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Good Pharmacovigilance Practices

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INTRODUCTION

Good Practices in Pharmacovigilance

Life cycle of medicines

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From 4 to 5 years

Discovery Basic Research

10,000 compounds

Pre-clinical Development

30-250 compounds

From 1 to 2 years

From 6 to 8 years

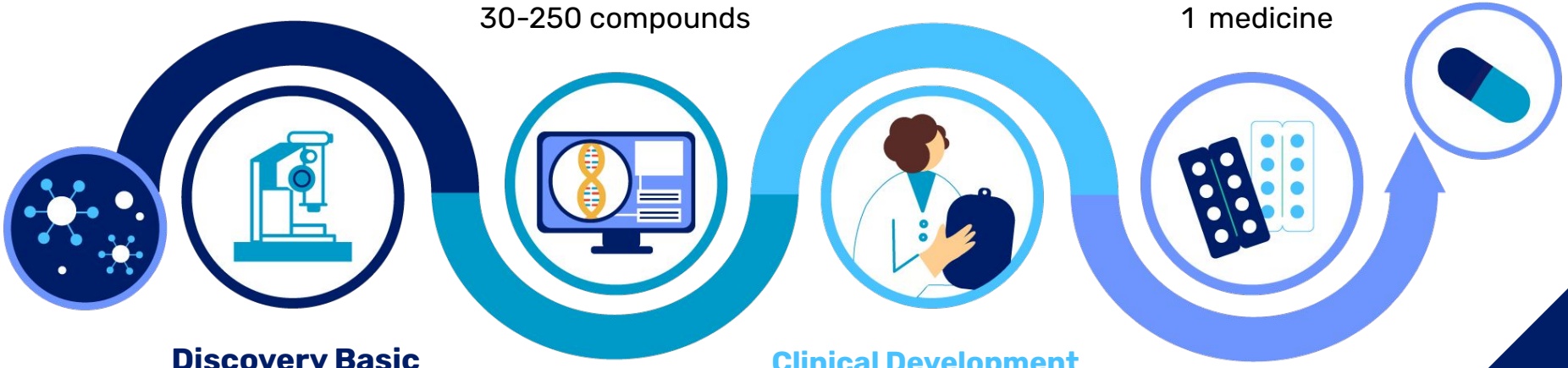
Clinical Development Phases I, II, III, IV

5 compounds

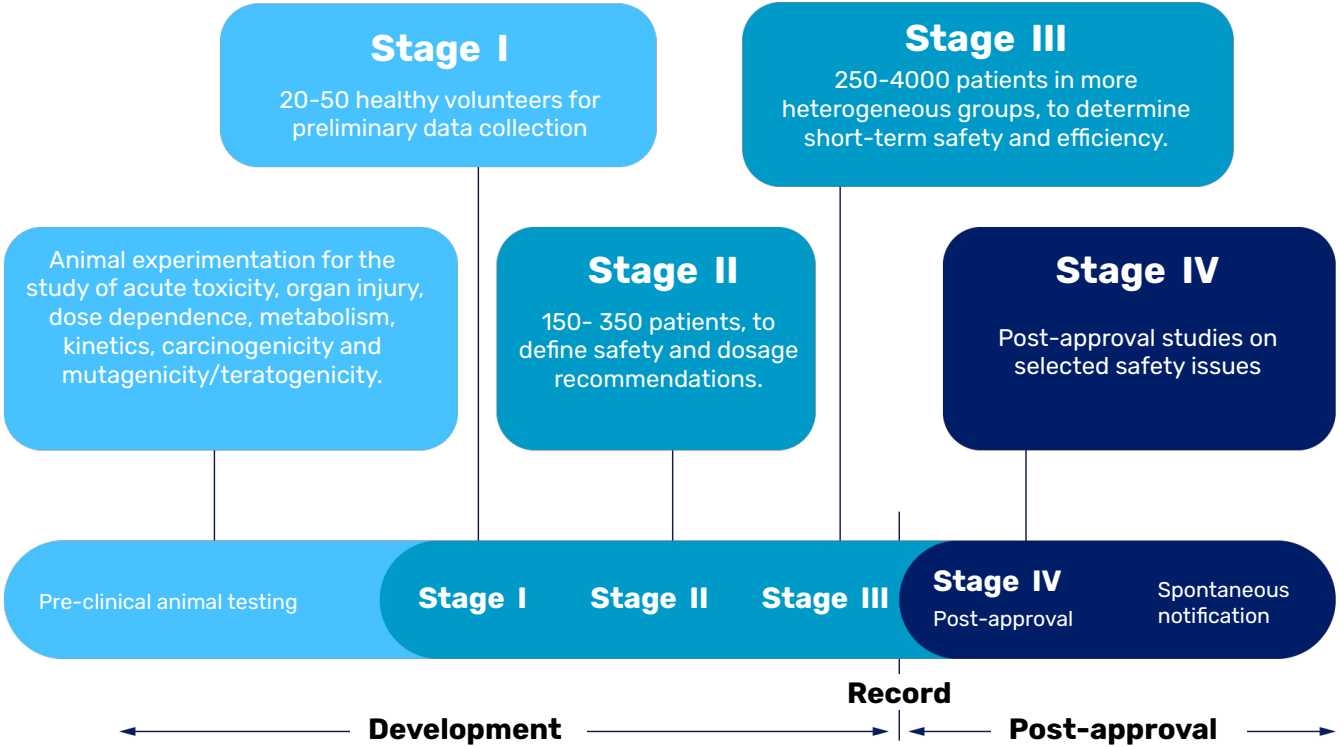
Registration and Marketing

1 medicine

From 1 to 2 years



Clinical drug development



Source: Pharmacovigilance: Guarantee of safety in the use of medicines. WHO (2004)
Available at: https://iris.who.int/bitstream/handle/10665/68862/WHO_EDM_2004.8_spa.pdf?sequence=1&isAllowed=y

Concept of Pharmacovigilance

The WHO defines **pharmacovigilance** as the science and activities relating to the **detection, assessment, understanding and prevention of adverse effects** or any other medicine/vaccine related problem.

Pharmacovigilance Objectives

- To ensure the care and safety of patients in relation to the use of medicines and all medical interventions.
- Improve public health and safety in the use of medicines.
- Detect problems related to medication use and communicate findings in a timely manner.
- Contribute with the evaluation of the benefits, harms, effectiveness and risks of medicines, allowing preventing harms and maximizing benefits.
- Encourage the use of medicines in a safe, rational and more efficient manner (including cost-effectiveness).
- Promote understanding, education and clinical training in pharmacovigilance and its effective communication to the public.

Methodology

Various methods are used to carry out pharmacovigilance activities:

Spontaneous notification system

It identifies and detects suspected adverse reactions, by healthcare professionals, in their daily practice and the forwarding of this information to a body that centralizes it.

This is the methodology used by the participating centers of the WHO International Pharmacovigilance Program.

Procedimientos de farmacovigilancia intensiva

Based on the systematic and detailed collection of data on all the harmful effects that can be assumed to be induced by drugs in certain population groups.

They are divided into two groups:
- drug-centered systems.
- patient-centered systems

Epidemiological studies

Its purpose is to test a hypothesis, i.e., to establish causality between the presence of adverse reactions to drugs and their use.

They can be:
- cohort studies
- case and control studies

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GENERAL PRINCIPLES

Good Pharmacovigilance Practices

Good Pharmacovigilance Practices are a quality standard for monitoring the safety of medicines and are intended to ensure:

The veracity of the data collected

The confidentiality of reporters and patients and patients

The use of uniform criteria in the evaluation of notifications and generation of signals or alerts.

General information

- To obtain a **pharmacovigilance system** that can comply with good pharmacovigilance practices, it is necessary to implement quality management methods that make the system more efficient.

- The quality system shall include the organizational structure, responsibilities, procedures, processes, as well as the appropriate management of resources, compliance and record keeping.

Procedures

The procedures should clarify and unify information on:

- What constitutes a notifiable adverse event.
- Who should notify an observation of suspected drug-related problems.
- The availability and guidance for filling out the notification forms.
- Guidelines for the submission and collection of information
- Guidance for the evaluation, follow-up and processing of case notifications to the corresponding institutions.
- Guide to the analysis of information and possible courses of action
- Good communication practices
- Indicators to measure the progress of the monitoring system

General information

Currently, several countries have published their Good Pharmacovigilance Practice manuals, as well as their compliance checklist. Here are some links with information:

Argentina

Peru

PAHO

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BASIC ACTIONS FOR THE ESTABLISHMENT OF A PHARMACOVIGILANCE CENTER

Good Pharmacovigilance Practices

Pharmacovigilance Center

A new pharmacovigilance center can be set up very easily.

However, the development of a **pharmacovigilance system** from an uncertain initial state to an effective and established organization is a process that requires time, vision, dedication, competence and continuity.

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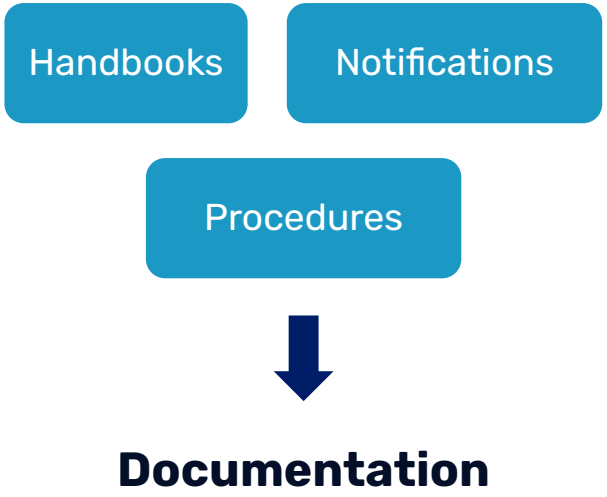
DOCUMENTATION

Good Pharmacovigilance Practices

Documentation

Complete and updated documentation is essential for the quality assurance system and good pharmacovigilance practices.

Their importance lies in the fact that notifications can generate signals and therefore their quality is decisive for an appropriate assessment of the possible causal relationship between the drug and the adverse events.



To ensure good pharmacovigilance practices, documentation should comply with the following characteristics:

- Designed, developed, reviewed and distributed according to its functionality
- Approved, signed and dated.
- Unambiguous wording
- Clear and legible documents
- Periodic review and updating

Handbooks

Quality

Describes the objectives, means and procedures for quality assurance.

Procedures

It brings together in an orderly and logical manner the standard operating procedures used in the operation and describes the interrelationship between them.

Procedures

Operating procedures are an important part of the documentation of a quality assurance system the documentation of a quality assurance system. They are defined as detailed, written instructions for achieving uniformity in the performance of a specific activity and form the basis for internal or external audits.

They should be oriented to describe at least the following activities:

1. Collection and transmission of safety information (including validation, documentation of the reaction, obtaining complementary information).

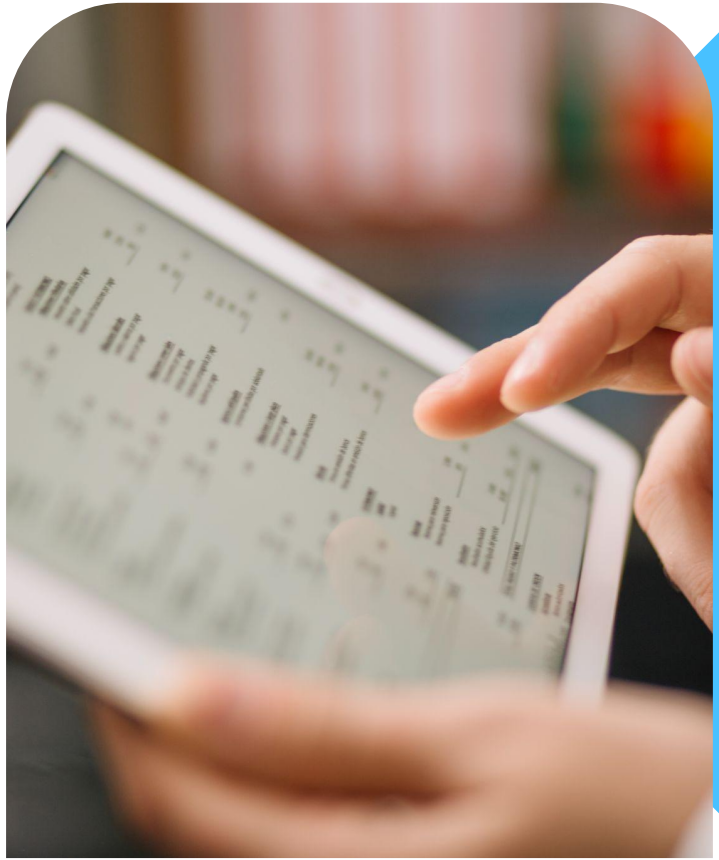
2. Activities of an administrative nature (archiving of documentation, protection of records).

3. Notification evaluation and reporting (including detection and management of signals or alerts).

Procedures

The procedures should be identified with the following data:

- Name of procedure
- Name and signature of author
- Name and signature of approver
- Code and date of editing
- Name and signature of QC
- Related procedures
- Target staff



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COMPUTERIZED SYSTEMS

Good Pharmacovigilance Practices

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These should be:

- Validated
- Regular backups
- List of authorized personnel
- Ensure traceability of information
- Periodic quality controls

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MANAGEMENT OF NOTIFICATIONS

Good Pharmacovigilance Practices

The management of notifications complies with the following characteristics:

- Evaluates notifications from health professionals.
- Requests complementary information when they are not physicians*.
- Contact of the health professionals when it comes from the patient.

Minimum information to be considered valid (NPDR):

1. Data from patient
2. Description of the adverse event
3. Suspect drug data
4. Notifier data.

Complete information:

5. Concomitant Medications
6. Risk factors
7. Event Diagnostics
8. Clinical evolution and results
9. Determinations from laboratories
10. Exposure and re-exposure information
11. Any other relevant information

*Follow-up to obtain additional information

Establishes procedures to encourage notification.

*Local data privacy laws in each country must be taken into account.

Processing Systems

Manual

When there are few cases

Computerized

It should include a hierarchical finding of drugs that allows them to be classified according to their generic component, trade name and therapeutic category.

Terminology that hierarchically classifies adverse reactions should be used.

Form of sending notifications

- Mail, fax and telephone
- E-mail or Internet: use systematic processing (e-Reporting /E2B)

How to improve notification

- Facilitate access to reporting media such as forms, e-mail or a website, etc.
- Acknowledge receipt of each suspected adverse reaction notification to thank the notificator.
- Provide feedback to notificators in the form of journal articles, adverse reaction bulletins fact sheets.
- Stimulate the participation of the centers' personnel in scientific meetings or educational courses, both undergraduate and graduate.
- Collaborate with local pharmacovigilance or drug committees and professional associations.
- Integrate pharmacovigilance in the development of clinical pharmacy and clinical pharmacology in the country.

Under-notification can delay signal detection and cause underestimation of the magnitude of a problem. However, it is not only the quantity of notifications that is important in signal detection, but also the relevance of the notified cases and the quality of the data.

Codification

- Use coding categories and terminologies adopted in international regulatory forums (such as international harmonization conferences).
- As established in the corresponding manual.
- Periodically control data quality to detect possible systematic errors in data entry and coding.
- Allow protection of the identity of both the notificator, patient, and the event.
- Ensure the completeness, accuracy, fiability, consistency and confidentiality of all information.
- Record the date of receipt and assign an identification number to each notification.
- For drugs and adverse reactions, internationally accepted terminology should be used: drug names with WHO drug dictionary, adverse reactions and WHO adverse reaction terminology (WHO-ART), or MedDRA (Medical Dictionary for Regulatory Activities).

Database review

- Local databases - and those of each institution - should be linked to those compiling regional and global information in pursuit of pharmacovigilance objectives.

- Documents related to the same notification of a suspected adverse reaction should be kept in the same file or, failing that, with a clear reference of their location to avoid duplication of notifications.

- Ensure the security and confidentiality of the information.

Evaluation of Notifications

- Quality of information
- Codification
- Importance: new medicine? Unknown reaction? Serious reaction?
- Identification of duplicated notifications.
- Causality assessment: temporal relationship, medical or pharmacological plausibility and probability or exclusion of other causes.

Evaluation of Causality

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Answer the questions:

- Is there an alternative explanation for the observed reaction?
- Were other medications not cited on the notification card administered?
- Is it certain that the patient took the medication as directed?
- Had the patient previously taken this drug or another analog?
- How many cases of this new reaction have been notified to the regional center, national center or UMC?

Chronological Sequence

- Is there a temporal relationship between taking the drug and the occurrence of the adverse reaction?

Relation from Causality

- Take into consideration that in some countries local authorities have determined the use of specific algorithms for causality assessment. Such as the Naranjo Algorithm - WHO Algorithm - FDA Algorithm - FDA Algorithm

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PHARMACOVIGILANCE IN CLINICAL STUDIES

Good Practices in Pharmacovigilance

Pharmacovigilance in Clinical Trials

Sponsor

- Responsible for the continuous evaluation of the safety of the products under investigation.
- It should promptly notify interested institutions and investigators and the regulatory authority of findings that could adversely affect the safety of subjects under study.
- You should notifify all serious and unexpected adverse drug reactions, along with all periodic safety updates and reports.

Local Regulation

- It must establish in detail the deadlines for notification.
- Notifications of clinical studies should be handled or identified separately from those of marketed products.