Vaccine Adverse Event Reporting System (VAERS)
Standard Operating Procedures for COVID-19
(as of 29 January 2021)

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Centers for Disease Control and Prevention
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Disclaimer

This document is a draft planning document for internal use by the Centers for Disease Control and Prevention, with collaborating contractors. Numerous aspects (including but not limited to specific adverse events to be monitored, timeframes for report processing, data elements to be reported, and data analysis) are dynamic and subject to change without notice.

Executive Summary

CDC and FDA will perform routine VAERS surveillance to identify potential new safety concerns for COVID-19 vaccines. This surveillance will include generating tables summarizing automated data from fields on the VAERS form for persons who received COVID-19 vaccines (e.g., age of vaccinee, COVID-19 vaccine type, adverse event).

Enhanced surveillance (i.e., automated data and clinical review) will be implemented after reports of the following adverse events of special interest (AESIs): death, COVID-19 disease, Guillain-Barre Syndrome (GBS), seizure, stroke, narcolepsy/cataplexy, anaphylaxis, vaccination during pregnancy, acute myocardial infarction, myopericarditis, coagulopathy (including thrombocytopenia, disseminated intravascular coagulopathy [DIC], and deep venous thrombosis [DVT]), Kawasaki’s disease, multisystemic inflammatory syndrome in children (MIS-C), multisystemic inflammatory syndrome in adults (MIS-A), transverse myelitis, Bells Palsy, and appendicitis. Abstraction of medical records associated with reports of these conditions will be performed using an internal CDC website (i.e., behind CDC’s firewall). Data entered into the abstraction website will be stored on CDC servers and used to populate data tables, from which automated reports will be generated and analyzed on a periodic basis. Enhanced surveillance (i.e., automated data and clinical review) will also be implemented after reports of pregnancy complications, stillbirths, congenital anomalies, and vaccination errors. However, abstraction of medical records after these conditions will be performed on an as needed basis. These efforts will assist in CDC’s efforts to monitor the safety of COVID-19 vaccines.

1.0 Introduction

The Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA) use the Vaccine Adverse Event Reporting System (VAERS) as a front-line system to monitor the safety of vaccines licensed for use in the United States. In addition to conducting general surveillance, each year VAERS activities focus on new formulations and types of vaccine, new populations who may be vaccinated because of changes in licensed indications or Advisory Committee on Immunization Practices (ACIP) recommendations, and any new safety concerns identified. This Standard Operating Procedures (SOP) document describes the following activities for COVID-19 vaccine safety monitoring:
1) Approach for CDC-FDA VAERS monitoring
2) Plans for coordinating with FDA VAERS staff, particularly around data mining and VAERS data interpretation
3) Overall COVID-19 vaccine safety monitoring coordination for The VAERS Team within CDC’s Immunization Safety Office (ISO)

This SOP does not describe details of FDA surveillance procedures for COVID-19 vaccine safety or CDC surveillance or evaluation of COVID-19 vaccines in systems other than VAERS.

**Vaccines to monitor:**

Pfizer/BioNTech (trade name TBD)
Moderna (trade name TBD)
Other COVID-19 vaccines as they are authorized or licensed for use in the United States

For each adverse event of special interest (AESI), the rationale for enhanced monitoring, case definitions (if available), and references are provided in Table 1:
Table 1: Adverse Events of Special Interest, with case definitions (if available)

<table>
<thead>
<tr>
<th>Adverse Event of Special Interest</th>
<th>Rationale for enhanced monitoring</th>
<th>Case definition (if available)*</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction (AMI)</td>
<td>• Has been reported as a presenting sign of COVID-19 disease and could indicate VAED</td>
<td>• International consensus case definition available at <a href="https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000000617">https://www.ahajournals.org/doi/epub/10.1161/CIR.0000000000000617</a></td>
<td><a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7179991/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7179991/</a></td>
</tr>
</tbody>
</table>
| Appendicitis                      | • Can be a medical emergency  
<table>
<thead>
<tr>
<th>Condition</th>
<th>Details</th>
<th>Brighton Collaboration case definition available at <a href="https://www.sciencedirect.com/science/article/pii/S0264410X16303139?via%3Dihub">source</a></th>
<th><a href="https://www.fda.gov/media/144245/download">source</a></th>
</tr>
</thead>
</table>
| Bell’s Palsy  | • Can affect daily functions  
• An imbalance between vaccinees and placebo was noted in clinical trials with the Pfizer/BioNTech COVID-19 vaccine                                                                 |                                                                                                                |                                                                                                                |
<p>| Coagulopathy  | • Thrombocytopenia, DIC, and DVT have all been reported as part of COVID-19 disease and could indicate VAED                                                                                          | • Brighton Collaboration case definition for thrombocytopenia available at <a href="https://www.sciencedirect.com/science/article/pii/S0264410X0700268X?via%3Dihub">source</a> | • <a href="https://www.thelancet.com/journal/s/lanhae/article/PIIS2352-3026(20)30151-4/fulltext">source</a>                   |
|               |                                                                                                                                                                                                                                                                  | • Scientific Standardization Committee of the International Society of Thrombosis and Haemostasis scoring for DIC available at <a href="https://www.tandfonline.com/doi/full/10.1080/17474086.2018.1500173">source</a> |                                                                                                                |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th>• Modified Wells’ score (widely acknowledged standard for DVT/PE) available at <a href="https://academic.oup.com/clinchem/article/57/9/1256/5620938">source</a></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Severe COVID-19 disease can be an indication of vaccine-enhanced disease (VAED)</td>
<td>Pre-publication Brighton case definition for VAED available at <a href="https://brightoncollaboration.us/vaed/">https://brightoncollaboration.us/vaed/</a></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>Public interest in deaths after vaccination, especially in children (&lt;18 years of age) and recipients of newly licensed vaccines</td>
<td>Report of death certificate or autopsy report</td>
<td><a href="https://academic.oup.com/cid/article/61/6/980/451431">https://academic.oup.com/cid/article/61/6/980/451431</a></td>
</tr>
<tr>
<td>Kawasaki’s disease</td>
<td>Could be confused with MIS-C, which could be an indication of VAED</td>
<td>CDC case definition available at <a href="https://www.cdc.gov/kawasaki/case-definition.html">https://www.cdc.gov/kawasaki/case-definition.html</a></td>
<td><a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm">https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm</a></td>
</tr>
<tr>
<td>Condition</td>
<td>Description</td>
<td>Case Definition</td>
<td>URL</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Children (MIS-C)</td>
<td>• Could be an indication of VAED</td>
<td>• Interim case definition available at <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm">https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm</a></td>
<td>• <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm">https://www.cdc.gov/mmwr/volumes/69/wr/mm6932e2.htm</a></td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Adults (MIS-A)</td>
<td>• Could be an indication of VAED</td>
<td>• Interim case definition available at <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm">https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm</a></td>
<td>• <a href="https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm">https://www.cdc.gov/mmwr/volumes/69/wr/mm6940e1.htm</a></td>
</tr>
<tr>
<td>Myopericarditis</td>
<td>• Has been reported as part of COVID-19 disease pathology and could indicate VAED</td>
<td>• Joint Smallpox Vaccine Safety Working Group of the Advisory Committee on Immunization Practices (ACIP) and the Armed Forces Epidemiology Board (AFEB) case definition available at <a href="https://www.cdc.gov/mmwr/PDF/wk/mm5221.pdf">https://www.cdc.gov/mmwr/PDF/wk/mm5221.pdf</a> (p. 494)</td>
<td>• <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7199677/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7199677/</a></td>
</tr>
<tr>
<td>Narcolepsy/Cataplexy</td>
<td>• Has been alleged as an adverse event associated with some adjuvanted vaccines; some COVID-19 vaccines might employ adjuvants</td>
<td>• Brighton Collaboration case definition available at <a href="https://www.sciencedirect.com/science/article/pii/S0264410X12017811?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S0264410X12017811?via%3Dihub</a></td>
<td>• <a href="https://www.cdc.gov/vaccinesafety/concerns/history/narcolepsy-flu.html">https://www.cdc.gov/vaccinesafety/concerns/history/narcolepsy-flu.html</a></td>
</tr>
<tr>
<td>Vaccination during pregnancy</td>
<td>• Public interest and concern over adverse pregnancy events and fetal outcomes</td>
<td>• Report of vaccinated person being pregnant (during or after vaccination)</td>
<td>• <a href="http://www.sciencedirect.com/science/article/pii/S0002937810011051">http://www.sciencedirect.com/science/article/pii/S0002937810011051</a></td>
</tr>
<tr>
<td>Stroke</td>
<td>• Has been reported with COVID-19 disease and might therefore be an indication of VAED</td>
<td>• American Heart Association/American Stroke Association consensus definition available at <a href="https://www.ahajournals.org/doi/epub/10.1161/STR.0b013e318296aeca">https://www.ahajournals.org/doi/epub/10.1161/STR.0b013e318296aeca</a></td>
<td>• <a href="https://jamanetwork.com/journals/jamaneurology/fullarticle/2768098">https://jamanetwork.com/journals/jamaneurology/fullarticle/2768098</a></td>
</tr>
</tbody>
</table>


* Draft case definitions for some conditions under development by the Brighton Collaboration.
In addition, selected AESIs will be monitored for awareness but not abstracted. These AESIs and available case definitions are listed in Table 2:

**Table 2: AESIs to monitor (but not abstract), with definitions and available case definitions**

<table>
<thead>
<tr>
<th>AESIs to monitor but not abstract*</th>
<th>Reference definitions and available case definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Respiratory Distress Syndrome (ARDS)</td>
<td><a href="https://www.thoracic.org/professionals/career-development/residents-medical-students/ats-reading-list/adult/ards.php">https://www.thoracic.org/professionals/career-development/residents-medical-students/ats-reading-list/adult/ards.php</a></td>
</tr>
<tr>
<td>Autoimmune disorders</td>
<td>Appendix 4.6 lists specific disorders to monitor</td>
</tr>
<tr>
<td>Other clinically serious neurologic AEs:</td>
<td></td>
</tr>
<tr>
<td>Multiple sclerosis (MS)</td>
<td>NIH (last updated 5 Aug 2019)</td>
</tr>
<tr>
<td>Optic neuritis (ON)</td>
<td>Guier et al (last updated 10 Aug 2020)</td>
</tr>
<tr>
<td>Chronic inflammatory demyelinating polyneuropathy (CIDP)</td>
<td>Gogia et al (last updated 9 Oct 2020)</td>
</tr>
<tr>
<td>Encephalitis</td>
<td>Sejvar et al (2007)</td>
</tr>
<tr>
<td>Myelitis</td>
<td>Sejvar et al (2007)</td>
</tr>
<tr>
<td>Encephalomyelitis</td>
<td>Merriam Webster (last accessed 7 Nov 2020)</td>
</tr>
<tr>
<td>Meningoencephalitis</td>
<td>Merriam-Webster (last accessed 7 Nov 2020)</td>
</tr>
<tr>
<td>Meningitis</td>
<td>CDC (last updated 21 Jan 2020)</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>NIH (last updated 27 Mar 2019)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>Johns Hopkins Medicine Dept of Neurology and Neurosurgery (last accessed 7 Nov 2020)</td>
</tr>
<tr>
<td>Non-anaphylactic allergic reactions</td>
<td>Varies with specific symptom; see Appendix 4.6</td>
</tr>
<tr>
<td>Vaccination errors</td>
<td>See Section 4.4</td>
</tr>
</tbody>
</table>

* Will be specified by a list of MedDRA PTs (see Appendix 4.6, p. 27)
2.0 Overview of VAERS Surveillance Activities

The specific tasks and frequency of these tasks for surveillance will be adjusted to meet public health needs, with consideration of staff time and resources. For example, in the event of a significant increase in the number of adverse events (AEs) reported to VAERS that warrant clinical review, additional ISO staff will be assigned to perform reviews. An algorithm of the process to monitor vaccine AEs is shown in Appendix 4.1.

CDC will perform clinical reviews for AESIs listed in Table 1. Results from automated data assessment will identify additional conditions potentially warranting further clinical review.

CDC will perform Proportional Reporting Ratio (PRR) analysis (see section 2.3.1, p. 14), excluding laboratory results, to identify AEs that are disproportionately reported relative to other AEs.

FDA routinely reviews all serious* and other medically important condition (OMIC) reports daily and performs data mining.

* Serious reports are defined by Code of Federal Regulations (FDA CFR 1997) if at least one of the following was reported: death, hospitalization, life-threatening illness, permanent disability and/or prolonged hospitalization, and congenital anomaly.

Summaries (or other deliverables, as needed) will be based on data processing, coding and follow-up, automated data, and clinical review, as well as field investigations as appropriate. COVID-19 vaccine safety coordination meetings among ISO team members and FDA will be scheduled weekly (or more frequently, as needed) to discuss results of the automated data and (if indicated) clinical review.

2.1 Data processing and coding and follow-up

The CDC contractor for VAERS receives, processes, and manages VAERS reports. The contractor receives reports online and by mail, fax, or telephone. Using standard procedures, contractor staff will review each U.S. report following COVID-19 vaccines and assign standard codes to each reported sign, symptom, and diagnosis using Medical Dictionary for Regulatory Activities terminology [10]. The staff will enter all MedDRA terms and other information from each VAERS report form into a computerized database. Vaccine type codes in the VAERS database are shown in Appendix 4.2.

Trained contractor staff will request additional information including hospital records and autopsy reports when appropriate (Appendices 4.3 and 4.4). Medical records are routinely requested for all serious reports, including deaths.
Contractor clinical staff will summarize data and assign additional MedDRA codes for symptoms, signs, and diagnoses identified from the requested additional information. They will then add these additional codes to the data originally entered into the database for the specific VAERS report.

Table 3 lists the AESIs for which medical records will be requested and reviewed. Manual review of serious reports is routinely performed by FDA (a more in-depth clinical review will be performed by CDC as indicated).

**Table 3: AESIs for which medical records will be requested and reviewed**

<table>
<thead>
<tr>
<th>AESI</th>
<th>Medical and vaccination records obtained by contractor</th>
<th>Clinical review by CDC*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Myocardial Infarction (AMI)</td>
<td>All reports (including manufacturer reports)</td>
<td>All reports (including manufacturer reports)</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appendicitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bell’s Palsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coagulopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>COVID-19 disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
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<tr>
<td>GBS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kawasaki’s disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Children (MIS-C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Adults (MIS-A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myopericarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Narcolepsy/ Cataplexy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Death Serious</td>
<td>All reports (including manufacturer reports)</td>
<td>As needed</td>
</tr>
<tr>
<td>Pregnancy and Prespecified Conditions</td>
<td>All reports (including manufacturer reports)</td>
<td>All reports (including manufacturer reports)</td>
</tr>
<tr>
<td>Seizure/Convulsion</td>
<td>All reports (including manufacturer reports)</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>All reports (including manufacturer reports)</td>
<td></td>
</tr>
<tr>
<td>Transverse myelitis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes review of VAERS form and available medical records by primary ISO staff. Initial review will be performed and documented within CDC internal COVID-19 medical abstraction website. More detailed review will be performed as needed.

All COVID-19 vaccine reports will be entered into the VAERS database and assigned a unique identifying (ID) VAERS number during normal business hours. The contractor will send daily e-mail alerts (Daily Priority Reports) to CDC/FDA with a list of VAERS ID numbers for all serious and non-serious reports of adverse events of special interest (AESIs) after COVID-19 vaccines. Reports of AESIs will be identified in the Daily Priority Reports and in a daily table (to be constructed, as described in section 2.4).
Appendix 4.3 provides details on how the prespecified conditions will be identified by the contractor.

2.1.1 Jurisdiction-specific data in VAERS reports after COVID-19 vaccines

ISO will make selected VAERS data available to Vaccine Safety Coordinators (VSCs) in requesting jurisdictions on a weekly basis via Epi-X. The selected data will include the following:

- Unredacted initial report data for reports of residents* within the VSC’s jurisdiction (i.e., local, state, or territorial health department) who experience AEs after receiving COVID-19 vaccines; report data of state or territorial jurisdictions will include unredacted report data of local jurisdictions within that state or territory. These unredacted data will not be accessible by other jurisdictions. These unredacted data will be refreshed on Epi-X weekly.

- Cumulative counts of VAERS reports after vaccination with COVID-19 vaccines, cross-tabulated in the following manner:
  - Rows listing each jurisdiction by total cumulative counts, stratified by seriousness (non-serious, serious non-death, and death)
  - Rows listing selected AESIs by total cumulative counts among all jurisdictions combined (to avoid small cell counts and potential unintended identification of affected persons), stratified by age group, in years (0–4, 5–17, 18–49, 50–64, 65–74, 75–84, ≥85, not reported, and total)
  - These cumulative counts will include all reports to date and will be refreshed on Epi-X weekly.

* Residency will be assigned in the following hierarchy: 1) state or territory of reported patient residency; if not available, 2) state or territory where COVID-19 vaccine was administered; if not available, 3) state or territory of person making the VAERS report; absent these data, residency will be decided per standard contractor business rules. Residence within a local jurisdiction will be determined in similar fashion, based upon city and ZIP code information comprising the local jurisdiction.

Weekly redacted data will be made available publicly via CDC WONDER (https://wonder.cdc.gov), HHS (https://vaers.hhs.gov), and Epi-X on the same date. Case counts on Epi-X and public websites should be equal; any differences in case counts may result from data processing (e.g., data cleaning) and will be reconciled as the data mature.

2.1.2 Vaccination Errors

Reports of vaccination errors will be identified by conducting an automated search using MedDRA preferred terms (PTs) and organized into vaccination error groups shown in Appendix 4.5.
• Some reports that use the MedDRA PT codes in Appendix 4.5 do not always document a vaccination error.
• If ACIP does not recommend vaccination with COVID-19 vaccines during pregnancy, reports where vaccination was contraindicated due to pregnancy, but still performed, will be captured under “contraindication to vaccination.” A previous review of reports coded as pregnancies revealed that for many reports, no vaccination error occurred. The PTs “exposure during pregnancy,” “fetal exposure during pregnancy,” and “maternal exposure during pregnancy” are not included in Appendix 4.5.

Vaccination errors will be summarized by vaccination error group based on automated data and include any error involving COVID-19 vaccines and any other coadministered vaccine(s). Clinical review of VAERS reports will be performed for vaccination error reports that are classified as serious (see p.11), and vaccination error PTs with elevated PRRs.

The data from this automated search will be provided as a weekly automated table that will be reviewed as described below in sections 2.4 and 3.0.

2.2 Automated tables:

A series of tables will be generated using the VAERS automated data.

2.2.1 VAERS daily table

A version of the cumulative count tables from section 2.1.1 will be refreshed daily for internal use (i.e., inside ISO). This version will be generated independently of the jurisdictional Epi-X/CDC WONDER data and will be almost identical in appearance and content, except that the data will be presented in aggregate and not at the local level. Because this internal version will use supplemental data not for public release, counts may vary from counts on Epi-X/CDC WONDER.

2.2.2 VAERS weekly tables

Data tables demonstrating frequency, reporting ratios and general characteristics will be generated automatically using pre-defined variables populated by VAERS data. The data in these tables will be summarized by whether the AE is classified as serious and by age group and sex, and will be presented in weekly and cumulative formats. Note that during the time period when demand for COVID-19 vaccines exceeds supply, the Advisory Committee on Immunization Practices (ACIP) recommended that 1) health care personnel (HCP) and 2) residents of long-term care facilities (LTCFs) be offered COVID-19 vaccination first. Appendix 1 explains how LTCF populations and HCP can be identified in VAERS. VAERS is collaborating with the National Healthcare Safety Network (NHSN) to stimulate VAERS reporting from HCPs and LTCFs. Appendix 2 explains how the contribution of NHSN-stimulated reporting to VAERS will be assessed.

The following weekly tables will be available every Monday (data as of the previous Friday):

Table 1. All reports following COVID-19 vaccines by severity and selected manufacturer/brand name

**AESI tables**

Table 2. Top 25 most frequently reported AEs

Table 3. Reports of the following AESIs after vaccination with COVID-19 vaccines, stratified by age group (ages <18 years, 18–49 years, 50–64 years, 75–84, years, 85+ years, unreported):

- Death
- COVID-19 Disease
- Guillain Barre Syndrome (GBS)
- Seizure
- Stroke
- Narcolepsy/Cataplexy
- Anaphylaxis
- Acute Myocardial Infarction
- Myopericarditis
- Coagulopathy
- Transverse Myelitis
- Multisystemic Inflammatory Syndrom in Adults (MIS-A)

Table 4. Reporting trends of the following AESIs after vaccination with COVID-19 vaccines, stratified by age group (<12 months, 12–35 months, 36–59 months, 5–11 years, 12–20 years, >20 years, unreported):

- Kawasaki Disease
- Multisystemic Inflammatory Syndrom in Children (MIS-C)

Table 5. Reporting trends of VACCINATION DURING PREGNANCY following vaccination with COVID-19 vaccines stratified by age group (ages <18 years, 18–29 years, 30–39 years, 40–49 years, ≥50 years, unreported)

Table 6. Reporting trends of Autoimmune Disorders by System Organ Class following vaccination with COVID-19 vaccines by age group (ages <18 years, 18–49 years, 50–64 years, 65–74 years, 75+ years, unreported)

Table 7. Reporting trends of AESIs to monitor but not abstract (Table 2, p. 8), following vaccination with COVID-19 vaccines by age group (ages <18 years, 18–49 years, 50–64 years, 75–84, years, 85+ years, unreported):
Table 8. Vaccination errors

Table 9, 10, etc. PRRs (number of tables TBD)

2.3 Signal detection methods and data analyses

The analyses for COVID-19 vaccine safety signals will focus on identifying deviations from preliminary safety data, and possibly from other vaccines, using disproportionality analyses and comparisons of reporting rates.

Two main approaches to data mining are Proportional Reporting Ratios (PRRs) and Empirical Bayesian Geometric Means [11–13]. Both have published literature suggesting criteria for detecting “signals” [14]. PRR will be used at CDC for potential signal detection; Empirical Bayesian data mining will be performed by FDA.

After initial licensure or approval of COVID-19 vaccines in the United States, initial reports may be too few to allow for data mining immediately. As the data mature, PRR and Empirical Bayesian data mining can then be used.

2.3.1 Proportional Reporting Ratio (PRR)

CDC will perform PRR data mining on a weekly basis or as needed. PRRs compare the proportion of a specific AE following a specific vaccine versus the proportion of the same AE following receipt of another vaccine (see equation below Table 4). A safety signal is defined as a PRR of at least 2, chi-squared statistic of at least 4, and 3 or more cases of the AE following receipt of the specific vaccine of interest.

CDC will apply appropriate comparator vaccines (e.g., adjuvanted vaccines like Shingrix and/or Fluad for adjuvanted COVID-19 vaccines) and adjust for severity and age distributions where applicable.

Table 4. Calculation of Proportional Reporting Ratio (PRR)

<table>
<thead>
<tr>
<th></th>
<th>Specific AE</th>
<th>All other AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific vaccine</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>All other vaccines</td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

PRR = \[\frac{a}{(a+b)}\]

\[\frac{c}{(c+d)}\]

2.3.2 Data mining

FDA will perform data mining at least biweekly (with stratified data mining monthly) using empirical Bayesian data mining to identify AEs reported more frequently than expected following vaccination with COVID-19 vaccines, using published criteria [12,
Vaccine product-specific AE pairs following specific COVID-19 vaccines with reporting proportions at least twice that of other vaccines in the VAERS database (i.e., lower bound of the 90% confidence interval of the Empirical Bayesian Geometric Mean [EB05] >2) will be evaluated. Data mining runs can be adjusted and/or stratified by possible confounding variables such as age, sex, season of administration, and type of vaccines. FDA and CDC will share and discuss results of data mining analyses and signals.

2.3.3 Crude reporting rates

If needed for internal purposes, crude reporting rates will be calculated based on COVID-19 vaccine doses distributed, when a source of doses distributed data becomes available.

2.4 Review of VAERS forms, medical records, and automated tables for reports of interest

- Daily priority reports will provide VAERS ID numbers and associated AESIs; these reports can be reviewed by VAERS personnel for initial information.
- Daily line list will provide VAERS ID numbers, associated AESIs, and assigned medical abstractor names. Medical abstractors will then access the VAERS VPN, review available medical records, and complete abstraction using the internal abstraction website (Figure).
  - Data from these medical abstractions will be used for supplemental tables to provide additional information on the automated summary tables (i.e., the cumulative daily data described in section 2.2.1.)
- Automated tables referenced in section 2.2.2 will be reviewed weekly for potential safety signals.
MedDRA terms identified as safety signals due to elevated PRR and/or a statistically significant finding on data mining will be reviewed as appropriate. The pattern or trend of PRR and data mining results over a period of time (e.g., several weeks) will be monitored before initiating a clinical review. Other factors, such as clinical importance, whether AEs are unexpected, seriousness, and whether a specific syndrome or diagnosis is identified rather than non-specific symptoms will be considered in determining if clinical review will be performed.

Identification of a cluster of reports or unexpected AEs will be further investigated, and additional information on serious AEs will be shared with CDC leadership. A list of lot numbers of vaccines that may be of concern will be requested from FDA. In the event of review of difficult or rare cases, subject matter experts (e.g., neurologist, the Clinical Immunization Safety Assessment network) may be consulted.

Clinical review will include reviewing reports (and associated medical records) containing the identified MedDRA terms, confirming appropriate coding, confirming diagnosis (e.g., by applying a case definition), confirming time from vaccination to symptom onset, reviewing the patient history and course of illness to identify risk factors, and potentially comparing to comparable data for another vaccine.

A summary of the data review described in this section will be provided monthly, or as needed, to pertinent stakeholders (e.g., Immunization Safety Office leadership, FDA partners).
2.5 Signal assessment

Signal detection can occur in VAERS surveillance through FDA empirical Bayesian data mining, through CDC PRR data mining, and through descriptive analysis. When a potential signal is detected, ISO VAERS staff shall take a series of steps to assess the potential signal. Steps may include, but are not limited to:

- Assess if the potential signal merits further investigation (e.g., expected AEs might not warrant further analysis)
- Consult with FDA colleagues to coordinate response
- Perform quality checks on data management and data analysis that led to signal detection
- Individual report review to:
  - Confirm the accuracy of MedDRA coding
  - Confirm the AE outcome and apply a standardized case definition if appropriate
  - Confirm onset interval to assess biological plausibility
  - Assess for other risk factors that might contribute to the AE
  - Assess the clinical seriousness
- Perform comparative analysis with other vaccines (e.g., compare frequencies and proportions with influenza vaccine)
- Analyze reporting rates and compare reporting rates with other vaccines or background rates

If, after an initial assessment, VAERS investigators determine a signal warrants further investigation, the VAERS team lead will notify ISO leadership and develop a coordinated response plan. Any appropriate investigation will be conducted in collaboration with FDA. FDA will share with CDC reports of possible concern based of the data mining results and assess product-specific or lot safety as appropriate. ISO leadership will be responsible for notifying NCIRD and the CDC COVID-19 Vaccine Task Force (VTF) in a timely manner.

3.0 Coordination and Collaboration

Meetings and conference calls will be scheduled as follows, subject to change as needed:

1) **Daily review by team lead and ISO leadership**, to review counts of reports and selected subgroups (e.g., deaths)

2) **Weekly VAERS Team COVID-19 Meeting** among VAERS team members
   a. To review the automated tables and clinical summary
   b. To analyze and interpret the VAERS data
   c. To discuss signals or potential events of concern

3) **Weekly (or as needed) CDC/FDA COVID-19 Safety Coordination Meeting** with ISO leadership, NCIRD representatives, and FDA
a. To present pertinent automated data and clinical summary (e.g., AEs resulting in signals) and FDA data mining results
b. To provide updates on ISO VAERS team and FDA COVID-19 vaccine activities (e.g., scientific projects/publications, regulations, data from other vaccine safety systems)

4.0 Appendices

4.1 Process of monitoring of COVID-19 vaccine adverse events

4.2 VAERS codes for COVID-19 vaccines [pending]

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>CDC code</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Fill as appropriate)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## 4.3 NURFU (Nurses Follow-up) Guidance: requesting additional information for selected AESIs

<table>
<thead>
<tr>
<th>Description</th>
<th>Report Type</th>
<th>Vaccine Brand/Manufacturer</th>
<th>Actions/ Documents Requested</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Serious (including manufacturer reports)</td>
<td>Unknown/ Not Specified</td>
<td>Vaccination records</td>
</tr>
<tr>
<td>Acute Myocardial Infarction</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Acute myocardial infarction, Myocardial infarction, Silent myocardial infarction</td>
<td>Clinical follow-up, Vaccination records</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Anaphylactic reaction, Anaphylactic shock, Anaphylactoid reaction, Anaphylactoid shock OR Clinical judgment (e.g. epinephrine given, severe allergic reaction)</td>
<td>Clinical follow-up, Vaccination records</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Appendicitis, Appendicitis noninfective, Appendicitis perforated, Complicated appendicitis</td>
<td>Clinical follow-up, Vaccination records</td>
</tr>
<tr>
<td>Bell’s Palsy</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Facial paralysis, Oculofacial paralysis</td>
<td>Clinical follow-up, Vaccination records</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Acquired amegakaryocytic thrombocytopenia, Amegakaryocytic thrombocytopenia, Axillary vein thrombosis</td>
<td>Clinical follow-up, Vaccination records</td>
</tr>
<tr>
<td>Condition</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes:</td>
<td>Clinical follow-up Vaccination records</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>-----------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Cavernous sinus thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral venous thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disseminated intravascular coagulation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embolism venous</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Immune thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intracranial venous sinus thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenteric vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary venous thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe fever with thrombocytopenia syndrome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subclavian vein thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenic purpura</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transverse sinus thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vena cava embolism</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vena cava thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GBS</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Guillian-Barre syndrome, Miller Fisher syndrome, Demyelinating polynueopathy</td>
<td>Clinical follow-up Vaccination records, Do NOT fill out GBS questionnaire</td>
</tr>
<tr>
<td>Kawasaki Disease</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Kawasaki's disease</td>
<td>Clinical follow-up Vaccination records</td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Children (MIS-c)</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Multisystem inflammatory syndrome in children</td>
<td>Clinical follow-up Vaccination records</td>
</tr>
<tr>
<td>Multisystem Inflammatory Syndrome in Adults (MIS-a)</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>Ages 21 and older AND</td>
<td>Clinical follow-up Vaccination records</td>
</tr>
<tr>
<td>Condition</td>
<td>Classification</td>
<td>MedDRA Codes</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-----------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>----------------------------</td>
</tr>
<tr>
<td>Myocarditis/Pericarditis</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Atypical mycobacterium pericarditis, Autoimmune myocarditis, Autoimmune pericarditis, Bacterial pericarditis, Coxsackie myocarditis, Coxsackie pericarditis, Cytomegalovirus myocarditis, Cytomegalovirus pericarditis, Enterovirus myocarditis, Eosinophilic myocarditis, Hypersensitivity myocarditis, Immune-mediated myocarditis, Myocarditis, Myocarditis bacterial, Myocarditis helminthic, Myocarditis infectious, Myocarditis meningococcal, Myocarditis mycotic, Myocarditis post infection, Myocarditis septic, Pericarditis, Pericarditis adhesive, Pericarditis constrictive, Pericarditis helminthic, Pericarditis infective, Pericarditis mycoplasmal, Pleuropericarditis, Purulent pericarditis, Viral myocarditis, Viral pericarditis</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>Narcolepsy/Cateplexy</td>
<td>Serious/Non-serious (including manufacturer reports)</td>
<td>MedDRA Codes: Narcolepsy, Cataplexy</td>
<td>Clinical follow-up</td>
</tr>
</tbody>
</table>
## Pregnancy and Prespecified Conditions

<table>
<thead>
<tr>
<th>Serious/Non-serious Conditions (including manufacturer reports)</th>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Abortion</td>
<td>- Abortion</td>
</tr>
<tr>
<td>- Aborted pregnancy</td>
<td>- Aborted pregnancy</td>
</tr>
<tr>
<td>- Abortion complete</td>
<td>- Abortion complete</td>
</tr>
<tr>
<td>- Abortion early</td>
<td>- Abortion early</td>
</tr>
<tr>
<td>- Abortion incomplete</td>
<td>- Abortion incomplete</td>
</tr>
<tr>
<td>- Abortion late</td>
<td>- Abortion late</td>
</tr>
<tr>
<td>- Abortion missed</td>
<td>- Abortion missed</td>
</tr>
<tr>
<td>- Abortion spontaneous</td>
<td>- Abortion spontaneous</td>
</tr>
<tr>
<td>- Abortion spontaneous complete</td>
<td>- Abortion spontaneous complete</td>
</tr>
<tr>
<td>- Abortion spontaneous incomplete</td>
<td>- Abortion spontaneous incomplete</td>
</tr>
<tr>
<td>- Abortion threatened</td>
<td>- Abortion threatened</td>
</tr>
<tr>
<td>- Congenital anomaly</td>
<td>- Congenital anomaly</td>
</tr>
<tr>
<td>- Drug exposure during pregnancy</td>
<td>- Drug exposure during pregnancy</td>
</tr>
<tr>
<td>- Exposure during pregnancy</td>
<td>- Exposure during pregnancy</td>
</tr>
<tr>
<td>- Foetal death</td>
<td>- Foetal death</td>
</tr>
<tr>
<td>- Maternal exposure during pregnancy</td>
<td>- Maternal exposure during pregnancy</td>
</tr>
<tr>
<td>- Stillbirth</td>
<td>- Stillbirth</td>
</tr>
</tbody>
</table>

OR

Text String:
Preg (Text String located in symptom_text, history, prex_illness) (*exclude ‘not pregnant’, ‘non-pregnant’, ’non pregnant’, ’nonpregnant’, and ‘no preg’) OR Pregnant Status (2.0 form-Q8) OR Congenital anomaly outcome (2.0 form-Q21)

Clinical follow-up including: prenatal visit documentation, delivery records, ER/hospital records during pregnancy, well child visits, infant hospitalization records; for congenital anomalies- infant records, ultrasounds, genetic studies Vaccination records

## Seizure/Convulsion

<table>
<thead>
<tr>
<th>Serious/Non-serious Conditions (including manufacturer reports)</th>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Atonic seizures</td>
<td>- Atonic seizures</td>
</tr>
<tr>
<td>- Atypical benign partial epilepsy</td>
<td>- Atypical benign partial epilepsy</td>
</tr>
<tr>
<td>- Autonomic seizure</td>
<td>- Autonomic seizure</td>
</tr>
<tr>
<td>- Clonic convulsion</td>
<td>- Clonic convulsion</td>
</tr>
<tr>
<td>- Complex partial seizures</td>
<td>- Complex partial seizures</td>
</tr>
<tr>
<td>- Convulsion in childhood</td>
<td>- Convulsion in childhood</td>
</tr>
<tr>
<td>- Convulsion</td>
<td>- Convulsion</td>
</tr>
</tbody>
</table>

Clinical follow-up Vaccination records
| Stroke | Serious/Non-serious (including manufacturer reports) | MedDRA Codes:  
Basal ganglia stroke  
Brain stem stroke  
Cerebellar stroke  
Cerebral infarction  
Cerebrovascular accident  
Emolic stroke  
Haemorrhagic stroke  
Haemorrhagic transformation stroke  
Ischaemic stroke  
Lacunar stroke  
Perinatal stroke | Clinical follow-up  
Vaccination records |
|---|---|---|
| Stroke | Serious/Non-serious (including manufacturer reports) | MedDRA Codes:  
Basal ganglia stroke  
Brain stem stroke  
Cerebellar stroke  
Cerebral infarction  
Cerebrovascular accident  
Emolic stroke  
Haemorrhagic stroke  
Haemorrhagic transformation stroke  
Ischaemic stroke  
Lacunar stroke  
Perinatal stroke | Clinical follow-up  
Vaccination records |
<table>
<thead>
<tr>
<th>Myelitis</th>
<th>Serious/Non-serious (including manufacturer reports)</th>
<th>MedDRA Codes: Myelitis transverse</th>
<th>Clinical follow-up Vaccination records</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transverse myelitis</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 4.4 VAERS triaging of reports in business days\(^1,2\)

<table>
<thead>
<tr>
<th>Type of report</th>
<th>Reported Vaccine</th>
<th>Serious reports</th>
<th>Non-serious reports</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scan within</td>
<td>Complete process within(^3)</td>
</tr>
<tr>
<td>1. US Deaths(^4)</td>
<td>COVID-19</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2. US Deaths(^4)</td>
<td>Non-COVID-19</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>3. US/Foreign 5-day</td>
<td>All</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>4. US 15-day</td>
<td>All</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>5. US</td>
<td>COVID-19(^5)</td>
<td>2*</td>
<td>3*</td>
</tr>
<tr>
<td>6. US</td>
<td>Seasonal Influenza(^6,7)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>7. US 30-day</td>
<td>All</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>8. US</td>
<td>List A(^8)</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>9. US</td>
<td>List B</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>10. Foreign Deaths</td>
<td>COVID-19</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>11. Foreign</td>
<td>COVID-19</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>12. Foreign</td>
<td>Non-COVID-19</td>
<td>5</td>
<td>90</td>
</tr>
</tbody>
</table>

---

1. Subject to change in response to new public health policies and/or events and/or funding availability after discussion between CDC and FDA
2. Not applicable for GBS reports where a patient is confined to facility longer than the time allowed for follow-up (e.g., patient in rehabilitation after GBS)
3. Completion includes scanning, data entry, and coding
4. If final autopsy report is not received within 2 months, make request every 2 months
5. If no records received within 5 days from the original request, make another request for Covid-19
6. If no records received within 7 days from the original request, make another request for Seasonal Influenza
7. Seasonal influenza reports will be prioritized as stated in Row 4 until March 31, 2021. On April 1, 2021, process reports as stated in Row 8.

* If report is of anaphylaxis, scan and initiation of follow-up will occur same day of report (i.e., 1 day), regardless of seriousness.

<table>
<thead>
<tr>
<th>List A</th>
<th>List B</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEPLISAV-B</td>
<td>All vaccines excluding List A and Seasonal Influenza</td>
</tr>
<tr>
<td>Shingrix</td>
<td></td>
</tr>
<tr>
<td>Gardasil 9</td>
<td></td>
</tr>
<tr>
<td>Yellow Fever</td>
<td></td>
</tr>
<tr>
<td>Other vaccines licensed in the U.S. for less than 12 months</td>
<td></td>
</tr>
<tr>
<td>Seasonal Influenza reports received after March 31, 2021</td>
<td></td>
</tr>
</tbody>
</table>
4.5 Vaccination error groups and MedDRA Preferred Terms (PTs) for COVID-19 vaccination errors

**Administration Errors**
- Accidental exposure to product
- Accidental exposure to product by child
- Drug administered in wrong device
- Exposure via direct contact
- Exposure via eye contact
- Exposure via skin contact
- Inadequate aseptic technique in use of product
- Incorrect product administration duration
- Incorrect product formulation administered
- Intercepted drug administration error
- Lack of administration site rotation
- Lack of injection site rotation
- Lack of vaccination site rotation
- Multiple use of single-use product
- Occupational exposure to product
- Paravenous drug administration
- Product administration error
- Product administered at inappropriate site
- Product commingling
- Product leakage
- Product use complaint
- Product use in unapproved indication
- Unintentional use for unapproved indication,
- Wrong technique in device usage process
- Wrong technique in product usage process

**Contraindication to vaccination**
- Contraindication to vaccination
- Contraindicated product administered
- Contraindicated product prescribed
- Documented hypersensitivity to administered product
- Labelled drug-disease interaction medication error
- Labelled drug-drug interaction medication error
- Labelled drug-food interaction medication error

**Equipment**
- Device connection issue,
- Device breakage
- Device defective
- Device difficult to use
- Device dislocation
- Device failure
- Device leakage
- Device issue

**General**
- Medication error
- Intercepted medication error
- Product use issue
- Vaccination error
- Unintentional use for unapproved indication

**Inappropriate schedule of drug administration**
- Inappropriate schedule of product administration
- Product administered to patient of inappropriate age
- Wrong schedule

**Incorrect dose**
- Accidental overdose
- Accidental underdose
- Booster dose missed
- Dose calculation error
- Extra dose administered
- Incomplete course of vaccination
- Incorrect dose administered
- Incorrect dosage administered
- Incorrect product dosage form administered
- Overdose
- Product dose omission
- Single component of two component product administered
- Underdose
- Wrong dose
- Wrong strength

**Prescribing and dispensing**
- Drug dispensed to wrong patient
- Inappropriate prescribing
- Intercepted drug dispensing error
- Intercepted drug prescribing error
- Intercepted product selection error
- Prescribed overdose
- Prescribed underdose
- Product dispensing error
- Product preparation error
- Product prescribing error
- Product prescribing issue
- Product selection error
- Transcription medication error

**Product quality**
- Expired product administered
- Discontinued product administered
- Incorrect product storage
- Poor quality product administered
- Product contamination
- Product contamination microbial
- Product contamination physical
- Product expiration date issue
- Product quality issue
- Product quality control issue
- Product preparation issue
- Product reconstitution issue
- Product reconstitution quality issue
- Product sterility lacking
- Product storage error

**Product labeling/packaging**
- Product barcode issue
- Product design confusion
- Product name confusion
- Product container issue
- Product dosage form confusion
- Product identification number issue
- Product label confusion
- Product label issue
- Product label on wrong product
- Product lot number issue
- Product name confusion
- Product packaging confusion
- Product packaging issue
- Product outer packaging issue
- Product packaging confusion

**Wrong Product**
- Interchange of vaccine products
- Intercepted wrong patient selected
- Product substitution error
- Wrong patient received product
- Wrong product administered
- Wrong drug
- Wrong product procured

Vaccination Error groups shown on this list were updated to include several new PT codes that became available in MedDRA. Reports of exposure during pregnancy, fetal exposure during pregnancy, maternal exposure during pregnancy are not included. A review of pregnancy coded reports revealed that many reports were documenting that the patient was pregnant without an error occurring. A contraindication to vaccination code has captured true vaccine contraindication reports in pregnant women.

While most reports are documenting a medical error, some reports that use the MedDRA PT codes are not necessarily vaccination errors (e.g., product quality issue, needle issue, syringe issue).
4.6 AESIs to monitor, and identifying PTs

* AESI to abstract

**Pre-specified Condition**

(*Abstraction Website*)

**Acute Disseminated Encephalomyelitis (ADEM)**

MedDRA Codes: Acute disseminated encephalomyelitis

**Acute Myocardial Infarction***

MedDRA Codes: Acute myocardial infarction

Myocardial infarction

Silent myocardial infarction

**Acute Respiratory Distress Syndrome (ARDS)**

MedDRA Codes: Acute respiratory distress syndrome

**Anaphylaxis***

MedDRA Codes: Anaphylactic reaction

Anaphylactic shock

Anaphylactoid reaction

Anaphylactoid shock

**Appendicitis***

MedDRA Codes: Appendicitis

Appendicitis noninfective

Appendicitis perforated

Complicated appendicitis

**Ataxia**

MedDRA Codes: Ataxia

Cerebellar ataxia

Cerebral ataxia

**Autoimmune**

MedDRA Codes: Acute cutaneous lupus erythematosus

Acute haemorrhagic leukoencephalitis

Acute haemorrhagic ulcerative colitis

Acute motor axonal neuropathy

Acute motor-sensory axonal neuropathy

Addison's disease

Administration site vasculitis

Alopecia areata

Alveolar proteinosis

Amyloidosis

Amyloidosis senile

Ankylosing spondylitis
Anti-erythrocyte antibody
Anti-erythrocyte antibody positive
Anti-insulin antibody
Anti-insulin antibody decreased
Anti-insulin antibody increased
Anti-insulin antibody positive
Anti-insulin receptor antibody
Anti-insulin receptor antibody decreased
Anti-insulin receptor antibody increased
Anti-insulin receptor antibody positive
Anti-islet cell antibody
Anti-islet cell antibody positive
Anti-myelin-associated glycoprotein antibodies positive
Anti-myelin-associated glycoprotein associated polyneuropathy
Anti-neuronal antibody
Anti-neuronal antibody positive
Anti-neutrophil cytoplasmic antibody positive vasculitis
Antiphospholipid antibodies
Antiphospholipid antibodies positive
Antiphospholipid syndrome
Anti-platelet antibody
Anti-platelet antibody positive
Antisynthetase syndrome
Aplasia pure red cell
Arteritis
Arteritis coronary
Atrophic thyroiditis
Autoantibody positive
Autoimmune aplastic anaemia
Autoimmune arthritis
Autoimmune colitis
Autoimmune demyelinating disease
Autoimmune dermatitis
Autoimmune disorder
Autoimmune encephalopathy
Autoimmune endocrine disorder
Autoimmune haemolytic anaemia
Autoimmune hepatitis
Autoimmune hyperlipidaemia
Autoimmune hypothyroidism
Autoimmune inner ear disease
Autoimmune lymphoproliferative syndrome
Autoimmune neuropathy
Autoimmune neutropenia
Autoimmune pancreatitis
Autoimmune pancytopenia
Autoimmune retinopathy
Autoimmune thyroid disorder
Autoimmune thyroiditis
Autoimmune uveitis
Autonomic nervous system imbalance
Axial spondyloarthritis
Axonal neuropathy
Basedow's disease
Behcet's syndrome
Bickerstaff's encephalitis
Biliary cirrhosis primary
Birdshot chorioretinopathy
Butterfly rash
Caplan's syndrome
Cardiac amyloidosis
Cardiac sarcoidosis
Castleman's disease
Cell-mediated immune deficiency
Central nervous system lupus
Cerebral amyloid angiopathy
Cholangitis sclerosing
Cholecystocholangitis
Chronic cutaneous lupus erythematosus
Chronic inflammatory demyelinating polyradiculoneuropathy
Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids
Chronic recurrent multifocal osteomyelitis
Coeliac disease
Cogan's syndrome
Cold agglutinins
Cold agglutinins positive
Cold type haemolytic anaemia
Colitis ulcerative
Collagen disorder
Collagen-vascular disease
Concentric sclerosis
Coombs positive haemolytic anaemia
Crest syndrome
Crohn's disease
Cryofibrinogenemia
Cryoglobulinaemia
Cutaneous amyloidosis
Cutaneous lupus erythematosus
Cutaneous sarcoidosis
Cutaneous vasculitis
Cystitis interstitial
Dermatitis herpetiformis
Dermatomyositis
diabetic mastopathy
Dialysis amyloidosis
Diffuse vasculitis
digital pitting scar
Dressler's syndrome
Encephalitis autoimmune
Endocrine ophthalmopathy
Eosinophilic fasciitis
Eosinophilic granulomatosis with polyangiitis
Erythema nodosum
Evans syndrome
Felty's syndrome
Gastrointestinal amyloidosis
Goodpasture's syndrome
Granulomatosis with polyangiitis
Granulomatous dermatitis
Haemolytic anaemia
Hashimoto's encephalopathy
Hashitoxicosis
Henoch-schönlein purpura
Henoch-schönlein purpura nephritis
Hepatic amyloidosis
Herpes gestationis
Human antichimeric antibody positive
Human anti-mouse antibody increased
Human anti-mouse antibody positive
Hypersensitivity vasculitis
Idiopathic pulmonary fibrosis
Immune agglutinins
Immune thrombocytopenic purpura
Immune-mediated adverse reaction
Immune-mediated necrotising myopathy
Immunoglobulin g4 related disease
Immunoglobulin therapy
Immunomodulatory therapy
Immunosuppressant drug level
Immunosuppressant drug level decreased
Immunosuppressant drug level increased
Immunosuppressant drug therapy
Inclusion body myositis
Injection site vasculitis
Insulin autoimmune syndrome
Interstitial granulomatous dermatitis
Intrinsic factor antibody
Intrinsic factor antibody abnormal
Intrinsic factor antibody positive
Juvenile idiopathic arthritis
Juvenile polymyositis
Juvenile psoriatic arthritis
Juvenile spondyloarthritis
Keratoderma blenorrhagica
Laryngeal rheumatoid arthritis
Latent autoimmune diabetes in adults
Lichen planus
Lichen sclerosus
Ligneous conjunctivitis
Limbic encephalitis
Linear iga disease
Liver sarcoidosis
Lupoid hepatic cirrhosis
Lupus cystitis
Lupus encephalitis
Lupus endocarditis
Lupus enteritis
Lupus hepatitis
Lupus myocarditis
Lupus nephritis
Lupus pancreatitis
Lupus pleurisy
Lupus pneumonitis
Lupus vasculitis
Lupus-like syndrome
Lymphocytic hypophysitis
Marine lenhart syndrome
Meniere's disease
Microscopic polyangiitis
Mixed connective tissue disease
Morphoea
Morvan syndrome
Multiple sclerosis plaque
Muscular sarcoidosis
Myasthenia gravis
Myasthenia gravis crisis
Myasthenia gravis neonatal
Myasthenic syndrome
Neonatal lupus erythematosus
Nephrogenic systemic fibrosis
Neuralgic amyotrophy
Neuromyelitis optica spectrum disorder
Neuromyotonia
Neuropsychiatric lupus
Neurosarcoidosis
Nodular vasculitis
Ocular myasthenia
Ocular pemphigoid
Ocular sarcoidosis
Ocular vasculitis
Overlap syndrome
Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection
Palindromic rheumatism
Palisaded neutrophilic granulomatous dermatitis
Parietal cell antibody
Parietal cell antibody positive
Paroxysmal nocturnal haemoglobinuria
Pemphigoid
Pemphigus
Pericarditis lupus
Peritonitis lupus
Pernicious anaemia
Pityriasis lichenoides et varioliformis acuta
Poems syndrome
Polyarteritis nodosa
Polychondritis
Polyglandular autoimmune syndrome type i
Polyglandular autoimmune syndrome type ii
Polyglandular autoimmune syndrome type iii
Polyglandular disorder
Polymyalgia rheumatica
Polymyositis
Postpericardiotomy syndrome
Primary amyloidosis
Progressive facial hemiatrophy
Psoriasis
Psoriatic arthropathy
Pulmonary amyloidosis
Pulmonary renal syndrome
Pulmonary sarcoidosis
Pulmonary vasculitis
Pyoderma gangrenosum
Pyogenic sterile arthritis pyoderma gangrenosum and acne syndrome
Radiculitis brachial
Radiologically isolated syndrome
Rasmussen encephalitis
Raynaud's phenomenon
Reiter's syndrome
Renal amyloidosis
Renal vasculitis
Retinal vasculitis
Retroperitoneal fibrosis
Reynold's syndrome
Rheumatoid factor decreased
Rheumatoid factor increased
Rheumatoid factor positive
Rheumatoid factor quantitative decreased
Rheumatoid factor quantitative increased
Rheumatoid lung
Rheumatoid neutrophilic dermatosis
Rheumatoid nodule
Rheumatoid scleritis
Rheumatoid vasculitis
Sarcoidosis
Satoyoshi syndrome
Schnitzler's syndrome
Sclerodactylia
Scleroderma
Scleroderma associated digital ulcer
Scleroderma renal crisis
Scleroderma-like reaction
Secondary amyloidosis
Septal panniculitis
Shrinking lung syndrome
Silent thyroiditis
Sjogren's syndrome
Sle arthritis
Stevens-johnson syndrome
Stiff leg syndrome
Stiff person syndrome
Subacute cutaneous lupus erythematosus
Susac's syndrome
Sympathetic ophthalmia
Systemic lupus erythematosus
Systemic lupus erythematosus rash
Systemic scleroderma
Systemic sclerosis pulmonary
Takayasu’s arteritis
Temporal arteritis
Testicular autoimmunity
Thromboangiitis obliterans
Thromboplastin antibody positive
Tolosa-hunt syndrome
Type 1 diabetes mellitus
Type iii immune complex mediated reaction
Undifferentiated connective tissue disease
Urticarial vasculitis
Vaccination site vasculitis
Vasculitis
Vasculitis cerebral
Vasculitis gastrointestinal
Vasculitis necrotising
Vitiligo
Warm type haemolytic anaemia

**Bell's Palsy***

MedDRA Codes:
Facial asymmetry
Facial nerve disorder
Facial palsy
Facial paralysis
Facial paresis
Oculofacial paralysis

**Chronic inflammatory demyelinating polyneuropathy (CIDP)**

MedDRA Codes:
Acquired amegakaryocytic thrombocytopenia
Amegakaryocytic thrombocytopenia
Axillary vein thrombosis
Cavernous sinus thrombosis
Cerebral venous thrombosis
Deep vein thrombosis
Disseminated intravascular coagulation
Embolism venous
Hepatic vein thrombosis
Immune thrombocytopenia
Intracranial venous sinus thrombosis
Mesenteric vein thrombosis
Portal vein thrombosis
Pulmonary embolism
Pulmonary thrombosis
Pulmonary venous thrombosis
Severe fever with thrombocytopenia syndrome
Subclavian vein thrombosis
Thrombocytopenia
Thrombocytopenic purpura
Thrombotic thrombocytopenic purpura
Thrombosis
Transverse sinus thrombosis
Vena cava embolism
Vena cava thrombosis
Venous thrombosis

**COVID-19 Disease***

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic COVID-19</td>
</tr>
<tr>
<td>COVID-19</td>
</tr>
<tr>
<td>COVID-19 Pneumonia</td>
</tr>
<tr>
<td>SARS-COV-2 test positive</td>
</tr>
</tbody>
</table>

**Death***

Died=Y

**Encephalitis**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalitis</td>
</tr>
</tbody>
</table>

**Encephalopathy**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Leukoencephalopathy</td>
</tr>
</tbody>
</table>

**Encephalomyelitis**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalomyelitis</td>
</tr>
<tr>
<td>Leukoencephalomyelitis</td>
</tr>
<tr>
<td>Noninfective encephalomyelitis</td>
</tr>
</tbody>
</table>

**GBS***

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guillain-Barre syndrome</td>
</tr>
<tr>
<td>Miller Fisher syndrome</td>
</tr>
<tr>
<td>Demyelinating polyneuropathy</td>
</tr>
</tbody>
</table>

**Kawasaki Disease***

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kawasaki's disease</td>
</tr>
</tbody>
</table>

**Meningitis**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
</tr>
<tr>
<td>Meningitis aseptic</td>
</tr>
<tr>
<td>Meningitis viral</td>
</tr>
</tbody>
</table>

**Meningoencephalitis**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningoencephalitis viral</td>
</tr>
</tbody>
</table>

**Multiple sclerosis**

<table>
<thead>
<tr>
<th>MedDRA Codes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>Multiple sclerosis relapse</td>
</tr>
<tr>
<td>Primary progressive multiple sclerosis</td>
</tr>
<tr>
<td>Progressive multiple sclerosis</td>
</tr>
</tbody>
</table>
Progressive relapsing multiple sclerosis
Relapsing multiple sclerosis
Relapsing-remitting multiple sclerosis
Secondary progressive multiple sclerosis
Tumefactive multiple sclerosis

Multisystem
Inflammatory
Syndrome in Adults (MIS-a)*
Ages 21 and older
MedDRA Codes:
Systemic inflammatory response syndrome

Multisystem
Inflammatory
Syndrome in Children (MIS-c)*
Ages 0-20
MedDRA Codes:
Multisystem inflammatory syndrome in children

Myelitis
MedDRA Codes:
Myelitis
Noninfectious myelitis

Myocarditis/Pericarditis*
MedDRA Codes:
Atypical mycobacterium pericarditis
Autoimmune myocarditis
Autoimmune pericarditis
Bacterial pericarditis
Coxsackie myocarditis
Coxsackie pericarditis
Cytomegalovirus myocarditis
Cytomegalovirus pericarditis
Enterovirus myocarditis
Eosinophilic myocarditis
Hypersensitivity myocarditis
Immune-mediated myocarditis
Myocarditis
Myocarditis bacterial
Myocarditis helminthic
Myocarditis infectious
Myocarditis meningococcal
Myocarditis mycotic
Myocarditis post infection
Myocarditis septic
Pericarditis
Pericarditis adhesive
Pericarditis constrictive
Pericarditis helminthic
Pericarditis infective
Pericarditis mycoplasmal
Pleuropericarditis
Purulent pericarditis
Viral myocarditis
Viral pericarditis

Narcolepsy/Cataplexy

* MedDRA Codes:
  Narcolepsy
  Cataplexy

Non-anaphylactic allergic reactions

  Allergy to vaccine
  Allergic bronchitis
  Allergic colitis
  Allergic cough
  Allergic cystitis
  Allergic gastroenteritis
  Allergic hepatitis
  Allergic keratitis
  Allergic pharyngitis
  Allergic reaction to excipient
  Allergic respiratory disease
  Allergic respiratory symptom
  Allergic sinusitis
  Conjunctivitis allergic
  Dermatitis allergic
  Encephalitis allergic
  Encephalopathy allergic
  Laryngitis allergic
  Nephritis allergic
  Pruritus allergic
  Rhinitis allergic
  Scleritis allergic

Optic neuritis (ON)

  MedDRA Codes:
  Optic neuritis

Pregnancy and Prespecified Conditions*

  MedDRA Codes:
  Abortion
  Aborted pregnancy
  Abortion complete
  Abortion early
  Abortion incomplete
  Abortion late
  Abortion missed
  Abortion spontaneous
  Abortion spontaneous complete
  Abortion spontaneous incomplete
  Abortion threatened
  Congenital anomaly
  Drug exposure during pregnancy
  Exposure during pregnancy
Foetal death
Maternal exposure during pregnancy
Stillbirth
OR
Text String 'preg' located in symptom_text, history, prex_illness (*exclude ‘not pregnant’, ‘non-pregnant’, ‘non pregnant’, ‘nonpregnant’, and 'no preg')
OR
Pregnant Status (2.0 form-Q8)
OR
Congenital anomaly outcome (2.0 form-Q21)

Seizure/Convulsion*
MedDRA Codes:
Atonic seizures
Atypical benign partial epilepsy
Autonomic seizure
Clonic convulsion
Complex partial seizures
Convulsion in childhood
Convulsion
Convulsions local
Epilepsy
Epileptic encephalopathy
Febrile convulsion
Febrile infection-related epilepsy syndrome
Generalised non-convulsive epilepsy
Generalised onset non-motor seizure
Generalised tonic-clonic seizure
Grand mal convulsion
Idiopathic generalised epilepsy
Myoclonic epilepsy
Neonatal seizure
Partial seizures with secondary generalisation
Partial seizures
Petit mal epilepsy
Seizure anoxic
Seizure cluster
Seizure like phenomena
Seizure
Simple partial seizures
Status epilepticus
Temporal lobe epilepsy
Tonic clonic movements
Tonic convulsion
Tonic posturing

Stroke*
MedDRA Codes:
Basal ganglia stroke
Brain stem stroke
Cerebellar stroke
Cerebral infarction
Cerebrovascular accident
Embolic stroke
Haemorrhagic stroke
Haemorrhagic transformation stroke
Ischaemic stroke
Lacunar stroke
Perinatal stroke
Spinal stroke
Thrombotic stroke
Vertebrobasilar stroke

Transverse Myelitis*
Myelitis transverse

Vaccination Error
Please see COVID19 SOP
5.0 References