Post-licensure vaccine safety

Key point

Spontaneous reporting is the cornerstone of most post-licensure safety monitoring systems because of its relative ease of implementation and ability to capture unexpected events.

Rotateq® vaccine example

Post-licensure surveillance

Post-licensure surveillance (also known as post-marketing surveillance) Pharmacovigilance conducted after a product has been licensed and introduced for use in a population of vaccine safety is critical. The conditions and reasons for safety monitoring change following licensure.

Licensure The granting of a license to conduct a regulated procedure, for example, to conduct a trial of a new vaccine or to approve a vaccine for routine delivery to the public in a vaccination programme, and introduction of a new vaccine.

- Vaccines are now in use in the general population and recipients are no longer monitored in clinical trials.

Clinical trial A systematic study of a medical intervention in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to the intervention. Clinical trials also study the absorption, distribution, metabolism, and excretion of the products with the objective of ascertaining their efficacy and safety. Clinical trials are generally classified into Phases I to IV. Phase IV trials are studies performed after the licensure and introduction of pharmaceutical products. They are carried out to expand the evidence base of the product characteristics for which the marketing authorization was granted, with narrow inclusion/exclusion criteria.

- Subpopulations commonly excluded in clinical trials (e.g. those with underlying medical conditions, preterm infants) get vaccinated,

- Large numbers of people are being vaccinated, for example, entire birth cohorts receive infant vaccines,

- Other factors that can lead to AEFIs, such as incorrect administration practices, need to be monitored for safety,

- Uncommon and rare vaccine reactions, and reactions with delayed onset, may not be detected before vaccines are licensed,
Health providers should understand that some commonly used vaccines have demonstrated rare and potentially serious adverse events. In these instances, policy-making bodies have judged that the individual and community benefits of vaccination outweigh the risks.

Post-licensure surveillance options

**AEFI surveillance**

*AEFI surveillance (also known as vaccine safety surveillance)* A surveillance system designed to collect adverse events temporally associated with receipt of vaccines. This type of surveillance typically relies on health professionals associating an adverse event in an individual as a possible consequence of vaccination and reporting it to the NRA or appropriate authority. Systems are specific to monitoring adverse events associated with vaccine use. In contrast, adverse drug reaction (ADR) surveillance systems are used to monitor suspected adverse reactions associated with medicines.

A range of surveillance

*Surveillance* The systematic collection, analysis, interpretation, and dissemination of health data on an ongoing basis, to gain knowledge of the pattern of disease occurrence and potential in a community, in order to control and prevent disease in the community. Options can be used to monitor the safety of vaccines and immunizations post-licensure. Click on each surveillance option to learn more.

**Passive surveillance systems**

Passive surveillance systems

- **Passive surveillance**

  *Passive surveillance (also known as spontaneous reporting)* A surveillance system designed to collect adverse events that follow vaccination. This type of surveillance typically relies on health professionals noticing and reporting adverse events in individuals after vaccination to the NRA or appropriate authority. Systems (or spontaneous reporting systems) are the cornerstone of most post-licensure safety monitoring systems because of their relative ease of implementation, their cost and ability to capture unexpected events.

  These reporting systems monitor events reported by health care providers and consumers and do not actively seek out and collect data or measure outcomes using study protocols.
Active surveillance systems

Post-licensure clinical trials and phase IV surveillance studies

- Vaccines may undergo clinical trials after licensure to assess the effects of changes in vaccine formulation, vaccine strain.

  Strain A specific genetic grouping of an organism. Many organisms, such as viral influenza, pneumococcus and meningococcus, have multiple strains that cause disease, age at vaccination, number and timing of vaccine doses, simultaneous administration and interchangeability of vaccines from different manufacturers on vaccine safety and immunogenicity.¹⁴

- To improve the ability to detect adverse events that are not detected during pre-licensure trials, some recently licensed vaccines in developed countries have undergone formal phase IV surveillance studies, involving cohorts as large as 100 000 often recruited from health maintenance organizations (HMOs), lasting four to six years.

Large linked databases (LLDBs)

- LLDBs are large administrative databases from defined populations (such as a single health care provider or HMO) that were created separately from each other and linked to enable the sharing of data across platforms. Such linked databases have become useful to vaccine safety surveillance.

- Because LLDBs cover enrollee populations numbering from thousands to millions, they can detect very rare adverse events. With denominator data on doses administered and the ready availability of appropriate comparison (i.e. unvaccinated) groups, these large databases provide an economical and rapid means of conducting post-licensure studies of the safety of drugs and vaccines. They also represent powerful tools to allow for testing hypotheses when signals.

  Signal Reported information on a possible causal relationship between an adverse event and a drug, the relationship being previously unknown or incompletely documented. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information, or allegations create suspicions of a possible vaccine safety issue.

- The Vaccine Safety Datalink (VSD) project is an example of a LLDB between the USA’s Centers for Disease Control and Prevention (CDC) and eight HMOs. The VSD project was established in 1990 to monitor immunization safety.

  Immunization safety The process of ensuring and monitoring the safety of all aspects of immunization, including vaccine quality, vaccine storage and handling, vaccine administration, disposal of sharps, and management of waste, and to address the gaps in scientific knowledge about rare and serious events following immunization.²⁰
Clinical centers, including the Clinical Immunization Safety Assessment (CISA) centers

- More recently, tertiary clinical centers have been used to conduct research on immunization-associated health risks.
- The USA's Clinical Immunization Safety Assessment (CISA) Network is a national network of six medical research centers with expertise in immunization safety conducting clinical research on immunization-associated health risks. Established in 2001 as a collaborative project between the CDC, six medical research centers, and American Health Insurance Plans, CISA conducts clinical research on vaccine adverse events and the role of individual variation.21