

## PHARMACOVIGILANCE IN CLINICAL TRIALS

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**ABSTRACT**

Pharmacovigilance has become an important tool for evaluation of adverse drug reactions (ADRs). During a clinical trial, ADRs can happen in any phase therefore strict vigilance is needed for the safety of the participants. Even after the drug has been approved, the effect of the drug has to be monitored in the larger population as during the trials, the study population is small and trial is under strict control due to robust inclusion and exclusion criteria. Once out in market, the medicine is consumed by a larger population, therefore the chances of occurrence of rare adverse effects are high. Due to this reason, Pharmacovigilance is very crucial even after approval of a drug. Lastly, in case of vaccines, AEFI surveillance and reporting is very important to find out the rare side effects of vaccination.

Pharmacovigilance is the science dealing with detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.

**ADR (Adverse drug reaction):** ADR is defined by the World Health Organization (WHO) as a response to a drug that is noxious, unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis or therapy of disease or for the modification of a physiological function.

Clinical trials can result in several complications related to the medical conditions of the participants involved in a clinical trial. During a clinical trial, these kinds of situations or events might happen. It is important to have a proper segmentation of events so that a quick and effective management plan can be implemented immediately. There are different reporting processes that need to be followed in different events. Two most common events in a clinical trial are Adverse Events (SE) and Serious Adverse Events (SAE).

**Adverse Event (AE):** Adverse Events refers to any situation where the candidates participating in a clinical trial shows some adverse medical symptoms. These symptoms may be revealed in the laboratory test reports or physical examination of the participants. This term is strictly applicable for the individuals who have been involved or associated with the research for any length of time, short or long.

The principal difference between an adverse event and an adverse drug reaction is that a causal relationship is suspected for the later, but is not required for the former.

In this framework, adverse drug reactions are a subset of adverse event reports.

**Serious Adverse Event (SAE)**

A Serious Adverse Event (SAE) is actually a special case of an adverse event where adverse outcomes are severe. It includes following events.

- Death of any of the participants associated with a clinical trial.
- An event which can lead to life-threatening complications or put the life of participants at risk as a result of participation in a clinical trial.
- Events that result in such a condition where the participants may require immediate hospitalization or increase the duration of hospitalization.
- Any events that lead to a permanent or temporary physical disability in the body of the participants. Any sort of incapacity is also regarded as SAE.
- Any events that lead to any type of congenital abnormalities. It also includes any cases of birth defects resulting from the clinical trials.
- Any events where an investigator or team of investigators finds feel that it can lead to significant hazards.

**Importance of pharmacovigilance**

In 1994, more than 100,000 deaths occurred because of adverse drug reactions. And in the period between 1999 and 2008, the adverse drug reactions were responsible for 26,399 deaths and 0.9% of the emergency hospital admissions, which means that adverse drug reactions are responsible for increasing the patient's morbidity and mortality worldwide.

### The importance of Pharmacovigilance in Clinical Trial Regulation

Although new medicine development is crucial for a large portion of patients, the random increase in the number of clinical trials may affect the function of ethics committees and regulators, which may lead to unethical patient practices, poor reporting of adverse effects, and poor patient monitoring during the phases of clinical trials. To overcome these challenges the pharmacovigilance took part in the clinical trial regulation to guarantee proper monitoring, reporting, and assessment of clinical data. The CIOMS (Council for International Organization of Medical Sciences) working groups on pharmacovigilance have the same roles, besides standardizing and coordinating the adverse drug reporting process internationally between the pharmaceutical manufacturers and the regulatory authorities.

### The Importance of Pharmacovigilance in the Post-Marketing Safety Monitoring

About 10% of the newly-approved drugs are withdrawn from the market after their release. Introducing a new medicine to the market after its approval does not guarantee its safety. Premarket studies can not determine the complete drug safety profile. Small sample size, short study duration, and also excluding some patient's categories, like the elderly and children, may affect the drug safety profile results. Besides, the pharmaceutical companies exert more effort to prove the drug efficacy rather than its safety. Therefore, the role of pharmacovigilance in the drug safety monitoring for any adverse drug events is necessary either for the new medicines or the old one. And here, the health care providers and the community have a vital role in reporting any adverse drug events to support the role of pharmacovigilance.

### The Role of Pharmacovigilance in Monitoring of Herbal and Traditional Medicines

Some herbs interact with particular drugs, resulting in an unwanted increase or decrease in drug concentration. Therefore, the National Pharmacovigilance included the herbal and traditional medicines in its programs to monitor their safety.

### The Importance of Vaccine Pharmacovigilance

Most people believe that any vaccine is safe, so any change in this belief will lead to serious outcomes. Vaccine's safety should be monitored to guarantee public compliance with the vaccine programs. Here the concept of vaccine pharmacovigilance arises: "It is the science and activities relating to the detection, assessment, understanding, prevention, and communication of adverse events following immunization, or any other vaccine- or immunization-related issues."

With the developing trends in health care industry, information technology (IT) has transformed the world health care and clinical medicine, to meet their standards,

thus improving the safety, efficacy of drugs, and reducing the costs. Booming of IT into clinical safety practice creates a strong platform, to establish pharmacovigilance systems for safety signal detection. Thus, it brought a significant change in conducting clinical research practice of medicines and medical safety monitoring. For an fruitful pharmacovigilance system to be effective, all the stakeholders need to be keen enough throughout the lifecycle of a drug in the market. Thus pharmacovigilance is very critical step involved in drug development process, which ensures new innovative drug meets the regulatory compliance, thus enhancing the clinical trials safety and post marketing surveillance.

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