REPUBLIC OF GUINEA

Work-Justice-Solidarity

MINISTRY OF HEALTH AND PUBLIC HYGIENE

NATIONAL DIRECTORATE OF PHARMACY AND MEDICINE

PHARMACOVIGILANCE GUIDELINES

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Abreviations list :

MA: Marketing Authorization

ANRP: National Authority for Pharmaceutical Regulation

CNP: National Pharmacovigilance Committee

CNTS: National Blood Transfusion Center

DNPM: National Directorate of Pharmacy and Medicine

EI: Undesirable Event

ADR: Adverse Drug Event

ICH: International Council for Harmonization of Technical Requirements for the Registration of Medicinal Products for Human Use

AEFI: Adverse Manifestation Post-Immunization

MedDRA: Medical Dictionary of Regulatory Affairs

EPI: Expanded Vaccination Program

EPI/SSP: Expanded Program for Immunization/Primary Health Care

PV: Pharmacovigilance

UMC: Uppsala Monitoring Center

I. INTRODUCTION

The National Pharmacovigilance System in the Republic of Guinea had its beginnings in the 1990s. Law N °L94/012/CTRN of 22 MARCH 1994, on pharmaceutical legislation, in its regulatory provisions section in its article R6 established the pharmacovigilance sub-committee among the specialized sub-commissions. The basic elements were materialized in 2008 with the training of executives at the poison control center in Morocco, the design of tools (notification form, surveillance guide), membership of the Uppsala Monitoring Center (UMC) in 2009 as an associate member.

The monitoring of side effects during the vaccination campaign against yellow fever in 2010 came to galvanize the achievements by the strengthening of technical capacities and the acquisition of experience through the experts deployed for this purpose.

The country became a full member of the international side effects monitoring system in 2013 (Uppsala Monitoring Center (UMC) based in Uppsala, Sweden,

The monitoring of adverse post-immunization events initiated by the WHO has made it possible to update the tools and to draw up the monitoring guide for these events. It also supported the process and strengthened the skills of actors at all levels.

The pharmacovigilance system is coordinated by the National Directorate of Pharmacy and Medicine according to the provisions of law L/2018/024/AN of July 13, 2018 relating to medicines, health products and the exercise of the profession of pharmacist. in its article 21, which is devoted to monitoring the risk of adverse effects resulting from the use of medicinal products.

The operation and organization of the pharmacovigilance system are defined by Order of the Minister in charge of Health.

It is a decentralized system with focal points at all levels of the Health pyramid. Nowadays, the pharmacovigilance section of the National Directorate of Pharmacy and Medicine ensures the implementation of Pharmacovigilance activities.

These guidelines are developed

To define the monitoring mechanisms (detection, notification, causal analysis, communication and dissemination of any information relating to the safety of use) during the use of the drug or other health product, but also the way in

which the various stakeholders must fulfill the obligations as well as the mechanisms of collaboration between them.

They are based on the guidelines of the International Council for Harmonization (ICH) for the registration of medicinal products for human use and may also contain additional requirements in accordance with the legislation in force. They bring together general guidance on the requirements, procedures, roles and activities in this area, for stakeholders in the national pharmacovigilance system.

The contents of this document should not be considered the sole interpretation of the Drugs and Other Health Products Regulations and is not intended to cover all possible cases. Any other means used to comply with the Regulation respecting medications and other health products may also be taken into consideration with the appropriate justifications.

It should be noted that, as with all guidance documents in rapidly changing technical areas, these guidelines are intended to be reviewed regularly.

II. PHARMACOVIGILANCE

In the interests of consumer protection, the public authorities give fundamental priority to procedures guaranteeing the quality of the drug and the Marketing Authorizations (MA). The drug is made available to health professionals and citizens taking into account the quality of the drug molecule sufficient to protect them from the harmful effects of its use.

The health and economic interest represented by the drug highlights its therapeutic value, relegating its undesirable effects to the background. The drug has certainly made it possible to reduce the mortality and morbidity of several diseases and even to eradicate some of them, but it can also be the cause of health, economic and social damage.

Adverse effects are generally considered to be those directly related to the drug, today include all effects resulting from, among other things, abuse of use, dependence, drug addiction, medication errors, even use of the drug outside of the regulatory circuit. Hence the interest of Pharmacovigilance for the management of all these elements.

To avoid causing harm to patients and thus improve public health, it is essential to have mechanisms in place to assess and monitor the safety of medicines used in clinical practice. In concrete terms, this means setting up a well-organized pharmacovigilance system.

Pharmacovigilance, an umbrella term used to describe the processes for monitoring and evaluating adverse drug reactions, is an essential component of effective drug regulatory systems, clinical practice, and public health programs.

The national system for managing adverse effects is decentralized with focal points for reporting information based on the country's health pyramid, taking into account all health system stakeholders.

II. 1. DEFINITION

Pharmacovigilance is defined by WHO as the science and activities related to the detection, evaluation, understanding and prevention of adverse drug reactions and other problems related to the use of drugs and any other health products. health.

II. 2. OBJECTIVES

II.2.1 General objective:

Improve patient safety by continuously monitoring the health impact of the use of health products and assessing the benefit/risk ratio of these products.

II.2.2 Specific objectives:

- Orient Providers to the early detection of new adverse effects;
- Detect the frequency of known adverse effects;
- Identify drug risk factors that may explain these effects;
- Assess the benefit/risk ratio;
- Disseminate the information necessary to improve the prescription and regulation of drugs;
- Promote the rational use of medicines;
- Improve the quality of care and patient safety.

II. 3. FIELDS OF APPLICATION

Pharmacovigilance applies to drugs and any other health product for human use:

1. Pharmaceutical products
   - Medicines as defined by the regulations;
   - homeopathic medicines;
   - Drugs in the clinical trial phase;
2. organic products
   - Blood products obtained by fractionation;
   - Vaccines and other biological products;
   - Cell therapy products;
   - Gene therapy products;
3. Food products
   - Food supplements;
4. Hygiene products
   - cosmetic products;
   - Insecticides and acaricides intended for application on humans;
5. Medical devices
   - Medical materials;
   - Laboratory reagents;
6. Medical gases
7. Radiopharmaceuticals ; _
8. Products from traditional medicine;
   - Plants ;
   - Medicinal herbal products.

Vigilance is also exercised on all other problems related to use such as: medication errors, treatment failures, inferior quality and falsified medicines (QIF), abuse of use, diversion of indication, misuse and other health products.

These guidelines do not apply, at this time, to the following products:

- Hard surface disinfectants;
- Whole blood and blood components;
- veterinary products.

III. NATIONAL PHARMACOVIGILANCE SYSTEM

The National Pharmaceutical Policy of the Republic of Guinea aims to provide its population with good quality, effective and affordable drugs **.**

In order to ensure the quality of drugs, the Ministry of Health and Public Hygiene has deemed it necessary to develop a pharmacovigilance system.

The implementation of an effective pharmacovigilance system is not only based on the development of a pharmacovigilance center, but requires the presence of an effective National Pharmaceutical Regulatory Authority (ANRP), capable of reacting to signals emanating from the center and to take the necessary regulatory measures. The decentralization of activities improves the exchange of information with health professionals and therefore makes it possible to obtain an overall view of the situation.

For its operation, the National Pharmacovigilance System includes: the National Pharmacovigilance Commission, the National Pharmacovigilance Technical Committee, the Pharmacovigilance Section of the National Directorate of Pharmacy and Medicine, the Pharmacovigilance Focal Points at each level of the health pyramid, Health Programs, Pharmaceutical Companies and the Public.

The National Pharmacovigilance System aims to:

- Detect as early as possible adverse effects due to the use of drugs and other health products under normal conditions of use and in the event of:
- Misuse ,
- Misuse,
- drug addiction,
- medication error,
- Drug ineffectiveness,
- Defective or substandard products.
- Establish the frequency and severity of known or newly discovered adverse effects;
- Promote patient safety in relation to the use of all health products;
- Ensure the training and information of health personnel and the public in terms of adverse effects;
- Give reasoned technical advice to personalities and organizations with decision-making power on the regulation of health products;

- Encourage and carry out studies on the mechanisms and consequences of the adverse effects of health products.

The Pharmacovigilance Section of the DNPM is responsible for the coordination and implementation of all system activities.

This implementation is based on:

- A network for collecting reports of adverse effects, including during clinical trials;
- Recording, analysis, evaluation of the quality of the information collected and its classification;
- Centralization and evaluation of all information on drug risks;
- Risk communication;
- Decision making ;
- Conducting studies on the safety of use of drugs and other health products.

IV. DIFFERENT PARTICIPANTS IN THE NATIONAL PHARMACOVIGILANCE SYSTEM

IV. 1 The National Pharmacovigilance Commission

The National Pharmacovigilance Commission sits with the Ministry of Health and Public Hygiene through the National Directorate of Pharmacy and Medicine.

It meets twice a year and decides on all the questions proposed by the Pharmacovigilance Technical Committee and also on the measures and decisions taken urgently outside the sessions and can call on any outside expertise if necessary.

The work of the National Commission is also held when necessary and when convened by its President.

The members of the National Pharmacovigilance Commission are bound by the obligation of confidentiality and are required to avoid conflicts of interest.

IV.1. 1 . Missions of the National Pharmacovigilance Commission

Its mission is to:

- Evaluate information on adverse effects of drugs and other health products;
- Give advice to the Minister in charge of Health at the request of the latter on any question relating to the area of competence of the Commission;
- Assess the risks incurred by subjects participating in a clinical trial and give its opinion to the DNPM on its continuation or termination;
- Inform the DNPM of all measures concerning the marketing and withdrawal of drugs;
- Give an opinion to the Minister in charge of Health on the measures to be taken to ensure the safety of patients in the face of the risks associated with the use of drugs or other health products.

IV. 1.2. Composition of the National Pharmacovigilance Commission

The National Pharmacovigilance Commission is composed as follows:

- Chairman: National Director of Pharmacy and Medicine
- Vice-president: National Coordinator of the Expanded Vaccination Program (EPI)
- Secretariat: Head of Pharmacovigilance Section (DNPM)
  Surveillance Focal Point (ENP/SSP Coordination)
  Members :
- The Legal Advisor of the Ministry of Health and Public Hygiene
- A Representative of the Ministry in charge of Trade and Industry;
- A Representative of the Ministry in charge of Security;
- A Representative of the National Directorate of Laboratories;
- A Representative of the National Directorate of Public and Private Hospital Establishments;
- A Representative of the National Customs Directorate;
- Three Head Pharmacists of the University Hospitals;
- Three Chief Biologists of the University Hospitals;
- A representative of the army health service;
- A representative of civil society;
- A Representative of the National Directorate of Community Health and Traditional Medicine;

- A Representative of the National Blood Transfusion Center (CNTS);
- Pharmacovigilance focal point for the various Health Programs;
- A representative of the order of doctors;
- A representative of the Order of Pharmacists;
- A Representative of the College of Dental Surgeons;
- A Representative of the National Drug Quality Control Laboratory.

IV.2. National Pharmaceutical Regulatory Authority (ANRP)

IV.2.1 Roles of the DNPM/ ANRP:

Through its pharmacovigilance section, its role is to:

- Organize the technical activities of pharmacovigilance at the national and regional level;
- Ensure the coordination of pharmacovigilance activities with health programs and all players in the system;
- Manage the national database of adverse reactions to health products
- Ensure relations with the UMC (International Center for Pharmacovigilance of Uppsala)
- Fill in the international database via Vigiflow;
- Collect and record adverse reaction reports;
- Receive statements, reports and all information transmitted to it;
- Evaluate information on adverse effects of drugs and other health products;
- Generate alerts in the field of pharmacovigilance and refer to the National Pharmacovigilance Commission, whenever necessary;
- Provide information on the rational use of the drug and adverse effects to authorities, health professionals, the media and the public;
- Ensure the training of health professionals on the adverse effects of health products and their notification;
- Coordinate the actions of the various stakeholders in the system;
- Ensure compliance with Good Pharmacovigilance Practice procedures;
- Transmit the report of the Technical Committee to the National Pharmacovigilance Commission;
- Prepare the meeting sessions of the National Pharmacovigilance Commission.

IV.3. National Pharmacovigilance Technical Committee

The National Technical Committee is an independent committee, made up of experts from different specialties. He is responsible for the analysis of the data, the clinical review of the cases, their classification, the validation of the tools and the final report as well as the communication of the report.

IV.3.1 Role and powers of the Technical Committee

- Schedule and decide on the appropriateness of pharmacovigilance surveys, including the quality control of the surveillance system and to examine the results;
- Evaluate the periodic reports sent to it;
- Assess the adequacy of notifications on substandard products ;
- Decide on the advisability of planning and coordinating additional investigations in order to confirm causality (quality control of health products, active surveillance, inspection and others…);
- Assess the potential causal links between the drug(s) and the adverse event and/or between the vaccines and the AEFI (imputability);
- Provide advice on issues related to the safety of use of medicines to the Pharmaceutical Regulatory Authority;
- Give the Regulatory Authority technical advice on the basis of the results of their exercise to manage the risks associated with health products (quarantine, batch recall, letter to prescribers, and others);
- Monitor the implementation of technical advice provided to the Pharmaceutical regulatory authority;
- Assess the impact of regulatory decisions recommended by the Risk Management Committee;
- Constitute technical or thematic sub-committees as needed (which report only to the technical committee);
- Consult a permanent unit of Pharmacology Specialists and Clinical Experts who can, if necessary, assess the risks incurred by humans and propose the measures to be taken to the National Medicines Commission;
- Respond to any request for scientific advice presented by the National Pharmacovigilance Commission or by the Pharmaceutical Regulatory Authority.

IV.3.2. Composition of the Pharmacovigilance Technical Committee

In view of this mission, the National Technical Committee is composed as follows:

1 President
1 Vice-president
2 secretaries

Members :

1. Pediatrician ;
2. Pharmacist/Medicine Epidemiologist;
3. Dermatologist ;
4. Gastroenterologist;
5. Infectiologist/Internal Medicine;
6. Neurologist/Neurosurgeon/Psychiatrist;
7. Forensic pathologist/Anatomopathologist;
8. Immunologist/ Toxicologist;
9. Communication Expert;
10. Expert in Socio-anthropology;
11. Expert in Pharmacognosy;
12. Quality Control Expert;
13. Clinical Pharmacist.

The Technical Committee may occasionally call on any other expertise if necessary. The structures of the Ministry of Health and Public Hygiene and the Technical and Financial Partners involved in the field will be observers of the work of the said Committee.

The Pharmacovigilance Section Head of the DNPM and the MAPI focal point of the EPI will provide the secretariat.

IV.4. Industry / Pharmaceutical Firms:

Pharmaceutical companies holding a Marketing Authorization (MA) are responsible for the drugs they market through the development of a functional pharmacovigilance unit in accordance with good pharmacovigilance practices. They must :

- Organize an internal pharmacovigilance system with a person qualified for pharmacovigilance;
- Encourage their medical representatives to collect cases of adverse effects reported by healthcare professionals. These cases are processed, imputed and sent to the DNPM;
- Promptly report all serious and unexpected side effects;
- Transmit updated information on the safety of health products as well as pharmacovigilance decisions taken in other countries;
- Transmit periodic pharmacovigilance reports (every 3 months) (Periodic safety update report PSUR) for new products and annually for other products;
- Respond to any query regarding their firm's drugs;
- Declare the spontaneous adverse effects notified to them;
- Provide the risk management plan on request from the DNPM if necessary.

All this information must be sent to the DNPM.

In the case of clinical trials:

a) Serious adverse effects occurring during a clinical trial must be notified to the DNPM within 7 days;
b) The notification of any new fact likely to harm the safety of the subjects participating in the trial is 15 days following the knowledge of the sponsor;
c) Non-serious adverse effects will be transmitted in the final report of the clinical study to the DNPM.

Industry participation in Pharmacovigilance surveys strengthens collaboration with the DNPM for the benefit of the patient.

An investigation carried out by the National Pharmacovigilance Commission gives rise to the obligation of participation of the pharmaceutical industry.

IV.5. HEALTH PROFESSIONALS

Doctors, dental surgeons, pharmacists, midwives, nurses, community health workers, etc. with a view to the safety of use of health products must declare as soon as possible:

- Any presumption of an adverse effect in relation to the consumption of one or more drugs or other health products under normal conditions of use, whether expected, unexpected, serious or non-serious;
- Any undesirable effect appearing outside the normal conditions of use (misuse, abusive use, medication error, therapeutic ineffectiveness);
- Any other effect it deems relevant to declare:

- drug interaction,
- drug addiction,
- Withdrawal syndrome,
- Effects on products of conception or drug exposure during pregnancy,
- Defective or counterfeit product.

In addition, healthcare professionals must:

- Keep the documents concerning the adverse reaction for additional information if necessary;
- Cooperate with the DNPM in the context of investigations;
- Inform and educate patients about adverse effects when prescribing, dispensing or administering the health product;
- Detect adverse effects;
- Ensure the care of patients with an adverse effect.

IV.6. The focal points

The focal points ensure the promotion of pharmacovigilance within their structure, they act as relays between their department and their reference structure. They are responsible for:

- Manage notification forms;
- Reporting adverse reactions;
- Centralize and transmit notifications to the Hierarchy;
- Monitor PV activities;
- Inform and educate health professionals about PV.

IV.7. Pharmacovigilance and Health Programs

On the recommendation of the WHO, it has been suggested to integrate Pharmacovigilance into Health programs in order to ensure the continuous and

exhaustive monitoring of all adverse events and to contribute to the evaluation of the benefit/risk ratio of the drugs used. in the treatment of target diseases.

Indeed, health programs distribute drugs and health products on a large scale from various sources and beneficiary populations may be exposed to adverse effects and treatment failures . It is therefore necessary to put in place a strategy aimed at the early detection and evaluation of any problem related to the use of these drugs.

The integration of pharmacovigilance in the various health programs allows them to:

- Reduce harmful consequences and the cost of drugs;
- Reduce failures and resistance to treatment;
- Improve clinical practice;
- Promote the rational use of medicines;
- Ensuring greater public confidence in health programs;

The coordinator of each health program has the role and responsibility of:

- Introduce the practice of pharmacovigilance in the development of strategies, guides, circulars during seminars and training workshops;
- Sit (by invitation if necessary) in the Pharmacovigilance Technical Committee in order to participate in the analysis of program data;
- Centralize data on the adverse effects of program drugs and share them with the DNPM;
- Validate notifications by evaluating the cause and effect relationship;
- Provide feedback to the dispensers of their products and to the DNPM.

IV.8. Professional Orders and Associations (Pharmaceutical, Medical and Paramedical)

The representatives of the Professional Orders of health are members of the National Commission of Pharmacovigilance.

IV.9. Audience

The involvement of the public makes it possible to fight against under-reporting and freely report adverse effects without influence from the nursing staff.

Patients or their representatives can report adverse effects suspected of being related to the use of a medicinal product by telephone (call, text message, email,

mobile application, etc.) or by consulting a healthcare professional. Feedback should be given to them.

In the event of a serious undesirable effect, the nursing staff must arrange for treatment.

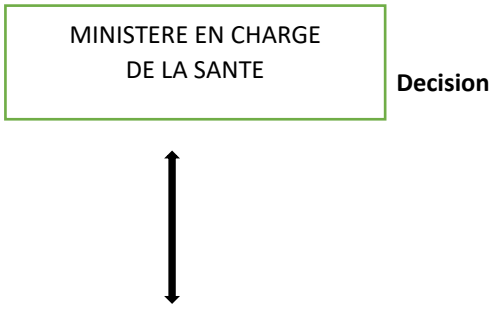
IV.10. Media

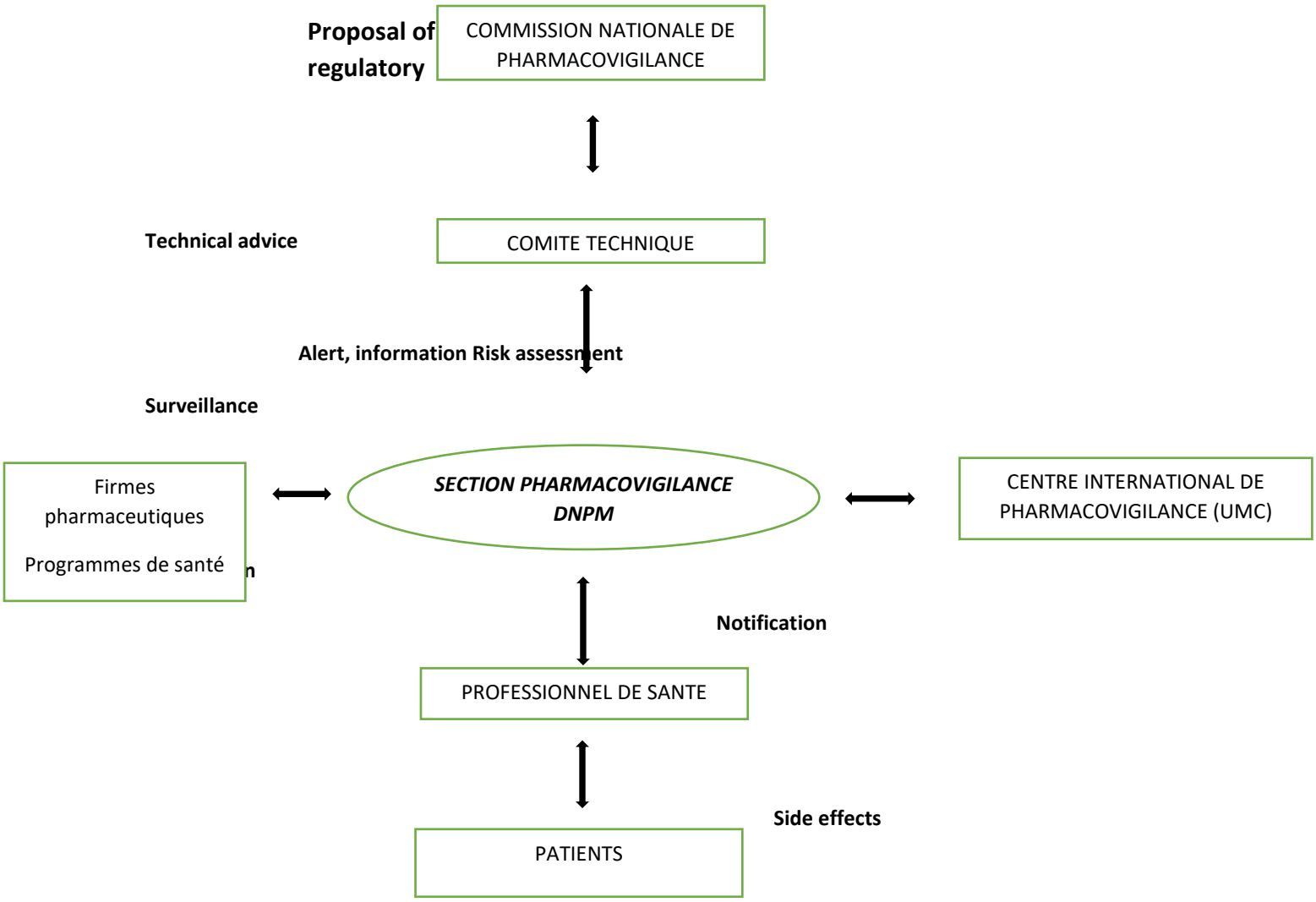
The media are used effectively and cautiously to convey pharmacovigilance information to the general public, the pharmaceutical industry and healthcare professionals.

IV.11. Other organizations

Drug promotion agencies, drug donor associations, the Agronomic and Veterinary Institute, consumer associations and any other organization with information on adverse drug reactions are required to notify the DNPM.

NATIONAL PHARMACOVIGILANCE SYSTEM SCHEME IN GUINEA





V. NOTIFICATION

Notification is the fact of reporting a case of adverse event following the use of a drug or any other health product.

All service providers must systematically notify AEs.

reporting is the cornerstone of any pharmacovigilance system. It provides all the information needed to detect AEs and improve care.

Any undesirable event must be notified even when it is the consequence of misuse or abuse.

V.1 Who must notify (Notifier)/declare?

Can notify:

- ✓ Health professionals (doctor, pharmacist, pharmacy assistant, pharmacy auxiliaries, nurse, midwife, dental surgeon, etc.);
- ✓ Community Agents;
- ✓ Pharmaceutical Laboratories;
- ✓ Applicants for clinical trials;
- ✓ The patient or his representative…

V.2 What to notify?

- ➢ Any adverse event as defined in this document. The effects to be notified may be symptoms and clinical signs (example: headache, drop in Blood Pressure, etc.);
- ➢ Changes in biological values (example: hypoglycaemia, etc.) or medication errors;
- ➢ Therapeutic failures:
- ➢ Drug interactions;
- ➢ Any observation of overdose, abuse or misuse;
- ➢ Any problem related to exposure during pregnancy or breastfeeding;
- ➢ Any observation of loss of efficacy, in particular with vaccines, contraceptives or other pharmaceutical products intended for the treatment of diseases involving life-threatening conditions;
- ➢ Any other effect deemed relevant to declare.

V.3 How to Notify

The notification is made on the national notification form designed by the DNPM (see appendix).

The notification form has four (4) sections, namely:

1°) The patient

This section includes **:**

- Surname, first name, age, address and telephone

- Personal clinical history, previous medication accidents (allergy, etc.)

To ensure confidentiality, the patient's initials will be recorded and the patient's age may be mentioned in place of the date of birth.

2°) The adverse event

The second section includes **:**

- The description of the adverse event, the time of appearance after taking the product(s), the corrective treatment if any, the concept of re-administration with or without relapse if it has been carried out ;
- Differential diagnoses with the data of the examinations carried out in order to support the diagnosis, associated factors favoring the appearance of the adverse effect;
- The severity and course of the adverse effect.

3°) The medicine(s) including the vaccine or any other health product taken by the patient

In this third section will be mentioned:

- The name of the product(s) administered;
- The start and end date of the treatment;
- Dosage and route of administration;
- The reason for the prescription.

It is important to mention the drug responsible for the adverse effect, but also the other drugs concomitantly taken by the patient because, certain adverse effects are the result of a drug interaction rather than the fact of the action of a single drug. especially.

4°) The notifier

The notifier needs to be identified as precisely as possible because it must be possible to contact him, to provide him with information concerning his notification or to help him deal with the adverse effect.

The section includes:

- The name and the first name

- The profession
- The place of exercise
- The phone
- Email
- Signature

The transmission of the notification of an adverse reaction likely to be due to a health product can be done:

- By mail in a sealed envelope to the address mentioned on the national notification form;
- By internet, by email or via the DNPM website;
- By telephone ;
- By hand delivery to DNPM PV staff.

It should be noted that the collection of notification forms will be done according to the circuit defined by the National Pharmacovigilance System, passing through the various focal points and according to the health pyramid.

V.4 Deadlines for transmission of notifications

All serious and unexpected adverse effects that are fatal or life-threatening, as well as those occurring during a clinical trial, must be notified to the DNPM expeditiously, i.e. as soon as the notifier becomes aware of them in in any case, within a period not exceeding 48 hours. Update notes may be provided within an additional period not exceeding 7-15 days.

All other serious or unexpected effects must be reported immediately, but within a period not exceeding 7 days.

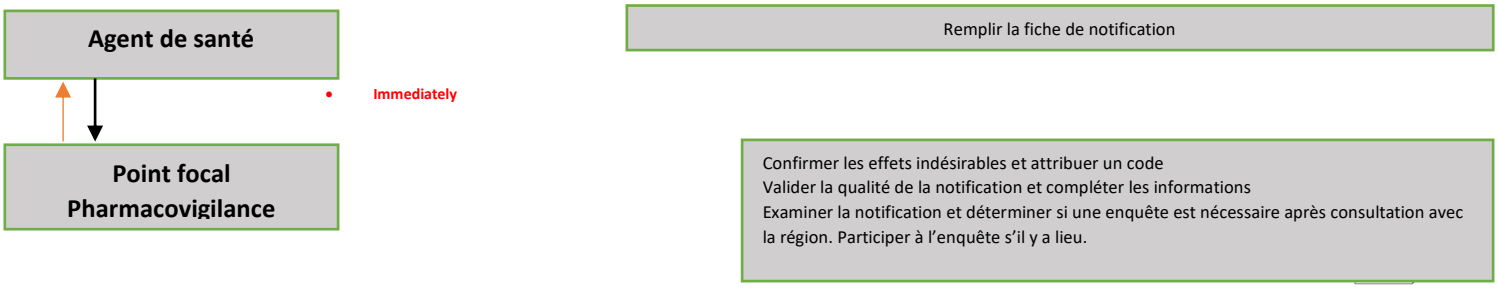
The count of days starts from the moment when the notifier becomes aware of the suspected adverse effect and the minimum conditions for notification are met.

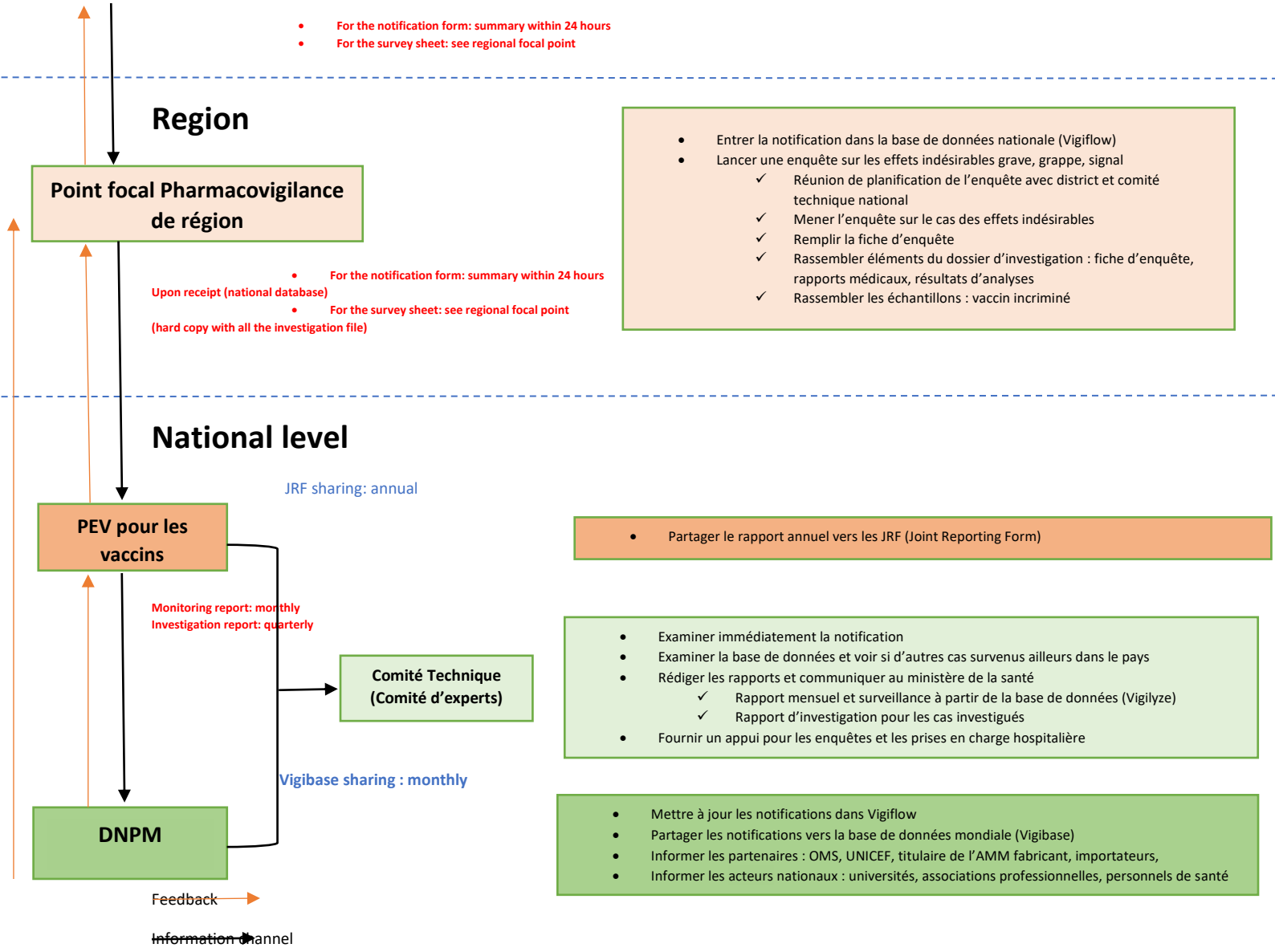
Notifier	**Time limit**	
	Non-serious effect	**Serious or unexpected effect**

Health professional	As soon as possible, not to exceed 7 days	24-48 hours In case of **death** : **immediately**
Regional Focal Point	Monthly	24-48 hours **Death: 24 hours**
Health program	Monthly	24-48 hours **Death: 24 hours**
Pharmaceutical industry	Monthly	24-48 hours **Death: 24 hours**

NOTIFICATION CIRCUIT FOR ADVERSE EFFECTS OF DRUGS INCLUDING THOSE OF TRADITIONAL MEDICINE AND OTHER HEALTH PRODUCTS, APPLICABLE DEADLINES AND ACTIONS

District





V.5 Assessment of notifications

For the assessment of the cases, the DNPM must assess the following elements:

- Quality of information: completeness and integrity of diagnostic quality data (notification form);
- Coding : Drug names should be coded in a systematic way using for example the WHO Drug Dictionary. For coding of adverse effects, the MedDRA tool will be used;
- Relevance: relating to the detection of a new reaction, the regulation of the product or the scientific or educational value of the observation;

- Identification of duplicates: certain characteristics of the observation such as sex, age, date of exposure to the drug, etc., can be used to identify cases declared twice;
- Imputability or the determination of the causal link.

V.6 Notification to the International Center for Pharmacovigilance Vigiflow ® database **.**

This database is made available to the various Pharmacovigilance Centers in the countries, in order to notify their Adverse Drug Effects (ADRs) as soon as possible and to improve the quality of the notifications.

Vigiflow ® allows each national pharmacovigilance center to have its own database of ADRs, to make statistical reports and searches, to directly access updates of terminologies used in pharmacovigilance: medical dictionary of regulatory affairs (**MedDRA**) drug dictionary (**WHO-DDE**).

Vigiflow ® is a simple, fast and reliable tool to improve all aspects of the notification of ADRs by pharmacovigilance centers, allowing the supply of **the database of** national and international ADR **data (VIGIBASE ™)** thus facilitating the generation of national or international alerts.

VI. ACCOUNTABILITY

Imputability is the clinical evaluation of the causal link likely to exist between an adverse event and the administration of a drug.

This evaluation aims to harmonize and standardize the imputation process, and to make it reproducible from one evaluator to another within the same center and between different centres.

VI 1 Methods of accountability

There are several methods of accountability. The most used are:

- The WHO method
- The French method

The WHO method is the one used by Guinea.

This method has been used by WHO Collaborating National Centers since 1987. It has the advantage of being internationally accepted and easy to use.

It is based on 3 considerations:

- The chronological relationship between the administration of the drug and the adverse event;
- Medical or pharmacological probability (signs and symptoms, laboratory tests, pathological data, mechanisms);
- The presence or absence of other causes.

For the definition of causality, six categories have been adopted by OM

1- **Very likely/certain:**
   - Clinical event for which there is a plausible temporal relationship to drug administration;
   - And which cannot be explained by a concomitant disease or by the Taking other drugs or chemicals;
   - And the regression of the effect must coincide with the discontinuation of the drug (pharmacological and pathological);
   - And the event must be explained by a pharmacological mechanism, or respond logically to re-administration if necessary.

2- **Likely :**
   - Clinical event for which there is a reasonable temporal relationship to the administration of a drug;
   - And which is unlikely to be attributable to a concomitant illness or to the taking of other drugs or chemicals;
   - And the clinical course is favorable to drug discontinuation.

3- **Possible :**
   - Clinical event for which there is a reasonable temporal relationship to the administration of a drug;
   - But that could also be explained by a concomitant disease or by taking other drugs or chemicals.

4- **Unlikely :**
   - Clinical event whose reasonable temporal relationship to drug administration makes a causal relationship unlikely;
   - But that could plausibly be explained by an underlying disease or by taking other drugs or chemicals.

5- **Unrelated:**

- Clinical event chronologically incompatible with the administration of the medicinal product;
- And that could be explained by an underlying disease or by taking other drugs or chemicals.

6- Unclassifiable:

- Clinical event for which there is insufficient information to identify and assess the cause.

VI 2 Measures to be taken following the evaluation of data on the adverse effect.

After evaluation of the data on the adverse effect by the Technical Committee and the National Pharmacovigilance Commission, the Authority (Minister in charge of Health) may decide to restrict the conditions of use, to extend the precautions for use, to suspend, withdraw or modify the Marketing Authorization.

The DNPM must immediately inform the focal points and the other actors of the National Pharmacovigilance System of the Authority's decision.

VII. SIGNAL MANAGEMENT AND ALERTS

The signal is an adverse event that has exceeded the accepted or set threshold.

A signal triggered by the International Center or by the National Center for Pharmacovigilance draws attention to the drug concerned and encourages closer monitoring; it may lead to the triggering of an alert.

The Alert is a stronger signal that leads to the establishment of surveys or studies to validate the drug's responsibility. It often results in:

- Decision-making by drug regulatory bodies: withdrawal of the MA, modification of the leaflet (indication, contraindication, precaution for use, etc.);

- A decision to train health professionals or inform the population to reduce the harmful effects of drug misuse or systematic error in the use of a drug.

The National Pharmacovigilance System is a system empowered to trigger and manage national and international alerts on health products. As a collaborating

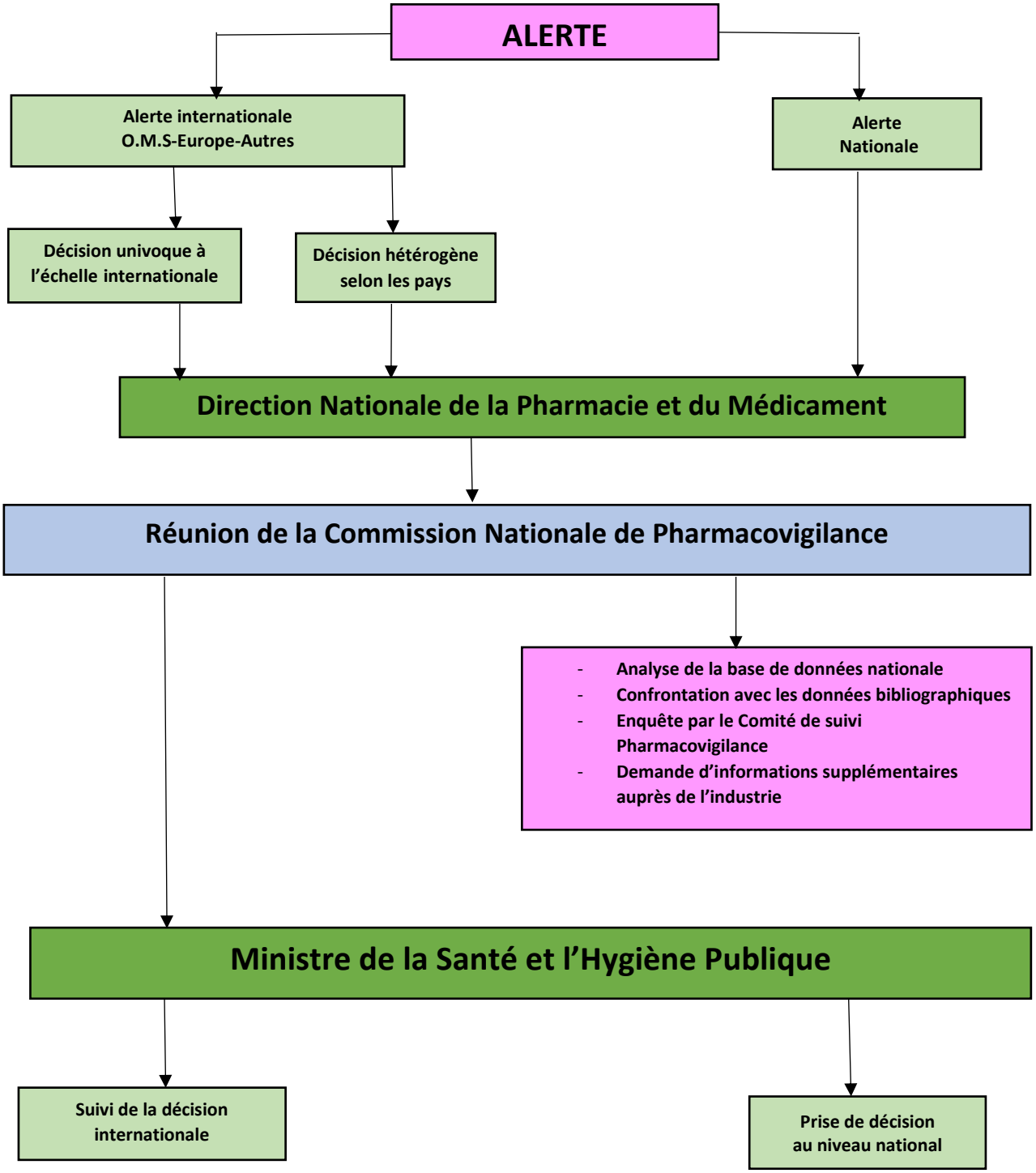
member of the WHO, the DNPM, through its Pharmacovigilance Section, receiving alerts on health products through the various international networks, is able to trigger national alerts by centralizing and managing its database. national ADR data.

The Pharmacovigilance Technical Committee analyzes serious cases of adverse effects linked to the use of health products, submitted to it by the DNPM or reported internationally. It supports the DNPM in proposing relevant cases to be studied to the National Pharmacovigilance Commission.

The DNPM, through the National Pharmacovigilance Commission, ensures that any alert is quickly analyzed and evaluated for a practical attitude in order to ensure patient safety.

After studying the file, the National Pharmacovigilance Commission makes proposals to the Minister in charge of Health who takes the final decision.

SCHEMA DE LA GESTION D'UNE ALERTE



OFFICIAL PHARMACOVIGILANCE INVESTIGATIONS IN THE CONTEXT OF AN ALERT

The main objective of the survey is to present the National Pharmacovigilance Commission with objective arguments concerning the tolerance of health products and to assess or reassess the benefit/risk ratio in our context.

Following a national or international alert, the National Directorate of Pharmacy and Medicine may suggest conducting an investigation. The opening of the investigation is decided by the Minister in charge of Health who judges its advisability and provides the conditions and means for its outcome.

Apart from alerts, other situations like the presence of substandard and falsified medicines that have caused harm can also trigger an investigation.

The request for the opening of an investigation by the DNPM must specify:

- The name of the drug/product concerned;
- The pharmaceutical form and dosage;
- The reasons for the investigation;
- Adverse effects;
- The location of the survey;
- The Investigation Committee.

Conduct of the investigation :

1 The investigation begins as soon as the Committee is set up;
2 The Committee appoints a rapporteur responsible for coordinating all stakeholders during the investigation (health authorities, clinicians, industrialists, epidemiologists, etc.), and also for presenting the progress of the investigation;
3 The Committee includes the rapporteur as well as the clinicians involved depending on the nature of the ADRs studied and the specialties. He is responsible for monitoring the study, proposing modifications or proposing an extension of the study;
4 The development of the protocol of the investigation is done by the committee , and often for all practical purposes, the person in charge of the AMM can be concerted;

5 To help the investigation run smoothly, the MA manager must provide all the necessary information on the products concerned (clinical trials, ADR cases, product monographs, etc.).

At the end of the investigation, the DNPM draws up a final report which is presented by the committee's rapporteur, first to the Technical Pharmacovigilance Committee for discussion, then to the National Pharmacovigilance Commission.

VIII. COMMUNICATION

Communication is an essential risk management tool for achieving the objectives of pharmacovigilance in terms of promoting the proper use of drugs and other health products and preventing risks. It is a key element to boost notifications.
Furthermore, it is important that competent authorities, pharmaceutical companies and health care providers communicate effectively on the risks of adverse effects in order to gain public confidence.
Communication is considered in the following situations:
- on the occasion of a health decision in connection with pharmacovigilance activities (suspension, withdrawal or not, renewal of the MA);
- on the occasion of a modification of the Marketing Authorization which requires specific information for healthcare professionals and users of the healthcare system (for example: new contraindication or warning, modification of therapeutic indications or dosage , …);
- when it is necessary to modify or remind the conditions of proper use of the drug (risks of misuse, medication error) or in the event of new recommendations for the management or prevention of an adverse effect (reduction of 'a risk) ;
- when a potential risk is being assessed and it is necessary to continue monitoring and/or communicate information on the management of this risk;
- when a potential or proven risk is the subject of strong media interest and requires clarification.

IX. FUNDING

Due to the significant health and economic consequences that the adverse effects of drugs can generate, continuity in the financing of pharmacovigilance

must be guaranteed while ensuring its independence vis-à-vis any pressure, any political or economic change.

The budget required for Pharmacovigilance is assessed according to the required notification rate and the size of the population.

The collection of quantitative and qualitative data, the evaluation of data as well as the dissemination of information obviously require expenditure. The Pharmacovigilance Section must have regular basic resources in order to ensure continuity in the work.

The budget comes from grants from the State and partners, health programs, drug registration fees (pharmacovigilance fees, namely Periodic Safety Update Report or periodic safety report PSUR **)** .

Apart from core resources, the section should receive additional funding from agencies or organizations with an interest in Pharmacovigilance.

These structures interested in the financing of pharmacovigilance are among others:

- Health insurance companies and health insurance funds;
- University departments;
- Professional associations;
- Government departments with an interest in the safe use of the drug.

Pharmacovigilance remains a dynamic clinical and scientific discipline.
For all drugs and other health products, it is necessary to know how to distinguish between the benefits and the potential harm. Harmful effects can be minimized by ensuring that medicines are of good quality, safe, effective and used rationally, taking into account patients' expectations and concerns in making treatment decisions. These actions make it possible to:

- Ensure that the risks associated with the use of medicines and other health products are anticipated and well managed;
- To serve public health and to nurture in patients a sense of confidence in the products they use and in health services in general;
- To provide Regulatory Authorities with the information necessary to modify recommendations concerning the use of medicinal products;

- Help healthcare professionals better understand the benefit/risk ratio of the drugs they prescribe;
- Improve communication between healthcare professionals and the public.

This is the very important role of Pharmacovigilance

An efficient Pharmacovigilance System is a guarantee for Patient Safety.

LEXICON

DEFINITION OF TERMS USED IN PHARMACOVOGILANCE

Abuse: excessive and voluntary, permanent or intermittent use of medicinal products not in accordance with the recommendations of the summary of product characteristics or with normal medical practice.

Alert: signal warning of a danger and calling for all useful safety measures to be taken.

In pharmacovigilance, the term "Alert" has a stronger meaning than the term "Signal": an alert justifies the implementation of a study or a decision.

Database: information organization system, designed for quick and easy location and updating of data. It is a computerized database in which all cases notified and validated by the Pharmacovigilance Center are entered.

Biovigilance: biovigilance consists of monitoring and preventing the risks associated with the use of elements and products derived from the human body and used for therapeutic purposes.

Biovigilance is a very complex discipline, which requires health monitoring at all stages of the chain, from the clinical and biological selection of the donor to the medical follow-up of patients, living donors or recipients.

Confidentiality: respect for the secrecy of the identity of the person for whom an adverse effect has been notified to a pharmacovigilance structure, which extends to any information of a personal or medical nature concerning him.

Confidentiality also concerns the identity of the notifier. The prevailing rule is comparable to a medical file.

Cosmetovigilance: all the means allowing collection, evaluation and monitoring adverse effects observed during or after use of cosmetic products under normal or reasonable conditions.

Development Safety Update Report (DSUR): format and content for periodic reports on drugs under development.

Source document: any original document related to a pharmacovigilance file, in particular:

- Telephone agreement report, initial letter from the notifier, internal memo from the medical visitor;
- Pharmacovigilance form (completed by the notifier or a person responsible for pharmacovigilance), copies of additional examinations or hospitalization reports;
- Couriers (initial, follow-up[s], conclusion);
- Transmission sheet, translations of the sheet;
- Printouts of computer entries (notices, summaries, tables) concerning the file.

Vaccine failure: occurrence of a biologically confirmed infection in a subject supposedly protected following complete immunization adapted to the age recommended by the manufacturer.

Adverse event : any harmful and unintended manifestation occurring in a subject during treatment. The term "adverse event", unlike "adverse effect", does not prejudge a causal link with exposure, in particular to a drug.

Post-vaccination adverse event (AEFI) : post-immunization event that may or may not be caused by the administration of a vaccine or by the immunization process.

Adverse Reaction : A harmful and unintended reaction to a drug or other health product, occurring at dosages normally used in man for the prophylaxis, diagnosis or treatment of disease or for the recovery, rectification or modification of a physiological function, or resulting from misuse of the drug or product.

Avoidable side effect : this is one that would not have occurred if the care had been consistent with the management considered satisfactory at the time.

Example: anaphylactic shock after administration of penicillin in a patient with a history of allergy to this drug could have been avoided if the prescriber had taken this history into account (by prescribing another antibiotic). An adverse effect resulting from a medication error is preventable .

Unexpected adverse reaction : any adverse reaction whose nature, severity or outcome does not correspond with the known authorized information for this medicinal product.

Adverse Drug Effect (ADR): harmful and unwanted reaction, occurring at dosages normally used in humans for the prophylaxis, diagnosis or treatment of a disease or the modification of a physiological function or resulting from misuse drug, constituting a withdrawal syndrome when stopping the product or a dependency syndrome, as well as any reaction resulting from misuse. It also includes any harmful reactions that may arise from poor quality of the drug.

Serious Adverse Effect (SAE) : an adverse effect that is lethal, or likely to be life-threatening, or resulting in disability or incapacity, or causing or prolonging hospitalization, or resulting in a congenital malformation.

Post-Vaccination Adverse Effect : A worrying medical incident that occurs following vaccination and is believed to be due to vaccination.

Adverse reaction linked to a programmatic error : an effect due to an error during the programming, handling, dispensing or administration of a given vaccine. The error is usually related to the person or the technique of handling the vaccine rather than the vaccine.

Minimum element of notification : from the perspective of reporting a suspected adverse reaction, the minimum elements are: an identifiable drug, an identifiable patient, an identifiable adverse reaction and an identifiable notifier.

Pharmacovigilance investigation : evaluation work, carried out at the request of the competent authorities by a Pharmacovigilance Center, in collaboration with the person responsible for pharmacovigilance of the company or organization exploiting the drug or product concerned, whenever there is reason to believe that a drug risk should be assessed or reassessed. There are two types of Pharmacovigilance investigations:

- *Pharmacovigilance monitoring, carried out with the aim of carrying out specific monitoring of the benefit of tolerance of the drug or product as soon as it is marketed, during the first years, or even for the entire duration of its marketing;*
- *The pharmacovigilance survey, carried out with the aim of reassessing the risk of a drug or product following an alert .*

Medication error : avoidable iatrogenic drug event (ADE), resulting from an unintentional dysfunction in the organization of the patient's therapeutic drug management. It can be secondary to several actions or situations:

- The prescription ;
- The communication of prescriptions;
- The labeling of medicines, their packaging and their name;
- Their preparation, deliverance, and dispensation;
- Their administration by a healthcare professional;
- Patient information and education;
- Therapeutic follow-up as well as the methods of use.

Clinical trial : clinical trial means any investigation on human and animal subjects, aimed at discovering or verifying the clinical, pharmacological or

adverse effects of one or more investigational products, with the objective of establishing their efficacy. and/or safety.

A clinical trial can take place at one or more sites.

Post-marketing authorization safety study (Post-Authorization Safety Study [PASS]): pharmacoepidemiological study or clinical trial carried out in accordance with the provisions of the Marketing Authorization, with the objective of identifying, characterize or quantify a risk or confirm the safety profile of the authorized medicinal product or assess the effectiveness of risk management measures.

Notification form: document completed by the notifier and containing the data necessary for the constitution of a notification file.

Generic: any medicinal product having the same quantitative and qualitative composition of active ingredient and the same pharmaceutical form as a reference medicinal product and for which bioequivalence with respect to the reference pharmaceutical (medicinal) product has been established by bioavailability studies appropriate.

Cluster or focus : term designating the observation, without prejudging an explanation, of a higher incidence of an event in a given region during a given period or in a region at a given period. In the case of a vaccine “cluster”, it is most often a problem of storage, dispensing or administration.

Haemovigilance : element of transfusion safety which aims to monitor, develop and prevent incidents and adverse effects occurring in donors or recipients of labile blood products (LBP).

Drug iatrogenics : set of potential or proven adverse health consequences of drugs prescribed or used in self-medication. The field of iatrogenics is therefore broader than that of undesirable effects alone (expected or unexpected) since it also includes the proven ineffectiveness of an inappropriate treatment, the effects induced by the context of the prescription (nocebo effect) and the induction of a state of dependence.

Imputability : case-by-case analysis of the causal link between taking a drug and the occurrence of an event.

Incident : any situation in which an event arises or new information in relation to an authorized medicinal product, and which may have an impact on Public Health.

An incident may relate to the efficacy, safety or quality of a drug product. In most cases, this will be a product safety or quality issue. Any situation, at first glance without gravity, but which is in the public domain – mediated subject or not – and which could cause public concern about a medicinal product, should be considered as an incident. Similarly, situations which could have a negative impact on the use of a medicine (which would cause patients to interrupt their treatment, for example) should be considered as incidents.

Triggering incident : cluster of adverse effects or single event (death, hospitalization or other) that alerts healthcare professionals to the need to take action, including investigation.

Missing information: any gap in knowledge about a medicine related to its safety or use and which could have a clinically relevant impact.

Materiovigilance : monitoring of incidents or risks of incidents resulting from the use of medical devices after they have been placed on the market.

Drug : any substance or composition presented as having curative or preventive properties with regard to human or animal diseases; as well as any product that can be administered to humans or animals with a view to establishing a medical diagnosis or restoring, correcting or modifying their organic functions.

Investigational drug : this is an experimental product under study or experimentation. This more specific term excludes placebos and drugs used as comparators in clinical trials, which are included in the definition of investigational drug product.

Risk Minimization Measure: activity aimed at preventing, limiting the probability of occurrence or reducing the severity in the event of occurrence of an adverse effect associated with exposure to a medicinal product.

Misuse : use of a drug that does not comply with the recommendations in the summary of product characteristics, excluding misuse.

Medication leaflet : paper containing information on the medication intended for the user and which accompanies the medication.

Notification: the act of reporting a case of an adverse event by an observer to a surveillance system, or the act of reporting a case to this system.
The notification must include at least: a person who notified and who is identifiable, an identifiable patient, one or more suspicious drugs, one or more suspicious adverse effects .

Spontaneous notification : this is a report made by a notifier (health professional or patient) to a pharmaceutical company, the regulatory authority or other competent organization describing one or more adverse effects likely to be due to the administration of one or more medicinal products occurring in a given patient at a given time and which does not come from a study or any other organized data collection system.

Notifier: any health professional, manufacturer or public who has noted a presumed adverse event of a drug, and who transmits it to a pharmacovigilance structure.

Overdose: administration of a quantity of medicine per dose or cumulatively which is greater than the maximum authorized doses according to the information on this medicine.

Periodic Safety Update Report (PSUR): Periodic Safety Update Report. It is a format and content for the submission of the benefit/risk assessment of a medicinal product, provided by an MA holder, at known regular time intervals to the Regulatory Authority in the post authorization period.

Its objective is:

1°) to assess the follow-up of the safety profile of a medicinal product or another health product with regard to the knowledge acquired and the information available;

2°) to consider, if necessary, a modification of the information on the medicine or the product, or even a reassessment of the benefit/risk ratio. This document contains an update of Pharmacovigilance data collected

worldwide during the period under review. It is transmitted immediately at the request of the National Pharmaceutical Regulation Authority and/or according to a defined periodicity after the registration of the drug or health product.

In practice, it includes a summary of all the pharmacovigilance data known to the organization using the drug or product, as well as any information useful for assessing the risks and benefits associated with the use of this drug. or product. This summary is accompanied by a scientific assessment of these risks and benefits.

Pharmacodependence: mental and sometimes physical state resulting from the interaction between a living organism and a drug. This interaction is characterized by changes in behavior and other reactions that always strongly urge the user to take the drug continuously or periodically in order to regain physical effects or sometimes to avoid withdrawal discomfort. This state may or may not be accompanied by tolerance. The same individual can be dependent on several drugs.

Pharmacovigilance : this is a medical specialty whose purpose is the detection, development, understanding and prevention of adverse effects and any other problem related to the use of health products. Its methodology is based on epidemiological, clinical and experimental data.

Phytovigilance: pharmacovigilance of medicinal plants or herbal medicines and herbal drugs. It takes care of monitoring plants, parts of plants (root, flowers, bark, seeds, etc.) and plant extracts (extracts, tinctures, etc.), whether fresh or dried, used for therapeutic purposes.
Its operation follows the same system as that of other health products, in this case that of medicines, with identical monitoring principles, whether nationally or internationally.

Risk Management Plan: This is a detailed description of the risk management system. This plan should identify or characterize the safety profile of the drug product concerned, as well as future characterizations of the profile. It must document the measures aimed at avoiding or minimizing the risk, including

the evaluation of the effectiveness of these measures and contain the post-marketing obligations which have been imposed as a condition for the granting of the MA.

Safety issue: this definition includes significant potential risks, significant identified risks and missing information.

Signal management process: includes the following activities: signal detection, signal validation, signal confirmation, signal analysis and prioritization, signal evaluation and recommendation for action. These activities are carried out to determine if there are new risks caused by a drug product or if the known risks have changed.

Cosmetic product: product intended to be brought into contact with the superficial parts of the human body with a view, exclusively or mainly, to cleaning, protecting, perfuming, maintaining them in good condition, modifying their appearance or correcting their smell.

Health Products: concern medicines (Vaccines, compendial preparation, divided compendial products, hospital preparation, biological and radiological diagnostic products, gases for human use, homeopathic products, biological products, stable blood derivatives, insecticide and acaricide intended to be applied on humans), plants and products of the traditional pharmacopoeia, cosmetics, medical devices, dietetic products and food supplements.

Reactovigilance: monitoring of incidents and risks of incidents resulting from the use of an in vitro diagnostic medical device (IVMD).

Injection reaction: reaction due to anxiety or pain at the injection site but not to the vaccine.

Summary of product characteristics (SPC): text written for the competent administrative authority when applying for Marketing Authorization for a pharmaceutical specialty and containing the basic information concerning it. It corresponds to the information intended for health professionals.

Benefit-risk ratio : this is the evaluation of the positive therapeutic effects of a product in relation to its risks.

Identified risk : adverse adverse reaction for which there is strong evidence of association with a medicinal product.
As an adverse effect adequately demonstrated by preclinical studies and then confirmed by clinical observations. Or an adverse effect documented by clinical trials or well-conducted epidemiological studies, for which the difference between the control group and the control is such that it suggests a causal relationship.

Significant risk: whether it is potential or identified, a risk is said to be significant if it can modify the benefit/risk ratio of a medicinal product, or have an impact from a public health point of view.
A risk that could be included as a contraindication or in the precautions for use of a drug should be considered important.

Risk associated with the use of a medicinal product: this is the probability of a harmful event occurring, linked to the quality, harmlessness or efficacy of a medicinal product with regard to the health of the patient or public health, or the likelihood of adverse environmental effects.

Potential risk: harmful effect for which there are elements that could lead to suspicion of an association with a medicinal product, which association has not yet been proven.

As a toxic effect observed by preclinical studies, but not yet observed in clinical studies. Or an adverse effect documented by clinical trials or well-conducted epidemiological studies, for which the difference between the control group and the control is not sufficient to suggest a causal relationship.

Signal: any event or exceeding of a fixed threshold, agreed as attracting attention during monitoring. In practice, we speak of a signal when the value of a parameter (number of cases of an event, incidence rate, etc.) deviates from what was expected or accepted. A signal after validation results in an

alert leading to decision-making or the implementation of an appropriate study.

Under notification: absence of notification to a surveillance structure of some of the cases of an adverse effect occurring in a given region.
Under-reporting can result from a large number of factors: absence of notification or observer time, absence of diagnosis of the event or failure to attribute this event to the drug.

Therapeutic follow-up: prospective study conducted on subjects treated with a drug under the conditions provided for in the Marketing Authorization.
Therapeutic follow-up is therefore generally equivalent to an observational-type treatment cohort.

Withdrawal syndrome: set of somatic disorders resulting from the abrupt withdrawal of the drug in a drug addict in a state of physical dependence, and which can be relieved by re-administration of the substance or by the administration of a similar substance.

Risk Management System: set of Pharmacovigilance activities, and interventions aimed at identifying, characterizing, preventing or minimizing the risk associated with a medicinal product, including an evaluation of the effectiveness of these interventions.

Teratovigilance: monitoring of risks related to exposure to health products during pregnancy. She is interested in the study of morphological and physiological malformations, as well as behavioral disorders coinciding with the intake of a health product during pregnancy.

Tolerance: property of a drug whose repeated use leads to a decrease in the effects initially obtained, hence the need to increase the doses to achieve the desired effect. It is often associated with the development of physical dependence.

Rational use of medicines: prescription of the most appropriate product, obtained in time and at a price affordable to all, correct dispensing and

administration according to the appropriate dosage and for an appropriate period of time.

Vaccinovigilance: early detection and rapid and adequate response to post-vaccination adverse events (EIPV) in order to minimize the impact on vaccination programs and on the health of individuals.

Signal validation: process of verifying documents supporting the detection of a signal to check whether they contain enough elements that could raise suspicion of a new risk or a new aspect of a known risk and therefore justify in-depth analyses.