# Harnessing Electronic Health Records to Enhance Reporting to the Vaccine Adverse Event Reporting System (VAERS): Phase 2, Implementation and Update - Final Report

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# History of Modifications

| Version | Date | Modification | Author |
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| 2.1 | 11/21/2019 | Final version with minor revisions from CDC accepted | Harvard Pilgrim Health Care, Department of Population Medicine |
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# Introduction

## *Background and Goals*

Routine vaccination is a cornerstone of modern preventive care. Vaccines have dramatically decreased the incidence of many serious diseases among Americans of all ages, races, and genders.[1] However, vaccines occasionally cause important adverse events that only become apparent after widespread use. The continued success of comprehensive vaccination campaigns depends upon building and maintaining public confidence in vaccine safety. Rigorous post-marketing and ongoing surveillance systems that can reliably detect rare and unexpected adverse events, confirm the frequency and severity of known adverse events, and detect manufacturer or lot-specific problems are critical ingredients to building public and professional trust in vaccines.

The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) jointly operate the Vaccine Adverse Event Reporting System (VAERS) to facilitate vaccine safety surveillance. VAERS is a passive reporting system that depends upon clinicians and patients to recognize possible adverse events and take the initiative to report them. There are few incentives for busy clinicians to do so and no widespread, automated mechanisms to ensure complete detection and electronic reporting of adverse events to VAERS. Consequently, the utility of VAERS data is diminished by substantial under-reporting and limited data from clinicians on their detailed understanding of their patients' clinical status and potential explanations of their condition.[2]

The Health and Medicine Division (HMD) of the National Academies of Sciences, Engineering, and Medicine (the National Academies), formerly the Institute of Medicine, and the Agency for Healthcare Research and Quality (AHRQ) have advocated the use of health information technology to improve the monitoring and detection of adverse events in healthcare.[3, 4] Electronic health record (EHR) systems offer an exciting and increasingly available opportunity for low-cost surveillance and reporting of adverse events. Building upon our previous work, our goal is to leverage EHR systems to improve the security of vaccination programs by improving the completeness, quality, and efficiency of vaccine adverse event (VAE) detection and reporting to VAERS.

ESP-VAERS scans live EHR data for possible adverse events for up to 42 days following immunizations, alerts providers using secure EHR-based clinical messages about possible adverse events, elicits clinicians' comments, and allows them to submit secure electronic case reports directly to the national VAERS program.[5] Our pilot implementation of ESP-VAERS demonstrated that automating VAE detection, engaging clinicians within their existing workflows to invite them to comment on events, and secure reporting to CDC/FDA's VAERS program is feasible. Although the pilot system remained in operation in a limited fashion, it required modifications to make it more suitable for widespread implementation. This task order supported development of the pilot system into a mature production product to make automated adverse event detection and reporting a realistic possibility for widespread adoption by EHR-users. We have enhanced our algorithms to decrease false positive alerts, partitioned the software code to make it more compatible with different EHRs, updated the system for ICD-10, enhanced documentation, created an implementation toolkit, and characterized the specific resources and effort needed for implementation.

## Vaccine safety and adverse events

Pre-licensure studies of vaccines are too small to exclude the possibility of rare but important adverse events. Some important risks of vaccines may only become apparent after FDA approval when the agent is administered to the general population. Unexpected adverse events of vaccines identified after licensure have included intussusception associated with rhesus-human rotavirus vaccine, myopericarditis associated with smallpox vaccine, alopecia associated with hepatitis B vaccine, and seventh cranial nerve palsies associated with intranasal influenza vaccine.[6-9] In addition, since vaccines are biological agents, there is constant risk of batch-specific variability during manufacturing and distribution that may affect large numbers of patients exposed to a specific lot.[10, 11] **Vaccines' widespread use, their public health significance, and the well-recognized limitations of pre-approval trials compel the creation and maintenance of robust safety surveillance systems to continually detect and characterize VAEs.**

## Passive surveillance systems for vaccine related adverse events

The CDC and FDA rely heavily on passive surveillance systems to identify unsuspected adverse events of approved products. VAERS accepts spontaneous reports from clinicians, pharmaceutical companies, and the public on the entire immunized population. The companion system for drugs is FAERS, the FDA Adverse Event Reporting System (formerly AERS). VAERS and FAERS rely upon clinician initiative to report potential adverse events via telephone, fax, or internet either directly to VAERS/FAERS, or to manufacturers who report on their behalf. Although providers are required to report adverse events from the VAERS table of reportable events, there are few incentives for busy physicians to submit these reports, information capture by VAERS and FAERS is idiosyncratic, and case documentation is often incomplete.[2] CDC estimates fewer than 5% of severe events, such as idiopathic thrombocytopenia after measles-mumps-rubella vaccine or hypotonic-hyporesponsive episodes after diphtheria-tetanus-pertussis vaccine,[12] are reported. For drugs, officials estimate that only about 1% of adverse reactions are reported to FAERS.[13] Many VAERS reports are poorly documented, particularly with regard to vaccine lot number and the precise date of administration.

## Opportunities to improve adverse event surveillance using ambulatory care data

EHR systems offer an opportunity to improve adverse event detection and reporting by automatically scanning EHR data for potential adverse events and eliciting clinical impressions and comments from providers. EHR systems offer three potential advantages over existing passive and claims-based vaccine safety surveillance systems: 1) EHRs include detailed clinical data including vital signs and laboratory test results, 2) EHR alerting can be near real-time rather than delayed by months or years as with claims-based systems, and 3) EHR systems make it possible to query patients' clinical providers for additional detail and evaluation while potential events are still current. As with claims data, EHR systems allow calculation of denominators in order to generate adverse event incidence densities, rather than simply adverse event counts. EHR systems are widespread, so a generalizable and portable automated adverse event surveillance approach based on existing EHR systems offers the opportunity to quickly ramp up adverse event surveillance and provide clinically rich reports at relatively low marginal cost.

## *ESP-VAERS – EHR-based automated adverse event surveillance and reporting*

The building blocks needed to create a comprehensive, prospective, EHR-based VAE detection and reporting system currently exist and have been integrated into a functional, scalable, reproducible system. Our group developed the ESP system, a sophisticated, generalizable, open-source, freely available EHR-based public health surveillance platform capable of analyzing large amounts of structured EHR data for events of public health importance and sending secure electronic case reports to public health agencies (esphealth.org).[5, 14, 15] We and others developed algorithms to survey EHR data for VAEs.[16-18] As described below, we have integrated these two technologies into ESP-VAERS, a pilot system funded through the SHEPheRD Task Order 200-2011-42037 that adds a feedback loop for clinicians to comment upon and endorse, or refute, automatically detected events, overcoming the two major limitations of extant, purely automated adverse event detection models: limited capability to capture idiosyncratic events and the high false positive rate of purely rule-based systems.[17, 19, 20]

## *Preliminary data*

The ESP-VAERS pilot system was rolled out to all MetroHealth System practices (~500 providers) in December 2012.[5] In the 8 months following implementation, 91,622 vaccinations were given. ESP-VAERS sent 1,385 messages to clinicians describing potential VAEs. Clinicians opened 1,304 messages, responded to 209, and confirmed 16 for transmission to VAERS. An additional 16 high probability VAEs were sent automatically. Reported events included seizure, pleural effusion, and lymphocytopenia. The odds of a VAERS report submission during the implementation period were 30.2 times greater than the odds during the comparable pre-implementation period.

The current work builds upon the success of the ESP-VAERS pilot, converting ESP-VAERS from a development version to a component of ESP that is usable by other ESP installations. We have also developed both technical documentation and a clinical users' guide.

## *Task order aims*

Aim 1: Design a clinical algorithm based on identification of vaccines administered and prospective capture of the patient's new diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions

Aim 2: Develop implementation program and documentation to introduce ESP-VAERS into the clinical practice

Aim 3: Characterize effort for implementation in no more than 4 multisite/ multispecialty practices designated as current ESP installation sites

Aim 4: Update ESP-VAERS so that it may be used with the new VAERS 2.0 form

Aim 5: Enhance ESP-VAERS system documentation to make it adaptable to other electronic health record systems

Aim 6: Produce reports after each phase, including a final written report

The sections in this report include the deliverables to fulfill the aims of the Task Order.

# Section One: Information for Practice Managers and Clinicians

This section is intended for use by sites who choose to implement the ESP VAERS system. It is a draft guide that can be adapted by sites to introduce their practice managers and clinicians to VAERS, discuss briefly how ESP VAERS works to detect possible vaccine-associated adverse events, and inform them of how they can confirm or reject reports.

## I. Clinical Guide for Practice Managers and Clinicians

*[Insert your local clinical practice name here]* is pleased to be implementing an EHR-based system that can alert clinicians to possible vaccine adverse events, elicit clinician feedback, and automatically submit electronic case reports to VAERS. Our vaccine adverse event detection system leverages the Electronic medical record Support for Public Health (ESP) system. ESP is a sophisticated, open-source, EHR-based public health surveillance platform (esphealth.org) [5, 14, 15]. ESP-VAERS uses algorithms to survey patients' diagnoses and laboratory test results for up to 42 days following vaccination to detect new diagnoses or conditions that may be attributable to a vaccine. If ESP-VAERS detects a suggestive new diagnosis or change in lab values, ESP-VAERS will notify the clinician diagnosing the event and invite him/her to comment upon and confirm or refute the purported event.

### *Background*

#### Vaccine adverse events and the Vaccine Adverse Event Reporting System (VAERS)

Vaccines' widespread use, their importance to public health, and the well-recognized limitations of pre-approval trials make it imperative to create and maintain robust safety surveillance systems to continually detect and characterize vaccine-associated adverse events. The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) jointly operate the Vaccine Adverse Event Reporting System (VAERS) to facilitate vaccine safety surveillance. VAERS is a passive reporting system that depends upon clinicians and patients to spontaneously recognize possible adverse events and take the initiative to report them. There are few incentives for busy clinicians to do so and no widespread, automated mechanisms to ensure complete detection and electronic reporting of adverse events to VAERS. Consequently, the utility of VAERS data is diminished by substantial under-reporting [2]. CDC estimates that fewer than 5% of severe events, such as idiopathic thrombocytopenia after measles-mumps-rubella vaccine or hypotonic-hyporesponsive episodes after diphtheria-tetanus-pertussis vaccine, are reported[5, 12]. Of the reports that *are* sent to VAERS, many are poorly documented, particularly with regards to vaccine lot number and the precise date of administration.

#### Automated adverse event surveillance and reporting via the ESP-VAERS system

Electronic health record (EHR) systems offer an opportunity to improve adverse event detection and reporting by automatically scanning EHR data for potential vaccine-associated adverse events and eliciting clinical impressions and comments from providers when the EHR record suggests a possible vaccine-associated adverse event.

A prototype of the current ESP-VAERS system was piloted at MetroHealth in Ohio in 2012-2013. The reporting rate increased 30-fold during the implementation period compared with prior to implementation. Of clinicians responding to the notifications of potential vaccine adverse events, 55%

found the messages helpful and not disruptive to workflow, and 79% considered the number of messages to be appropriate. The pilot demonstrated that automating vaccine-associated adverse event detection was feasible using EHR data, engaging clinicians within their existing workflows to comment on events and report plausible or possible vaccine-associated adverse events to CDC/FDA's VAERS program[15].

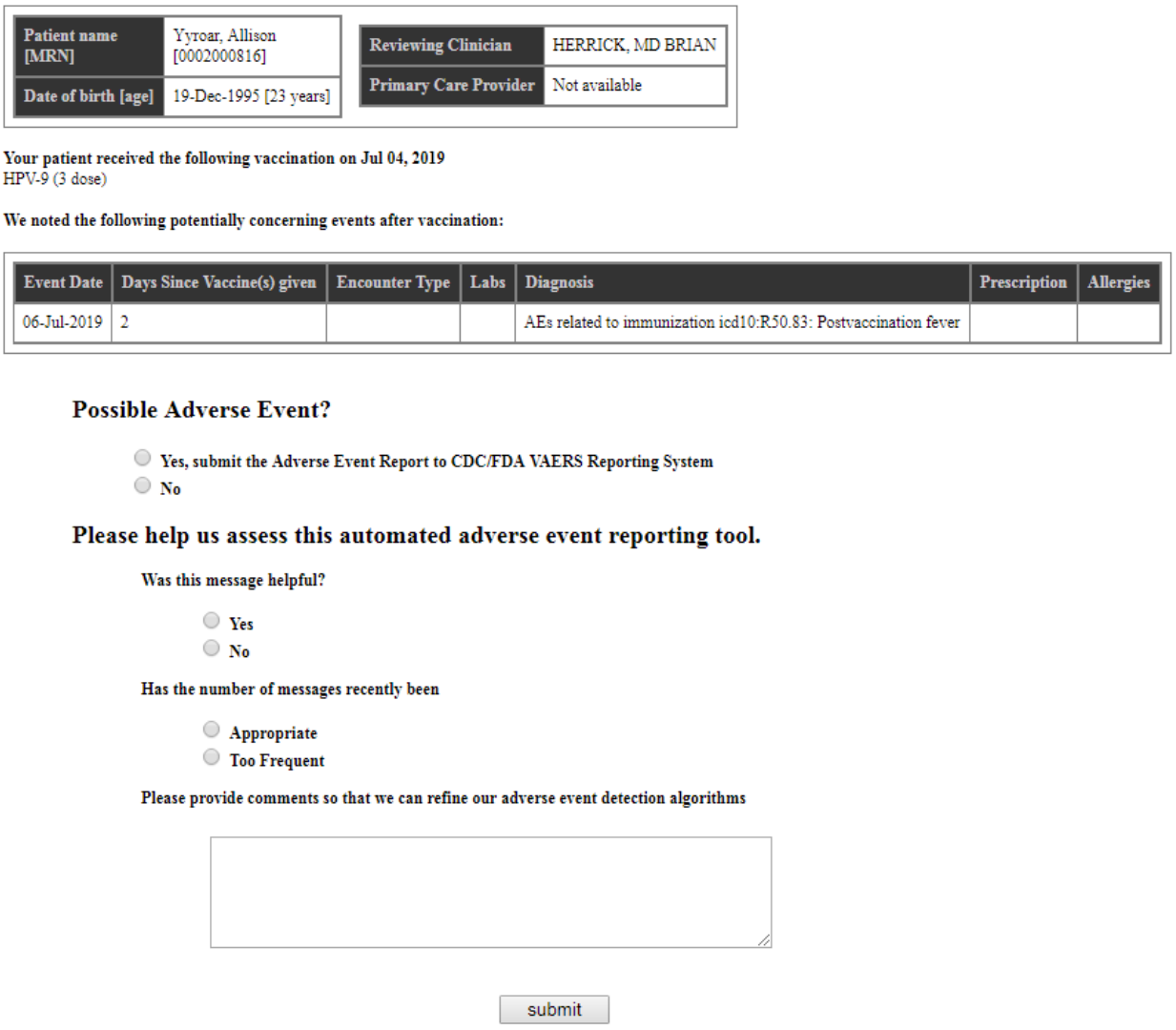
### Adverse events that should be reported to VAERS

Healthcare providers, as well as patients and parents, are asked to report to VAERS any adverse event that occurs after vaccination. As stated by VAERS,

*"You should report any adverse event that happens after getting a vaccine, even if you are not sure that the vaccine caused the adverse event. It is especially important to report any adverse event that resulted in hospitalization, disability, or death."*

## *Completing the VAERS report using ESP-VAERS*

If a possible vaccine-associated adverse event occurring within 42 days of vaccination is detected via the ESP VAERS algorithms, an automated message will go to the in-basket of the clinician who diagnosed the condition. The message will provide summary information about the patient's potential adverse event, along with the immunization and triggering event. This document becomes part of the patient's medical record. The message will include a web link back to the ESP system. If you click on the link in the message, a screen like the following appears:



| Patient name [MRN] | Yyroar, Allison [0002000816] |
|---|---|
| Date of birth [age] | 19-Dec-1995 [23 years] |

| Reviewing Clinician | HERRICK, MD BRIAN |
|---|---|
| Primary Care Provider | Not available |

**Your patient received the following vaccination on Jul 04, 2019**
HPV-9 (3 dose)

**We noted the following potentially concerning events after vaccination:**

| Event Date | Days Since Vaccine(s) given | Encounter Type | Labs | Diagnosis | Prescription | Allergies |
|---|---|---|---|---|---|---|
| 06-Jul-2019 | 2 | | | AEs related to immunization icd10:R50.83: Postvaccination fever | | |

**Possible Adverse Event?**

- Yes, submit the Adverse Event Report to CDC/FDA VAERS Reporting System
- No

**Please help us assess this automated adverse event reporting tool.**

Was this message helpful?

- Yes
- No

Has the number of messages recently been

- Appropriate
- Too Frequent

Please provide comments so that we can refine our adverse event detection algorithms

submit

If, as in this example, you answer “No” to “Possible Adverse Event?” then no further action is needed, although you have the option of answering three brief questions to help your local ESP VAERS promoters evaluate whether the system is useful and acceptable to you and other clinicians.

If you answer “Yes” to “Possible Adverse Event?” then a few additional important pieces of information are solicited, as shown in this screen:

# ESP — Electronic medical record Support for Public Health (ESPnet)

| | | | |
|---|---|---|---|
| Patient name [MRN] | Testlastname, Testy [0123wxyz] | Reviewing Clinician | Smith, MD James P. |
| Date of birth [age] | 21-Sep-1947 [71 years] | Primary Care Provider | Smith, MD James P. |

**Your patient received the following vaccination on Apr 19, 2019**
PNEUMOCOCCAL POLYSACCHARIDE 23 VALENT (PPSV23) (CVX=33)

**We noted the following potentially concerning events after vaccination:**

| Event Date | Days Since Vaccine(s) given | Encounter Type | Labs | Diagnosis | Prescription | Allergies |
|---|---|---|---|---|---|---|
| 27-Apr-2019 | 8 | | | Ataxia icd10:R26.2 | | |

## Possible Adverse Event?

- (●) Yes, submit the Adverse Event Report to CDC/FDA VAERS Reporting System
- ( ) No

Has the patient recovered from the adverse event(s)?

- ( ) Yes
- ( ) No
- ( ) Unknown

Result or outcome of adverse event(s): (Check all that apply)

- [ ] Doctor or other healthcare professional office/clinic visit
- [ ] Emergency room/department or urgent care
- [ ] Hospitalization
  - Number of days (if known)
  - Hospital Name
  - City State
- [ ] Prolongation of existing hospitalization (vaccine received during existing hospitalization)
- [ ] Life threatening illness (immediate risk of death from the event)
- [ ] Disability or permanent damage
- [ ] Patient Died -- Date of death (mm/dd/yyyy) mm / dd / yyyy
- [ ] Congenital anomaly or birth defect
- [ ] Unknown
- [ ] None of the above

Please provide details on the likelihood and severity of this possible event

## Please help us assess this automated adverse event reporting tool.

Was this message helpful?

- ( ) Yes
- ( ) No

Has the number of messages recently been

- ( ) Appropriate
- ( ) Too Frequent

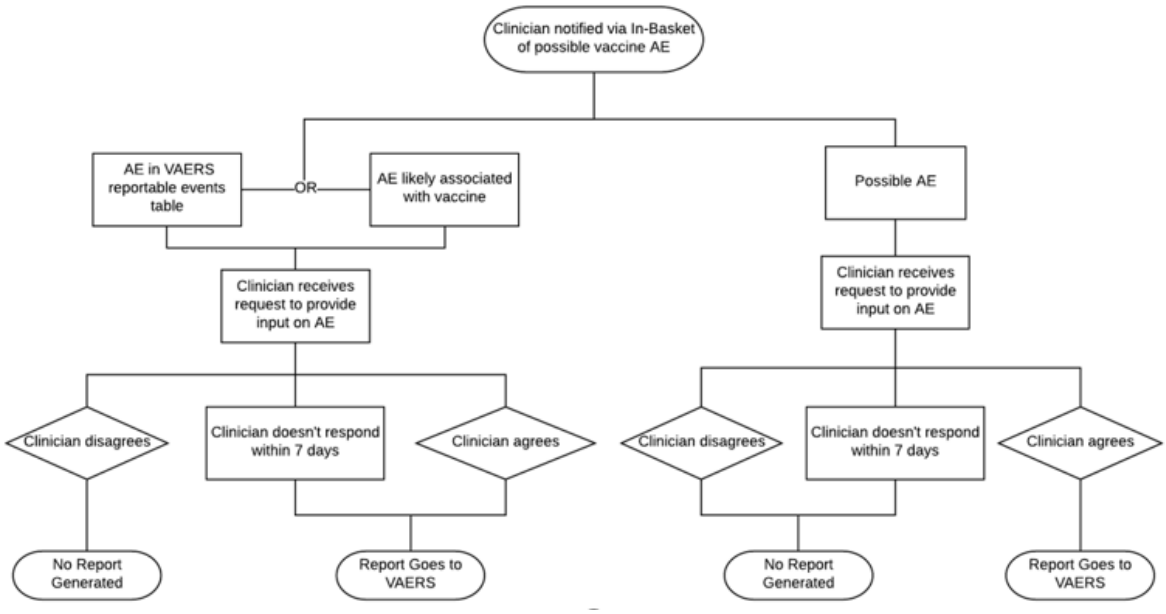
Please provide comments so that we can refine our adverse event detection algorithms

submit

This additional information about the adverse event is incorporated into an online VAERS form, the rest of which is filled out automatically. You then click on "Submit" to send the form to VAERS. A notice that a VAERS report was sent via ESP VAERS (but not the filled-out form itself) is placed in your patient's record, including reference to the specific vaccination(s) and the triggering event.

If you do not electronically comment on the event within 7 days, what happens next depends on the nature of the adverse event. In the case of *rare, serious, known adverse events* or *adverse events considered to be likely associated with vaccination*, reports will automatically go to VAERS. In the case of *possible adverse events*, no automatic reports will go to VAERS—you must explicitly confirm that such an event might be vaccine-associated in order for a report to VAERS to be generated.

These scenarios are presented graphically in the figure below:




## *Frequently asked questions*

1. <u>What is VAERS and how can I find out more about it?</u>

   VAERS is the national Vaccine Adverse Event Reporting System maintained by the CDC and FDA to receive spontaneous reports of adverse events after vaccination with U.S. licensed vaccines. Monitoring and analysis of these reports allows safety problems to be detected. An article by Shimabukuro et al. [21] sums up the history of VAERS and its relationship to the National Childhood Vaccine Injury Act as follows:

   > *"VAERS was established in 1990 [22, 23] to fulfill a requirement of the National Childhood Vaccine Injury Act of 1986 [24]. By law, vaccine manufacturers are required to report adverse events that come to their attention, and healthcare professionals are required to report adverse events that*

*are considered a contraindication to further doses of vaccine and those specified in the VAERS Table of Reportable Events Following Vaccination [25-28]. The National Childhood Vaccine Injury Act of 1986 also authorized establishment of the National Vaccine Injury Compensation Program [24]. Adverse events on the VAERS Table of Reportable Events Following Vaccination mirror the "illness, disability, injury or condition covered" conditions in the National Vaccine Injury Compensation Program's Vaccine Injury Table [26] used to help adjudicate petitioner claims of vaccine related injury."*

Resources:

VAERS website:
https://vaers.hhs.gov/

CDC website on VAERS:
https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vaers/index.html

VAERS Table of Reportable Events:
https://vaers.hhs.gov/docs/VAERS_Table_of_Reportable_Events_Following_Vaccination.pdf

2. Why do I need to report possible vaccine adverse events to VAERS?

Pre-licensure clinical trials are not conducted in large or diverse enough study populations to detect very rare true adverse events of vaccination. Reporting of possible vaccine-associated adverse events to VAERS is one of the most important ways by which previously unknown adverse events of vaccination come to the attention of public health authorities after new vaccines are licensed. Analysis of VAERS reports can also help identify risk factors for certain kinds of adverse events and batch- or lot-specific safety problems. Under-reporting of adverse events to VAERS reduces its power and utility for identifying safety problems.

Clinically important and unexpected adverse events, especially, should be reported, even if one is not sure they were caused by vaccination.

3. What happens when the ESP-VAERS system detects a potential vaccine adverse event?

A message goes to the in-basket of the clinician who diagnosed the health event. It will be similar in format to this one:

*Dear Dr. JONES*
*Your patient Sam Adams may have suffered an adverse event from a recent vaccine. Sam Adams was diagnosed with MENINGITIS on AUGUST 12 2019, 7 days after receiving MEASLES VACCINE. If you think the MENINGITIS might have been due to the vaccine, we can automatically submit an electronic report to CDC / FDA's Vaccine Adverse Event Reporting System on your behalf.*

There will be a web link (URL) in the message. When you click on this, an input screen will open. If you think that the adverse event in question *might* be a vaccine adverse event, you select "Yes" in

the input screen, which will open another screen with a few more questions to answer. The report will then go to VAERS without your having had to fill in all the fields manually.

4. What if I do not believe that this health care event was related to vaccination?

   In such a case, you should answer "No" to the question of whether you think the event is a possible vaccine-associated adverse event. No report to VAERS will be generated if you click "No" within 7 days of receipt of the message.

5. What happens if I don't respond to or even look at a possible vaccine adverse event message from ESP-VAERS?

   It depends on the nature of the adverse event. If it is rare, serious, and/or considered likely to be associated with vaccination and you do not respond to the message within 7 days, a report will automatically be sent to VAERS. Otherwise, no report will be sent.

6. Under what circumstances does information about a possible vaccine-associated adverse event detected by ESP VAERS go into my patient's chart?

   Whenever the ESP VAERS algorithms detect a possible vaccine adverse event, a note about the immunization and the triggering event goes into your patient's chart. The note remains in the medical record regardless of whether or how you respond to it.

7. What if I or another health care professional or the patient already reported the adverse event to VAERS?

   There is no problem with multiple reports of an event being sent to VAERS. VAERS analysts can sort out the duplicates.

8. What is the reporting impact of ESP-VAERS?

   During the pilot study of ESP-VAERS at MetroHealth, the reporting rate increased 30-fold[5]. A largely automated reporting system like ESP-VAERS has the potential to substantially reduce the problem of under-reporting to VAERS if implemented on a large scale.

## II. Clinical Characteristics of the ESP-VAERS notifications sent to clinicians and VAERS reports transmitted

The algorithms went through several cycles of testing and revision. The last test used data from the two participating sites for the 12-month period 8/1/2018-7/31/2019. Between the two sites, 356,995 doses of vaccine were administered, and 23,566 notifications were produced, of which 0.8% were Category One (rare, severe adverse event on VAERS Table of Reportable Events Following Vaccination), 0.4% were Category Three (adverse event likely to be associated with the vaccination), and 99% were Category Two (possible novel adverse event not previously associated with vaccine). Of the Category One events,

thrombocytopenia was the most common at both sites. Of the Category Three events, "adverse effect of vaccines and biological substances, initial encounter" was the most common at both sites. The findings by site are summarized in the table below.

Aggregate results of test run using penultimate version of HOI case-finding algorithms at two sites, 8/1/2018-7/31/2019

| | Reports (cases) | | Conditions | | Most common condition(s) |
|---|---|---|---|---|---|
| | N | % | N | % | |
| **Site 1** | (125,168 vaccine doses administered) | | | | |
| Rare | 60 | 0.6% | 13 | 1.2% | Thrombocytopenia, unspecified |
| Reportable | 31 | 0.3% | 6 | 0.6% | Adverse effect of vaccines and biological substances, initial encounter |
| Possible | 9351 | 99.0% | 1046 | 98.2% | Top 10%: Rash, then nonspecific GI conditions |
| Total | 9442 | | 1065 | | |
| **Site 2** | (231,827 vaccine doses administered) | | | | |
| Rare | 119 | 0.8% | 21 | 1.6% | Thrombocytopenia, unspecified |
| Reportable | 54 | 0.4% | 8 | 0.6% | Adverse effect of vaccines and biological substances, initial encounter |
| Possible | 13951 | 98.8% | 1289 | 97.8% | Top 10%: Rash, then nonspecific GI conditions |
| Total | 14124 | | 1318 | | |

The conditions responsible for the top 20% of "possible"-category cases at Site 1 were: rash, nonspecific GI conditions grouped (including diarrhea, nausea, vomiting), cough, fever, syncope, pain, dysuria, anemia, and headache. The corresponding top conditions in the "possible" category at Site 2 were: rash, non-specific GI conditions grouped, cough, hyperlipidemia, anemia, fever, abnormal electrocardiogram, nasal congestion, syncope, dysuria, and dizziness and giddiness.

Upon review of these results, the clinician-members of the study team further modified the algorithms for Category Two events, attempting to strike a compromise between the competing goals of capturing previously unknown vaccine adverse events and not flooding the in-boxes of busy clinicians. There were two kinds of modifications. One was to exclude certain non-specific events such as cough and nasal congestion. The other was to tighten the inclusion criteria of certain other conditions responsible for numerous reports. For example, in the case of rash, the risk window was narrowed to Days 1-4 or, if and only if after varicella-containing vaccine, Days 5-26. Another example was unspecified fever, for which the risk window was narrowed to Days 1-7 or, if and only if after measles-containing vaccine, Days 8-14.

These and earlier refinements are reflected in the updated algorithm document and exclusions table, available at https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation.

# Section Two: Modifications to ESP VAERS

This section discusses modifications made to the ESP VAERS detection algorithm to include information on the VAERS reporting form v2.0, add ICD-10 codes, and reduce the number of false positives generated. This section also discusses changes made to ESP VAERS to make it possible to implement in other EHR systems.

## I. Update of the clinical algorithm for use with the VAERS 2.0 form, reduce false positives and add ICD-10 codes

### *Introduction*

Aim 1 and sub-aims from our proposal are as follows:

Aim 1: Design a clinical algorithm based on identification of vaccines administered and prospective capture of the patient's new diagnostic codes, laboratory tests, allergy lists, vital signs, and medication prescriptions

a) Refine the adverse event detection algorithms by improving the exclusion rules for certain high frequency conditions and integrating multiple streams of data from the EHR for event detection
b) Update the system to utilize ICD-10 as the required dictionary for coding diseases and diagnoses

In this section and two online documents, we address these aims by presenting the laboratory- and ICD-10-code-based algorithms we use to capture post-vaccination health outcomes of interest (HOIs), diagnoses to exclude and exclusion criteria, and steps taken to reduce false positives compared with the pilot ESP VAERS project.[1]

### *Algorithms for specific outcomes*

The current algorithms for capturing abnormal laboratory values and specific HOIs are presented in "**ESP_VAERS Algorithm_v2.6_2019-09-19docx"** (available at https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation). This document is based on the one used for the pilot but has been updated in several ways:

1. It is based on ICD-10 codes
2. Some outcomes have been excluded (e.g., poisoning) and others included (e.g., arthus phenomenon)
3. A category of adverse events, reactions, complications, and contamination related to immunization has been added
4. A more general category of adverse events, complications, and abnormal reactions related to medical care but not specific to vaccines has been added

5. Some of the algorithms have been made more specific in an attempt to reduce false positives (see "Reduction of false positives" below for more on this)

The maximum follow-up period remains 42 days. If a case occurs outside of its respective pre-specified risk window (e.g., Days 1-30, Days 0-7, Days 7-42, etc., depending on the outcome), it will be excluded.

## *Other outcomes to be reported*

In order to capture potential unanticipated vaccine-associated adverse events, codes for diagnoses other than the ones explicitly listed in the algorithm document will be reported under the following conditions:

1. They occur in the data during Days 1-30 after vaccination
2. They are not in the exclusions table, which is on the "exclusions" tab of "**ICD 10 code exclusions and inclusions 2019-09-24.xlsx**" (available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation)
3. The same code is not on the patient's current problem list prior to the encounter in question
4. The patient has had no diagnosis code having the same first 4 characters/digits (e.g.,K22.1) in the prior 36 months

## *Exclusions*

As referred to above, there is a new table of diagnoses to exclude, on the "exclusions" tab of "**ICD 10 code exclusions and inclusions 2019-09-24.xlsx**" (available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation). ICD-10-CM diagnosis codes to be excluded were chosen on the basis of generally broad criteria or characteristics and include the following:

- Infectious diseases, other than ones known to occur after vaccination
- Cancers, because unlikely to be diagnosed within 30 days
- Hereditary and congenital disorders and malformations
- Chronic conditions
- Injuries and certain other outcomes ascribed to external causes (except for adverse events ascribed to vaccination)
- Diseases due to external agents, e.g., respiratory conditions due to inhalation of chemicals, gases, fumes, and vapors
- Pregnancy and pregnancy-related diagnoses, other than spontaneous abortion
- Outcomes associated with diseases or conditions classified elsewhere
- Very general and/or very common diagnoses, e.g., unspecified sleep disorders

## *Reduction of false positives*

We took two general approaches to reducing false positives, as mentioned in the section on Clinical Characteristics of ESP-VAERS Notifications above. One approach was to exclude certain diagnoses. We

implemented a new ICD-10-based exclusions table, along with a new criterion by which reports of diagnoses are suppressed if the diagnosis was preceded by one with the same first 4 characters/digits in the prior 36 months. The exclusions table was refined over the course of testing and clinical review in the current project. For instance, conditions that are frequent, non-specific, and often not serious, such as cough, nasal congestion, and snoring, were added to the list of conditions to exclude. The current version of the exclusions table is available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation.

The other approach was to refine algorithms of outcomes that produced false positives in the pilot and/or that produced a relatively high volume of notifications for non-specific conditions during testing in the current project. This usually entailed restricting the post-vaccination period during which cases would generate a notification to a biologically plausible period. Baker et al. [5] reported the following from the pilot:

The most common diagnoses among the 193 false positives, with frequencies in parentheses:

- Cellulitis (14)
- Bronchospasm (13)
- Nonspecific skin eruption (9+)
- Fever (7)
- Seizure (4)

The most common diagnoses among the 1163 alerts without a response and not automatically sent:

- Nonspecific skin eruption
- Eosinophilia
- Seizure
- Fever
- Leukopenia
- Lymphocytopenia

Investigators involved in the pilot noted that syncope, too, generated several false positives.

The table below summarizes how the algorithms for most of the above-listed outcomes were made more specific, compared to the pilot:

| Condition | In either VAERS or vaccine injury table? | In list of specific diagnoses from pilot? | Changes made to reduce false positives | Comments |
|---|---|---|---|---|
| Bronchospasm | No, except in footnote about anaphylaxis in HRSA vaccine injury table | Yes | Excluded, except "wheezing," which is one of many signs and symptoms codes, most of which are not being excluded | Wheezing will generate alerts if during Days 1-30. |

| Condition | In either VAERS or vaccine injury table? | In list of specific diagnoses from pilot? | Changes made to reduce false positives | Comments |
|---|---|---|---|---|
| Fever | No | No | Risk window reduced from Days 1-30 to Days 1-7, or Days 1-14 for measles-containing vaccine | It was in 2 of the 16 clinician-confirmed reports to VAERS during the pilot. |
| Rash and other non-specific skin eruption | No | No | Risk window reduced from Days 1-30 to Days 1-4, or Days 5-26 for varicella-containing vaccine | Rash and viral exanthem were in 5 of the 16 clinician-confirmed reports to VAERS during the pilot. |
| Seizure | No, except in footnotes | Yes | • Keep febrile convulsions but restrict to ED/hospital settings<br>• Exclude convulsions of newborn and myoclonus | It was in 2 of the 16 clinician-confirmed reports to VAERS during the pilot. We now use Action Category Three (report to VAERS if no comment from clinician within 7 days) instead of Two. |
| Syncope | Yes | Yes | Restricted to Days 0-4 instead of Days 0-7 | |
| Dizziness and giddiness | No | No | Risk window reduced from Days 1-30 to Days 0-4 to match syncope | |
| Several unspecified GI symptoms, e.g., diarrhea unspec., vomiting unspec. | No | No | Risk window reduced from Days 1-30 to Days 0-7 | |
| Abnormal lab values for leukocytes, eosinophils, lymphocytes, AST | No | Yes | Raise eosinophil thresholds by 0.2 $x10^9$/L<br>For all labs, exclude if any of last 3 (instead of just last 1) known values appearing in last 2 years is abnormal (per definition in algorithm document) | Although often not responded to by clinicians in the pilot, abnormal values of each of these 4 components were cited in 1-2 of the 16 clinician-confirmed |

| Condition | In either VAERS or vaccine injury table? | In list of specific diagnoses from pilot? | Changes made to reduce false positives | Comments |
|---|---|---|---|---|
| | | | | reports to VAERS during the pilot. |

### *Summary*

We have developed a new ICD-10-based list of algorithms to capture HOIs and a new ICD-10-based table of diagnoses to exclude and have refined the criteria for including and excluding diagnoses in order to reduce false positive notifications.

## II. ESP Enhancements and adaptations for general use with EHRs

### *Introduction*

Aims 4 and 5 were to enhance the ESP VAERS system, including documentation of adaptations for use with other EHR systems.

ESP VAERS needs to be able to perform the following to provide successful AE identification and reporting to VAERS:

1. Interface with an EHR system to obtain daily access to patient data sufficient to identify potential Vaccine AEs
2. Identify potential patient Vaccine AEs using specified detection algorithms
3. Notify the physician of the potential Vaccine AE using a document that can be entered into the patient EHR.
4. Provide the physician an interface to confirm or reject the Vaccine AE.
5. If confirmed:
   5.1. Send confirmed VAERS-2 reports to the CDC.
   5.2. Notify the physician of the VAERS report using a document that is entered into the patient EMR.

All but item 2 requires an interface specification. The status of these items involving an interface (1, 3, 4, 5.1, 5.2) is described below.

During this stage of work, we investigated a number of new technologies in hopes of utilizing one or more of these.

- **HL7 FHIR API.** CMS has recently released a proposed rule that would require government health plans and health plans sold on the federal ACA exchanges to give patients free access and control over their health information by 2020 and to implement an HL7 FHIR-based API to open up data access to third party apps and developers. Early in the current VAERS project, we explored the potential to use the HL7 FHIR API for much of the data exchange and

interoperability requirements for the project. Unfortunately, the Epic technical representatives were not prepared to test the new technology with the current project. By 2020, (next year), there will be an opportunity to update the ESP VAERS system using the FHIR standard, but it wasn't quite ready for this project.

- **FDA Regional Technical Specifications for ICH E2B (R3) Implementation for Postmarket Submission of Individual Case Safety Reports (ICSRs) for Drugs, Biologics and Vaccines**. This standard could have been used for VAERS-2 form reporting. Upon review of this specification, it was determined that while it was extremely flexible and complete for its intended purpose, it was over-engineered as a solution for the VAERS messaging project. Use of this specification would have required GDIT and Commonwealth Informatics to completely rebuild their interface systems. The simpler solution for both parties was to update the existing HL7 standard used for VAERS-1 forms, to support VAERS-2.
- **Direct messaging and HL7 CCD template OID 1.3.6.1.4.1.19376.1.5.3.1.3.13 "Allergies and Other Adverse Reactions"**. Direct Messaging is a new standard for secure messaging directly between healthcare systems. The HL7 Continuity of Care Document (CCD) message standard is built around a set of standard templates for building message documents containing patient medical records data. One template is specific for conveying information about Allergies and other Adverse Reactions. Upon review of this specification, it seemed quite tenable that the VAERS system could use this for communicating with the EHR system about Vaccine AEs identified by ESP (items 3 and 5.2 above). Our initial hope was that we could modernize the VAERS interface to the EHR using these new standards and technologies. During initial discussions, the MetroHealth and CHA Epic technical support representatives raised the issue that URLs contained in the CCD message body could not be made as active links in Epic, and the only solution was to provide a PDF containing that link. Commonwealth created a test PDF and set up a "sandbox" for testing direct message transfers to MetroHealth. We prepared an initial test of simply transferring a text message with the PDF attached but were informed by MetroHealth Epic technical support that the message must include a CCD document as part of the message. We requested Epic technical documentation, via MetroHealth, for specifications of the Direct Message body including how to attach a CCD document and PDF, but these were never provided. We fell back to a pre-existing message transfer standard, HL7 2.3.1 MDM_T02. The use of this standard has been extensively documented and is currently supported by EHR vendors. This is described in "Notify the physician of the potential Vaccine AE" below.

## *Interface with an EHR system to obtain daily access to patient data*

ESP is currently in operation at approximately twelve sites across the US, in Massachusetts, Texas and Ohio. There are installations underway in Pennsylvania and Washington. For all sites, data is extracted on a nightly basis from the EHR, and all new or updated data is written to a set of text files. These files are described in "**ESP_Filespec_v1.5_VAERS**" (available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation). Once set up, the extraction process runs nightly and provides the data interface between the EHR system and ESP VAERS.

The ESP system must be installed in the same network enclave or data center as the source EHR. The extraction process generates the data files from the EHR and places them in the ESP incoming data folder. ESP loads all available data files once a day, or as often as data updates are provided.

There are a number of data extract scripts to generate the daily ETL data. These are available at the ESP source code site for Epic, GE Centricity, and Cerner EHR systems. These can be modified to conform to any EHR sites needs and set up fairly easily. These are available for download from https://gitlab.com/ESP-Project/esp_tools/tree/master/sample_etl.

An additional file at this site provides an example of how to schedule the nightly data extraction and load process. This file is "daily_batch.sh" and is located in the same folder as the sample ETL scripts.

## *Notify the physician of the potential Vaccine AE*

The HL7 MDM message specification provides a standard interface for Medical Document Management. This message specification is provided in Section 9 of the HL7 2.3.1 specification document (available from hl7.org). In particular, we are using MDM_T02 to provide a notification of a potential adverse event, along with a link to the ESP system to view the patient AE information and confirm or reject the case.

The messages are generated from ESP and are placed in a secure location accessible to a data loading process that runs once daily. Once loaded to Epic, the message appears in the Clinician Inbasket, and also becomes part of the patient EHR data.

The MDM_T02 specification document is available for download – please see "**ESP VAERS 2 MDM_T02 specification**" link in Resources; it is also available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation.

## *Provide the physician an interface to confirm or reject the Vaccine AE*

After receiving the message, the clinician will click the URL link and will be taken to a web interface displaying the patient information about the possible vaccine AE.

**ESP – Electronic Medical Record Support for Public Health (ESPNet)**

Status Nodis Vaers Administration About Logout

| | | | |
|---|---|---|---|
| Patient name [MRN] | William McFake [xyz1234] | Reviewing Clinician | Dr. Stanley Steamer |
| Date of birth [age] | 30 Feb 1980 [39] | Primary Care Provider | Dr. Fred Astaire |

Your Patient received the following vaccination on Feb 05, 2019
Influenza, intradermal, quadrivalent, preservative free

We noted the following potentially concerning events after vaccination:

| Event Date | Days since vaccines(s) given | Encounter type | Labs | Diagnosis | Prescription | Allergies |
|---|---|---|---|---|---|---|
| Feb 6, 2019 | 1 | ER | | R50.83 Postvaccination fever | | |

**Possible Adverse Event?**

- O Yes, submit the adverse event report to CDC/FDA VAERS Reporting System
- O No

**Please help us assess this automated adverse event reporting tool**

Was this message helpful?

- o Yes
- o No

Has the number of messages recently been

- o Appropriate
- o Too Frequent

Comments:

If the clinician selects “Yes, submit the adverse event report to CDC”, the screen expands to request information that cannot be obtained from the patient EHR.

## ESP – Electronic Medical Record Support for Public Health (ESPNet)

Status Nodis Vaers Administration About Logout

| | | | |
|---|---|---|---|
| Patient name [MRN] | William McFake [xyz1234] | Reviewing Clinician | Dr. Stanley Steamer |
| Date of birth [age] | 30 Feb 1980 [39] | Primary Care Provider | Dr. Fred Astaire |

Your Patient received the following vaccination on Feb 05, 2019
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We noted the following potentially concerning events after vaccination:

| Event Date | Days since vaccines(s) given | Encounter type | Labs | Diagnosis | Prescription | Allergies |
|---|---|---|---|---|---|---|
| Feb 6, 2019 | 1 | ER | | R50.83 Postvaccination fever | | |

## Possible Adverse Event?

- ● Yes, submit the adverse event report to CDC/FDA VAERS Reporting System
- O No

Has the patient recovered from the adverse event(s)? ○ Yes ○ No ○ Unknown
Result or outcome of adverse event(s): (Check all that apply)

- ● Doctor or other healthcare professional office/clinic visit
- ● Emergency room/department or urgent care
- ○ Hospitalization: Number of days (if known) ____
  Hospital Name ____ City ____ State ____
- ○ Prolongation of existing hospitalization (vaccine received during existing hospitalization)
- ○ Life threatening illness (immediate risk of death from the event)
- ○ Disability or permanent damage
- ○ Patient died – Date of death: (mm/dd/yyyy) ____
- ○ Congenital anomaly or birth defect
- ○ None of the above

Additional adverse reaction information:

**Please help us assess this automated adverse event reporting tool**

Was this message helpful?
- o Yes
- o No

Has the number of messages recently been
- o Appropriate
- o Too Frequent

Comments:

Once the information is collected, the clinician may select "Submit", and the system will generate a VAERS-2 message, as described below.

### *Send confirmed VAERS-2 reports to the CDC*

Confirmed VAERS cases will be sent to the CDC via the GDIT managed PHINMS route. The cases will be transcribed to the HL7 2.3.1 message transfer standard, as specified in the document "Implementation Guide for Immunization Data Transactions using Version 2.3.1 of the HL7 standard Protocol, version 2.2, June 2006". We have created an additional document which describes extensions to this specification in order to support the transmission of VAERS cases using the VAERS-2 report. Please see "**VAERS 2.0 HL7 2.3.1 Messaging Update Documentation**," available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation.

ESP will generate these messages and transfer them securely to the PHINMS message transfer server. The PHINMS application will take the message files and route them to the GDIT VAERS-2 route, where they will be received, parsed and loaded into the CDC VAERS database.

### *Notify the physician of the VAERS report*

When a VAERS-2 report is sent to the CDC, the ESP VAERS system automatically notifies the physician with a notice of the patient's VAERS report. This becomes part of the patient's medical record. This interface will use the MDM_T02 document format.

The MDM_T02 specification document is available for download – please see "**ESP VAERS 2 MDM_T02 specification**" available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation.

## III. Acceptability of the system to clinicians

Clinicians seeing lists of potential adverse event reports generated by the ESP VAERS system were queried about the acceptability of the system to themselves and their fellow clinicians. The overall response was positive. Remembering to report a suspected adverse event to VAERS and then locating the form were considered barriers to reporting, so the relative ease and speed with which potential AEs could be reported to VAERS by the ESP VAERS system—due to the largely automated filling of demographic, vaccine, and other data fields in the VAERS form—was noted as a major advantage over conventional, largely manual vaccine AE reporting. One clinician commented, "I'm glad our health system decided to install ESP VAERS because it makes it easier to contribute post-marketing surveillance data."

The fact that the occurrence of post-vaccination health outcomes would be brought to the attention of the clinician was seen as a strength, as clinicians may not always connect an outcome to a recent vaccination. The step involving clinical judgment to confirm or rule out cases was considered a useful feature. However, one clinician observed that some of the "possible" AEs (e.g., fever, cough, rash, vomiting), which generated a relatively high volume of reports, seemed generic and hard to attribute to a vaccine. He felt the algorithms were too sensitive. In general, there was an appreciation among the clinicians that two of the goals of ESP VAERS are at odds with each other, namely the goal of discovering unknown AEs (which would favor maximizing sensitivity) and the goal of not overwhelming clinicians with lots of false alarms (which would favor maximizing specificity), and that it could take further adjustment of the algorithms to achieve the optimal balance.

# Section Three: ESP Installation and Message Transmission

This section discusses how the electronic message is sent to the VAERS system and how to implement and install ESP in a new practice site.

## I. Optimal Transmission of VAERS 2.0 Reports to GDIT

### *The pre-existing ESP VAERS system*

The pre-existing ESP VAERS system was piloted at MetroHealth in Cleveland, Ohio in 2012. The ESP software would take a nightly data feed of patient clinical data from the MetroHealth Epic Clarity Electronic Medical Record (EMR) system and identify potential vaccine adverse events. A notification would then be sent to health care providers via the Epic Clinicians' Inbox with a link to review the evidence that ESP had found. The link would take the health care provider to a web page with details concerning the detected event-and would allow the clinician to review the data and make a determination as to whether or not the event represented a vaccine adverse reaction. If the clinician confirmed the event as an AE, an electronic VAERS report was generated and sent to the CDC via the secure Public Health Information Network Messaging System (PHIN-MS, see https://www.cdc.gov/phin/tools/phinms/index.html) as managed by SRA (now GDIT). (Some events were categorized to be automatically sent if no response was obtained from the clinician within a week.)

The pre-existing ESP VAERS system was developed using the VAERS-1 form and the 2006 electronic message specification document "Implementation Guide for Immunization Data Transactions using Version 2.3.1 of the Health Level Seven (HL7) Standard Protocol, Implementation Guide Version 2.2, June 2006". This CDC-authored document provided a detailed specification for use of HL7 2.3.1 for generating data files containing VAERS-1 form fields. When an event was confirmed as an AE, the ESP VAERS system would use this specification to generate an electronic VAERS report message file. These electronic VAERS message files would be placed in a computer folder that was actively checked by a PHIN-MS service. The PHIN-MS software service would encrypt the files and then send them to an SRA managed network site where their data would be parsed and loaded into the CDC VAERS database.

The VAERS-1 form fields transmitted by the pre-existing ESP VAERS system included:

| Box# on VAERS form | Description | Included? | Comments |
|---|---|---|---|
| | Patient name (Last, First MI), address, phone | YES | |
| | Vaccine administered by Name (Last, First, MI) , Facility name, address, phone | YES | |

| Box# on VAERS form | Description | Included? | Comments |
|---|---|---|---|
| | Form completed by | YES | |
| 1 | State | YES | |
| 2 | County | NO | |
| 3 | Date of birth | YES | |
| 4 | Age at time of vaccination | YES | |
| 5 | Sex | YES | |
| 6 | Date form completed | YES | |
| 7 | Describe adverse event | YES | This included all trigger ICD9 codes, lab results, allergy entries, and prescriptions. The reviewing clinician was asked to comment in the ESP VAERS web form, and that comment was included here. |
| 8 | Check all appropriate | YES | Electronic message included items answerable within the short time frame when the AE alert was sent to the clinician (within 1 day of the adverse event diagnosis, lab test, prescription, or allergy). Specifically, we included if the adverse event required an ER visit or doctor visit, or required hospitalization. Inpatient or outpatient/ED encounter information was used. |
| 9 | Patient recovered | NO | This cannot be reliably discerned from EHR data. |
| 10 | Date of vaccination | YES | |
| 11 | Adverse event onset | YES | Date patient presented to medical attention with symptoms. |
| 12 | Relevant diagnostic tests/laboratory data | YES | Triggering laboratory values and a last known lab value prior to vaccination for comparison<br>(frequency and duration if known) |
| 13 | Enter all vaccines given on date listed in 10 | YES | Vaccine type, manufacturer, lot, route, site |

| Box# on VAERS form | Description | Included? | Comments |
|---|---|---|---|
| 14 | Any other vaccinations within 4 weeks prior to the date listed in 10 | YES | Vaccine type, manufacturer, lot, route, site, date given |
| 15 | Vaccinated at | YES | Public health clinic/hospital Private doctor's office/hospital |
| 16 | Vaccine purchased with | NO | |
| 17 | Other medications | YES | Included trigger medications, but not other medications. |
| 18 | Illness at time of vaccination | NO | |
| 19 | Pre-existing physician-diagnosed allergies, birth defects, medical conditions | NO | |
| 20 | Have you reported the event previously | YES | An AE was resent if new information was obtained about the case. |
| 21 | Adverse event following prior vaccination | YES | Included if ESP VAERS has reported it in the past |
| 22 | Birth weight | NO | |
| 23 | No. of brothers and sisters | NO | |
| 24 | Project report number | YES | We were given a specific project ID by the CDC. |

## *Current project*

For the current project, much of the pre-existing ESP VAERS system was used to support updated electronic VAERS messaging to the CDC. The system continued to use the PHIN-MS secure message-file transfer system. However, two new developments were taken into account:

1. The VAERS-2 form was released, which includes a number of modified and new fields. We needed to assess the available ESP data and the changes required.
2. The FDA published a specification for using the International Conference on Harmonization's E2B (R3) message format for VAERS messaging. "FDA Regional Technical Specifications for ICH E2B (R3) Implementation. Postmarket Submission of Individual Case Safety Reports (ICSRs) for Drugs, Biologics and Vaccines." This superseded use of HL7 2.3.1 VAERS reporting standard and represented a complete change in message transfer specification. We needed to assess if this new specification could be used within the scope of the current project, and if not, what our other options were.

These developments are discussed below.

| Q# in 1.0 form | Q# in 2.0 form | Description of field | Included in Original ESP VAERS | Comparison | Notes regarding inclusion in new VAERS electronic message |
|---|---|---|---|---|---|
| -2 | 1 | Patient name and address | YES | New: county of residence and e-mail requested | County not in ESP data, email not in ESP data |
| -1 | 14 | Person administering vaccine, responsible MD, facility name and address | YES | New: "Best [person] to contact about AE" (instead of old form's person administering vaccine or "responsible physician") | Define rule for identifying provider contact |
| -1 | 15 | Facility name and address | YES | New: fax no. requested | Fax no. not in ESP data |
| 0 | 13 | Person completing form, relation to patient, address | YES | New: checkbox options for "relation" are different; e-mail requested | Email not in ESP data |
| 1 | 1 or 15 | State | YES | New: state of residence is in Q1, state of vaccination is in Q15 | |
| 2 | absent, but Q1 has co. of residence | County where administered | NO | New: county *of residence* is requested in Q1 (among several bits of address info) | County not in ESP data |
| 3 | 2 | Date of birth | YES | New: year in 4 digits | |
| 4 | 6 | Patient age | YES | New: fields for years and months instead of blank area | |
| 5 | 3 | Sex | YES | New: includes "unknown" | |
| 6 | 7 | Date form completed | YES | New: "today's date;" year in 4 digits | |
| absent | 8 | Pregnant at vaccination? | | If "yes," details are to go into Q18 free text space | Use ESP algorithm for pregnancy time span |

| Q# in 1.0 form | Q# in 2.0 form | Description of field | Included in Original ESP VAERS | Comparison | Notes regarding inclusion in new VAERS electronic message |
|---|---|---|---|---|---|
| 7 | 18 | Description of AE | YES | New: outcome explicitly requested (also in Q21) | This included all trigger ICD9 codes, lab results, allergy entries, and prescriptions. The reviewing clinician was asked to comment in the ESP VAERS web form, and that comment was included here. Outcome is not something ESP can generate from EMR data |
| 8 | 21 | Outcomes (several checkbox options) | YES | New: ER/doctor visit separated into two; hospital name, city, state requested; year (of death) in 4 digits; congenital anomaly or birth defect added | Can split ER/doctor out; need to make it easy for clinicians to respond--ask them in their alert; if they say "yes, AE," they'll be taken to screen with checkboxes from Q21. |
| 9 | 20 | Patient recovered? (y/n/unk) | NO | | |
| 10 | 4 | Date and time of vaccination | YES | New: year in 4 digits | |
| 11 | 5 | Date and time of AE onset | YES | New: year in 4 digits | ESP has date of event we attribute to AE onset, but not time |
| 12 | 19 | Relevant diagnostic tests/lab data | YES | New: says "(include dates)" | ESP has this per the AE detection heuristic, with dates. |
| 13 | 17 | List of all vaccines given on same date | YES | New: brand name requested (w/o its own field); route and site separated; dose no. instead of no. of previous doses | While ESP has vaccine history from the EMR system, it doesn't have any information about vaccine at other sites, so dose number will not be reliable. |

| Q# in 1.0 form | Q# in 2.0 form | Description of field | Included in Original ESP VAERS | Comparison | Notes regarding inclusion in new VAERS electronic message |
|---|---|---|---|---|---|
| 14 | 22 | Any other vaccines given in prior 4 wks/1 mo. | YES | New: in prior 1 mo. instead of 4 wks; brand name requested (w/o its own field); route and site separated; dose no. instead of no. of previous doses | Same as above regarding dose number |
| 15 | 16 | Vaccinated at (4 checkbox options for kinds of facilities) | YES | New: more checkbox options but no military option | |
| 16 | absent | Funds used to purchase vaccine (4 check-boxes for kinds of funds) | NO | | ESP does not have this data. |
| 17 | 9 | Other medications | YES | New: both prescription and non-prescription substances explicitly solicited (instead of old form's simple "other med's") | ESP only has medication orders. This will primarily be prescription drug data. |
| 18 | 11 | Illness at time of vaccination (specify) | NO | | |
| 19 | 10 | Pre-existing MD-diagnosed allergies, birth defects, medical conditions (specify) | NO | New (Q10): allergies don't have to be MD-diagnosed | ESP does have allergies data, but not birth defects. |
| 19 | 12 | | | New (Q12): chronic health conditions explicitly solicited (instead of old form's vaguer "pre-existing … medical conditions") | |
| 20 | **absent** | Have you reported this AE before? | YES | | |

| Q# in 1.0 form | Q# in 2.0 form | Description of field | Included in Original ESP VAERS | Comparison | Notes regarding inclusion in new VAERS electronic message |
|---|---|---|---|---|---|
| 21 | 23 | AE following prior vaccination? | YES | New: age at vaccination instead of at AE; vaccination date(s); brand name; no dose no.; no info requested on AEs in siblings | |
| 22 | **absent** | Birth wt. (for children ≤ 5) | NO | | |
| 23 | **absent** | No. of sib's | NO | | |
| 24 | 26 | Report no. (only for report submitted by mfr or imm. proj.) | | New: immun. proj. report no., nothing about mfr | We will continue using the original project Identifier. |
| 25 | **absent** | Date received by mfr or imm. proj. | | | |
| 26 | **absent** | 15-day report? | | | |
| 27 | **absent** | Report type (initial vs. f/u) | | | |
| absent | 24 | Race | | | This is available in ESP data |
| absent | 25 | Ethnicity | | | This is available in ESP data |
| absent | 27 | For DoD, DoD status at vaccination (active duty, reserve, National Guard, beneficiary, other) | | | NA for current project |
| absent | 28 | For DoD, vaccinated at DoD site? | | | NA for current project |
| absent | unnumbered | Any additional information (free text) | | New: large blank space at end of form | Provider comment in ESP VAERS form for provider |

## *HL7 versus E2B (R3) message structure.*

When the current project was originally proposed, we assumed that we would be incrementally upgrading our existing VAERS message structure. There is a document published by the American Immunization Registry Association and the CDC: "HL7 Version 2.5.1: Implementation Guide for Immunization Messaging". While the latest version of this document available from the CDC website is from 2014 and does not have a specific section for VAERS messages, the HL7 2.5.1 specification is very similar to the HL7 2.3.1 specification referenced earlier in this document. Our assumption was that for

this project we would be upgrading our current HL7 message generation process to use the newer HL7 format 2.5.1.

When we contacted the GDIT group who would receive and process the electronic VAERS messages, we learned that the HL7 specification had been superseded by a more recent FDA published specification. This specification uses the International Conference on Harmonization's E2B (R3) message format for VAERS messaging: "FDA Regional Technical Specifications for ICH E2B (R3) Implementation. Postmarket Submission of Individual Case Safety Reports (ICSRs) for Drugs, Biologics and Vaccines." The ICH E2B specification is a highly flexible electronic message format for compiling and transferring data regarding adverse events and related information.

However, the current project had envisioned updating rather than rebuilding the electronic VAERS messages format when estimating the scope of work. To migrate from the HL7 specification to the E2B specification would have required the project IT vendor, Commonwealth Informatics Inc (CII), to redesign and rebuild the ESP module that generates the electronic VAERS message file. In order to receive the new messages and load them to the CDC VAERS database, the GDIT group would have needed to redesign and rebuild the message parsing and loading system. The newly developed systems would have required extensive testing. While the CII and GDIT groups were willing to accept the significant additional work required, both groups expected that a redeveloped and sufficiently tested system would not be ready in time to meet the existing project delivery date for a working system.

After discussions between the CDC and GDIT and between CII and GDIT, the decision was taken to extend the existing HL7 2.3.1 specification to support the VAERS-2 form fields. This extension of the specification was ongoing work between CII and GDIT at the time this deliverable was sent to CDC. The following table outlines the updated HL7 2.3.1 message file structure for VAERS-2 form fields.

## VAERS 2.0 form fields

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| **Patient (one patient allowed)** | | | | |
| 1 | | First Name | PID | |
| 1 | | Last Name | PID | |
| 1 | | Street Address | PID | |
| 1 | | City | PID | |
| 1 | | State | PID | *2 character state abbreviation, Foreign=FR* |
| 1 | **New** | County | **PID** | |
| 1 | | Zip Code | PID | |
| 1 | | Phone | PID | |
| 1 | **New** | Email Address | **PID** | |
| **Patient Information (one patient allowed)** | | | | |
| 2 | | Date of Birth | PID | |
| 3 | | Sex | PID | *Male, Female, Unknown* |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| 4 | | Date of Vaccination | OBX, Date of vaccination | |
| 4 | **New** | Time of Vaccination | **OBX, Date and time of vaccination** | |
| 5 | | Date adverse event started | OBX, Adverse event onset date and time | |
| 5 | | Time adverse event started | OBX, Adverse event onset date and time | |
| 6 | **New** | Age at Vaccination Year | **OBX, Age at vaccination year** | |
| 6 | **New** | Age at Vaccination Month | **OBX, Age at vaccination month** | |
| 8 | **New** | Report is about vaccine administered to a pregnant woman | **OBX, Pregnant at time of vaccination** | *Yes, No, Unknown* |
| 9 | | Prescriptions, over-the-counter medications, dietary supplements or herbal remedies being taken at time of vaccination | OBX, Other medications | |
| 10 | **New** | Allergies to medications, food, or other products | **OBX, Allergies** | |
| 11 | | Other illness at the time of vaccination and up to one month prior | OBX, Illness at time of vaccination (specify) | |
| 12 | | Chronic or long-standing health conditions | OBX, Pre-existing physician diagnosed allergies, birth defects, medical conditions | |
| **Form completed by (one allowed)** | | | | |
| 13 | | Form completed by Name | NK1, Form completed by (Name) | |
| 13 | | Relation to Patient | NK1, Form completed by (Name) | *Healthcare professional/staff*<br>*Patient*<br>*Parent/guardian/caregiver*<br>*Other* |
| 13 | **New** | Relation to Patient Other Text | **NK1, Form completed by (Name)** | |
| 13 | | Street Address | NK1, Form completed by (Name) | |
| 13 | | City | NK1, Form completed by (Name) | |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| 13 | | State | NK1, Form completed by (Name) | *2 character state abbreviation, Foreign=FR* |
| 13 | | Zip Code | NK1, Form completed by (Name) | |
| 13 | | Phone | NK1, Form completed by (Name) | |
| 13 | **New** | Email Address | **NK1, Form completed by (Name)** | |
| **Best doctor or healthcare professional to contact about the patient (one allowed)** | | | | |
| 14 | **New** | Name | **NK1, Best Healthcare Professional to Contact** | |
| 14 | **New** | Phone | **NK1, Best Healthcare Professional to Contact** | |
| 14 | **New** | Ext | **NK1, Best Healthcare Professional to Contact** | |
| **Facility/clinic name (one allowed)** | | | | |
| 15 | | Facility/clinic name | ORC | |
| 15 | **New** | Fax | **ORC** | |
| 15 | | Street Address Line 1 | ORC | |
| 15 | | Street Address Line 2 | ORC | |
| 15 | | City | ORC | |
| 15 | | State | ORC | *2 character state abbreviation, Foreign=FR* |
| 15 | | Zip Code | ORC | |
| 15 | | Phone | ORC | |
| **Type of facility (one allowed)** | | | | |
| 16 | | Type of Facility | OBX, Vaccinated at | *Doctors office or hospital*<br>*Pharmacy or drug store*<br>*Workplace clinic*<br>*Public health clinic*<br>*Nursing home or senior living facility*<br>*School/student health clinic*<br>*Other*<br>*Unknown* |
| 16 | **New** | Type of Facility Other Text | **OBX, Vaccinated at** | |
| **All vaccines given on date listed in # 4 (8 sets allowed)** | | | | |
| 17 | | Vaccine | OBX, Vaccine type | |
| 17 | | Manufacturer | OBX, Manufacturer | |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| 17 | | Lot number | OBX, Lot number | |
| 17 | | Route | OBX, Route | *Intradermal - ID*<br>*Intramuscular - IM*<br>*Intranasal - IN*<br>*Needle Free Jet Injector Device - JET*<br>*Other - OT*<br>*Per Oral - PO*<br>*Subcutaneous - SC*<br>*Needle and Syringe (not specified further) - SYR*<br>*Unknown - UN* |
| 17 | | Body site | OBX, Site | *Arm - AR*<br>*Buttocks - GM*<br>*Left Arm - LA*<br>*Leg - LG*<br>*Left Leg - LL*<br>*Mouth - MO*<br>*Nose - NS*<br>*Other - OT*<br>*Right Arm - RA*<br>*Right Leg - RL*<br>*Unknown - UN* |
| 17 | **New** | Dose number in series<br>*(definition of field has changed; it is no longer "Number of previous doses")* | **OBX, Dose number in series** | *1*<br>*2*<br>*3*<br>*4*<br>*5*<br>*6*<br>*7+*<br>*Unknown*<br>*N/A* |
| **Adverse event information (one of each allowed)** | | | | |
| 18 | | Describe event(s), treatment and outcomes(s), if any | OBX, Vaccination adverse events and treatment, if any | |
| 19 | | Medical tests and laboratory results related to event(s) | OBX, Relevant diagnostic tests/lab data | |
| 20 | | Patient has recovered from event | OBX, Patient recovered | *Yes, No, Unknown* |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| **Result or outcome of event (multiple allowed)** | | | | |
| 21 | **New** | Doctor or other healthcare professional office/clinic visit | **OBX, Doctor or other healthcare professional office/clinic visit** | |
| 21 | **New** | Emergency room or emergency department visit | **OBX, Emergency room or emergency department visit** | |
| 21 | | Hospitalization | OBX, required hospitalization | |
| 21 | | Number of days hospitalized | OBX, Number of days hospitalized due to vaccination adverse event | |
| 21 | **New** | Hospital name | **OBX, Hospital Name** | |
| 21 | **New** | City | **OBX, Hospital City** | |
| 21 | **New** | State | **OBX, Hospital State** | *2 character state abbreviation, Foreign=FR* |
| 21 | **New** | Prolongation of existing hospitalization (vaccine received during existing hospitalization) | **OBX, Prolongation of existing hospitalization** | |
| 21 | | Life threatening illness (immediate risk of death from the event) | OBX, Life threatening illness | |
| 21 | | Disability or permanent damage | OBX, Resulted in permanent disability | |
| 21 | | Patient Died | OBX, Patient died | |
| 21 | | Date of Death | PID | |
| 21 | **New** | Congenital anomaly or birth defect | **OBX, Congenital anomaly or birth defect** | |
| 21 | | None of the above | OBX, None of the above | |
| **Any other vaccines received within one month prior to the date listed in # 4 (8 sets allowed)** | | | | |
| 22 | | Vaccine | OBX, Vaccine type | |
| 22 | | Manufacturer | OBX, Manufacturer | |
| 22 | | Lot number | OBX, Lot number | |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| 22 | | Route | OBX, Route | *Intradermal - ID*<br>*Intramuscular - IM*<br>*Intranasal - IN*<br>*Needle Free Jet Injector Device - JET*<br>*Other - OT*<br>*Per Oral - PO*<br>*Subcutaneous - SC*<br>*Needle and Syringe (not specified further) - SYR*<br>*Unknown - UN* |
| 22 | | Body site | OBX, Site | *Arm - AR*<br>*Buttocks - GM*<br>*Left Arm - LA*<br>*Leg - LG*<br>*Left Leg - LL*<br>*Mouth - MO*<br>*Nose - NS*<br>*Other - OT*<br>*Right Arm - RA*<br>*Right Leg - RL*<br>*Unknown - UN* |
| 22 | **New** | Dose number in series<br>*(definition of field has changed; it is no longer "Number of previous doses")* | **OBX, Dose number in series** | *1*<br>*2*<br>*3*<br>*4*<br>*5*<br>*6*<br>*7+*<br>*Unknown*<br>*N/A* |
| 22 | | Date given | OBX, date given | |
| **Adverse event for prior vaccines received (NEW LAYOUT - one allowed)** | | | | |
| 23 | **New** | Has the patient ever had an adverse event following any previous vaccine? | **OBX, Adverse event following any previous vaccine** | *Yes, No, Unknown* |
| 23 | **New** | If yes, describe and include patient age, vaccination dates, and vaccine type and brand name | **OBX, Adverse event following any previous vaccine Text** | |

| Form 2.0 Box # | | Form 2.0 Field Name | Segment, Keyword in HL7 File | Possible Values |
|---|---|---|---|---|
| **Race (multiple allowed)** | | | | |
| 24 | **New** | American Indian or Alaska Native | **OBX, American Indian or Alaska Native** | |
| 24 | **New** | Asian | **OBX, Asian** | |
| 24 | **New** | Black or African American | **OBX, Black or African American** | |
| 24 | **New** | Native Hawaiian or Other Pacific Islander | **OBX, Native Hawaiian or Other Pacific Islander** | |
| 24 | **New** | White | **OBX, White** | |
| 24 | **New** | Unknown Race | **OBX, Unknown Race** | |
| 24 | **New** | Other Race | **OBX, Other Race** | |
| 24 | **New** | Other Race Text | **OBX, Other Race Text** | |
| **Ethnicity (one allowed)** | | | | |
| 25 | **New** | Patient's ethnicity | **PID** | *Hispanic or Latino, Not Hispanic or Latino, Unknown* |
| **Other Information (one allowed)** | | | | |
| 26 | | Immunization project report number | OBX, Mfr./Imm. Proj. report no | |
| | **New** | Use the space below to provide any additional information | **OBX, Additional information** | |
| **Military status at time of vaccination (multiple allowed)** | | | | |
| 27 | **New** | Active Duty | **OBX, Active Duty** | |
| 27 | **New** | Reserve | **OBX, Reserve** | |
| 27 | **New** | National Guard | **OBX, National Guard** | |
| 27 | **New** | Beneficiary | **OBX, Beneficiary** | |
| 27 | **New** | Other Military Status | **OBX, Other Military Status** | |
| 27 | **New** | Military Status at Time of Vaccination Other Text | **OBX, Other Military Status Text** | |
| **Military/DoD (one allowed)** | | | | |
| 28 | **New** | Vaccinated at Military/DoD site | **OBX, Vaccinated at Military/DoD site** | *Yes, No* |

## VAERS-1 fields no longer used or superseded.

| Form 1.0 Box # | Form 1.0 Field Name | Comments |
|---|---|---|
| **Patient** | | |
| | MI | |

| Form 1.0 Box # | Form 1.0 Field Name | Comments |
|---|---|---|
| | Street Address Line 2 | |
| | Street Address Line 3 | |
| | | |
| **Vaccine Administrator** | | |
| | First Name | |
| | MI | |
| | Last Name | |
| | | |
| **Responsible Physician** | | |
| | First Name | |
| | MI | |
| | Last Name | |
| | | |
| **Facility** | | |
| | Street Address Line 3 | |
| | | |
| **Form completed by** | | |
| | Street Address Line 2 | |
| | | |
| **Box #** | | |
| 2 | County where vaccine was administered | |
| 4 | Age | Replaced with "Age at Vaccination Year" and "Age at Vaccination Month" |
| 6 | Date Form Completed | |
| | | |
| **Result or Outcome of Event** | | |
| 8 | Required emergency room/doctor visit | Replaced with "Doctor or other healthcare professional office/clinic visit" and "Emergency room or emergency department visit" |
| 8 | Resulted in prolongation of hospitalization | Replaced with "Resulted in prolongation of existing hospitalization" |
| | | |
| **Vaccines** | | |

| Form 1.0 Box # | Form 1.0 Field Name | Comments |
|---|---|---|
| 13 | Number of previous doses | Replaced with "Dose number in series" |
| | | |
| **Vaccines within 4 weeks prior** | | |
| 14 | Number of previous doses | Replaced with "Dose number in series" |
| | | |
| **Vaccinated At (drop down)** | | |
| 15 | Military clinic/hospital | |
| 15 | Other/unknown | |
| | | |
| **Box #** | | |
| 16 | Vaccine Purchased With | |
| 20 | Have you reported this adverse event previously? | |
| | | |
| **Adverse event for prior vaccines received** | | |
| 21 | Relationship | |
| 21 | Adverse Event | |
| 21 | Onset Age Year/Mo | |
| 21 | Vaccine | |
| 21 | Manufacturer | |
| 21 | Dose | |
| | | |
| **Box #** | | |
| 22 | Birth Weight (lb, oz) | |
| 23 | Number Brothers and Sisters | |
| 25 | Date Received by Immunization Project | |
| 26 | 15 day report | |
| 27 | Report Type | |

# II. Optimal Installation of ESP-VAERS in additional health care systems

## *Overview*

ESP-VAERS is a software system for detecting vaccine adverse events (VAEs) and reporting those events to public health authorities using the VAERS reporting structure.

The system is installed as follows:

1. A data extraction and transfer process must be developed to move data from the clinical EHR system to ESP. (See "Building the ETL system" below).
2. An ESP server must be set up with ESP installed, the data loaded and configured (See "Installation and Configuration of ESP VAERS" below).
3. An initial VAE detection run must be completed, and the VAE_Listing generated for review and verification that VAEs are being correctly detected. Updates to the system configuration may be indicated (See "Running VAE detection and VAE_Listing" below for review of configuration).
4. The potential VAE cases will be used to create messages for clinical review. The messages are generated in HL7 2.3.1 MDM-T02 format. The EHR system must have an interface to accept these messages, which become part of the patient medical record and which provide a link back to an ESP web page for confirmation or rejection. There are two types of EHR interface messages: messages indicating a potential VAE, and messages indicating a confirmed VAE and VAERS report sent (See "MDM-T02 message interface" below).
5. The confirmed VAE cases are used to create VAERS messages for transfer to the PHIN-MS secure message transfer service to the CDC's electronic VAERS message receiving address as managed by GDIT (see "Setting up PHINMS and sending VAERS messages" below).

## *Building the Extraction-Transformation-Load (ETL) system.*

ETL is the process for moving data from one data processing system to another. For ESP, this is the process of copying data from the clinical practice EHR system to the ESP data warehouse. For any site installing ESP-VAERS, the first step of the process is understanding the data requirements for the ESP system. ESP is an enterprise-level data warehouse-based application, which is provisioned nightly with all new and updated patient clinical data available in the clinical practice EHR system. There is a common misconception that ESP searches the clinical practice EHR system for VAEs, then extracts the necessary data for reporting, but this is not the case. All relevant patient data is copied to ESP, where it can be searched, VAE cases identified, and VAERS reports compiled. The VAERS reporting form requires PHI data, so ESP data provisioning requirements include all new and updated:

- Patient demographic information such as name, address, phone number, race, date of birth.
- Health care provider information such as name, address, phone number, care facility.
- Vaccination information such as date and time of vaccination, vaccine manufacturer, lot number, vaccine body site.
- Prescription information such as prescription name, order date, start date.
- Lab results data such as test name, order date, result date, results.
- Clinical Diagnosis data such as diagnosis code (ICD10), date of diagnosis.

- Clinical problems such as diagnosis codes and date of problem recording.

The ESP ETL system is built and installed according to the following steps:

1. Understanding the structure and content requirements of the ESP data load files.
2. Determining the source data elements from the clinical practice EHR that correspond to the target data elements in the ESP data load files.
3. Writing the code to extract the data from the clinical practice EHR and transform the data into the ESP data load file structure.
4. Determining how the nightly ETL process will be run, and how the ESP data load files will be made available to the ESP load system.

We review these steps in sequence below. The first two steps can be completed prior to the ESP installation. The third step cannot be completed until an ESP instance is installed and ready for testing the data. The fourth step requires an ESP installation. ESP installation is described in "Installation and Configuration of ESP VAERS" below.

### Understanding the structure and content requirements of the ESP data load files.

Currently, the ESP data warehouse is provisioned by generation of a set of delimited text files created from the clinical practice EHR[a]. These files are described in the "**ESP_Filespec_v1.5_VAERS,**" available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation. This document is an Excel workbook. The workbook tabs are arranged in the optimal order of review to understand the ESP ETL file structure requirements. The first tab provides an overview of the Workbook contents and provides descriptions of columns of interest. The second tab describes the files to be produced, including the file naming requirements and the file column layouts. The subsequent tabs describe the data contents of each of the ETL delimited files.

The ESP system is used to support a number of disease reporting and surveillance activities, and the data requirements for those activities are more extensive than required for VAERS reporting. The data requirements for the ESP system must be based on the overall reporting and surveillance purposes of the ESP system, but if the system will only be used for VAERS reporting, the workbook tab for each file specification includes a column "VAERS Required". These fields must be populated from the EHR to support VAERS reporting. Additional fields are optional; however, the developer must keep in mind that the order of delimited fields is critical, and if a field is omitted, delimiters must still be used to maintain the correct column count.

Delimited text files can be created by many data reporting systems. Any data reporting system that can produce delimited text files can be used to develop the ESP data provisioning interface. Most clinical practice EHR system support SQL-based reporting systems, and the ESP code repository includes a number of SQL data extract script samples that can be adapted to generate the daily ETL data. These samples include SQL for Epic Clarity, GE Centricity, and Cerner EHR systems. These can be modified to conform to any EHR sites needs and set up fairly easily. These are available for download from https://gitlab.com/ESP-Project/esp_tools/tree/master/sample_etl. Every clinical practice EHR is unique, and these sample scripts must be modified and tested for use at any site.

[a]A separate project is developing an ESP data load system to use HL7 CCD documents. This capability will be ready by fall 2019 and could be used for ESP-VAERS system installations.

### Determining the source data elements from the clinical practice EHR that correspond to the target data elements in the ESP data load files.

For clinical practice sites using EHR systems for which sample extract scripts are not available, an extraction process must be developed for the ESP installation. This involves identifying how the corresponding data is stored in the clinical practice EHR and determining how this data can be extracted into the data structure required for the delimited file. The ESP_filespec document is a useful tool for designing and documenting this process. For each file to be developed, the workbook tab for that file should be used to determine the required field (VAERS Required), and additional columns can be added to the spreadsheet to specify the data source(s) in the clinical practice EHR. This document then becomes the ETL design specification for developing the ETL code.

### Writing the code to extract the data from the clinical practice EHR and transform the data into the ESP data load file structure.

The ETL process must meet the following basic requirements:

1. It must be able to extract all relevant patient clinical data as specified in the ESP_filespec document.
2. It must be able to create file structures matching the forms specified in the ESP_filespec document.
3. It must be able to generate these files for healthcare services provided on a specified date.
4. It must be able to run as a scheduled unattended process on a daily (or otherwise regular) basis.

The ETL code, once developed or modified from the available samples, must be tested. Depending on the site, a formal or informal testing plan should be developed. Tests should be performed to assess the following:

1. Does the ETL file format match the specification?
2. Can ESP load the data without errors?
3. Does the data provided correctly correspond to data in the clinical practice EHR for the specified extraction date?

### Determining how the nightly ETL process will be run, and how the ESP data load files will be made available to the ESP load system.

The ESP system must be installed in the same network enclave or data center as the source EHR. The extraction process generates the data files from the EHR and places them in the ESP incoming data folder. ESP loads all available data files once a day, or as often as data updates are provided.

Once set up, the extraction process runs nightly and provides the data interface between the EHR system and ESP VAERS. Each site will design and develop its own nightly scheduled ETL process, in order to meet site-specific policy and procedure requirements and in order to work most efficiently with the clinical practice EHR. Here are actual use-case examples of how this can be done:

1. Direct pull from ESP server: Python scripts, with embedded SQL code are run as a scheduled job at a specific time each night on the ESP server. These scripts query the EHR for the required data and generate the required files. The ETL files are written to a file folder on the ESP server. When the ETL scripts are complete, the scheduled job moves on to the next step of loading the data to ESP, then running the VAE detection algorithms, and so on.

2. Indirect pull from ESP server: MUMPS scripts are run against a Cache database from a scheduled job at a specific time each night from the EHR data server. The ETL files are created in a folder accessible via sFTP from the ESP server. A separate job on the ESP server checks this folder on a regular basis for new files and moves them over to the ESP server when they are available. Once moved, the rest of the ESP load and detect processes are run.
3. Push to ESP: C# programs are created with embedded t-SQL to run data queries on a MS SQL-Server database containing clinical practice EHR data. These files are streamed to a shared filesystem that is available to both the ETL process running against the MS SQL-Server database, and ESP's data load process. ESP regularly checks this filesystem folder for new files and loads them when they are available.

The nightly data load and detection run on the ESP server is controlled by a shell script that is installed into the Linux crontab utility. An sample file is available at https://gitlab.com/ESP-Project/esp_tools/blob/master/sample_etl/daily_batch.sh. This file is a simple example of how to set up a scheduled load and detection process on the ESP side.

## *Installation and Configuration of ESP VAERS*

The ESP system installation and configuration will follow these steps:

1. Determine the storage and processing requirements of the ESP server.
2. Obtain the server (physical or virtual) and install into the network enclave or data center.
3. Install ESP
4. Load data from EHR system
5. Configure ESP data mappings for Labs and Immunizations.

### Determining the storage, memory and processing requirements of the ESP server

The storage, memory and processing requirements for the ESP server must be determined before a server is acquired and installed. There are two factors to take into account when determining these server size characteristics:

1. How much data will the EHR be providing on a nightly basis?
2. How long will EHR data be maintained in the ESP system (how much historic patient data will be maintained)?

To determine the first factor, it is necessary to query the clinical practice EHR to determine the basic counts of the following with respect to the ETL files created on a nightly basis for two sources:

- How many new or updated lab result file rows?
- How many new or updated encounter file rows?

These are typically among the largest files generated nightly, and the encounter and lab data is subjected to the most processing and review, and so these are the best indication of nightly data processing load requirements. With the information about data flow rates for these two files, server size can be calculated. A basic ESP system supporting a Postgres database and the Python processes that run the VAE detection process must have two CPUs (cores). From there:

- Add an additional CPU if you will be processing more than 40,000 encounter rows per day, and an additional CPU for each multiple of 40,000.

- Add an additional CPU if you will be processing more than 40,000 lab records per day, and an additional CPU for each multiple of 40,000.

For example, a system that processes an average of 20,000 encounters and 38,000 lab result rows per day will find that 2 CPUs (cores) are sufficient. A system with 75,000 encounters and 125,000 lab results per day would need at least 6 CPUs.

Storage requirements are a function of the number of patients under active care and the amount of historic patient data that the system will maintain. For ESP-VAERs reporting, the system must maintain at least a year of patient prior histories. Many of the VAE detection algorithms look back into the patients' medical records for exclusionary events. In addition, for validation purposes, it is useful to maintain an additional year of patients' medical histories so that test VAE cases can be created and reviewed when the system is installed. If the ESP installation is being used for other disease case reporting and surveillance purposes, additional years of patient histories will be required.

A simple heuristic for determining storage requirements for ESP-VAERS is based on the number of active patients and the number of years of patient medical histories the system will maintain. Active patients are patients with at least one encounter with a care provider in a year.

Count of active patients * number of years * 0.00025 = Gigabytes of storage required

For example, a system with 300,000 patients and 3 years of data would require:

300,000*3*0.00025=225Gb storage

This estimate includes storage for the ESP relational database tables, compressed delimited text files, compressed database backup dumps, and 15% free space overhead. This assumes that only the required VAERS data fields are populated.

ESP stored data in a relational database management system (RDBMS), typically PostgreSQL. RDBMS performance is highly dependent on the amount of system memory available. The larger your RDBMS, the more memory your system can utilize to improve performance.

A rule-of-thumb we use is for each 50GB of storage used by the RDBMS, you should have 2GB of memory. Keep in mind that the storage heuristic above is for ALL storage plus overhead, not just the database. The RDBMS will take up about 50% of the used storage. Also keep in mind that a new ESP system will not have as much data stored as a machine that has been collecting and maintaining patient histories for several years. It may be appropriate to start out with a smaller amount of system memory and expand this along with the size of your database.

### Installing the server into the network enclave or data center

Once the server size requirements have been obtained, an ESP server must be set up in the network enclave or data center. This may be a physical or virtual server. Basic server requirements are:

- An actively supported Linux distribution release.
- OpenSSH installed
- A static IP number assigned

## *Install ESP*

To complete an ESP installation, one follows the step-by-step instructions in "**How To - Install and Configure ESP on Ubuntu 18.04**" (a link to a download can be found in the Resources section of this

document; it is also available at: https://espnet.atlassian.net/wiki/spaces/EP/pages/815235073/ESP+VAERS+Documentation). These instructions are specific to Ubuntu 18.04, but they contain high-level instructions for installation on other Linux distributions as well. The installation follows these steps:

1. Create the ESP user and install the required software infrastructure.
2. Download the ESP software and run the installation
3. Create the ESP database and ESP database user
4. Create the filesystem locations required by ESP input and output processes
5. Configure the Apache web server for the ESP administrative interface
6. Configure iptables for controlled access to the server
7. Configure the basic ESP system and create the admin user

## Load data from EHR system

The ETL system developer under "Building the Extraction-Transformation-Load (ETL) system" above is now implemented for use with ESP. This includes extracting and loading patient histories (at least one year, optimally two years, optionally more), as well as setting up and running the automated nightly ETL process.

## Configure ESP data mappings for Labs and Immunizations

Once data is loaded to ESP, there are two final configuration steps which must be completed prior to running.

1. Mapping local lab test codes to ESP lab concepts
2. Mapping local vaccine codes to CDC standard vaccine codes

These mapping tasks must be completed after patients' medical history data are loaded, and as part of system maintenance on a regular basis going forward. The mapping must be a standard maintenance task in order to detect and map any new labs and vaccines that appear in the medical records at a clinical practice.

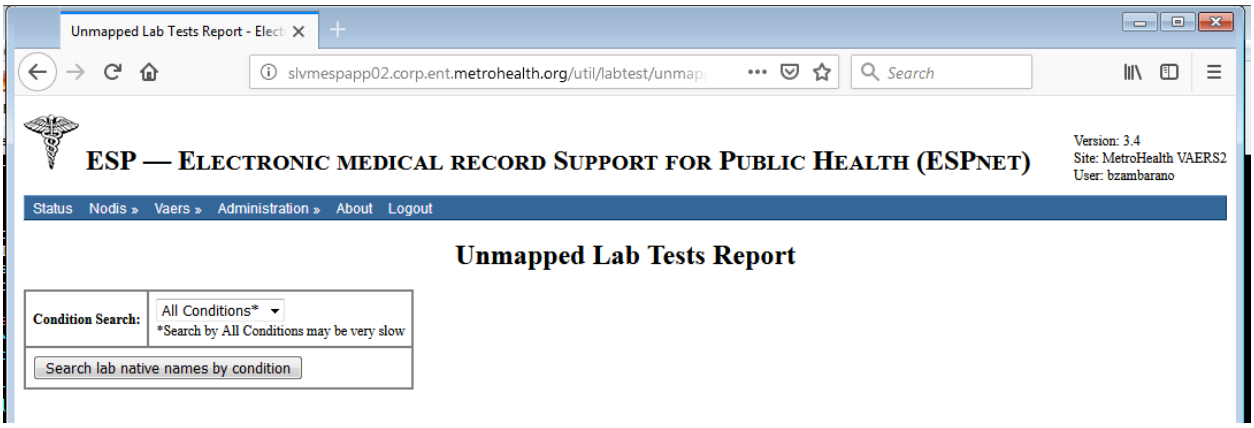
A number of ESP VAEs are determined based on lab test results. Most health care organizations do not maintain lab test records uniformly coded to national standards. In order for the ESP to correctly assess a lab test results as pertaining to a VAE, the local lab test code and lab test name must be mapped to an ESP lab concept. ESP VAE detection does not require mapping of lab test codes and names to any standard code system.

Before lab test mapping can be performed, an ESP command must be run that populates the data table used to determine the set of available local labs. From the Linux command line, run the command:

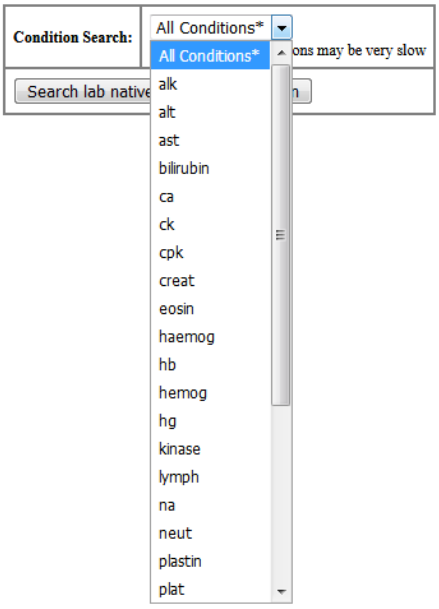
[$ESPHOME]/bin/esp concordance

The concordance command must be run prior to using the lab mapping interface with the ESP system in order to detect any new lab tests in the medical record.

The lab test mapping process is performed via the ESP administrative interface, which provides an interactive "Unmapped Lab Tests Report".




The report provides a simple dialog with a drop down pick list.




The user should pick one of the test name abbreviations on the list then select the button labelled "Search lab native names by condition". If there a large number of unmapped labs, and the user picks "All conditions", the interface will become very slow.

Below we have searched for "white". The target was tests for White Blood Cell counts, but that is not what was turned up:

## Unmapped Lab Tests Report

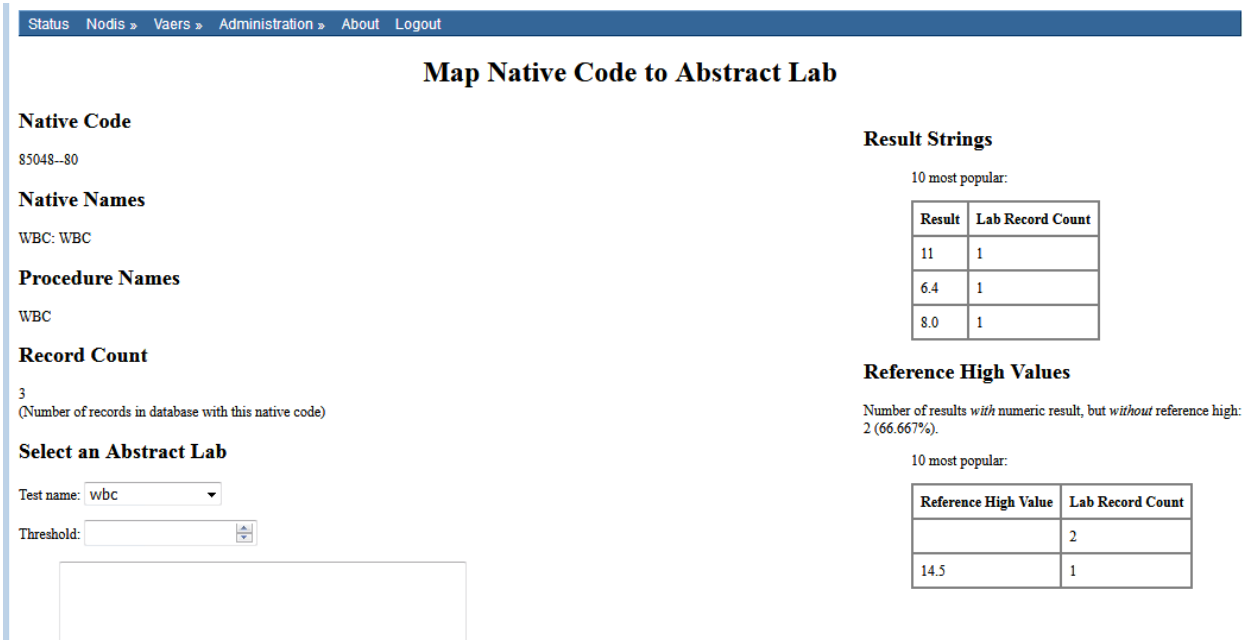
| Condition Search: | white<br>*Search by All Conditions may be very slow |
|---|---|
| Search lab native names by condition | |

| | Native Name | Native Code | Procedure Name | Lab Record Count | |
|---|---|---|---|---|---|
| ☐ | FOOD ALLERGEN PANEL 1: EGG WHITE | RAST F20--1233443 | FOOD ALLERGEN PANEL 1 | 1094 | map |
| ☐ | FOOD ALLERGEN PANEL 1: EGG WHITE CLASS | RAST F20--1233442 | FOOD ALLERGEN PANEL 1 | 1094 | map |
| ☐ | FOOD ALLERGEN PANEL 2: EGG WHITE | 86003--1233443 | FOOD ALLERGEN PANEL 2 | 101 | map |
| ☐ | FOOD ALLERGEN PANEL 2: EGG WHITE CLASS | 86003--1233442 | FOOD ALLERGEN PANEL 2 | 101 | map |
| ☐ | INHALANT ALLERGEN PANEL 2: WHITE ASH | RAST 19--1233548 | INHALANT ALLERGEN PANEL 2 | 1813 | map |
| ☐ | INHALANT ALLERGEN PANEL 2: WHITE ASH CLASS | RAST 19--1233547 | INHALANT ALLERGEN PANEL 2 | 1813 | map |
| ☐ | INHALANT ALLERGEN PANEL 2: WHITE MULBERRY | RAST 19--1233554 | INHALANT ALLERGEN PANEL 2 | 1813 | map |
| ☐ | INHALANT ALLERGEN PANEL 2: WHITE MULBERRY CLASS | RAST 19--1233553 | INHALANT ALLERGEN PANEL 2 | 1813 | map |

Ignore Selected Codes

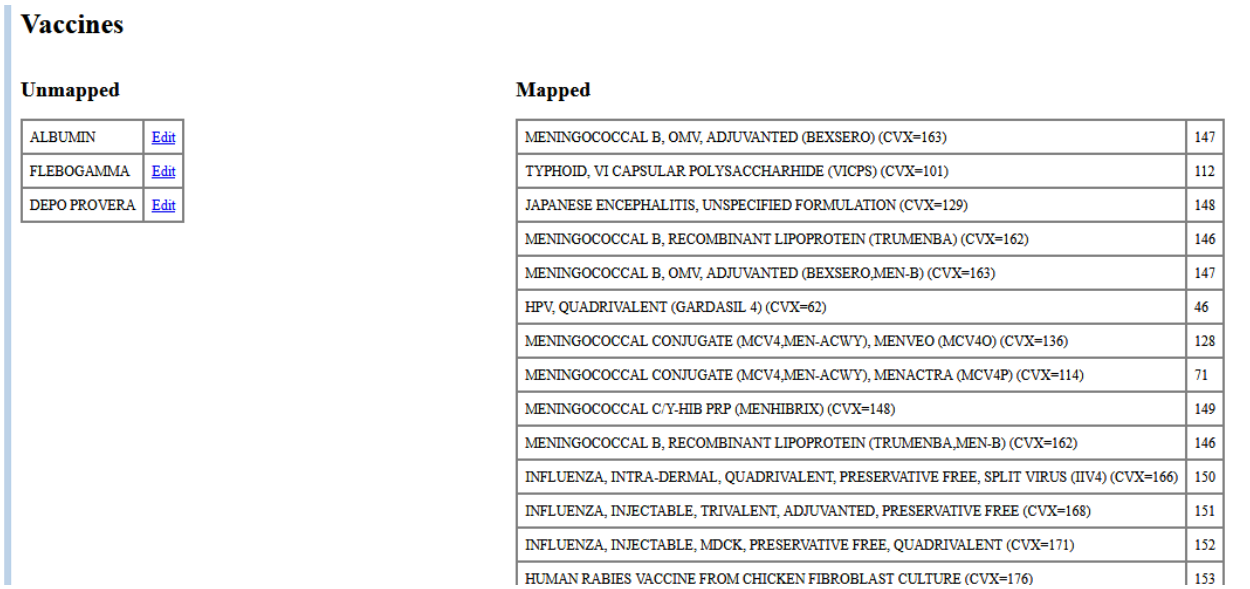
These codes may be permanently ignored so they don't turn up in future mapping searches. Click on the box on the left side of each row and then click on the "Ignore Selected Codes" button.

Alternatively, if a test had been available for mapping, the link at the right side of the row is available for mapping the test to a lab concept. The lab mapping interface looks like so:




The only field that MUST be set is the value for "Test name:" on the lower left side in this view. The remain values have correct defaults.

Mapping vaccines uses a simpler interface.



**Vaccines**

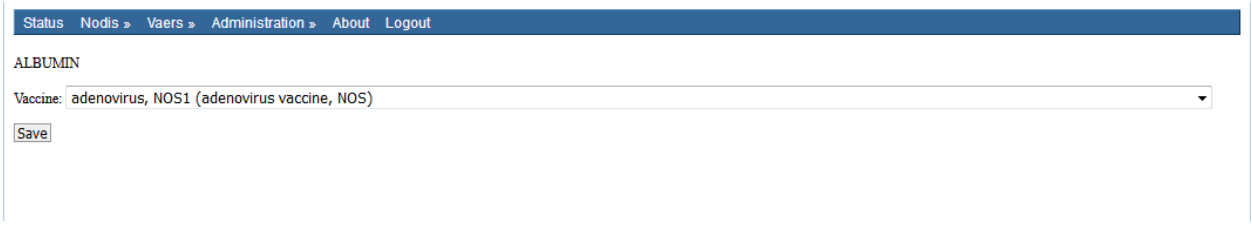
**Unmapped**

| | |
|---|---|
| ALBUMIN | Edit |
| FLEBOGAMMA | Edit |
| DEPO PROVERA | Edit |

**Mapped**

| | |
|---|---|
| MENINGOCOCCAL B, OMV, ADJUVANTED (BEXSERO) (CVX=163) | 147 |
| TYPHOID, VI CAPSULAR POLYSACCHARHIDE (VICPS) (CVX=101) | 112 |
| JAPANESE ENCEPHALITIS, UNSPECIFIED FORMULATION (CVX=129) | 148 |
| MENINGOCOCCAL B, RECOMBINANT LIPOPROTEIN (TRUMENBA) (CVX=162) | 146 |
| MENINGOCOCCAL B, OMV, ADJUVANTED (BEXSERO,MEN-B) (CVX=163) | 147 |
| HPV, QUADRIVALENT (GARDASIL 4) (CVX=62) | 46 |
| MENINGOCOCCAL CONJUGATE (MCV4,MEN-ACWY), MENVEO (MCV4O) (CVX=136) | 128 |
| MENINGOCOCCAL CONJUGATE (MCV4,MEN-ACWY), MENACTRA (MCV4P) (CVX=114) | 71 |
| MENINGOCOCCAL C/Y-HIB PRP (MENHIBRIX) (CVX=148) | 149 |
| MENINGOCOCCAL B, RECOMBINANT LIPOPROTEIN (TRUMENBA,MEN-B) (CVX=162) | 146 |
| INFLUENZA, INTRA-DERMAL, QUADRIVALENT, PRESERVATIVE FREE, SPLIT VIRUS (IIV4) (CVX=166) | 150 |
| INFLUENZA, INJECTABLE, TRIVALENT, ADJUVANTED, PRESERVATIVE FREE (CVX=168) | 151 |
| INFLUENZA, INJECTABLE, MDCK, PRESERVATIVE FREE, QUADRIVALENT (CVX=171) | 152 |
| HUMAN RABIES VACCINE FROM CHICKEN FIBROBLAST CULTURE (CVX=176) | 153 |

Unmapped values in the local vaccine list are shown on the left, the list of mapped values is shown on the right. If a local vaccine value is not considered a vaccine, it should be left unmapped. Click on the "Edit" link to map an unmapped entry.




Use the drop-down list to pick a CDC standard vaccine name to map the local value to, then click save.

One additional step is required to complete the configuration of local vaccination data. As noted above, some data may be transferred to ESP which does not represent vaccines. This may include various other injections and infusions. The local name string for these non-vaccines must be included in the table "immuexclusion." After completing the mapping for vaccine names using the mapping interface, run the following sql command as the ESP database user:

```
INSERT INTO immuexclusion (non_immu_name)
SELECT native_name FROM vaccinecodemap
WHERE canonical_code IS NULL;
```

## *Running VAE detection and VAE_Listing for review of configuration*

Once the ETL has been developed and tested and the ESP system has been installed and configured and the ETL process has been used to load patient data, the next steps are to run VAE detection against the loaded data and generate a VAE listing of all detected cases for review and validation.

## Running VAE detection

Running VAE detection requires submission of an ESP command from the Linux command line. The command does accept a number of arguments and requires at least one. The command syntax is:

[$ESPHOME]/ bin/esp vaers [options]

The options explained:

| | |
|---|---|
| -b BEGIN_DATE | The start of VAE detection period |
| -e END_DATE | The end of the VAE detection period |
| -l | Run Lab Results Heuristics |
| -d | Run Diagnostics Heuristics |
| -p | Run Prescription Heuristics |
| -a | Run All Heuristics |

You must include one of l, d, p, or a (lab, diagnostic, prescriptionor all heuristics).

For example:

[$ESPHOME]/bin/esp vaers -a -b 20180101

The above command would run VAE detection for all heuristics from 20180101 until the present.

## Running the VAE listing

Similarly, running VAE listing is done from the command line:

{$ESPHOM]/bin/esp vae_listing

The command will accept one optional argument: use -p to generate a listing containing PHI, otherwise the report will obscure all PHI. For the default report, dates are provided as only years, dates of service are provided as days offset from the vaccination date. No patient information is provided.

The listing should be reviewed to confirm that the system configuration is generating VAEs correctly. The PHI version of the listing can be used to conduct chart review to examine the potential VAE cases to determine

# *MDM-T02 message interface*

Once VAE cases have been generated, subsequent command can be used to generate HL7 version 2.3.1 MDM-T02 messages, which contain a brief report concerning the potential VAE. These messages are generated by ESP but must be transferred to the EHR system and imported. The MDP-T02 message is a standard message format for providing external documents regarding a patient clinical issue, to the attention of a physician. The process for transfer of the messages must be designed by the site, with coordination between the ESP system administrator and the EHR HL7 interface developer.

Once these messages are loading into the EHR system, the notified care provider will have a brief message describing the potential VAE, and a URL link back to an ESP web page where the VAE data can be reviewed. The care provider will be able to confirm or reject the VAE. Confirmed VAEs will accept additional information from the care provider, and when saved the results will be used to generate a VAERS message for transfer to the VAERS reporting system.

When VAERS messages are sent, an additional MDM-T02 message is generated as well. This message informs the care provider that a VAERS message has been sent to the reporting system, and this is saved as part of the patient's medical record.

## *Setting up PHINMS and sending VAERS messages.*

Once VAEs have been confirmed, or for category 3 VAEs older than a week, VAERS reports may be generated for transfer to the VAERS messaging system.

VAERS messages are generated via the command:

[$ESPHOME]/bin/esp vaers_hl7

This command has no options. VAERS message files are written to a directory location based on the ESP installation configuration.

PHINMS installation and operation is documented extensively elsewhere: https://www.cdc.gov/phin/tools/phinms/installation.html.

# III. Technical Guide for ESP system managers

This technical guide provides a "How-To" for obtaining, installing, configuring, implementing and maintaining ESP-VAERS. It is intended for a technical audience. Before using this guide, you should read Section Three, Part II above, "Optimal Installation of ESP-VAERS". The Optimal Installation write-up is intended for both a technical and less-technical audience; it provides a narrative context for the steps outlined below. Many parts of this guide are maintained elsewhere and are simply provided as web links in the text below. Web resources for ESP can be found here: https://www.esphealth.org/

Resources specific to ESP-VAERS can be found here: https://espnet.atlassian.net/wiki/x/AYCXM

## *ESP-VAERS Installation and configuration*

### Determine the server hardware requirements for ESP

Storage capacity requirements heuristic:

> Count of active patients * number of years * 0.00025 = Gigabytes of storage required

For example, a system with 300,000 patients and 3 years of data would require:

300,000*3*0.00025=225Gb storage

Memory (RAM) requirements heuristic:

> 2 * ((Storage capacity requirements / 2) / 50) = Gigabytes of memory required

For example, a system that requires 225GB of storage would require:

2 * ((225 / 2) /50) = 4.5Gb memory

You would want to round up as necessary.

CPU requirements heuristic:

2 + CEILING(number of new encounter records per day / 40,000) - 1 + CEILING(number of new lab records per day / 40,000) -1 = Number of CPUs

For example, a system that processes 20,000 encounters and 50,000 labs a day would require:

2 + CEILING(20000/40000) -1 + CEILING(50000/40000)-1 = 3 CPUs

These are rough estimates. If you are able to dynamically allocate resources to your ESP server (this is straight-forward for many virtual hosting environments), it is of course acceptable to start with fewer resources and allocated additional resources as required.

## Install ESP

To complete an ESP installation, follow the instructions in "HowTo - Install and Configure ESP on Ubuntu 18.04". (This link will always provide the most up-to-date version of these instructions: https://espnet.atlassian.net/wiki/x/H4CPAg).

Step 14: Setting Up Basic Disease Detection can be ignored, unless you will be using ESP for disease detection as well as VAERS reporting.

There are some ESP-VAERS specific configuration requirements when editing application.ini under the reporting section. Instructions for setting these values are provided in the default INI:

```
phinms_server = 'your_phinms_server'
phinms_username = 'your_phinms_sftp_username'
phinms_path = 'your_phinms_path'
# Path to vaers line listing reports (PHI and no-PHI)
# Must exist and must have esp read-write access
# Default value is ESP home directory, fine for test and dev
# Alternative below is suggestion for production implementation
vaers_linelist_path = '/home/esp/'
# Is sending AE reports via PHIN-MS enabled?
# set to True to use this feature
vaers_send_report = 'False'
# Is the EMR updated via the transcription interface when a VAERS
report is transmitted to CDC?
vaers_update_emr = 'True'
# Login details for SFTP server where transcription interface messages
will be sent
update_emr_server = 'your_update_sftp_server'
update_emr_username = 'your_update_sftp_username'
update_emr_path = 'your_update_sftp_path'
# If set, send "suspected vaccine AE" message to the specified provider
instead of the normal reviewer
# This must be a valid "Natural_Key" value from the EMR_PROVIDER table,
with corresponding data to identify the override clinician reviewer
vaers_override_clinician_reviewer = ''
# The VAERS autosender is the clinician identified by the site as the
point of contact for auto-sent vaers reports.
vaers_autosender = ''
```

## Install PHINMS

PHINMS is the VAERS message transfer software that provides secure authenticated and authorized transfer of VAERS messages to the CDC VAERS reporting system. This is installed on a MS Windows system and does not require anything more than a single CPU and sufficient storage for the OS and a

relatively small number of VAERS message files: An additional 5Gb of storage beyond the needs of the OS will be more than sufficient.

PHINMS installation and operation is documented extensively elsewhere: https://www.cdc.gov/phin/tools/phinms/installation.html.

PHINMS installation is likely to require Network support to ensure that routes through the firewall are opened for PHINMS traffic.

## Set up the data feed from the ETL process, configure daily data load and VAE detection process

The data feed is mentioned briefly in the Installation how-to. Section Three, Part II, "Optimal Installation of ESP VAERS" above provides guidance on how to set up the ETL system for the data feed. With the ETL developed and testing, implementation is as follows.

1. Determine the amount of historical data required for the system. This is typically a minimum of two years. Run the ETL process to generate the historical data files in the ESP incoming data folder, as specified during the ESP system installation and configuration.
2. Execute the following ESP command from the Linux shell:
   - $> [$ESPHOME]/bin/esp load_epic

   The command should be run from a detachable process, such a tmux or nohup, as it can take considerable time to complete. This can be several days to several weeks depending on the amount of historic data being loaded. The command name "load_epic" is vestigial – ESP was originally developed to work with an Epic system. The command will load ETL data from any EHR system.
3. Monitor the historic load. When it is complete, configure the lab test and vaccine mapping data. From the Linux command line, run the command:

```
[$ESPHOME]/bin/esp concordance
```

   Login to the ESP administrative interface you set up during the ESP installation. Navigate to Admin>Unmapped Lab Tests Report. Use the lab mapping interface to map local lab codes to the required ESP lab concepts. When done, navigate to VAERS>Vaccine Mapping. Map the local immunization names to the CDC standard names. This is described in some detail in the "Optimal Installation of ESP VAERS"above.

4. Prepare a shell script that will run the ETL process on a regular basis and then run the VAE detection and messaging processes. Here is an example:

```
#!/bin/bash

ESP_DIR=/srv/esp
LOGFILE=$ESP_DIR/log/daily_cron.log.$$
VAERS_ESP=$ESP_DIR/vaers/test/bin/esp

exec 5>&1 6>&2 >>$LOGFILE 2>&1

. $ESP_DIR/vaers/test/bin/activate
export PIP_RESPECT_VIRTUALENV=true
export PIP_REQUIRE_VIRTUALENV=true
python $ESP_DIR/scripts/esp_etl.py -i $ESP_DIR/scripts/esp_vaers.ini
```

```
#The esp_etl.py script runs the ELR process.  Default mode is to
#  generate data collected from the prior day and save to the ESP
#  data incoming folder.
deactivate

($VAERS_ESP load_epic -l --reload && \
 $VAERS_ESP immunization_checker && \
 $VAERS_ESP vaers -a && \
 $VAERS_ESP vaers_hl7 && \
 $VAERS_ESP status_report --send-mail)

exec 1>&5 2>&6
```

Besides load_epic, the ESP commands include above are:

- immunization_checker updates immunization records to exclude non-immunization data (tb tine test, gamma globulin, etc.)
- vaers run the VAE detection process
- vaers_hl7 generates the various hl7 message files and transfers them as appropriate
- status_report generates an email describing the outcome of the various commands.

Add this shell script to the ESP users crontab.  It should be run daily at off-hours.

## ESP-VAERS ongoing operations

Daily operations include: review the daily status report email.

Weekly operations include: (all these activities can be monitored via automated alerting systems.)

- review the ESP and PHINMS system and auth logs for any suspicious events
- check and confirm that ESP backups have been running
- run the ESP concordance command, and check for unmapped labs and vaccines
- check the unused storage capacity of the ESP and PHINMS systems and ensure there is sufficient available storage for ongoing operations
- check the PHINMS administrative interface and confirm that any new messages have be routed and received.

On an as needed basis: when unmapped labs or vaccines are encountered, use the administrative mapping interfaces to map as appropriate.

There should be a schedule for performing system updates to apply security patches, and for testing backups.

The PHINMS system relies on a certificate pack with an expiration setting.  New certificates must be requested and installed, typically on a once-yearly basis.

# Section Four: Implementation at Cambridge Health Alliance and MetroHealth

This section discusses the implementation of the updated ESP VAERS algorithm at two health care systems, Cambridge Health Alliance based in Cambridge, MA and MetroHealth based in Cleveland, OH.

## I. Implementing, testing, and refining ESP-VAERS at CHA and MetroHealth

### *Overview*

ESP-VAERS is a software system for detecting vaccine adverse events (VAEs) and reporting those events to public health authorities using the VAERS reporting structure.

ESP VAERS is now installed at two sites: MetroHealth in Cleveland, OH, and Cambridge Health Alliance (CHA) in MA. Implementation, testing and refining progress at these two sites is reported below.

### *MetroHealth*

#### Implementation:

Implementation at MetroHealth is complete:

- installation of the ESP VAERS system
- installation and configuration of the Epic Clarity data interface to ESP including nightly data loading
- the installation of the PHINMS system
- the generation and internal review of all types of VAERS cases
- the generation of all types of HL7 messages including the MDM-T02 interface message and the VAERS-2 messages.
- Implementation of the MDM T02 interface
- Installation and implementation of the PHINMS messaging system

#### Testing

**The Epic Clarity Data interface to ESP**: We have tested and confirmed via independent SQL queries that the Epic Clarity data interface is working correctly. Daily logs and status reports are generated automatically and we have reviewed these and noted no errors in data processing.

**The PHINMS system**: We have completed configuration and preliminary testing of the new version of the PHINMS system.

**Generation and review of VAERS cases**: We have completed a number of cycles of review of the VAERS cases using the non-PHI listing available from ESP. This uncovered several issues for correction:

- A number of injectable medicines are including in the MetroHealth immunization data, which are not vaccines. This include gamma globulin and TB tine test. These "immunization" items are marked as "not an immunization" so they don't continue to generate AEs.
- Several specific rules were reviewed in light of the number of messages they create. Several were modified to change their status as "automatically" sent.
- A number of rule bugs and transcription errors were found and corrected.

**Generation for HL7 messages**. Testing of messaging occurred in conjunction with the MetroHealth project team for the MDM T02 messages, and with GDIT staff to test the VAERS 2 messages.

### Refining

Refinements due to testing and discovery of system issues were limited to

- two updates to the status values for AEs.
    - Syncope – change to category 2
    - Fever, unspecified – change to category 2
- Non vaccine identifications:
    - ALBUMIN
    - FLEBOGAMMA
    - DEPO PROVERA
    - RHO(D) IMMUNE GLOBULIN (IV OR IM) (CVX=156)
    - RHO(D) IMMUNE GLOBULIN (IM) (CVX=157)
    - IMMUNE GLOBULIN (IG), INTRAMUSCULAR (CVX=86)
    - RABIES IMMUNE GLOBULIN (RIG) (CVX=34)
    - RSV-MAB (SYNAGIS) (CVX=93)
    - IVIG (GAMMASTAN) (CVX=87)
    - TST-PPD, INTRADERMAL (PPD) (CVX=96)
- Rule bug and transcription errors included:
    - Some AE categories depend on which Vaccine they follow. This was not working correctly, but is now fixed.
    - Some lab AEs were hard-coded into the software from the prior pilot. These have been removed.
    - Cut-off values were mis-transcribed for a number of AEs. This has been corrected.
    - Day zero was being included in AEs that were not supposed to look for events on day zero. This is fixed.
    - The order of precedence for action category had not be set correctly. This is fixed.
    - Minimum age at vaccination was working correctly for lab AEs, but not diagnosis AEs. This is fixed.

## *CHA*

### Implementation:

Implementation at CHA is complete through:

- installation of the ESP VAERS system
- installation and configuration of the Epic Clarity data interface to ESP including nightly data loading

- the installation of the PHINMS system
- the generation and internal review of all types of VAERS cases
- the generation of all types of HL7 messages including the MDM-T02 interface message and the VAERS-2 messages.
- Implementation of the MDM T02 interface
- Installation of the PHINMS messaging system
- Implementation steps not completed: The PHINMS messaging system is installed but not tested at CHA

### Testing

**The Epic Clarity Data interface to ESP**: We have tested and confirmed via independent SQL queries that the Epic Clarity data interface is working correctly. Daily logs and status reports are generated automatically and we have reviewed these and noted no errors in data processing.

**The PHINMS system**: We have completed configuration and preliminary testing of the new version of the PHINMS system.

**Generation and review of VAERS cases**: We have completed one cycle of review of the VAERS cases. No significant issues have been uncovered.

**Generation of HL7 messages**. Testing of messaging occurred in conjunction with the CHA project team for the MDM T02 messages.

### Refining

No system refinements have been needed based on CHA evidence.

# II. Cost and Effort for Implementation of ESP-VAERS

## *Overview*

ESP-VAERS is a software system for detecting vaccine adverse events (VAEs) and reporting those events to public health authorities using the VAERS reporting structure.

ESP VAERS is now installed at two sites: MetroHealth in Cleveland, OH, and Cambridge Health Alliance (CHA) in MA. Implementation at CHA was performed after Implementation and testing at MetroHealth. The staff involved in the system implementation were provided all documentation developed as part of this project and were provided additional instructions as documented below. Hours and materials used were tracked and are reported below.

## *ESP setup:*

### Virtual Server creation

CHA set up a virtual Linux server for a new ESP installation. Basic system specifications are:

- 850GB of disk storage
- 8GB of memory
- 2 CPUs

| Cost item | Cost |
|---|---|
| Initial virtualization system setup costs will depend on the host system features but shouldn't exceed $2500 for a system of this size. | $2500 |

The remaining categories are for staff hours.

## Installation

| Task and staff expertise | Hours |
|---|---|
| CHA Linux server administration staff installed the Linux OS. Some network configuration issues took some time for network engineers to troubleshoot in order to establish VPN access. | 8 hours |
| CII staff installed the ESP software and software dependencies. Skills include Linux system administration, PostgresSQLdatabase administration, and apache web server administration. | 16 hours |

## Integration of EHR data

| Task and staff expertise | Hours |
|---|---|
| CII consultant migrated the Epic Clarity data system to the new ESP server. Skills required include PostgreSQL database admin skills and knowledge of the Epic Clarity data extraction system and file structure for ESP. | 45 hours |

## Configuring ESP data and running VAE detection

| Task and staff expertise | Hours |
|---|---|
| Setting up the configuration data. Using the lab mapping interface, using the vaccine mapping interface, developing custom reports to confirm configuration sufficiency. Skills required include PostgreSQL database administration skills, as well as ESP software system knowledge and expertise. | 40 hours |
| Running the VAE detection process, review results, debug data configuration issues. Skills required include PostgreSQL database administration skills, as well as ESP software system knowledge and expertise. | 15 hours |

## Configuring reporting interfaces

| Task and staff expertise | Hours |
|---|---|
| CII staff created test patient data and test messages for the interfaces. Provided test messages. Set up the automated process to generate and move messages to a shared folder. The ESP VAE review web pages were set up and tested. Generating listing of links for CHA clinical review. Skills required include PostgreSQL database administration skills, ESP software system knowledge and expertise, HL7 standards knowledge and expertise. | 30 hours |
| CHA staff designed the Epic system interface, then developed and implemented it. Skills required include knowledge of the Epic interface system. | 20 hours |
| CHA clinical staff reviewed the first set of VAERS AEs | 5 hours |

## Project management overhead

| Task and staff expertise | Hours |
|---|---|
| The current project involved project management for both CHA and for CII staff. | 20 hours |

## Configuring reporting interfaces

| Task and staff expertise | Hours |
|---|---|
| Testing and setup of HL7 interfaces must be completed. This will require about equal amounts of time from CII and CHA | 40 hours |
| Clinical review of VAE content, with cycles for feedback and updates. | 20 hours |

## Roll-out for general use

| Task and staff expertise | Hours |
|---|---|
| Presentation of system to clinical staff. Training, and support. | 20 hours |
| Gathering of feedback and managing updates to system. | 20 hours |

## Project management overhead

| Task and staff expertise | Hours |
|---|---|
| Ongoing project supervision and support | 20 hours |

# Section Five: Recommendations, and Next Steps

EHR systems offer an opportunity to improve vaccine adverse event detection and reporting by automatically scanning EHR data for potential adverse events and eliciting clinical impressions and comments from providers. Because these systems are widespread, a generalizable and portable automated adverse event surveillance approach based on existing EHR systems offers the opportunity to quickly ramp up adverse event surveillance and provide clinically rich reports at relatively low marginal cost. This task order expanded the ESP-VAERS pilot system into a comprehensive, prospective, EHR-based VAE detection system that is scalable and reproducible in other ESP installations. We also developed both technical documentation and a clinical users' guide. In testing the installation process, we were able to quantify the effort and cost of installation as well as additional work required by individual sites.

Key to the success of any expansion efforts will be the establishment of the necessary interoperability. The EPIC EHR systems we were working with for this project did have sufficient capabilities to enable the necessary interoperability, but to some extent we were required to customize these interfaces, and they were based on an older interoperability standard. There are new interoperability standards available, such as HL7 FHIR, HL7 C-CDA, and Direct messaging, which would streamline the installation process. Unfortunately, the EHR vendor was not ready to support them, or there was insufficient support available for adopting them at the data partner sites and the EHR vendor would not make supporting documentation available to a third-party contractor. The ESP VAERS installation and configuration process will remain somewhat complex until the uniform adaptation and support of newer interoperability standards can be achieved.

Clinicians viewing lists of cases detected by the system regarded ESP VAERS in a net-positive light, commenting on the ease with which AEs could be reported to VAERS compared with the previous manual procedures. However, during the testing process, clinicians at both participating sites expressed concern over the volume of identified potential AEs and the amount of time this would require for clinical review. There is an inherent tension between two objectives of the system—on the one hand, to detect unsuspected vaccine adverse events and, on the other, to avoid overwhelming busy clinicians with false-positive notifications. We conducted several cycles of testing and algorithm-adjustment to reduce false positives, but more could be done in this regard without unduly harming sensitivity. Alternatively, the system could be configured such that notifications of possible AEs go to a clinical informatics team for screening before going to clinicians. This would require a modification to the ESP interface.

In conclusion, we recommend that ESP sites adopt the ESP VAERS system in order to facilitate reporting of adverse events to VAERS. It may be appropriate to roll the system out in stages at a site, in order to build support and familiarity. For example, it should be possible to begin production use with category 1 and 3 AEs, while review of category 2 AEs continues and algorithms are further refined so as to reduce the volume of false positive messages.

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