

The Rise of **PHARMACOVIGILANCE**



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Introduction

Pharmacovigilance is a critical step in the long and exhaustive process of drug development. It occurs after clinical trials have been completed and a drug has been released to the general population. The aim of pharmacovigilance is to carefully monitor and report any possible adverse drug reactions (ADR) that had not previously been detected.

Pharmacovigilance has been defined by the World Health Organization as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problem” (Pharmacovigilance, n.d.). It is considered a critical tool to “prevent, identify and treat preventable and non-preventable adverse reactions to medications” (Vazquez-Alvarez et al., 2017).

Pharmacovigilance serves an important function in the development of a drug. It aims to “enhance patient care and patient safety in relation to the use of medicines; and to support public health programs by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines” (Pharmacovigilance, n.d.).

Background

Pharmacovigilance began as a reaction to a major and unfortunate oversight in the testing of a popular pharmaceutical drug. In 1961, thousands of infants were born deformed due to in utero exposure to an unsafe medicine (World Health Organization, 2002). This medicine — thalidomide — was tested on animals and found to be safe; however, the tests did not examine the effects of the drug during pregnancy (Thalidomine, n.d.). This pharmaceutical disaster led to the first organized efforts to address drug safety issues after its release to the general population.

In 1963, the Sixteenth World Health Assembly adopted a resolution that reaffirmed the need for early action regarding reporting adverse drug reactions. This assembly ultimately led to the creation of the World Health Organization (WHO) Pilot Research Project for International Drug Monitoring (World Health Organization, 2002).

From these efforts emerged pharmacovigilance. Systems were developed throughout the world to collect and evaluate individual cases of ADRs, creating an international database of ADR reports. It was decided that special attention would be paid to new drugs, and special reference centers would be required to provide data regarding drug safety issues (World Health Organization, 2002).

The practice of pharmacovigilance has gained significant momentum since its beginnings in the 1960s. By the end of 2010, the World Health Organization Pharmacovigilance Program listed 134 countries as members (Pharmacovigilance, n.d.). Today, pharmacovigilance is a standard practice in the development and testing of pharmaceutical drugs.



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Importance of Pharmacovigilance

It is critical for pharmaceutical companies to monitor and report adverse reactions to their medicines. ADRs that are not detected can pose considerable risks for patients — in 2014, they were the “fifth most common cause of hospital deaths” in the EU (Pontes, Clemet, & Rollason, 2014). Due to these significant dangers, health regulation authorities are emphasizing the adoption of pharmacovigilance practices by pharmaceutical companies.

Although pharmaceutical companies must complete rigorous testing to ensure a product’s safety prior to its release, many organizations have recognized that it would not be possible to identify all possible safety concerns during the initial phases of testing. Clinical trials test ADRs on only a small sample of individuals. When a drug has been released to a larger population, the risk of side effects rises substantially. In fact, “many ADRs are identified only after a drug has been marketed when it is used by a larger and more diverse population than during clinical trials” (Ventola, 2018).

Pharmacovigilance serves to track, analyze and report these adverse effects — a practice that is critical to the protection of public health (Ventola, 2018). Therefore, “collection and risk assessment based on observational data are critical for evaluating and characterizing a product’s risk profile and for making informed decisions on risk minimization” (Guidance for Industry: Good Pharmacovigilance Practices and Pharmacovigilance Assessment, 2005).

Modern Challenges of Pharmacovigilance

An extensive report by the World Health Organization (2002) outlines the challenges of pharmacovigilance.

1. **Globalization:** Today's global economy impacts all industries, including pharmaceutical companies. Distribution of pharmaceutical drugs is on a larger scale than ever, increasing exposure of these medicines to massive populations. Because so many people have access to these medicines, it is more critical than ever before to carefully monitor potential dangers of newly released drugs.
2. **Web-based Sales and Information:** Technology has a major impact on the way that new drugs can be disseminated. The internet has helped to facilitate uncontrolled sales of new medications "across national borders" (World Health Organization, 2002), which can often be dangerous. Additionally, the internet can be used to market new drugs — which can often result in "excessive, and probably irrational, use of medicines" (World Health Organization, 2002).
3. **Broader Safety Concerns:** Pharmacovigilance continues to grow in scope as the range of new medicines increases. According to the World Health Organization report, pharmaceutical companies are now responsible for monitoring problems that could arise from "irrational drug use, overdoses, polypharmacy and interactions, increasing use of traditional and herbal medicines with other medicines, illegal sale of medicines and drugs of abuse over the Internet, increasing self-medication practices, substandard medicines, medication errors, and lack of efficacy" (World Health Organization, 2002).

To adapt to this growing list of challenges, pharmaceutical companies must review and further develop their own pharmacovigilance systems. Taking advantage of available research tools is critical in the gathering and analyzing of complex information.



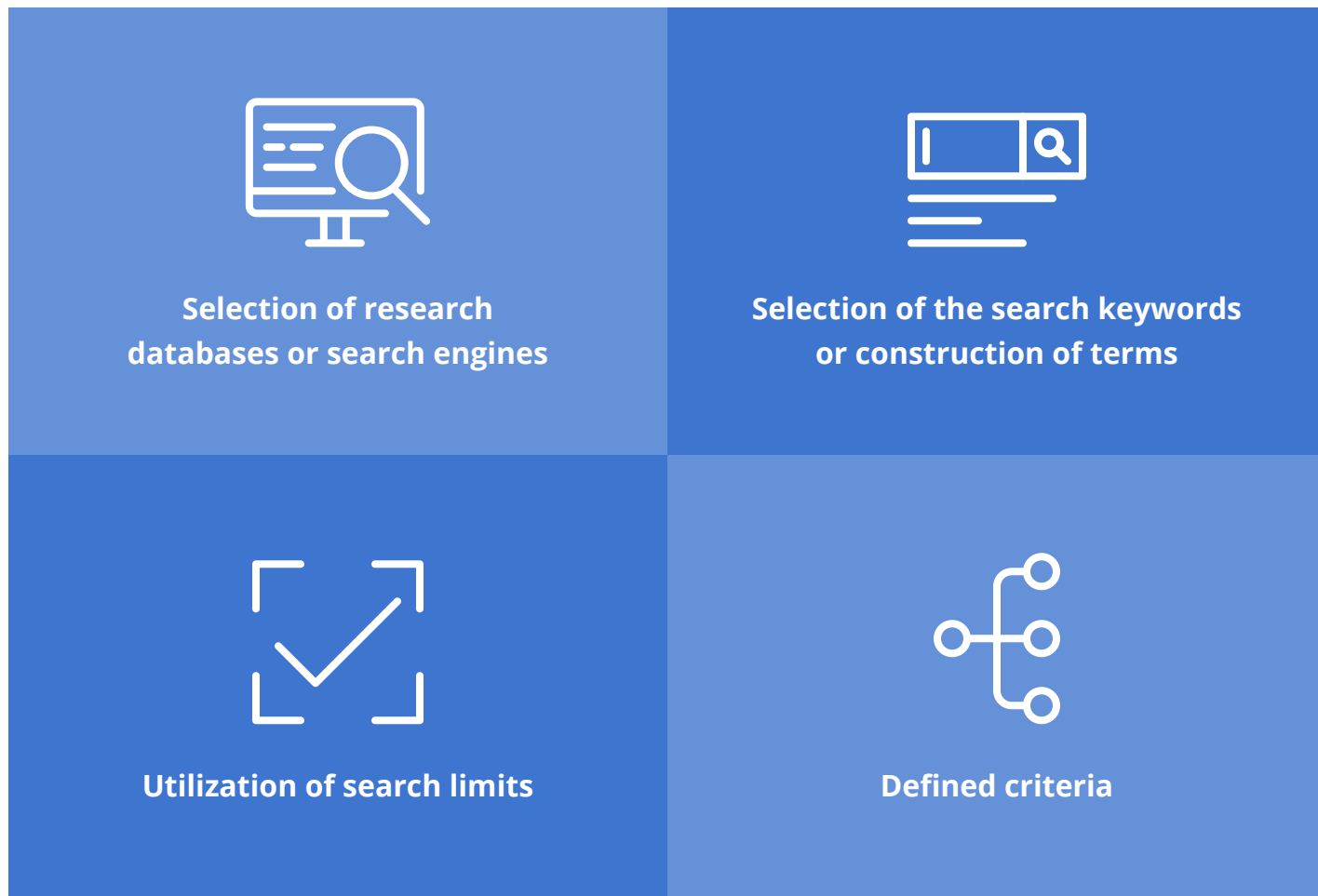
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Research Tools for Pharmacovigilance

Although technology can pose challenges for pharmacovigilance, it can also serve as a tool to make pharmacovigilance more effective and efficient. Big data has been employed to assist in the gathering of and distribution of pharmaceutical information. Big data can be defined as "a large volume of diverse, dynamic, distributed structured or unstructured data..." (Ventola, 2018).

Today, a number of databases exist with the sole purpose of storing data used for pharmacovigilance. "The use of big data for pharmacovigilance involves novel electronic methods that are applied to analyze the large and growing volume of information about ADEs (adverse drug events) in spontaneous reporting systems (SRS) databases and other digital sources" (Ventola, 2018). These methods are critical for analyzing information to understand any potential patterns between drugs, side effects and risk factors.

Additionally, scientific literature can provide a significant source of information for pharmacovigilance. Pharmaceutical companies must employ a strategic approach to collecting information about suspected ADRs from literature sources using reference databases such as MEDLINE or EMBASE. During the literature review, the search should focus on articles containing safety relevant information through “review articles, meta-analyses, observational studies, epidemiologic studies, etc.” (Pontes, Clemet, & Rollason, 2014). To obtain the best results, it is recommended (Pontes, Clemet, & Rollason, 2014) that the researcher considers the following:



To ensure that researchers are reviewing the most relevant and reliable information, it is recommended that pharmaceutical companies invest in a specialized database to streamline pharmacovigilance research. EBSCO's [*Biotechnology Source*](#) offers a single-search platform that allows researchers to search thousands of full-text pharmaceutical journals. Additionally, it offers the largest collection of full-text content indexed in MEDLINE, EMBASE and BIOSIS. This invaluable database will make pharmacovigilance research easier than ever.



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Special Cases: Developing a Plan

The development of most products requires only routine pharmacovigilance. However, in some instances, developing a more in-depth pharmacovigilance plan is necessary. This is important for products that pose unusual safety risks that have become evident prior to approval or after the product has been marketed. The development of such a plan can be useful “at the time of product launch or when a safety risk is identified during product marketing” (Guidance for Industry: Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment, 2005).

According to the U.S. Department of Health and Human Services (2005), the plan should include one or more of the following elements:

1. Submission of specific serious adverse event reports in an expedient manner beyond routine reporting
2. Submission of adverse event report summarized at more frequent intervals
3. Active surveillance to identify adverse events that may or may not be reported through passive surveillance
4. Additional pharmacoepidemiologic studies using cohort, case-control, or other appropriate study designs
5. Creation or registries or implementation of patient or health care provider surveys
6. Additional controlled clinical trials

Common web-based tools to assist in the practice of pharmacovigilance:

- Spontaneous reporting systems (SRS) that can be used to analyze adverse drug effects in patients
- Electronic health records that provide information that can help researchers identify possible associations between a drug and adverse effects
- MEDLINE, a bibliographic database of academic journals that specialize in medical and pharmaceutical information, can assist in recognizing drugs and associated adverse effects
- Medical literature can be used to predict drug and adverse effect associations based on chemical structures, as well as identify vaccines and adverse effect signals based on molecular information
- Databases such as Embase®, which consist of published literature to support pharmacovigilance in complying with the regulatory requirements of a licensed drug



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Conclusion

Pharmacovigilance is a critical step to the drug development process. As medicine becomes a globalized industry, it is more important than ever to understand the adverse effects of drugs on larger and more diverse populations. Although technology poses some challenges to the pharmaceutical industry, it can also assist in gathering critical information that can help researchers make more informed decisions.

To prepare for and develop a pharmacovigilance process, pharmaceutical companies should invest in tools that will help to perform in-depth research. EBSCO Corporate Solutions offers *Biotechnology Source*, a single-search platform to thousands of full-text journals, industry publications and unique titles for biotechnology and pharmaceutical research. For more information, contact an EBSCO representative today.

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