tragedies, regulations in general and national pharmacovigilance centers were set up to follow up drugs once they were authorized and marketed.

The World Health Organization (WHO) defines pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. The goals of pharmacovigilance are to identify and evaluate safety signals and to mitigate the risks of each product, in a timely manner" (WHO, 2002).

A WHO article summarizes the specific aims of pharmacovigilance as being to "improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions, improve public health and safety in relation to the use of medicines, contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost effective) use, and to promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public" (WHO, 2004).

Pharmacovigilance can be passive, such as the routine monitoring of spontaneous reports, or it can be active, which requires putting in place appropriate risk management activities for specific risks associated with use of the product. Most of the benefit–risk information obtained in the postmarket setting comes from spontaneous reports of adverse events, which may be provided by patients, caregivers, health care professionals, and market authorization holders. Some of the databases that collect reports of adverse events include the EudraVigilance Database of the European Medicines Agency, the Uppsala Monitoring Center of the WHO, the FDA Adverse Event Reporting System (FDA AERS), and the Canada Vigilance database. Identification of signal(s) from these reports involves a process of hypothesis generation, assessment of the available information for causality, and derivation of conclusions based on the scientific evidence. However, there are certain drawbacks with spontaneous adverse event reports such as the quality of reporting, details of the information provided, and patient-related confounding factors that make adequate assessment of causal association of an adverse event to the drug difficult, or sometimes impossible.

Underreporting is a major limitation of spontaneous adverse event reporting systems, as many adverse events may go undetected, or there may not be enough evidence to link the drug to the adverse event of concern. New data-mining techniques and the analytical methods that are now available to the pharmacovigilance specialist have greatly enhanced the way pharmacovigilance is done (Meyboom et al., 1997; ICH, 2004; Poluzzi et al., 2012). In recent years, there has been a shift to more proactive pharmacovigilance. This has led to the introduction of risk management plans as tools for planning pharmacovigilance and risk minimization activities. Risk management plans are used to address some of the uncertainties, especially those related to the potential risks that exist at the time a drug is authorized for market. Some of the activities that may be requested as part of a pharmacovigilance plan are postauthorization studies and/or registries, in order to better characterize the benefit–risk profile of the drug throughout its life cycle.