MINISTRY OF HEALTH

GUIDELINES FOR THE IRAQI PHARMACOVIGILANCE SYSTEM (IPhvC)

INDIVIDUAL CASE SAFTEY REPORT (ICSR) FOR HELTH CARE PROFESSIONALS

2012

IRAQI PHARMACOVIGILANCE CENTER
Version 1

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Table of contents

Abbreviations

ADR Adverse Drug Reaction

AEFI Adverse event following immunization

DGI Directorate of general inspection

DOH Directorate of health

DTA Directorate of technical affairs

EMA European medicines agency

EPI Expanded program on immunization

HCPs Health care professionals or providers

ICSR Individual Case Safety Report

IPhvC Iraqi Pharmacovigilance Centre

MAH Marketing Authorization Holder

MHRA Medicines and health regulatory agency

MOH Ministry of Health

NBDS National Board for Drugs Selection

NCDCR National center for drug control and research

PSUR Periodic Safety Update Report

PV Pharmacovigilance

SPC Summary of product characteristics

UMC Uppsala Monitoring Centre

WHO World Health Organization

ACKNOWLEDGEMENT

We owe a great many thanks to a great many people who helped and supported us during the writing of this guidelines.

The special thank goes to the deputy minister for technical affairs and the general manager for the directorate of technical affairs **Dr. Sattar jabbar Alsaedy** and his assistant **Dr.Adnan Shannon Atti** for their encourage, support and helpful supervision .

Big contribution and hard worked from pharmacist **Manal Mohammed Younus** , The supervision and support that she gave truly help the progression and smoothness for writing these guidelines .

Great appreciations go to the Iraqi pharmacovigilance center staff pharmacist **jaafer Kurmanji , firas ali and marwa faisal** ,that help us from time to time during the writing of these guidelines.

Iraqi Pharmacovigilance system guidelines

Introduction

Medicines have significant benefits to our lives and lead to significant reduction in morbidity and mortality. However, even though they are generally seen as having beneficial effects, all medicines (including their excipients e.g. coloring agents, lubricants, preservatives, etc), have a potential for producing adverse or unwanted effects no matter how skillfully they are used.

With the increasing use of medicines for the management and control of diseases, there has been a mounting need to monitor adverse drug reactions (ADRs), as ADRs have been shown to rank among the top 10 leading causes of mortality in some countries despite the fact that most of the ADRs are preventable. In addition suitable services to treat ADRs impose a high financial burden on health care due to the hospital care of patients with drug related problems. It is therefore of major importance to set up a Pharmacovigilance system to control the increasing in the use of medicines through continuous monitoring for the ADRs and other drugs related problems to insure the safety of medicines at all times and at all levels of the health care system.

The world health organization (WHO) with the view to early detection of unknown adverse reactions and interactions, increase in frequency of known adverse reactions and identification of risk factors and possible mechanisms underlying adverse reactions.

The Ministry of health in Iraq is charged with the responsibility of ensuring the availability of safe, efficacious and good quality medicines to all Iraqis. To attain the objective, the Ministry of health, through the technical affairs directorate (including the National Drug Regulatory

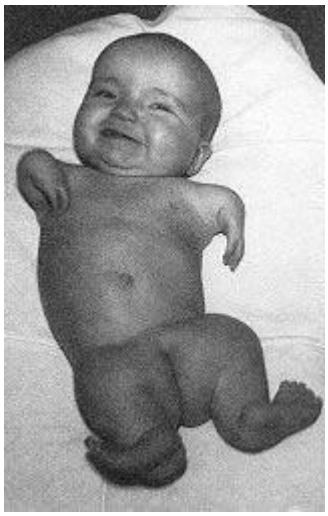
Authority in Iraq) has been implementing strategies aimed at ensuring that products used in Iraq are safe, efficacious, of good quality and are supplied and handled by qualified personnel. in the past , Safety and efficacy surveillance of medicines has not received the required attention. To address this, the Iraqi Pharmacovigilance center has developed these Guidelines for the National Pharmacovigilance System in Iraq. The Pharmacovigilance system is necessary for the prevention of drug - related illnesses, early detection and assessment of adverse drug reactions and to minimize the financial costs associated with preventable adverse events. The role out of a Pharmacovigilance system is an indication of the Ministry's commitment to safeguarding the Health of all Iraqi people.

The Guideline for the National Pharmacovigilance System in Iraq is to guide healthcare workers on the operations of the Pharmacovigilance system. It gives an overview of what Pharmacovigilance is, how to detect and classify ADR's and the structural organization of the system in Iraq. It also describes the reporting system to the National Pharmacovigilance Centre and expected outcomes.

All healthcare workers are encouraged to actively participate in Pharmacovigilance and to report all suspected adverse drug reactions to help protect the health of all Iraqis.

All medicines have potential risks as well as benefits. The potential risks of medicines came into sharp focus during the story of thalidomide tragedy in the late of 1950's and early 1960's in western Europe and North America , the mothers had taken the drug for morning sickness , babies born with phocomelia (shortening of the limbs), among other birth defects.

Following this tragedy till now, all the governments have tried formulating legislations and regulations that ensure the safety, efficacy and quality of medicines used in their countries.



Thalidomide induced phocomelia - *Birth - defects where babies are born without limbs or with serious deformities*

What is Pharmacovigilance?

According to the WHO, Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse events or any other possible drug-related problems.

Iraqi pharmacovigilance center deal with any serious adverse drugs events, decrease or lack of effectiveness , any medication errors lead to serious ADR.

Importance of Pharmacovigilance

The information collected during the pre-marketing phase is incomplete with regard to adverse drug reactions and this is mainly because:

- Tests in animals are insufficient to predict human safety.
- Patients used in clinical trials are selected and limited in number, the conditions of use differ from those in clinical practice and the duration of trials is limited ; By the time of licensing a product,

exposure of less than 5000 human subjects to a drug allows only the more common ADR to be detected;

- Information about rare but serious adverse reactions, chronic toxicity use in special groups (such as children, the elderly or pregnant women) or drug interactions is often incomplete or not available. Therefore, post-marketing surveillance is important to permit detection of less common but sometimes very serious ADRs.

Thus, post-marketing surveillance is important to permit detection of less common, but sometimes very serious ADRs. Therefore health professionals worldwide should report on ADRs as it can save lives of their patients and others.

The objectives of the Pharmacovigilance system

- ❖ To Improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions,
- ❖ To Improve public health and safety in relation to the use of medicines,
- ❖ To Detect problems related to the use of medicines and communicate the findings in a timely manner,
- ❖ To Contribute to the assessment of benefit, harm, effectiveness and risk of medicines, leading to the prevention of harm and maximization of benefits,
- ❖ Encourage the safe, rational and more effective (including cost effective) use of medicines,
- ❖ Promote understanding, education and clinical training in Pharmacovigilance and its effective communication to the public.

The goals of Pharmacovigilance

The ultimate goals of Pharmacovigilance are:

- The Rational and safe use of medicines.
- The assessment and communication of the risks and benefits of drugs on the market.
- Educating and informing patients on safety of medicines.

Classification of Adverse Drug Reactions

❖ Type A

Augmented pharmacologic effects - dose dependent and predictable (medicine actions) are those which are due to (exaggerated) pharmacological effects. Type A effects tend to be fairly common, dose related (i.e. more frequent or severe with higher doses) and may often be avoided by using doses which are appropriate to the individual patient. Such effects can usually be reproduced and studied experimentally and are often already identified before marketing.

❖ Type B effects

Bizarre effects (or idiosyncratic) - dose independent and unpredictable (Patient reactions) characteristically occur in only a minority of patients and display little or no dose relationship. They are generally rare and unpredictable, and may be serious and are notoriously difficult to study. Type B effects are either immunological or non-immunological and occur only in patients, with - often unknown - predisposing conditions.

Immunological reactions may range from rashes, anaphylaxis, vasculitis, inflammatory organ injury, to highly specific autoimmune syndromes. Also non-immunological Type B effects occur in a minority of predisposed, intolerant, patients, e.g. because of an inborn error of metabolism or acquired deficiency in a certain enzyme, resulting in an abnormal metabolic pathway or accumulation of a toxic metabolite. Examples are chloramphenicol aplastic anaemia and isoniazid hepatitis.

❖ **Type C effects**

Chronic effects refer to situations where the use of a medicine, often for unknown reasons, increases the frequency of a "spontaneous" disease. Type C effects may be both serious and common (and include malignant tumors) and may have pronounced effects on public health. Type C effects may be coincidental and often concern long term effects; there is often no suggestive time relationship and the connection may be very difficult to prove.

❖ **Type D effects**

Delayed effects (dose independent)

Carcinogenicity (e.g., immunosuppressants)

Teratogenicity (e.g., fetal hydantoin syndrome)

❖ **Type E effects**

End-of-treatment effects

❖ **Type F effects**

Failure of therapy

Introduction to the Iraqi Pharmacovigilance system

The Iraqi Pharmacovigilance center (IPhvC) has been established in the directorate of technical affairs (DTA), Ministry of Health to be responsible for the **collection** and **evaluation** of information on pharmaceutical products marketed in Iraq with particular reference to adverse reactions. Furthermore, IPhvC is taking all appropriate measures to:

A. Encourage physicians , pharmacists and other healthcare professionals to report the suspected adverse reactions to IPhvC
B. Oblige marketing authorization holders to systematically collect information on risks related to their medical products and to transmit them to IPhvC
C. Provide information to HCPs and end-users through adverse drug reaction news bulletins, drug alerts and seminars.

Who should report ADRs?

- All health care professionals/workers, including clinicians, pharmacists, dentists, nurses, traditional medicine practitioners are encouraged to report.
- Marketing authorization holder (MAH), being primarily responsible for the safety of their products, they are obligated to report **serious** adverse drug reactions they receive about their Products to IPvC. While the Non-serious ADRs should be included in the periodic safety update report (PSURs).

What is to be reported?

- For the new medicines: Report all suspected adverse reactions including minor ones for the newly marketed medicines in Iraq for

5 years regardless the nature and intensity of the ADRs. (Medicines are still considered "new" up to five years after marketing authorization).

- For the established medicines : Report all the serious ADRs including:

1. rare
2. unexpected
3. fatal or life-threatening
4. permanently / significantly disabling
5. required or prolong hospitalization
6. cause a congenital anomaly

- Report if an **increased frequency** of a given reaction is suspected.
- Report all suspected ADRs associated with drug-drug, drug food or drug-food supplements (including herbal and complementary products) **interactions**.
- Report ADRs occurring from overdose or **medication error**.
- Report when suspected ADRs are associated with medicine withdrawals.
- Report ADRs in special fields of interest such as medicine abuse and medicine use in **pregnancy** (teratogenicity) and during lactation.
- In **children** under the age of 18, all suspected ADRs occurring, should be reported regardless of whether the medicine is licensed for use in children. Children are often not exposed to medicines during clinical trials and many medicines are used in children even if they are not licensed for this purpose. This means that monitoring of medicine safety is particularly important for this age group.

As soon as possible
Reports on all suspected adverse reactions
- known or not, serious or not –
are welcome and useful
If there is any doubt about whether or not it is an ADR;
always it is best practice to submit a report

What happens to the reported ADRs?

1. The information obtained from your report will be used to promote safe use of medicines in the local, national and international levels.

2. The report you submit will be entered into the national database of adverse drug reactions and be analyzed by expert reviewers on a regular basis.

A well - completed and duly submitted ADR reported by you may result in:

- Additional investigations into the use of the medicine in Iraq
- Appropriate changes in the package insert
- Change the schedule of the medicine
- Enhancing educational initiatives to improve the safe use of that medicine
- Other regulatory and health promotion interventions as the situation may warrant including withdrawal / recall.

Thus, the ultimate purpose of ADR reporting and monitoring is to reduce risks associated with drug prescribing and administration and improve patient care, safety and treatment outcome.

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Expectedness of the adverse drug reaction

The expectedness of the reaction is assessed in accordance with the approved product information; the reaction is **defined as expected** if it is included in package insert or the summary of product characteristics (SPC).

On the other hand the **unexpectedness** of the reaction includes the following:

- The reaction is not included in the package insert or the summary of product characteristics (SPC).
- The reaction is included in the package insert or the summary of product characteristics (SPC) but showed changes in its known frequency.
- The reaction is included in the package insert or the summary of product characteristics (SPC) but showed changes in its known severity i.e. the change in the severity of a known adverse drug reaction is considered as unexpected to that medicine.

What are the benefits of these reports?

The health care provider and patient stand to benefit as:

- Improvement on the quality of care offered to patients.

- Reduction of drug related problems leading to better treatment outcome.
- Improved patient confidence in professional practice, hence professional growth.
- Improved knowledge.
- Access to feedback information on drug related problems reported within the country and internationally.
- Satisfaction for the fulfillment of a moral and professional obligation.
- Participitation of some of the important ADRs in the meetings of Pharmacovigilance.
- Letters of thanks dedicated to the health care professionals.

Will reporting have any negative consequences on the reporter?

- The adverse drug reaction report **does not** constitute an admission that you or any other health professional or the drug contributed to or caused the event in any way.
- The outcome of the report, together with any important or relevant information relating to the reaction you have reported, will be communicated to you as appropriate.
- The details of your report are stored in a confidential database at the Iraqi pharmacovigilance center and the analyzed report will be sent to the Uppsala Monitoring Center (UMC).
- The names of the reporters or any other health professionals named on the report and the patient will be removed before any details

about a specific adverse drug reaction is used or communicated to others.

- The information obtained from your report will not be used for commercial purposes. It is only meant to improve our understanding and use of medicines in Iraq.

You can reduce suffering and Save thousands of patients' lives by doing just one thing:

REPORTING ALL SUSPECTED ADVERSE DRUG REACTIONS

Including lack of effect.

How to obtain the reporting form

At each hospital or health center, you will find the ADRs reporting form in the pharmacy department section, or you can get it directly from the ministry of health website.

In the future:

- A Pharmacovigilance coordinator will be assigned (preferred to be the clinical pharmacist, or the drug information centers pharmacist), the reporting forms will be available at the hospital Pharmacovigilance coordinator for the hospital health care professional.
- In addition, the reporting forms will be available on the **IPhvC web site** for health care professional & patients to be downloaded.
- A web based dynamic reporting module will be available at **IPhvC** website to be completed and submitted online.

- A Special stand for the reporting form will be available in the community pharmacies (mainly for community pharmacists & may be for the nearby private clinics).

How to submit ADR report ?

After filling the ADR reporting form; All ADR reports can be sent to the IPhvC by:

- By official letter to the DOH then to the IPhvC.
- E-mail
- By Hand

In case of serious ADRs,
Call the IPhvC as fast as possible while you report the ADRs form

In the future, there will be collaboration with the pharmaceutical distribution companies to inform the IPhvC about any medicines problems especially the ADRs.

Serious reports should be submitted in expedited manner
i.e as soon as possible & no later than 15 calendar days
Thus they best submitted by Email

While other reports can be submitted on regular basis (every month) by any of the above means.

The Basic principles of efficient reporting

- **In-time reporting**

✓ Report the suspected adverse drug reaction as soon as it occurs- the report involves less work and is more accurate.

✓ Send the report quickly to the Iraqi Pharmacovigilance center.

- **Strong suspicion and follow-up**

✓ Continue your strong suspicion of the medicine-induced illness in the same patient and in other patients

✓ Keep a vigil for signs and symptoms that may now enhance or exclude the possibility of a medicine induced reaction

✓ All follow - up / supplementary information should be documented and submitted to the Iraqi Pharmacovigilance center "FOLLOW - UP REPORT" clearly indicated on the top right corner of the form.

✓ Make sure that the patient names and patient code are the same in the 1st report & the Follow up report. As it is very important that follow-up reports are accurately identified and linked to the original report.

- **Accuracy and completeness**

✓ Ensure that each reported Suspected ADR Reporting Form is filled in accurately and with all the necessary information, as much as is available to you. This is very important for assessing the causality of the medicine to have caused that reaction.

✓ Remember the 4 basic components that make a report reliable are:

  - An identifiable patient
  - An identifiable health-care professional

- An identifiable Adverse reaction or product problem
- An identifiable medicine (suspected)

If the above information is missing, the report may not be useful.

✓ Remember to fill in all information accurately and in clear legible writing.

How to recognize ADRs in patients ?

ADRs are difficult and sometimes impossible to distinguish from the disease being treated since they may act through the same physiological and pathological pathways. However, the following approach is helpful in assessing possible drug-related ADRs:

1) Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised.

2) Take a proper history and do a proper examination of patient

- A full medicine and medical history should be taken
- An ADR should be your first differential diagnosis at all times
- Ask if this adverse reaction can be explained by any other cause e.g. patient's underlying disease, other medicines including over-the-counter medicines or traditional medicines, toxins or foods
- It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is.
- A medicine-related cause must be considered, especially when other causes do not explain the patient's condition.

3) Establish time relationships by answering the following question: *Did the ADR occur immediately following the medicine administration?*

Some reactions occur immediately after the medicine has been

given while others take time to develop. The time from start of therapy to the time of onset of the suspected reaction must be logical.

4) Carry out a thorough physical examination with appropriate laboratory investigations if necessary:

- Remember: only a few medicines produce distinctive physical signs.
- Exceptions include fixed medicine eruptions, steroid-induced dermal atrophy, acute extra-pyramidal reactions.
- Laboratory tests are important if the medicine is considered essential in improving patient care or if the laboratory tests results will improve management of the patient.
- Try to describe the reaction as clearly as possible- Where possible, provide an accurate diagnosis.

5) Effect of Dechallenge and Rechallenge should be determined

- Dechallenge (withdrawal of the suspected medicine): Positive dechallenge is the improvement / resolution of ADR when the suspected medicine is withdrawn in a strong, though not conclusive indication of medicine-induced reaction.

- Rechallenge (re-introducing the suspected medicine after a dechallenge) .

Rechallenge is only justifiable when the benefit of reintroducing the suspected medicine to the patient overweighs the risk of recurrence of the reaction, which is rare. In some cases the reaction may be more

severe on repeated exposure. Rechallenge requires serious ethical considerations**.**

6) Check the known pharmacology of the medicine :

- Check if the reaction is known to occur with the particular suspected medicine as stated in the package insert or other reference.
- Remember: if the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular suspected medicine.

7) Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the Iraqi Pharmacovigilance Centre.

Causality assessment

Causality assessment is the method by which the extent of relationship between a medicine and a suspected reaction is established i.e. to attribute clinical events to medicines in individual patients or in case reports

The WHO scale of assessment and the Naranjo's scale are the most commonly used scales.

Most commonly reported ADRs
Rash
Vomiting
Nausea
Abdominal pain
Headache
Renal failure
Hypertension
Fever
Tinnitus
Death

Drug classes commonly reported with ADRs
Non- steroidal anti-inflammatory drugs
Anti -depressants
Antibiotics
Anti- epileptics
Analgesics and antipyretics
Bronchodilators
Immunosuppressant
Anti malarial
Anti emetics
Anti diabetics

Various causality terms are in use but the below is used most widely. Some people, however, do not use all the terms. For instance, many do not believe that a "certain" classification is possible for a single report and others make no distinction between "probable" and "possible".

Where only "possible" or "unlikely" are used to describe reactions it must be understood that "possible" include those reactions which are called by others "probable" and "certain", as well as "possible".

Whilst "conditional/unclassified" and "unassessible/unclassifiable" are not causality terms, they describe the status of adverse reaction reports and therefore allow for practical communication about ADR issues.

WHO probability scale

TERM	DESCRIPTION
Certain	▪ **A clinical reaction, including laboratory test abnormality, occurring in a plausible time relationship to medicine administration, and which** ▪ **Cannot be explained by concurrent disease or other medicines or chemicals.** ▪ **The response to withdrawal of the medicine (dechallenge) should be clinically plausible.** ▪ **The reaction must be definitive pharmacologically or phenomenologically, (i.e. an objective and specific medical disorder or a recognized pharmacological phenomenon)** ▪ **Using a satisfactory rechallenge procedure if necessary.**
Probable / Likely	▪ **A clinical reaction, including laboratory test abnormality, with** ▪ **A reasonable time sequence to administration of the medicine,** ▪ **Unlikely to be attributed to concurrent disease or other medicines or chemicals, and which** ▪ **Follows a clinically reasonable response on withdrawal (dechallenge).** ▪ **Rechallenge information is not required to fulfill this definition.**
Possible	▪ **A clinical reaction, including laboratory test abnormality, with** ▪ **A reasonable time sequence to administration of the medicine, but which could also be explained by concurrent disease or other medicines or chemicals.** ▪ **Information on medicine withdrawal may be lacking or unclear.**
Unlikely	▪ **clinical reaction, including laboratory test abnormality, with** ▪ **a temporal relationship to medicine administration which makes a causal relationship improbable, and** ▪ **Other medicines, chemicals or underlying disease provide plausible explanations.**
Conditional/ Unclassified	▪ **A clinical reaction, including laboratory test abnormality**
Unassessable/ Unclassified	▪ **More data is essential for a proper assessment or the additional data are under examination.**

NARANJO's Algorithm

QUESTION	YES	NO	DON'T KNOW
Are there previous conclusion reports on this reaction?	+1	0	0
Did the adverse reaction appear after the suspect medicine was dministered?	+2	-1	0
Did the AR improve when the medicine was discontinued or a specific antagonist was administered?	+1	0	0
Did the AR reappear when medicine was readministered?	+2	-1	0
Are there alternate causes [other than the medicine] that could solely have caused the reaction?	-1	+2	0
Did the reaction reappear when a placebo was given?	-1	+1	0
Was the medicine detected in the blood [or other fluids] in a concentration known to be toxic?	+1	0	0
Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0
Did the patient have a similar reaction to the same or similar medicines in any previous exposure?	+1	0	0
Was the adverse reaction confirmed by objective evidence?	+1	0	0

Scoring for NARANJO's Algorithm

- > **9 = definite ADR**
- 5-8 = probable ADR
- 1-4 = possible ADR
- 0 = doubtful ADR

(ADR REPORTING FORM)

وزارة الصحة

دائرة الأمور الفنية / المركز العراقي للرصد الدوائي

REPORT OF SUSPECTED ADVERSE DRUG REACTIONS استمارة الابلاغ عن الاعراض الجانبية المشتبه بها

I- PATIENT DETAILS

Patient initials: _____

Age: _____ ☐ Years Weight: _____ Kg Sex: ☐ Female ☐ Male

II- DETAILSE OF ADVERSE DRUG REACTION (ADR)

Onset Date: ☐☐☐☐☐☐ (d d / m m / y y)

End date ☐☐☐☐☐☐ (d d / m m / y y)

Outcome: ☐ Recovered *(Date)*: _____ ☐ not yet recovered
☐ Fatal *(Date of death)*:_____ ☐ unknown

Duration: _____ min,hr,day,week,month,year

Description of ADR(S)

_____

_____

_____

Suspected drug(s) *(please specify brand name & batch No. if known)*	Dosage	Frequency	Route	Date started	Date stopped	Indication(s) for using drug
1.						
2.						
3.						
Concomitant drugs *(Including self medication taken at the same time and/or 3 months before)*						
1.						
2.						
3.						
4.						
5.						

Other relevant information: e.g. medical history, allergies, pregnancy, smoking, alcohol use, please enclose any relevant laboratory results.

_____

_____

_____

III. - MANAGEMENT OF ADVERSE REACTION

Drug(s) discontinued ☐ Yes ☐ No Improvement on discontinuation ☐ Yes ☐ No

Hospitalization *(following the ADR):* ☐ yes No ☐ Already hospitalized ☐

Do you consider the reaction to be serious? ☐ Yes ☐ No

If yes, please tick (✓) to indicate why the reaction is considered to be serious:

☐ Patient died due to reaction ☐ Involved or prolonged in – patient hospitalization

☐ Life threatening ☐ Involved persistent or significant disability or incapacity

☐ Congenital anomaly ☐ medically significant, please give details:_____

Treatment given: ☐ No ☐ Yes(please specify):_____

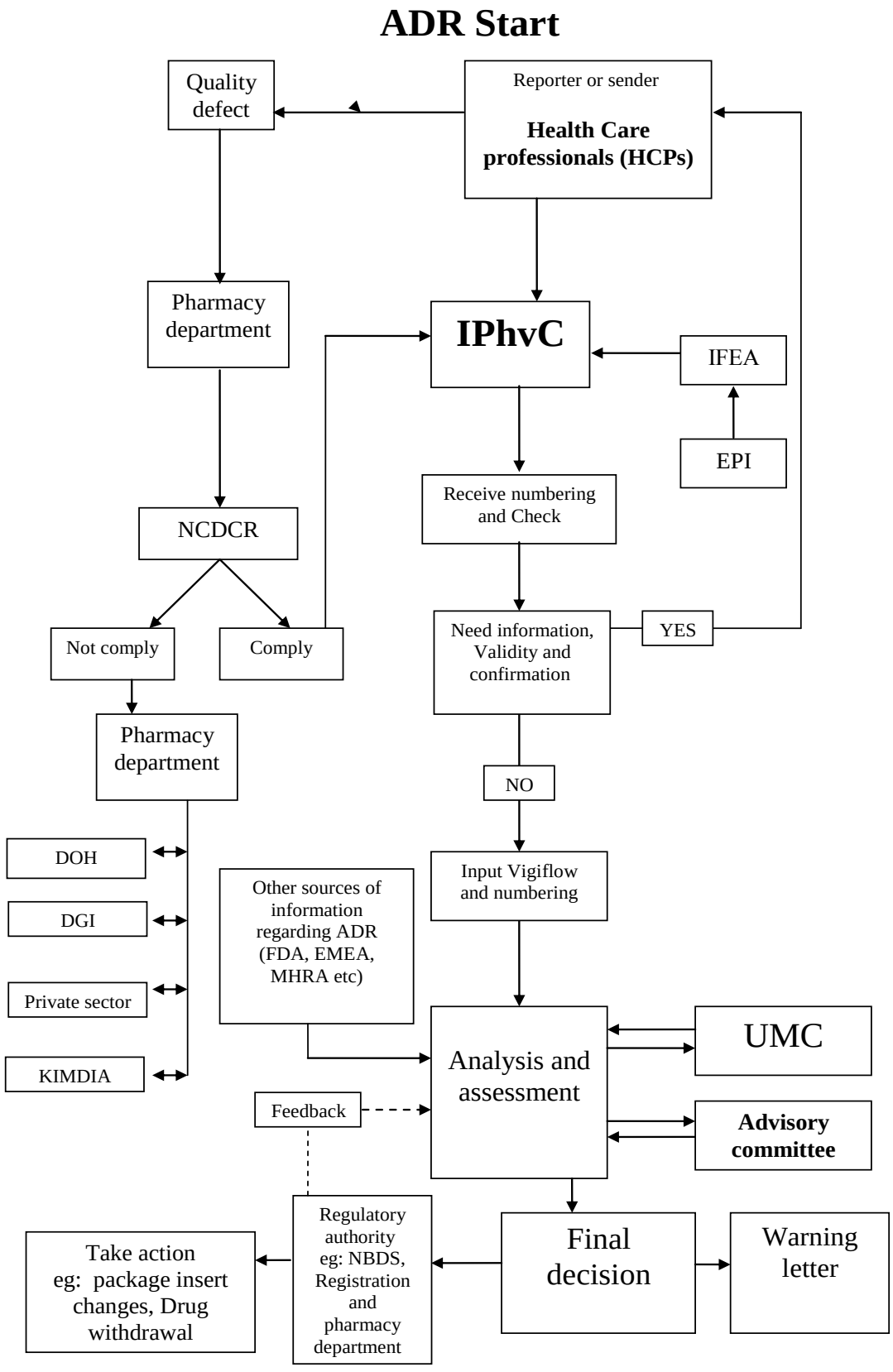
IV- REPORTER DETAILS

Name: _____ Profession: _____ Signature:_____

Contact no: _____ Email address: _____ Date: _____

THANK YOU FOR TAKING CARE OF YOUR PATIENT

The Workflow shows how Pharmacovigilance team process the ADRs reports



Glossary of important terms used in Pharmacovigilance

Adverse Event/ Adverse Experience

Any untoward medical occurrence that may present during treatment with a pharmaceutical product but which does not necessarily have a causal relationship with this treatment.

Adverse Drug Reaction

A response to a drug which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease, or for the modification of physiological function.

An adverse drug reaction, contrary to an adverse reaction, is characterized by the suspicion of a causal relationship between the medicine and the occurrence, i.e. judged as being at least possibly related to treatment by the reporting or a reviewing health professional.

Case Control Study

Study that identifies a group of persons with the unintended medicine effect of interest and a suitable comparison group of people without the unintended effect. The relationship of a medicine to the medicine reaction is examined by comparing the groups exhibiting and not exhibiting the medicine reaction with regard to how frequently the medicine is present.

Clinical Trial

A systematic study on pharmaceutical products in human subjects (including patients and other volunteers) in order to discover or verify the effects of and/or identify any adverse reaction to investigational products, and/or to study the absorption, distribution, metabolism and excretion

of the products with the objective of ascertaining their efficacy and safety.

Clinical trials are generally classified into Phases: I to IV. Phase IV trials are studies performed after marketing of the pharmaceutical product. They are carried out on the basis of the product characteristics for which the marketing authorization was granted and are normally in the form of post-marketing surveillance.

Cohort Study

A study that identifies defined populations and follows them forward in time, examining their rates of disease. A cohort study generally identifies and compares exposed patients to unexposed patients or to patients who receive a different exposure.

Causality assessment

The evaluation of the likelihood that a medicine was the causative agent of an observed adverse reaction. Causality assessment is usually made according established algorithms.

Drug/ Medicine

Any substance in a pharmaceutical product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient. The term drug/medicinal product is used in a wider sense to include the whole formulated and registered product, including the presentation and packaging, and the accompanying information.

Drug Alerts

The action of notifying a wider audience than the initial information holder(s) of a suspected association between a drug and an adverse reaction. Note that the term is used in different contexts that can be confusing, for example, an alert may be from a manufacturer to a regulator or from a regulator to the public.

Dechallenge

The withdrawal of a medicine from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed.

Individual Case Safety Report (ICSR)

A document providing the most complete information related to an individual case at a certain point of time. An individual case is the information provided by a primary source to describe suspected adverse reaction(s) related to the administration of one or more medicinal products to an individual patient at a particular point of time.

Lack of Efficacy

Unexpected failure of a medicine to produce the intended effect as determined by previous scientific investigation.

National Pharmacovigilance Centre

A single, governmentally recognized centre (or integrated system) within a country with the clinical and scientific expertise to collect, collate, analyze and give advise on all information related to medicine safety.

Pharmacoepidemiology

The study of the use and effects of medicines in large numbers of people.

Pharmacovigilance

The science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem.

Prescription Event Monitoring

A system created to monitor adverse drug events in a population. Prescribers are requested to report all events, regardless of whether they are suspected adverse events, for identified patients receiving a specified medicine.

Rechallenge

The point at which a medicine is again given to a patient after its previous withdrawal. (see Dechallenge).

Record Linkage

Method of assembling information contained in two or more records, e.g., in different sets of medical charts, and in vital records such as birth and death certificates. This makes it possible to relate significant health events that are remote from one another in time and place.

Serious Adverse Event or Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose results in:

- Death
- Is life-threatening
- Requires inpatient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability/incapacity
- Congenital Anomaly
- Medically important event or reaction

To ensure no confusion or misunderstanding of the difference between the terms ‘serious’ and ‘severe’, the following note of clarification is provided:

The term ‘severe’ is not synonymous with serious. In the English language, ‘severe’ is used to describe the intensity (severity) of a specific reaction (as in mild, moderate or severe); the reaction itself, however, may be of relatively minor medical significance (such as severe headache).

Seriousness (not severity) which is based on patient/reaction outcome or action criteria serves as guide for defining regulatory reporting obligations.

Side Effect

Any unintended effect of a pharmaceutical product occurring at doses normally used in humans, which is related to the pharmacological properties of the medicine.

Signal

Reported information on a possible causal relationship between an adverse reaction and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the reaction and the quality of the reaction and the quality of the information.

Spontaneous Reporting

A system whereby case reports of adverse drug reactions are voluntarily submitted from health professionals and pharmaceutical manufacturers to the national regulatory authority.

Unexpected Adverse Reaction

An adverse reaction, the nature or severity of which is not consistent with domestic labeling or market authorization, or expected from characteristics of the medicine.

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