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04-Jan-2016

Circular No. ....../

**The Secretary General,  
The Inspector General,  
The Directors of the Central Administration  
The Directors of the University Hospitals  
The Regional Healthcare Directors**

**RE:** Organisation of the National Pharmacovigilance System

Within the context of the organization of the national Pharmacovigilance system, this circular has the purpose of defining the concepts and the organization of pharmacovigilance and describing how its activities are operated. It gives concrete expression to the activity assigned to it in the 2012-2016 sectorial strategy of the Ministry of Health through action 60 pertaining to the strengthening of healthcare monitoring measures.

Pharmacovigilance is defined by the World Health Organization (WHO) as being: *“The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem”*.

A medicinal product is defined in law no. 17-04 containing the provisions governing medicinal products and pharmaceuticals (2006) as: *“Any substance or preparation presented as having curative or preventive properties as regards human or animal diseases, as well as any product that can be administered to humans or animals with the aim of establishing a medical diagnosis or restoring, correcting or modifying their organic functions”*.

Pharmacovigilance also concerns other healthcare products, namely, vaccines, contraceptive products, medical devices, diet products, food additives, plants, products listed in the herbal pharmacopoeia, homeopathic remedies and cosmetics (WHO guide on the creation and operating of a pharmacovigilance centre).

An adverse event is described as being: *“a harmful or unwanted reaction, occurring at doses normally used in humans for the prophylaxis, diagnosis or treatment of a disease or the modification of a physiological function or resulting from the misuse of a medicinal product, constituting a withdrawal state on stopping the product or a dependence syndrome, as well as any reaction resulting from improper use or a medication error. It also comprises any harmful reaction that could result from a low-quality medicinal product”*.

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## I- AIMS OF THE NATIONAL PHARMACOVIGILANCE SYSTEM

The main aims of the national pharmacovigilance system are:

- Promote patient safety with regard to the use of all healthcare products;
- As quickly as possible detect adverse events due to the use of healthcare products in normal conditions of use and in the case of misuse, improper use, drug dependence, medication error, treatment inefficacy, reactions caused by a defective or low-quality product;
- Establish the frequency and severity of known or newly-discovered adverse events;
- Develop training for healthcare professionals and the public as regards healthcare product-related adverse events;
- Develop studies on the mechanisms and consequences of adverse events of healthcare products;
- Give reasoned technical advice to those administrative bodies and organisations having the power to make decisions on the regulation of healthcare products;
- Improve patient confidence in authorised healthcare products on the market in Morocco.

## II- ORGANISATION OF THE NATIONAL PHARMACOVIGILANCE SYSTEM

The National Pharmacovigilance System comprises:

### *At a central level*

- o The National Pharmacovigilance Committee,
- o The National Pharmacovigilance Centre,
- o The Technical Pharmacovigilance Committee.

### *At a regional level*

- o Pharmacovigilance representatives

### *Other players*

- o Healthcare service providers and prescribing doctors,
- o Pharmaceutical and healthcare product companies,
- o Patients,
- o Consumer and user associations.

### 1- **The National Pharmacovigilance Committee (CNP)**

The National Pharmacovigilance Committee plays an **advisory role** for the decisions to be submitted to the Ministry of Health. Its operation and remit are defined through regulation for the implementation of law no. 17-04 containing the provisions governing medicinal products and pharmaceuticals. Whilst awaiting its implementing provisions, circular no. 3 [of the] medicinal product and pharmaceutical management department (DMP) dated 28-Jan-1997 defines its modes of operation.

### 2- **The National Pharmacovigilance Centre (CNPV)**

The National Pharmacovigilance Centre (CNPV) works in tandem with the National Toxicovigilance Centre (CNTV) in a single structure called the Morocco Poison control and

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Pharmacovigilance Centre (CAPM). The two Centres share human skills (those of its doctors, pharmacists, scientists, technicians and administrators etc.), operating means (24-hour telephone service, Pharmacology and toxicology laboratory, Database) and the methods, techniques and tools used.

The National Pharmacovigilance Centre's (CNPV) mission is to put in place the technical procedures for running the National Pharmacovigilance System and the management of adverse event-related reports and risks and to promote and supervise the regional pharmacovigilance structures. It ensures compliance with the procedures of Good Pharmacovigilance Practices. The CNVP is responsible for:

**a- Managing reports:**

- Collecting adverse event reports for medicinal products and other healthcare products;
- Validating and analysing each adverse event reported (causal link, whether or not the event could have been avoided, investigation of the underlying cause etc.) and responding to reporters [of those adverse events] when necessary. It shall regularly send all cases to the WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre (UMC));
- Launching, maintaining and managing the National Database of adverse events of medicinal products and other healthcare products;
- Creating alerts for qualitatively or quantitatively abnormal unwanted symptoms;
- Validating the alerts by carrying out the necessary investigations and notifying the National Pharmacovigilance Committee, or any other relevant department, whenever necessary;
- Participating in the implementation of measures to minimise risks in coordination with the relevant departments.

**b- Managing pharmacovigilance activity:**

- Organising technical pharmacovigilance activities at a national and regional level;
- Maintaining relations with Uppsala Monitoring Centre;
- Training staff working at a regional level in the methods used in pharmacovigilance for collecting and validating adverse event data, establishing a causal link and performing investigations;
- Providing technical advice on the safety of medicinal products and other healthcare products;
- Participating in the teaching and training of healthcare professionals as regards healthcare product-related adverse events;
- Running public awareness campaigns to reduce morbidity and mortality linked to the irrational use of healthcare products;
- Submitting the Technical Pharmacovigilance Committee's report to the National Pharmacovigilance Committee and to the relevant departments;
- Participating in investigations and studies.

**3- The technical pharmacovigilance committee (CTPV)**

To support the activities of the CNPV, a CTPV has been created, which is an independent clinical and scientific committee whose mission is to:

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- Provide technical advice on all issues of a scientific nature submitted to the CNPV,
- Schedule pharmacovigilance investigations, determine the need for said investigations and examine the results thereof,
- Respond to any request for a scientific opinion made by the National Pharmacovigilance Committee,
- Plan the annual programme of scientific activities and research to be undertaken at a national and regional level.

The Technical Committee is presided over by the Director of the CAPM.

Its members are:

- The head of the National Pharmacovigilance Centre,
- The head of the National Toxicovigilance Centre,
- The heads of the regional Pharmacovigilance Centres,
- The pharmacovigilance coordinators of different healthcare programmes,
- The representative of the Medicinal product and Pharmaceutical directorate,
- Four specialist doctor experts,
- A private doctor,
- A dispensing pharmacist,
- Two pharmacologists,
- An epidemiologist,
- A statistician.

The Technical Committee may appoint any additional person if necessary.

It meets regularly once per quarter and at the request of the chairman, whenever there is an urgent issue on the agenda.

The Technical Pharmacovigilance Committee extends to a regional level to support the activity of the Regional Pharmacovigilance Centres.

#### **4- Regional Pharmacovigilance Representatives (CRPV)**

At a Regional level, a person (doctor or pharmacist) trained in pharmacovigilance is appointed as a regional pharmacovigilance representative (CRPV) by the Regional Healthcare Director in coordination with the Poison control and Pharmacovigilance Centre.

The CRPV is responsible for developing pharmacovigilance activity at the various hospitals within its region as well as at the level of the department for regional outpatient infrastructure and action (SIAAP) and coordinates activity with the departments of Pharmacovigilance within University Hospitals.

The CRPV is responsible for:

- Collecting adverse event reports for medicinal products and other healthcare products at a regional level;
- Validating and analysing each adverse event reported (causal link, whether or not the event could have been avoided, investigation of the underlying cause etc.)

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- Responding to reporters [of those adverse events] when necessary and regularly sending all cases to the National Pharmacovigilance Centre;
- Launching, maintaining and managing the National Database of adverse events of medicinal products and other healthcare products;
- Working with the National Centre to create alerts and validating these alerts;
- Working in collaboration with the National Centre to implement measures to minimise risks;
- Providing information on the rational use of healthcare products and adverse events to the healthcare professionals in the region.

### III- OPERATING PROCEDURES

Spontaneous adverse event (AE) reporting as regards medicinal products and other healthcare products is the basis of all pharmacovigilance systems.

#### 1- *Those people reporting (AE) [sic] concerning medicinal products and other healthcare products are:*

- Healthcare professionals: general practitioners or specialist doctors, dental surgeons, pharmacists, nurses, physiotherapists and midwives working in the public, private or military sector;
- Those working in the pharmaceutical industry;
- Members of the public;
- Organisations: learned society, the consumer protection society, the Poison control Centre, medical laboratories, the Institute of Agriculture; all of these may also participate in the notification of adverse events.

Healthcare professionals and manufacturers are obliged to report medicinal product-related adverse events.

Pharmacovigilance centres are bound by confidentiality as regards data relating to the patient and the person reporting the AE.

#### 2- *Methods for reporting adverse events*

- The reporting of adverse events concerns any presumed Adverse Event relating to any healthcare product occurring in normal conditions of use or any misuse, improper use, drug dependence, withdrawal state, inefficacy, medication error, drug interaction, and any adverse event relating to a defective product (contaminated, adulterated, counterfeit, out-of-date etc.)
- It also concerns any adverse event occurring in the conceptus following exposure to a drug during pregnancy
- The reporting of adverse events concerns adverse events whether or not they are expected or unexpected, serious or not serious and regardless of whether they are observed in clinical practice, during clinical trials or during pharmacoepidemiology studies
- The report contains the following information relating to:

##### a- **The patient**

- Identification and socioeconomic status;
- Previous medical history and previous adverse events;

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#### **b- Medicinal and healthcare product-related adverse events (AE)**

- Description of the AE;
- Time of onset after taking the medicinal product;
- Notion of re-administration with or without relapse if this has been done;
- Associated factors promoting the onset of an AE;
- Corrective treatment given;
- Differential diagnoses with the data from the tests carried out to support the diagnosis;
- Severity;
- Progress of the AE after stopping or reducing the dose.

#### **c- The suspected medicinal or healthcare product**

- Treatment start and end date;
- Dose and route of administration;
- Reason for its prescription (indication);
- Information on all concomitant medicinal or healthcare products; including those taken in the two weeks prior to the onset of the AE.

#### **d- The reporter: name, contact details and signature**

AE are reported using the yellow notification form, in hardcopy or electronic format. These reports can be submitted via all means of communication:

- CMPV website [www.capm.ma](http://www.capm.ma);
- Telephone;
- Fax;
- Regular post;
- Onsite appointment.

#### **IV- ROLE OF THE PHARMACEUTICAL INDUSTRY**

All Marketing Authorisation (MA) holders of a specialty are responsible for the safety of the medicinal product that they manufacture. They must have a department dedicated to the collection, recording and evaluation of adverse events managed by a person qualified in the area of pharmacovigilance, in accordance with law no. 17-04 containing the provisions governing medicinal products and pharmaceuticals.

- Cases of adverse events reported by medical representatives after collection from prescribing doctors, must be processed, causality must be determined and they must be submitted to the CNPV.
- Updates made to information on the safety of healthcare products as well as pharmacovigilance decisions made in other countries must be submitted by the manufacturers to the Medicinal Product and Pharmaceutical Directorate and the CNPV.
- **Periodic Safety Update Reports (PSUR)** are submitted every three months to the Medicinal Product and Pharmaceutical Directorate with a copy sent to the CNPV.

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The Head Pharmacist at the pharmaceutical company laboratory must respond to any request from the Regulatory Authorities as regards the medicinal products manufactured by their company.

**For marketed medicinal products:**

- The CNPV must be notified of serious adverse drug reactions within 7 calendar days in the event of death or a life-threatening reaction, whilst all other serious effects must be reported to them within 15 days of the date on which they are discovered;
- Non-serious adverse events will be submitted to the CNPV and the Medicinal Product and Pharmaceutical Directorate on a quarterly basis;
- Pharmaceutical company laboratories may also request **a report of the adverse events linked to the medicinal products** that they manufacture, on a quarterly basis.

**With regard to clinical trials:**

- The CNPV must be notified of serious adverse drug reactions occurring during a clinical trial within 7 calendar days in the event of death or a life-threatening reaction, whilst all other serious effects must be reported to them within 15 days of the sponsor becoming aware of said effect;
- Any new development that could affect the safety of those people taking part in the trial, must be reported within 15 calendar days of the sponsor becoming aware of said knowledge;
- Non-serious adverse events are to be submitted to the CNPV and the Medicinal Product and Pharmaceutical Directorate at the time of submission of the final clinical study report.

<p>The Health Minister</p> <p>One signature in handwriting (-)</p> <p>El Houssaine LOUARDI</p>
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**Copy to:**

- The Representatives of the Ministry of Health in the Provinces and prefecture and arrondissement prefectures
- The Directors of the Regional, Provincial and Prefectural Hospitals
- The Chairman of the National Board of Doctors
- The Chairman of the National Board of Pharmacists
- The Chairman of the National Board of Dentists
- The Chairman of the Board of Industrial Pharmacists and Distributors
- The Chairman of the Moroccan Pharmaceutical Industry Association
- The Chairman of the "Pharmaceutical Companies" Association (Formerly "Morocco Innovation and Health" [MIS])
- The Chairman of the Moroccan Association of Generic Drugs



## Appendix

This circular takes into account and integrates all of the provisions mentioned in the different texts which precede it:

### \* Laws

- Law No. 84-12 pertaining to medical devices: in which medical devices vigilance is mentioned (2013);
- Law No. 11-08 pertaining to the use of in vitro diagnostics: in which IVD medical device safety monitoring is mentioned (2010);
- Law No. 17-04 containing the provisions governing medicinal products and pharmaceuticals (2006): in which the national pharmacovigilance committee is mentioned;
- Law no. 03-94 pertaining to the donation, drawing and use of human blood (Dahir no. 1-95-133 dated 19 Safar [February] 1416: in which haemovigilance is mentioned (1995).

### \* Circulars:

- Circular No. 104 DMP/00 dated 23-Oct-2014 pertaining to the registration of cosmetic and personal hygiene products (2004);
- Circular No. 3/DMP dated 28-Jan-1997 pertaining to the national pharmacovigilance, toxicovigilance, IVD medical device safety monitoring and medical devices vigilance committee (1997);
- Circular No. 2DR/10 pertaining to the national poison control and pharmacovigilance organisation (1992).

### \* Manuals and Guides:

- Morocco Good Pharmacovigilance Practices Manual: First edition (2003) and second edition (2011);
- WHO Guide: The importance of pharmacovigilance (Safety Monitoring of medicinal products) (2002);
- WHO guide for the creation and running of a pharmacovigilance centre: Monitoring the Safe Use of Medicinal Products (2000);
- WHO guideline on reporting and learning systems for medication errors: the role of pharmacovigilance centres;
- WHO guideline: Pharmacovigilance in Public Health Programmes

The Health Minister

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