

Vaccine safety signal detection and assessment

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Rapidly detecting and assessing vaccine safety signals is an essential component of vaccination programs and helps guide regulatory, policy, and clinical decisions about vaccination. Many definitions for a “signal” exist and recently, the Council for International Organizations of Medical Sciences (CIOMS) proposed a signal as: “information...from one or multiple sources ..., which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action.”¹

Spontaneous reporting systems (SRSs) provide the cornerstone of signal detection, particularly for rare or unusual adverse events (AEs) that may not have been detected in clinical trials. Signals may also be identified through other sources including the literature, clinical inquiries, media and by using large linked databases.² In the United States, the Vaccine Adverse Event Reporting System (VAERS), an SRS jointly managed by the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA), serves as the nation’s primary system for detecting vaccine safety signals.^{3,4} Healthcare providers and manufacturers are required to report certain AEs to VAERS but VAERS accepts reports from anyone. For reports coded as serious (death, life-threatening illness, hospitalization, prolonged hospitalization, disability or congenital anomalies), additional medical records are requested. VAERS has limitations including biased reporting, incomplete or inaccurate data, and lack of denominator data on the number of persons vaccinated; VAERS is not designed to assess causality.

Two complementary methods are used to detect signals in VAERS: traditional methods (e.g., case individual report and case series reviews) and statistical data mining methods to detect disproportionate reporting of specific vaccine-event combinations.^{1,5} Initial signal assessment involves reviewing the reports to characterize clinical features, verify diagnoses, assess other potential risk factors, and evaluate the interval between vaccination and the AE. Further signal assessment can include reviewing the literature, assessing for similar findings in other data sources, and considering the biological plausibility of a relationship between the vaccine and AE.

More definitive signal assessment may be warranted through carefully designed observational or clinical studies using appropriate comparison groups. Prioritizing signal assessment can vary based on the severity of the AE, number of people impacted, and potential to mitigate risk. Two examples of vaccine safety signals will be presented: Guillain-Barré syndrome (GBS) shortly after the introduction of a new meningococcal conjugate vaccine (MCV4, Menactra[®]) for adolescents^{6,7} and febrile seizures after the combination measles-mumps-rubella-varicella (MMRV, ProQuad[®]) vaccine.^{8,9,10}

*Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the views CDC.

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