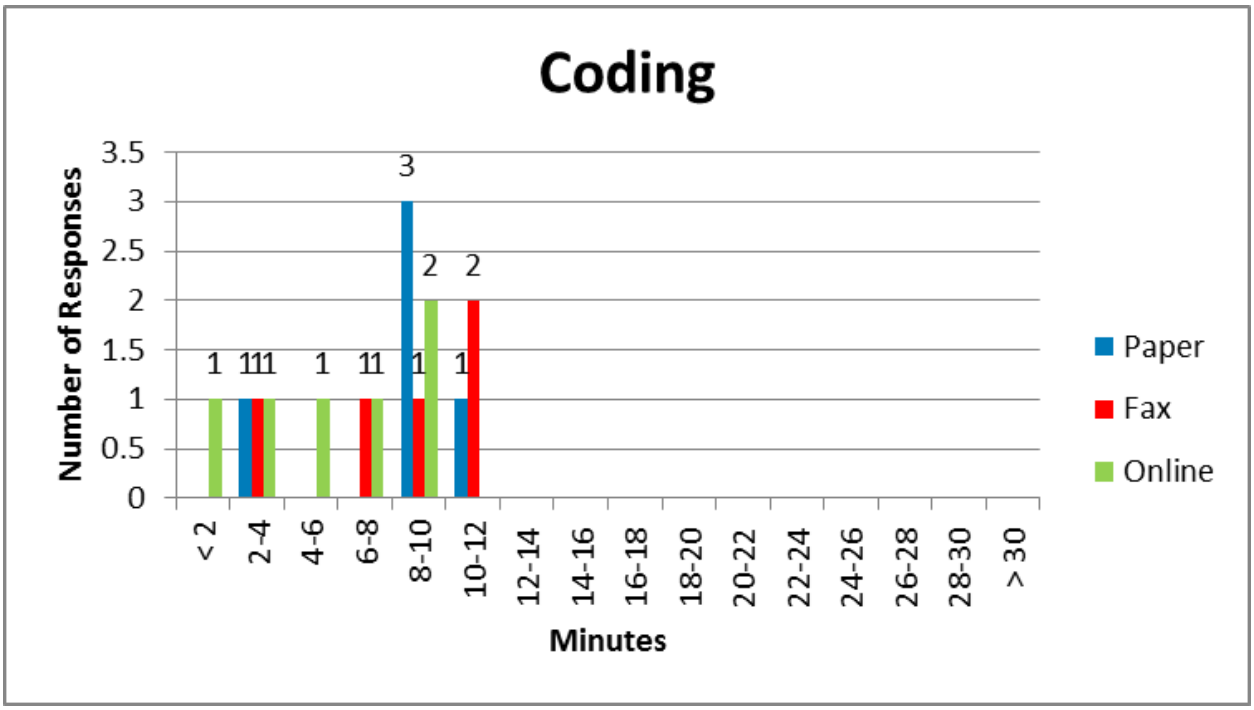


Figure 27: Processing time of adverse event reports for Coding staff

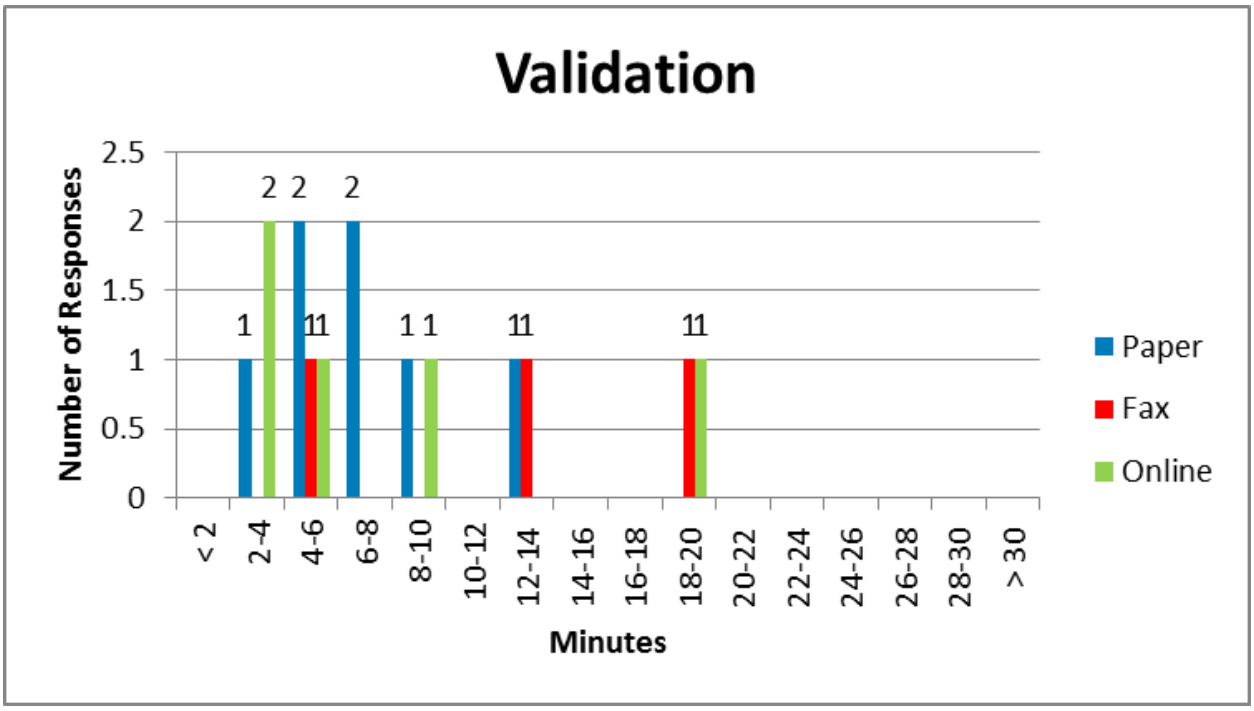


Figure 28: Processing time of adverse event reports for Validation staff