ADVERSE EVENTS REPORTING GUIDELINES FOR HEALTHCARE PROFESSIONALS

Document Number: **PHSR/GL/RGHP/007**
Document History: **2nd Edition**
Effective Date: **20th October, 2025**

Drug Regulatory Authority of Pakistan
Islamabad-Pakistan

1. HISTORY

This is the second edition of this document.

2. APPLICATION - Guidance Document.

This document is for the guidance and support of healthcare professionals for reporting adverse events to NPC, DRAP.

3. PURPOSE:

HCPs are responsible for the timely identification, documentation, and reporting of AEs and their contribution is essential to the early detection and reporting of an AE as they have face to face interaction with a patient and can extract maximum information. Lack of knowledge, fear of accountability, ambiguity about ADR and understanding of reporting system of the country are inter-alia factors responsible for underreporting by HCPs. The purpose of this document is to. -

3.1. Guide and enlighten HCPs about reporting AEs to NPC, DRAP;

3.2. To enhance the participation of HCPs in the reporting system of the country; and

3.3. To develop a spontaneous reporting culture in the country to ensure therapeutic good's safety.

Table of Contents

1. HISTORY 2
2. APPLICATION - Guidance Document. 2
3. PURPOSE: 2
4. INTRODUCTION: 4
5. DEFINITION AND ACRONYMS: 4
6. WHY TO REPORT? 7
7. ARE THERE NEGATIVE CONSEQUENCES OF REPORTING? 7
8. WHAT TO REPORT: 8
9. WHERE AND HOW TO REPORT: 9
10. HOW TO FILL IN THE REPORTING FORMS: 11
11. WHEN TO REPORT: 18
12. MEDICATION ERRORS: 18
13. HIGH ALERT MEDICATIONS/ DRUGS LIST. 20
14. ASSESSMENT OF AE REPORTS: 20
15. INITIAL SIGNAL DETECTION BY HCPs: 25
16. WHAT HAPPEN TO THE REPORT: 26
17. REFERENCES: 27
18. ANNEX A: YELLOW FORM 28

ANNEX B: DOWNLOADING VIGIMOBILE APPLICATION 31

4. INTRODUCTION:

Therapeutic goods such as drugs, vaccines and biologicals are extensively tested in humans during clinical trials yet everything related to their safety i.e. ADRs cannot be determined during clinical trials. The limitations of clinical trials are: the numbers of trials subjects are less than patients of real practice; trials subjects are highly selective and vulnerable groups such as pregnant women, the elderly, children and patients with other diseases and patients with concomitant drugs are excluded in clinical trials; and duration of clinical trials is of few years as compared to real practice. That is why after registration of therapeutic goods when these are released into the market and a large population is exposed to them, some new and unexpected serious ADRs can occur. Therefore, there is a dire need to have a vibrant national pharmacovigilance centre to monitor the therapeutic goods after these are registered and released into the market. In line with international practices, the DRAP has established the National Pharmacovigilance Centre (NPC), under the Division of Pharmacy Services, DRAP, Islamabad, to monitor therapeutic goods' safety across the country. NPC has developed different reporting forms that are available through the official website and a mobile application for HCPs for reporting of any AEs and accordingly play their part in ensuring the safety of therapeutic goods.

Reporting adverse drug events (ADEs) including medication errors and near misses equips the policymakers and healthcare system as a whole, with important knowledge about the products or therapeutic goods associated with errors, or for harmful/fatal outcomes for a patient as a result of an error. Moreover, reporting helps in understanding the circumstances that lead to such errors and the steps which can be taken to avert them in the future (e.g. system or process upgrade, policy development, training and education etc.). It can also help in identifying the product package or nomenclature issues (e.g. Look-alike, Sound-alike – LASA products) that contribute to ADEs so that necessary improvements in the product design can be done to avoid further mishaps.

5. DEFINITION AND ACRONYMS:

Abuse of therapeutic good: means persistent or sporadic, intentional excessive use of therapeutic good which is accompanied by harmful physical or psychological effects;

ADR: "*Adverse Drug Reaction*" means response to drug or therapeutic goods which is noxious and unintended that occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease or for the restoration,

correction or modification of physiological function. A response in this context means that a causal relationship between a therapeutic good and an adverse event is at least a reasonable possibility. An adverse reaction, in contrast to an adverse event, is characterised by the fact that a causal relationship between a therapeutic good and an occurrence is suspected.

AE: "*Adverse Event"* means any untoward medical occurrence in a patient or clinical investigation subject administered a drug or therapeutic good and which does not necessarily have a causal relationship with this treatment.

AEFI: *"Adverse Event Following Immunizations*" means any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine

DRAP: The Drug Regulatory Authority of Pakistan.

Causality Assessment: means the evaluation of the likelihood that medicine or therapeutic good was the causative agent of an observed adverse reaction;

HCP: "*Healthcare Professional"* means any member of the medical, dental, pharmacy, nursing professions, any allied health professional or any other person who in the course of his professional activities may prescribe, recommend, purchase, supply, sell or administer a therapeutic good including medical technologies as registered or enlisted by the Authority

Medication Error: means any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer

Near Miss: WHO defines a near miss as "an error that has the potential to cause an adverse event (patient harm) but fails to do so because of chance or because it is intercepted" ("An error caught before reaching the patient")

NPC: National Pharmacovigilance Centre working under DRAP.

Occupational Exposure*:* an exposure to a therapeutic good as a result of one's professional or non-professional occupation at the workplace. It does not

include the exposure to one of the ingredients during the manufacturing process before the release as a finished product at a pharma company.

Off Label Use: Refers to the use of an approved medicine under the direction or supervision of a healthcare professional for an unapproved indication, age group, dosage, route or form of administration.

Overdose of Therapeutic good: means administration of a quantity of a therapeutic good given per administration or cumulatively which is above the maximum recommended dose according to the registered therapeutic good information

PV: *"Pharmacovigilance"* means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other therapeutic good related problems.

Serious ADRs or AEs: means an untoward medical occurrence that at any dose results in patient death, is life-threatening, requires inpatient hospitalization or results in prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect or is judged to be a medically important event or reaction;

Spontaneous Reporting: a system whereby case reports of adverse drug events are voluntarily submitted from health professionals and registration holders to the national regulatory authority; or

unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization such as World Health Organization, and poison control centre that describes one or more adverse drug reactions in a patient who was given one or more therapeutic goods and that does not derive from a study or any organized data collection scheme

Therapeutic Goods: Includes drugs or alternative medicine or medical devices or biologicals or other related product as may be notified by DRAP. Further explanation of each class of the therapeutic goods is given in Schedule II of the DRAP Act, 2012.

WHO-UMC: World Health Organization Uppsala Monitoring Centre.

6. WHY TO REPORT?

Even though therapeutic goods such as drugs, vaccines and biological are extensively tested in humans during the clinical trials (initial testing in humans) before they are registered, not everything about their safety in the form of ADRs can be determined during these trials. Many therapeutic goods display unexpected ADRs that can vary from individual to individual. Many of these effects are identified during the drug development, but, since clinical trials are conducted in selected subjects with disease conditions, it is likely that some rare ADRs may not be observed during these phases. Therefore, new information about the safety of therapeutic goods that was not previously determined during the clinical trials may be identified when these are registered and used by a wider population. AEs and AEFIs reported spontaneously by HCPs play a substantial role in the detection of risks and confirmation of ADRs that may lead to subsequent risk minimization measures.

Medication errors are failures in the treatment process that leads to or has the potential to lead to harm to the patient. As per the World Health Organization patient safety website. Globally, as many as 4 in 10 patients are harmed in primary and outpatient healthcare. Up to 80% of harm is preventable. The most detrimental errors are related to diagnosis, prescription and the use of medicines. Likewise, in high-income countries, it is estimated that one in every 10 patients is harmed while receiving hospital care. The harm can be caused by a range of adverse events, with nearly 50% of them being preventable. Medication errors are a leading cause of injury and avoidable harm in health care systems. Reporting medication errors and sharing with patients and other colleagues these errors and near misses provide opportunities to reduce the effects of errors and prevent the likelihood of future errors by, in effect, warning others about the potential risk of harm.

7. ARE THERE NEGATIVE CONSEQUENCES OF REPORTING?

Across the world, HCPs are reluctant to report AEs and medication errors the reasons being; lack of knowledge, fear of accountability and the busy schedule of HCPs. Fear of accountability is the main reason that leads to under-reporting. It is a misconception on the part of HCPs that AE and AEFI are caused by their negligence that will lead to the loss of their job. The occurrence of AEs has nothing to do with the negligence of HCPs. An AE could still happen in a patient that is being continuously watched upon and provided with standard treatment without any error. The data submitted by HCPs contains confidential details of the patient and

the reporter (that is HCP) containing details of name, address, email address and contact numbers. NPC-DRAP don't share this data and treats the details of the reporter and patient as confidential data. The only purpose of spontaneous AE reporting is to gather more data about the safety of therapeutic goods from the HCPs and ensure their safety for all. Therefore, by reporting AEs and medication errors, HCPs can help to provide more information about therapeutic goods, which will ultimately help to make them safer for all. Furthermore, it is also the ethical responsibility of HCPs to report AEs and medication errors. Reporting AEs and suspected ADRs offers an opportunity to identify and further investigate previously unknown or poorly described adverse reactions and helps in continuous monitoring of the safety of the therapeutic good throughout its life

8. WHAT TO REPORT:

8.1. Types of Reports.

The HCPs can submit the following type of reports:

8.1.1. Known or unknown serious spontaneous suspected ADRs or AEs reports with therapeutic goods;

8.1.2. Known or unknown non-serious spontaneous suspected ADRs or AEs reports with therapeutic goods;

8.1.3. AEFIs report with vaccines;

8.1.4. Reports of lack of therapeutic efficacy in the case of vaccines, contraceptives, antibiotics, and medicines used in critical conditions or life-threatening conditions;

8.1.5. AEs with quality problems; and

8.1.6. Reports that are associated with adverse outcomes as a result of an overdose, abuse, misuse, off-label use, occupational exposure and medication error of therapeutic goods.

8.2. Mandatory & Essentially Required Information.

HCPs should collect all the information required to be filled in the AE reporting forms. In case complete information is not available, then all the essentially required fields/ information should be filled. In case essentially required information is not available, then reporting form must contain all the mandatory information. Mandatory information is the minimum criteria for reporting therefore a form without mandatory information will not be accepted.

Mandatory Information	Essentially Required Information.
1. Patient information. **2. One or more suspected reaction (s).** The reaction terms or event summary must be given in case ADRs or ADE/medication error has reached to the patient **3. One or more suspected drug (s).** **4. Reporter information.**	1. Patient initials, and age at the time of reaction or event. 2. Sex of the patient. 3. Reaction term (s) or incident summary 4. Time-to-onset of reaction (start date/time of suspected drug +start date/time of reaction) 5. Suspected drug (s) (dose, strength, dosage form) 6. Indication for use. 7. The seriousness of reaction or event 8. The outcome of the reaction or event 9. De-challenge (in case of ADR) 10. Re-challenge (not always ethical to perform) (in case of ADR) 11. Reporter information (designation, contact details) 12. Case Narrative in free text (chronology of happening of ADRs or AEs) 13. Date of report.

9. WHERE AND HOW TO REPORT:

9.1. Report the AEs to the Pharmacovigilance Officer of the Hospital.

HCPs, who are working in a hospital, should at first report the AE or suspected ADR to the pharmacovigilance officer or pharmacovigilance focal person of the hospital. Public and private sector hospitals may have notified their pharmacovigilance officers for coordination with the provincial pharmacovigilance centres. The pharmacovigilance officer documents the reported AE or suspected ADR and takes a further course of action. HCPs should also manage the AEs to prevent harm to the patient.

9.2. Report the AEs directly to NPC, DRAP.

HCPs who are working in private clinics or some hospitals and do not have access to pharmacovigilance officers or a focal person of pharmacovigilance can report the suspected ADR or AE directly to NPC, DRAP through any of the following means:

9.2.1. Yellow form reporting

NPC, DRAP has developed suspected ADR reporting (yellow form) for HCPs

(Annex A) that is available on the DRAP website that can be mailed to NPC either on an email address or mailing address. Necessary contact details of the national centre are as under:

National Pharmacovigilance Centre
Division of Pharmacy Services
Drug Regulatory Authority of Pakistan
Prime Minister's National Health Complex, Park Road
Islamabad.
Phone No: 051-9255981
Email Address: npc@dra.gov.pk
Website: www.dra.gov.pk

9.2.2. Online Reporting through Med Vigilance E Reporting System.

AEs can also be reported to NPC, DRAP through Med Vigilance E Reporting System that is available through the official website. A telephone number of the reporter in the relevant field of the E-Reporting system should be provided in case staff from NPC, DRAP intends to get further information from HCP in the form of follow-up. For guidelines on how to report through Med Vigilance E Reporting System please see **section 10.2.**

9.2.3. Reporting through VigiMobile Application.

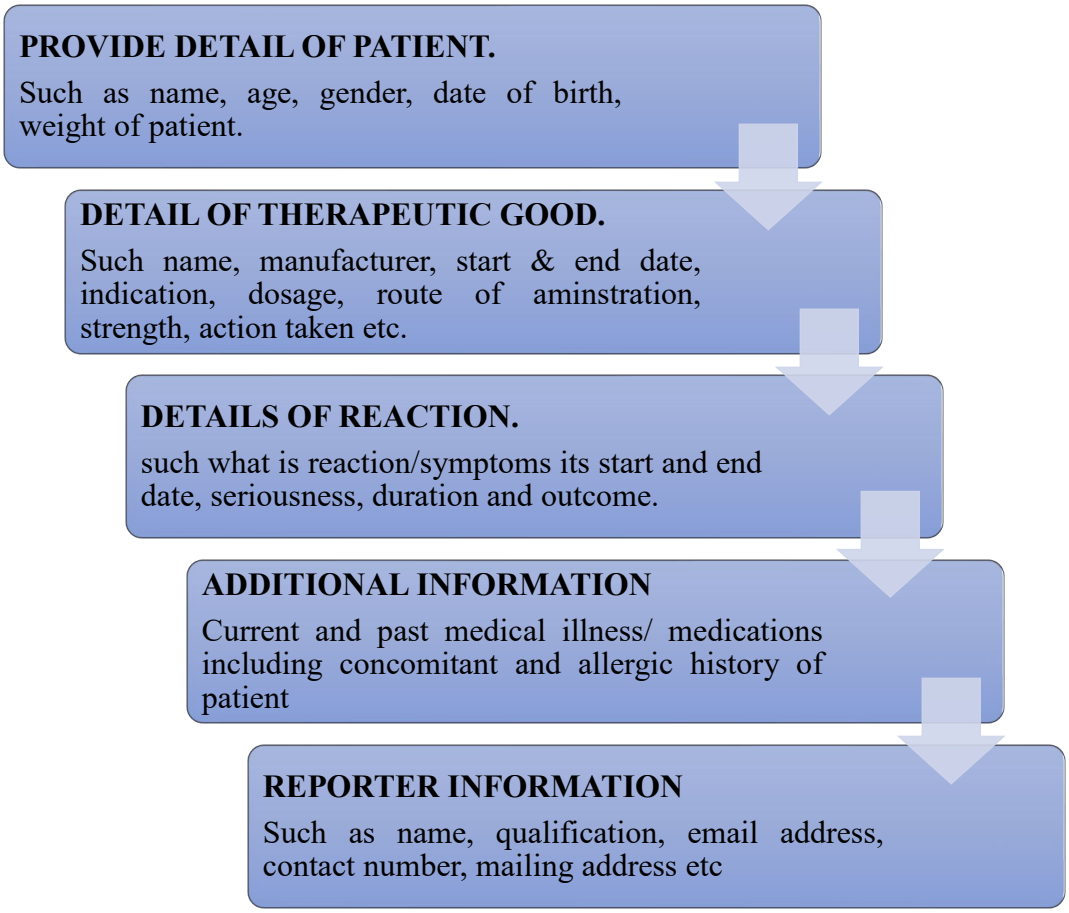
Similarly, there is a VigiMobile Application available that has been developed for AEs reporting through mobile phones. HCPs can directly report AEs to NPC, DRAP through this mobile application. Necessary guidelines on downloading the mobile application are available in **Annex B.** For guidelines on how to report through the VigiMobile Application please see **section 10.3**

9.3. Avoid Reporting Through Multichannel to Avoid Duplication.

In some cases, HCP reports the AE or suspected ADR to the pharmacovigilance officer of the hospital or provincial pharmacovigilance centre. If the pharmacovigilance officer has already reported it to the provincial pharmacovigilance centre then HCP should avoid reporting the same to NPC, DRAP. Likewise, only one channel should be used for reporting to DRAP i.e. either through E-Reporting or yellow form or through Med Safety Mobile App. The HCP should keep one thing in mind which is to "report an adverse event through the one channel only", to avoid duplication of reports.

10. HOW TO FILL IN THE REPORTING FORMS:

There are three methods to report AEs to NPC, DRAP as per section **9.2**. Overall, the data filling in the yellow form, Med Safety Mobile App and Med Vigilance E-Reporting system are approximately the same as you have to provide the information depicted in the below diagram:



10.1. Filling of Yellow Reporting Form.

NPC, DRAP has designed yellow form in hard format **(Annex A)** for the collection of suspected ADRs or AEs reports from HCPs. There are fields of mandatory and essentially required information in this reporting form that need to be filled in properly for proper assessment of the report. Following are the points to be filled in the said reporting form.

10.1.1. Patient Information

a. *Patient Initial or Name*: healthcare professionals can either write the initials of a patient's name like for example "MA" for Muhammad Arif or can write their full name. If healthcare professionals provide full names it would be kept confidential.

b. *Identification Number*: Hospital or ward admission numbers can be provided so that healthcare professionals can easily access patient files in case follow-up information is required.

c. *Sex*: Mention the gender of the patient. If the patient is female, then the healthcare professional must provide information, about whether she is pregnant or not.

d. *Age at the time of reaction or event:* The age of the patient should be provided in this section along with a proper unit for example hours, days, weeks, months, years etc. Suppose an infant is of 8 hours then the reporter needs to mention the hours unit with a numerical value.

10.1.2. Suspected Drug (s)/Vaccine (s)/ Alternative Medicine(s)

a. *Drug/ Vaccine/Alternative Medicine Name:* Both generic and brand shall be provided.

b. Batch No: Batch number shall be provided in case the drug has a quality problem, it would be helpful to trace the drug and recall it.

c. Manufacturer Importer: If the reporter has provided a generic name then he must provide details of the manufacturer/ importer.

d. *Route of Administration and daily doses:* Route through which the drug was given

e. Dosage and Strength:

f. Start date: administration date of the drug. It would be helpful to build a relationship between the drug and the event and will determine a time to onset of reaction.

g. Stop Date: when the drug was withdrawn. It would also help in the assessment of reports by providing information on the De-challenge of a drug.

h. Prescribed for: The indication for which the drug was administered.

10.1.3. Suspected Reaction (s)

a. When Reaction started: Mention the date on which reaction started, it would be helpful to determine the casual relationship of reaction with drug and will determine the time to onset of reaction.

b. When Recovery Started: Mention the date on which the reaction ended or recovery started, it would be helpful to determine whether the reaction subsides when the suspected medicine is stopped.

c. *Describe the reaction(s):* Complete narrative/ description of the reaction should be provided; how the patient developed the reaction, nature, localization etc.

d. *Details of treatment given for management of ADR:* If any treatment is provided for the management of ADR, then please provide in the section of the case narrative/description of the reaction, complete details of treatment including name, strength, dose and route etc.

e. *The outcome of the treatment provided.* Similarly, the outcome of the treatment provided should also be provided in the section of the case narrative/description. The outcomes such as whether the patient has recovered or is recovering or fatal (lead to death). The outcome of the treatment could also be provided in the outcome section as described below in sub-section k.

f. *Other relevant histories of the patient (Allergies, Smoking, Alcohol Use, Hepatic/Renal Problems, and Pre-Existing Medical Problems etc.*: Write the relevant history persistent to a patient including pre-existing conditions (allergies, smoking, alcohol use, hepatic or renal dysfunction, surgical procedure, risk factors etc.) and current medical condition if any.

g. *Relevant tests/Laboratory data with dates:* write all tests and procedures performed to diagnose or confirm the reaction/event, including those tests done to investigate a non-drug cause.

h. *The seriousness of the reaction:* If the reporter considers the reaction to be serious then he must tick all that apply out of the following:

- *Patient Died*: If the patient died due to an adverse event. It would be appropriate to mention the cause of death in the reaction narrative along with the date of death.
- *Life-Threatening:* If the patient was at substantial risk of dying at the time of the adverse event.
- *Involved or Prolonged Inpatient Hospitalization:* If due to adverse the patient was hospitalized or already hospitalized patient's stay was prolonged.
- *Disability or incapacity:* If due to an adverse event the patient normal life function is affected.
- *Congenital Anomaly/ Birth Defect:* When exposure to the drug during pregnancy has resulted in an adverse outcome in the infant in the form of birth defect.

- *Other serious events:* Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious such as important medical events that might not be immediately life-threatening or result in death or hospitalisation but might jeopardise the patient or might require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or the development of drug dependency or drug abuse.

i. *De-challenge details:* Withdrawal of medicine from a patient following an adverse event.

- *Yes:* If reaction abates/subsides after the suspected drug is stopped or the dose reduced.
- *No:* If the reaction does not abate/ subsides after the suspected drug is stopped or the dose reduced.
- *Does not apply:* If de-challenge is not applicable as in case of vaccines, anaesthesia, where a single dose is given, in case of death, or in a case where treatment is completed prior to reaction or event. De-challenge is also meaningless in the case of myocardial infarction and stroke.

j. *Re-Challenge details:* Reintroduction of the medicine under the same conditions as previously (same dose, form, route of administration), following withdrawal and recovery from the adverse event.

- *Yes:* When the suspected drug is reintroduced the reaction again appeared.
- *No:* When the suspected drug is re-introduced the reaction does not appear.
- *Does not apply:* If re-challenge is not applicable as in the case of anaphylaxis.

k. *The outcome of the reaction/event and treatment:*

Provide details if the suspected drug stopped what was the outcome or if the treatment was started what was the outcome.

- *Fatal:* If the patient dies.
- *Recovering:* If the patient is recovering from the reaction.
- *Unknown:* If the outcome is unknown.
- *Continuing:* If the patient is continuing to experience the reaction/event.
- *Recovered:* If the patient has completely recovered from the reaction/event.

l. *Cause of the Reaction/event:*

- *Quality problem:* If the reaction the patient experience was due to a quality problem. However, healthcare professionals can also inform NPC about the visible sign of quality defects.

- *Medication Error:* Inappropriate medication use or patient harm, when the medicine was in the control of a healthcare professional or consumer.
- *Adverse Event/ Reaction:* if the patient develops a reaction or event in spite of the fact that medicine has no quality defect and the healthcare professional does not use the medicine inappropriately.

m. *Causality Assessment:* The reporter (if trained) must perform the causality assessment and justify the assessment.

10.1.4. Other Concomitant Drug(s)/ Vaccine (s)/ Alternative Medicines (s)

Information is the same as a suspected drug. But, here only the information about the additional medication the patient is using shall be written.

10.1.5. Suspected Medical Devices (s)

a. Medical Device Common Name/ Brand Name: Brand name is on a label attached to a durable device; on a package of a disposable device; or is on the labelling materials of an implantable device. The generic or common name of the suspect medical device or a general descriptive name (e.g., urological catheter, heart pacemaker, patient restraint). Please do not use broad generic terms such as "catheter", "valve", "screw", etc.

b. Lot No/ Batch Name: This number can be found on the label or packaging material and help in tracking the device in the market and its production record at the time of recall.

c. Manufacturer/ Importer:

d. Model No: The exact model number found on the device label or accompanying packaging.

e. Unique Identifier No: This number can be found on the device, its label, or accompanying packaging. The number is located below the barcode and begins with one of the following three elements: 01; +; or =. Record all numbers, letters, parentheses, and symbols included in the UDI Number.

f. Serial No: It is assigned by the manufacturer and should be specific to each device.

g. Implantation date:

h. Ex-plantation date:

10.1.6. Reporter Details

a. *Name of Reporter:* The reporter needs to mention his name on the form.

b. Professional Address: The reporter must also mention his professional address for communication.

c. Speciality: Clinician, Pharmacist, Nurse, Physiotherapist.

d. Telephone No: For communication, if any information is required by the officers of NPC.

e. Email Address: For communication

f. Date of this report: mention the date on which she/he report the adverse reaction/ event.

g. Signature: Sign of the reporter

h. Reporting to other stakeholders: the reporter needs to mention whether he or she has reported the same ADR/ AE to the provincial centre and registration holder of therapeutic good or is reporting directly to NPC.

10.2. How to report through Med Vigilance E Reporting System?

Med Vigilance E-Reporting system online reporting form is divided into different sections/tabs such as patient, drugs, reactions, additional information and reporter. To move to the next section, you have to fill in/ answer the previous sections. The fields in sections/tabs are structured into drop-down lists, calendar selections, ticks or open fields where data could be typed. There are some mandatory fields in each section if these are not filled the report would not move forward and you would be asked to fill in the mandatory information. Overall, the fields are the same as of yellow reporting form but these are customized into web-based for easy reporting by healthcare professionals and patients. There are also options of *"add another reaction"* and "*add another medicine*" where you can add more than one reaction or medicine.

FOR HEALTHCARE PROFESSIONALS.

1. On the very **First Page**, you will be asked to report either as a patient/relative of the patient or as a healthcare professional. You have to select "*I'm reporting as a healthcare professional*".
2. In the section "**User of Medicine,"** you have to provide initials or name, sex, age or date of birth and weight of the patient.
3. In the **s**ection of "**Describe What Happened"**, you have to provide details of reaction/symptoms such as its start and end date, seriousness, duration and outcome. There is also a field of description where you can narrate how, when and where the event occurs. Also tick one of the seriousness categories provided, if the reaction is

serious. If you intend to add more than one reaction select add another reaction at the bottom.

4. In the section of "**Medicine(s)"**, you have to provide details of medicine such as its name, producer/manufactures, strength, dosage, batch number, route of administration, start and stop date, duration of treatment, reason of use and action taken after the reaction had developed. If you intend to add more than one medicines click add other medicines at the bottom.
5. In the "**Additional Information"** section, details of current and past medical illness and medications of a patient and any additional comments can be provided
6. In the **s**ection of "**Contact Detail"**, a given family name, profession, health facility details, contact number and email address of a healthcare professional need to be provided.
7. **Upon completion** of the online reporting form, a summary report would be generated for your review and you would be asked to send the report to NPC. A confirmation email will be sent to you once the report is received at NPC, DRAP.

10.3. How to report through VigiMobile Application?

This is a mobile application developed by the Uppsala Monitoring Centre (UMC) for the National Pharmacovigilance Centre of the DRAP. The application can be accessed through the QR codes available in Annex-B or on the official website of DRAP, wherein it can be scanned from Android or iOS devices and added to the home screen or application section. It is to be noted that the application is not available in the google or apple play stores. The reporting form and sections are the same as that of Med Vigilance E-reporting system. The form is available in English and Urdu Versions for ease of reporting and understanding.

Scan the below QR code to access the mobile application

11. WHEN TO REPORT:

The HCP should report a serious AE as soon as possible to NPC, DRAP. Sometimes, the adverse reaction might be unexpected and might be posing harm to other patients. Therefore, an earlier reporting of an adverse reaction by the HCP will help to prevent harm in other patients. As a general practice, serious AEs with therapeutic goods are mostly reported within fifteen calendar days and non-serious AEs are reported on a monthly basis. The NPC appreciate the reporting of AEs as per these timelines.

12. MEDICATION ERRORS:

The United States National Coordinating Council for Medication Error Reporting and Prevention defines a medication error as:

> *"Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. Such events may be related to professional practice, healthcare products, procedures, and systems, including prescribing, order communication, product labelling, packaging, and nomenclature, compounding, dispensing, distribution, administration, education, monitoring, and use".*

There are a number of different approaches to classifying medication errors. One approach is to base the classification on the stage in the sequence of the medication use process (treatment process), such as prescribing, transcribing, dispensing, administration or monitoring. Another approach is to consider the types of errors occurring, such as wrong medication, dose, frequency, administration route or patient. A further approach classifies errors according to whether they occur from mistakes made when planning actions (knowledge-based or rule-based mistakes) or errors in the execution of appropriately planned actions (action-based errors, known as "slips", or memory-based errors, known as "lapses"). Errors may also be classified according to their level of severity.

12.1. Types of Medication Errors.

S #	Type	Examples
1	**Prescribing errors**	Errors in prescribing can be divided into irrational prescribing, inappropriate prescribing, ineffective prescribing, under-prescribing and overprescribing, and errors in writing the prescription.

		Errors of omission, Ambiguous or illegible order Incorrect dose, Wrong drug, Inappropriate or not required drug, Wrong dosage, Wrong frequency, Wrong duration, Wrong time, Wrong route of administration
2	**Dispensing error**	Wrong drug, Incorrect directions/labelling, Incorrect preparation or compounding, Incorrect storage (e.g. temperature, use by date, light exposure)
3	**Medicine preparation error**	Preparation, or admixture, errors are generally considered to occur within the pharmacy department, but they can occur anywhere in the continuum of care. Common preparation errors include wrong concentration, wrong drug, wrong dose, wrong base solution/diluent, wrong volume, preparations made for the wrong patient, and preparations prepared for administration by the wrong route.
4	**Administration error**	Common administration errors include wrong patient, wrong route, wrong dosage form, wrong time, wrong dose or rate, and wrong drug. Additional errors in this category may include errors of omission or missed doses.
5	**Monitoring error**	1. **Failure to monitor medication effects.** An example may include not checking a scheduled blood glucose level and checking the level but not reacting to the level. 2. **Incorrect interpretation of laboratory data used to monitor medication effects.** An example may include checking the blood glucose level but giving the wrong amount of corrective or sliding-scale insulin for the value 3. **Incorrect transcription of laboratory test values.** An example may include transposed numbers or numbers being transcribed in the wrong place 4. **Incorrect timing of monitoring** may occur when a blood glucose level is taken at the wrong time relative to meals or an aminoglycoside level is not taken as a true trough level 5. **Incorrect timing of serum concentration monitoring**
6	**Drug identification errors due to Product packaging or nomenclature**	This is commonly referred to as Look-Alike drugs' packaging and design, and Sound-Alike or Read-Alike drugs' names with phonetic similarities (e.g. losec-lasic, vincristine-vinblastine etc.)

12.2. Identification and Reporting of Medication Errors.

Identifying medication errors and finding their underlying causes are the first steps in establishing prevention strategies to avoid their recurrence. In certain situations, medication errors are easily recognized by practitioners, but in other cases, medication errors are not clearly visible and are then reported as ADRs. In healthcare practice, the following are the most common methods used for the detection of medication errors namely: incident report review; patient chart review; direct observation; interventions by pharmacists; and trigger tools.

All types of medication errors identified during the practice of healthcare professionals should be reported to the hospital pharmacovigilance centre so that the recurrence of the same medication errors in other patients could be minimized. Medication errors associated with adverse outcomes could also be reported to NPC through the available means mentioned earlier.

13. HIGH ALERT MEDICATIONS/ DRUGS LIST.

High Alert Medications (HAMs) are medications that bear a heightened risk of causing significant patients harm when these medications/ drugs are used in error or inappropriately. The consequences of errors or inappropriate use of the following drugs can be more devastating and of serious concern. NPC, DRAP has developed a high alert medications/drugs list for Pakistan in collaboration with the Pakistan Society of Health-System Pharmacists (PSHP) that is available on the DRAP website. NPC, DRAP intends to encourage HCPs to actively monitor the safety of high alert medications/ drugs available on the list by avoiding their inappropriate use. If any adverse drug reaction (ADR) or ADE occur with or without inappropriate use, it should be managed properly and must be reported to National Pharmacovigilance Centre, DRAP through the available means.

14. ASSESSMENT OF AE REPORTS:

14.1. Adverse Drug Reactions (ADRs) Analysis:

Causality assessment is the evaluation of the likelihood that medicine or therapeutic good was the causative agent of an observed adverse reaction. In another way, it is a structured approach to determine the relationship between reported events and therapeutic good.

Nevertheless, causality assessment has become a common routine procedure in pharmacovigilance. These systems are largely based on four considerations:

- The association in time (or place) between drug administration and event;
- Pharmacology (including current knowledge of nature and frequency of adverse reactions);
- Medical or pharmacological plausibility (signs and symptoms, laboratory tests, pathological findings, mechanism); and
- Likelihood or exclusion of other causes.

These systems mainly fall into three categories.

i. Algorithms e.g. Naranjo, RUCAM;

ii. 'Global introspection' qualitative (e.g. WHO-UMC) or quantitative (e.g. French imputability system); and

iii. Probabilistic methods e.g. Bayesian.

14.1.1. Causality Assessment by HCPs.

Since HCP have maximum interaction with a patient who has experienced any AE or ADR and is the first one whom the patient visits after experiencing the event; therefore, NPC, DRAP advises HCPs to perform an initial causality assessment of suspected ADR, where possible, either through Naranjo or WHO-UMC method before reporting. Details of the two methods are discussed in detail in the preceding paragraphs.

14.1.2. Naranjo Algorithm Causality Assessment Method.

Naranjo is one of the most widely used methods. It is a questionnaire designed by Naranjo et al, to determine the likelihood of whether an ADR is actually due to the drug rather than the result of other factors**.** It uses a series of 10 questions and these questions can be answered as Yes, No or do not know. Answers are weighted with scores (-1 to +2) and the total score is ranked on four probability scales, the answer of the aggregate score is the result of causality assessment:

i. "*Definite" (Certain):* if the score is more than 9.

ii. *"Probable":* if the score is between 5 -8.

iii. *"Possible":* if the score is between 1-4.

iv. "*Doubtful" (Unlikely):* if is less than 1.

S. No	Question	Yes	No	Don't Know	Score
1.	Are there previous conclusive reports on this reaction?	+1	0	0	
2.	Did the adverse event appear after the suspected drug was administered?	+2	-1	0	
3.	Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	
4.	Did the adverse event reappear when the drug was re-administered?	+2	-1	0	
5.	Are there alternative causes that could on their own have caused the reaction?	-1	+2	0	
6.	Did the reaction reappear when a placebo was given?	-1	+1	0	
7.	Was the drug detected in blood or other fluids in concentrations known to be toxic?	+1	0	0	
8.	Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	
9.	Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	
10.	Was the adverse event confirmed by any objective evidence?	+1	0	0	

Naranjo scores of 9 or 10 indicate that an event was "definitely" an ADR; scores of 5-8 rate the likelihood as "probable"; scores of 1-4 are "possible"; and scores of less than 1 are "doubtful."

Naranjo CA, Busto U, Sellers EM, et al. A method for estimating the probability of adverse drug reactions.
Clin Pharmacol Ther. *1981;30:239-245.*

14.1.3. The WHO-UMC System for Standardized Case Causality:

The WHO-UMC system for standardised case causality assessment has been developed in consultation with the National Centres participating in the Programme for International Drug Monitoring and is meant as a practical tool for the assessment of case reports. It is a combined assessment considering the clinical-pharmacological aspects of the case history and the quality of the documentation of the observation. Since pharmacovigilance is particularly concerned with the detection of unknown and unexpected adverse reactions, other criteria such as previous knowledge and statistical chance play a less prominent role in the system. It is recognised that the semantics of the definitions are critical and that individual judgement may therefore differ. Other algorithms are either very complex or too specific for general use. This method gives guidance to the general arguments which should be used to select one category over another. WHO-UMC causality assessment system considers the following criteria: timing of event; alternative explanations (disease or drugs); response to de-challenge (withdrawal of drug); and response to re-challenge (re-exposure to a drug). Based on the above criteria the

ADR can be classified into the following six categories:

A. Certain
B. Probable/Likely
C. Possible
D. Unlikely
E. Conditional/ Unclassified
F. Unassessable/ Unclassifiable

Causality term	Assessment criteria*
Certain	• Event or laboratory test abnormality, with plausible time relationship to drug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible (pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon) • Rechallenge satisfactory, if necessary
Probable/ Likely	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable time relationship to drug intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional/ Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable/ Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory • Data cannot be supplemented or verified

*All points should be reasonably complied with

14.2. Medication Errors / Near Miss Analysis:

Quality improvement & patient safety programs within healthcare organizations must include mechanisms for reporting medication errors, examining and evaluating causes of errors, analysing aggregate data to determine trends and making necessary changes within their healthcare delivery system to prevent errors from occurring.

Timely analysis of the medication error reports from clinical settings could identify opportunities for quality improvement and system changes. In general, there are two steps for error analysis,

- The first is to identify individual problems and deficiencies in an event that can lead to the error; and
- The second is to analyse the defective design of the system.

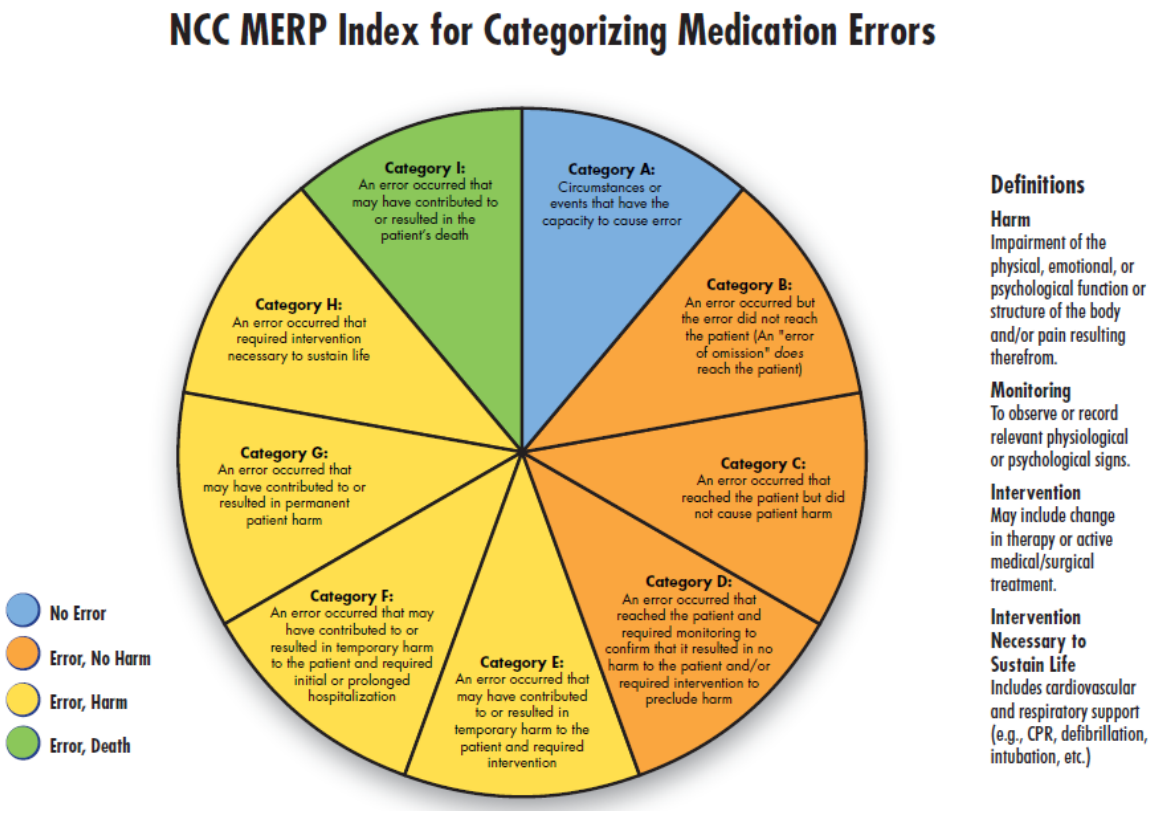
Institute for Safe Medication Practices (ISMP) emphasizes that the cause of a medication error is rarely the fault of a single person practising within the vast and complex medication-use process. Rather, medication errors are often the result of a breakdown of at least 1 of 10 key elements that affect medication use. These key elements are interrelated subprocesses of the 5 core steps in the medication-use process i.e.: medication prescribing, order processing, dispensing, administration, and monitoring.

When performing a root cause analysis, the following 10 key elements that affect the core medication use steps should be thoroughly evaluated to determine the cause of the error:

1. **Patient information** that is accessible and accurate (e.g. demographics, lab reports, history etc.).
2. **Drug information** that is accessible, accurate, and usable (e.g. information on how to safely order, dispense, administer a drug and monitor its effects).
3. **Communication** between providers that is consistent and not complicated (e.g. medication information communicated during hand-offs between shifts or when the patient is transferred or discharged).
4. **Drug labelling and packaging** that facilitates safety and the consistent use of appropriate nomenclature (e.g. products that are look-alike or sound-alike – LASA).
5. **Drug storage and stock** that facilitates appropriate distribution with standardized drug concentrations and administration times.
6. **Drug device acquisition:** methods that ensure proper use and monitoring (e.g. infusion pumps, syringe pumps etc used for administration of medicines).
7. **Work environments:** that provide an appropriate workload and limit

unfavourable conditions such as poor lighting, noise, and interruptions.

8. **Staff competency** That is assessed and can be improved with opportunities for continuing education.
9. **Patient education:** That is accurate and provided consistently.
10. **Medication use processes** that are evaluated for quality and can be redesigned to improve safety.



15. INITIAL SIGNAL DETECTION BY HCPs:

World Health Organization define a signal as "reported information on a possible causal relationship between an adverse event and a drug or a therapeutic good, 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 event and the quality of the information. The publication of a signal usually implies the need for some kind of review or action"

The more recent definition of a signal is given by the CIOMS Medical Sciences working group in its report of 2010 which is defined as under:

"*Information that arises from one or multiple sources (including observations and experiments), which suggests a new potentially causal association, or a new aspect of a known association, between an intervention and an event or set of related events, either*

adverse or beneficial, that is judged to be of sufficient likelihood to justify verificatory action".

HCPs should look for any unusual or unexpected AE with therapeutic goods. If they experience any unusual event with a specific therapeutic good not earlier reported in the package inserts they should flag that report, collect maximum data, perform proper assessment and timely report to the pharmacovigilance officer, provincial pharmacovigilance centre or NPC as the case may be. Sometimes, there might be a cluster with a therapeutic good that is the number of reports of a given AE or of a group of AE terms with the same therapeutic good. Case series are important in the detection of quality problems; therefore, these should be timely reported so that quality analysis could be performed timely and harms to other patients can be prevented.

16. WHAT HAPPEN TO THE REPORT:

NPC collect reports of AEs from healthcare professionals, patients, provincial pharmacovigilance centres, public health programme, and pharmaceutical companies having registration of therapeutic goods. Staff at NPC, at first, check the report for mandatory and essentially required information. If there is any missing mandatory information, the reporter is contacted. The staff also contacts the reporter for more information about serious AEs. Likewise, NPC performs a complete assessment of individual reports that will be discussed along with other similar reports received with the same therapeutic goods through different means.

The reports are checked for new signals by safety experts to determine if there is any new information about the safety of the therapeutic. After evaluation of the safety signals, NPC, DRAP may issue new warning/ contraindication, remove indication of therapeutic goods for specific diseases or age groups, advise on how the therapeutic good should be used, or in some cases even stop the use of therapeutic goods.

Overall, the processing at NPC, DRAP is to monitor the safety of therapeutic goods in order to optimize the use of therapeutic goods with minimum harm to the patient. NPC also transfer the report to the global database of the World Health Organization Uppsala Monitoring Centre, Sweden, where the AEs and ADRs reported by you are also assessed along with similar reports with the same drug from other countries. The organization also perform its evaluation and share any new safety signal with NPC, DRAP.

17. REFERENCES:

1. Take & Tell Brochure of the Uppsala Monitoring Centre, Sweden.
2. European Medicine Agency adverse reaction reporting guidelines.
3. The Importance of Pharmacovigilance Safety Monitoring of Medicinal Product, by World Health Organization (2002)
4. The WHO-UMC standardized method for causality assessment.
5. ASHP Guidelines on Preventing Medication Errors in Hospitals
6. A Root Cause Analysis Project in a Medication Safety Course.
7. Guidelines on National Pharmacovigilance System (Edition 04)

18. ANNEX A: YELLOW FORM

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

This form is for voluntary reporting of adverse drug reactions caused by therapeutic goods marketed in Pakistan.

For Healthcare Professionals

National Pharmacovigilance Centre (NPC)
Pharmacy Services Division, Drug Regulatory Authority of Pakistan (DRAP)
Ministry of National Health Services, Regulation & Coordination,
3rd Floor, TF-Complex, 7-Mauve Area, G-9/4, ISLAMABAD.
Telephone No: +92519107413

For DRAP's Office Use Only
Report No. _____

A. PATIENT DETAILS

Patient's Initials or Name: _____ Identification Number (Medical/Hospital Ref): _____
Sex: **Male / Female**: _____, If Female, **pregnant or not**: _____ Age (at the time of reaction): _____ Weight (kg) _____

B. SUSPECTED DRUG(S)/VACCINE(S)/ALTERNATIVE MEDICINE(S) *(use additional pages if necessary)*:

Drug/Vaccine/Alternative Medicine (Brand Name & Generic Name)	Batch No:	Manufacturer /importer	Route of Administration & Daily Doses	Dosage & Strength	Start Date	Stop Date	Prescribed For

C. SUSPECTED REACTION(S) *(use additional pages if necessary)*:

1. When reaction started (DD/MM/YY): _____ 2. When recovery started (DD/MM/YY): _____

3. **Describe the reaction(s):** *(use additional pages if necessary)*:

4. **Other relevant history of the patient (Allergies, Smoking, Alcohol Use, Hepatic/Renal Problems, and Pre-Existing Medical Problems etc.:**

5. **Relevant tests/Laboratory data with dates:** *(use additional pages if necessary)*:

6. **Do you consider the reaction(s) to be serious?** Yes/No
If yes, please tick all that apply of the following:
- ☐ Patient died due to reaction:
- ☐ Life Threatening:
- ☐ Involved or prolonged inpatient hospitalization:
- ☐ Involved persistent or significant disability or incapacity:
- ☐ Congenital anomaly/Birth Defects:
- Other Serious (Medically Important Condition): please give details: _____

7. **Reaction abated after use stopped or dose reduced?** ☐ Yes ☐ No ☐ Doesn't apply
8. **Reaction reappeared after reintroduction?** ☐ Yes ☐ No ☐ Doesn't apply

9. **Outcomes:** ☐ Fatal ☐ Recovering ☐ Unknown ☐ Continuing ☐ Recovered
Other _____

10. **You consider the problem related to which of the following:** ☐ Quality Problem ☐ Medication Error ☐ Adverse Event/Reaction
If other, please specify _____

D. OTHER CONCOMITANT DRUG(S)/VACCINE(S)/ALTERNATIVE MEDICINE(S) *(use additional pages if necessary)*:

Drug/Vaccine/Alternative Medicine (Brand Name & Generic Name)	Batch No:	Manufacturer /importer	Route of Administration & Daily Doses	Dosage & Strength	Start Date	Stop Date	Prescribed For

E. SUSPECTED MEDICAL DEVICE(S) fill this area for suspected Device only *(use additional pages if necessary)*:

Medical Device Common Name / Brand Name	Lot No/ Batch No:	Manufacturer /importer	Model No:	Unique Identifier No:	Serial No:	If Implanted enter date	If Explanted enter date

F. REPORTER DETAILS

Name: _____ **Professional Address:** _____
Specialty: _____ **Tel No:** _____, **Email Address:** _____
Date of this report: _____ **Signature** _____
Have you reported this problem to Provincial Pharmacovigilance Centre or Manufacturer? If yes, please specify: _____

"This form neither has any legal value nor can be presented before any Court of Law as an Evidence."

SECOND FOLD HERE

GUIDELINES FOR ADVERSE DRUG REACTION (ADR) REPORTING
"ADVERSE DRUG REACTION (ADR) REPORTING IS ETHICAL AND MORAL DUTY OF HEALTH CARE PROFESSIONALS"

Please use this form for reporting:

- Suspected Adverse Drug Reactions with **THERAPEUTIC GOODS**
- Suspected Adverse Drug Reactions with **NEW THERAPEUTIC GOODS**
- Suspected Adverse Drug Reactions for **ALL VACCINES**
- **LACK OF EFFICACY** in the case of vaccines, contraceptives, antibiotics, and lifesaving medicines.
- Adverse outcome due to suspected **QUALITY PROBLEM** in therapeutic good.
- Adverse outcomes as a result of an overdose, abuse, misuse, off-label use or medication errors.

✓ **THERAPEUTIC GOODS** include the following: Drugs, Vaccine, Biological or alternative medicine or medical devices or biologicals or other related product as may be notified by DRAP

✓ Fatal reactions, life-threatening, disabling or incapacitating, result in or prolong hospitalization, congenital anomaly or birth defect and other serious medically important conditions are considered serious.

✓ Health care professionals shall comment on the causal relationship of each suspected drug/vaccine/alternative medicine with each reaction as per the World Health Organization (WHO) causality assessment scale which comprises of the following six categories, namely:

i. Certain ii. Probable iii. Possible iv. Unlikely v. Unclassified vi. Unclassifiable

For the Greater Good & in Public Interest, Please Report ADRs to DRAP even if you are unsure.

For More Information/Queries, please contact:

National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan, Telecom Foundation (TF) Complex, 7-Mauve Area, G-9/4, ISLAMABAD, Pakistan.
Website: www.dra.gov.pk **Email:** *npc@dra.gov.pk*
Phone No: 051-91-7413 & 051-9167299

FIRST FOLD HERE

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

This form is for voluntary reporting of adverse drug reactions caused by therapeutic goods marketed in Pakistan.

For Health Care Professionals (Additional page)

B. SUSPECTED DRUG(S)/VACCINE(S)/ALTERNATIVE MEDICINE(S) *(continued)*:

Drug/Vaccine/Alternative Medicine (Brand Name & Generic Name)	Batch No:	Manufacturer /importer	Route of Administration & Daily Doses	Dosage & Strength	Start Date	Stop Date	Prescribed For

C. SUSPECTED REACTION(S) *(continued)*:

3. Describe the reaction(s) *(continued)*:

4. Other relevant history of the patient (Allergies, Smoking, Alcohol Use, Hepatic/Renal Problems, and Pre-Existing Medical Problems etc. *(continued)* **:**

5. Relevant Tests/Laboratory Data with Dates *(continued)*:

D. OTHER CONCOMITANT DRUG(S)/VACCINE(S)/ALTERNATIVE MEDICINE(S) *(continued)*:

Drug/Vaccine/Alternative Medicine (Brand Name & Generic Name)	Batch No:	Manufacturer /importer	Route of Administration & Daily Doses	Dosage & Strength	Start Date	Stop Date	Prescribed For

E. SUSPECTED MEDICAL DEVICE(S) *(continued)*:

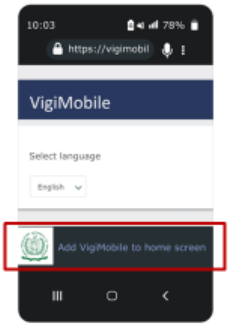
Medical Device Common Name / Brand Name	Lot No/ Batch No:	Manufacturer /importer	Model No:	Unique Identifier No:	Serial No:	If Implanted enter date	If Explanted enter date

ANNEX B: DOWNLOADING VIGIMOBILE APPLICATION

Install on Android (Chrome)

1 Scan QR code

2 Add VigiMobile to home screen



3 VigiMobile now appears as an app

Uppsala Monitoring Centre

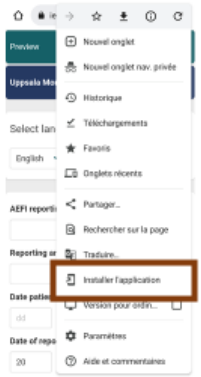
Install on Android

The prompt to download VigiMobile as an app is only sent the first time the webpage is visited. If a user wants to download the app at a later stage the process is:

1 Scan QR code

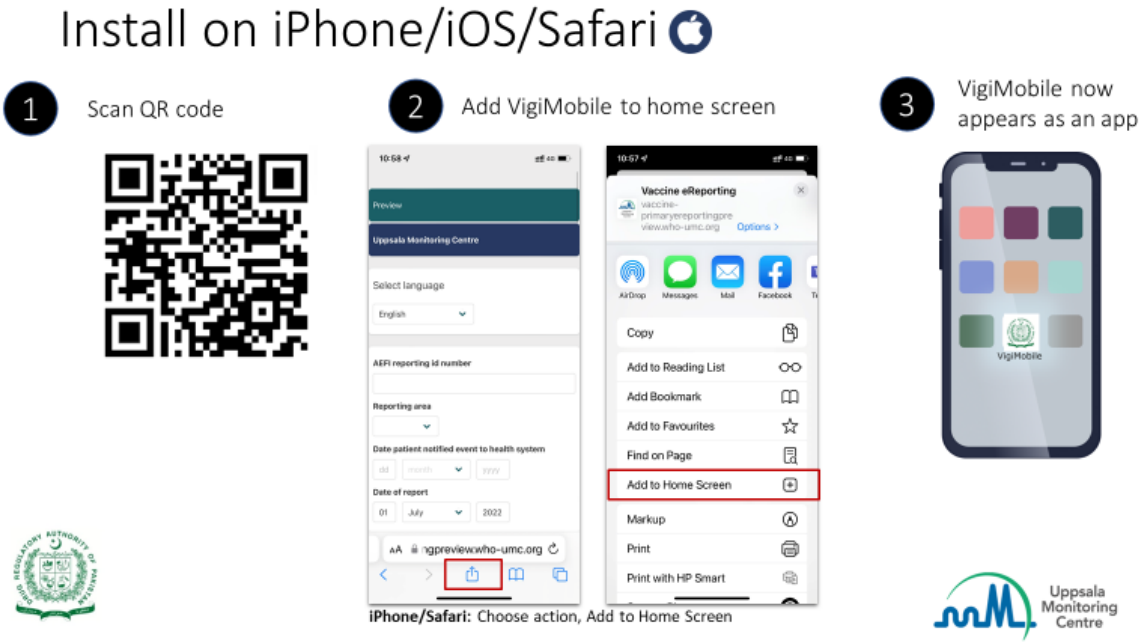
2 Click the three dots in top-right corner

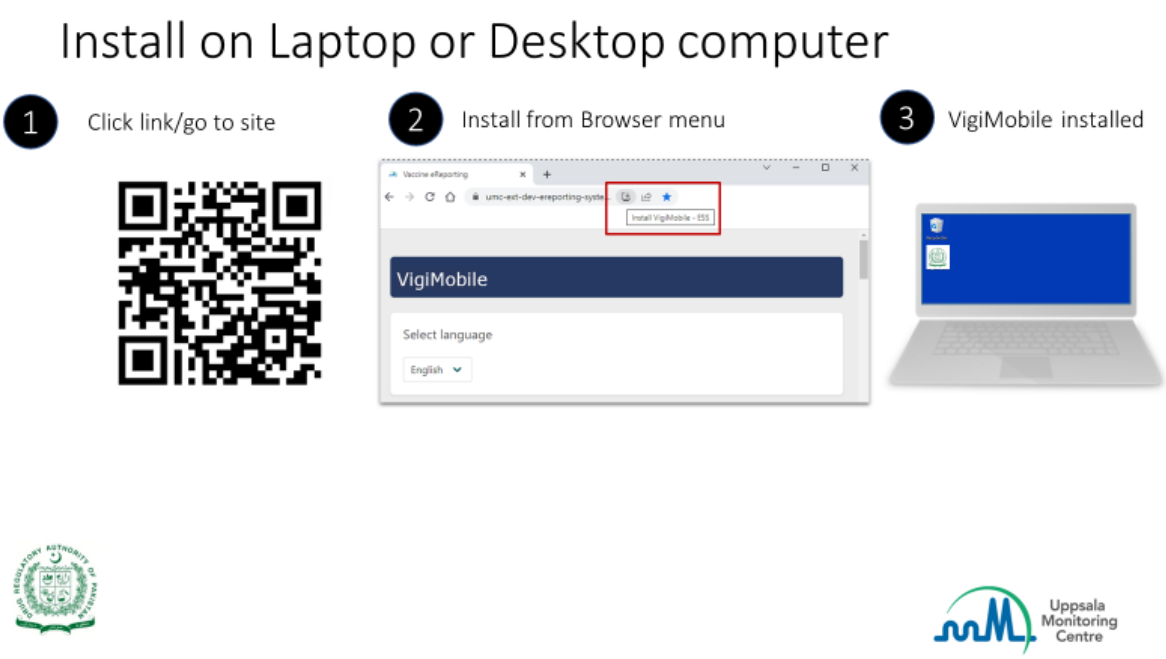
3 Chose *Install app*



4 VigiMobile now appears as an app

Uppsala Monitoring Centre





National Pharmacovigilance Centre
Pharmacy Services Division
DRUG REGULATORY AUTHORITY OF PAKISTAN
Prime Minister's National Health Complex, Park Road, Islamabad
Phone No. 051-9255981
Email: npc@dra.gov.pk
Website: www.dra.gov.pk