INTRODUCTION

The purpose of this Guide is to help health professionals to participate in the very important process of continuous surveillance of safety and efficacy of the pharmaceutical products which are used in their clinical practice. Continuous evaluation of their benefit and harm will help to achieve the ultimate goal to make safer and more effective treatment available to patients.

The objectives of the Guide are to raise awareness of the magnitude of the drug safety problem and to convince health professionals that reporting of adverse reactions is their moral and professional obligation.

The ultimate goal of the Guide is to reduce drug morbidity and drug mortality by early detection of drug safety problems in patients and improving selection and rational use of drugs by health professionals.

It is a model guide which can be translated into national languages and modified as the local situation may require.

WHO would be grateful to receive any comments on experience gained from the practical use of the Guide which would help in developing it further. Please contact the Department of Essential Drugs and Medicines Policy (EDM) with your comments:

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GLOSSARY

The terms are from “Safety Monitoring of Medicinal Products”:

1. An adverse drug reaction (ADR) is ‘a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man’.

2. An unexpected adverse reaction is ‘an adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorisation, or expected from characteristics of the drug’.

3. A drug or medicine is ‘a pharmaceutical product, used in or on the human body for the prevention, diagnosis or treatment of disease, or for the modification of physiological function’.

4. A side effect is ‘any unintended effect of a pharmaceutical product’.
occurring at doses normally used by a patient which is related to the pharmacological properties of the drug.'

L’exemple des bourdonnements d’oreilles lors de la prise de la Quinine et la sécheresse de la bouche lors de la prise de l’atropine.

Essential elements in this definition are the pharmacological nature of the effect, that the phenomenon is unintended, and that there is no deliberate overdose.

5. An **adverse event** or **experience** is defined as ‘any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment’. The basic point here is the coincidence in time without any suspicion of a causal relationship.

C’est le cas de l’épidémie de diarrhées rapportées chez les enfants de moins de cinq ans ayant reçu la vaccination antipoliomyélite à Kinshasa pendant la période de la saison sèche. Des rumeurs ont circulé que cette diarrhée était due au VOP, alors que les analyses bactériologiques et virologiques n’ont mis en évidence l’existence des rotavirus qui apparaissent fréquemment pendant la saison sèche.

6. A **serious adverse event** is any event that:
   - Is fatal
   - Is life-threatening
   - Is permanently/significantly disabling
   - Requires or prolongs hospitalization
   - Causes a congenital anomaly
   - Requires intervention to prevent permanent impairment or damage

Ceci peut se voir lors de la prise de certains médicaments comme le cotrimoxazole ou la sulfadoxine-pyrimethamine.

7. A **signal** refers to ‘reported information on a possible causal relationship between an adverse event 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 event and the quality of the information.

Nous pouvons relever la survenue des malformations congénitales chez les mères ayant pris des médicaments pendant le premier trimestre de la grossesse.

**The magnitude of the problem**

During the last decades it has been demonstrated by a number of studies that medicine morbidity and mortality is one of the major health problems which is beginning to be recognized by health professionals and the public. It has been estimated that such adverse drug reactions (ADRs) are the 4th to 6th largest cause for mortality in the USA. They result in the death of several thousands of patients each year, and many more suffer from ADRs. The percentage of hospital admissions due to adverse drug reactions in some countries is about or more than 10% in Norway 11.5% France 13.0%
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. Some countries spend up to 15-20% of their hospital budget dealing with drug complications. Il est difficile de déterminer le coût de la prise en charge liée à ces effets adverses chez nous car, peu d’informations sont disponibles.

Beside ADRs, medicine-related problems include also – drug abuse, misuse, poisoning, therapeutic failure and medication errors. Nous relevons parfois des problèmes liés aux erreurs d’étiquetage des produits faisant de sorte qu’un médicament donné est administré à la place d’un autre. C’est le cas du Chlorpropamide(antidiabétique) donné à la place du metronidazole(anti amibien) en 1986.

There is very limited information available on ADRs in developing countries and countries in transition. However, one may expect that the situation is worse rather than better. This problem is also caused by a lack, in some countries, of legislation and proper drug regulations, including ADR reporting, a large number of substandard and counterfeit products circulating in their markets, a lack of independent information and the irrational use of drugs.

**Why postmarketing surveillance and reporting ADR is needed**

The information collected during the pre-marketing phase of drug development is inevitably incomplete with regard to possible ADRs. 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 exposure of less than 5000 human subjects to a drug allows only the more common ADR to be detected;
- At least 30,000 people need to be treated with a drug to be sure that you do not miss at least one patient with an ADR which has an incidence of 1 in 10,000 exposed individuals;
- 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;

Thus, post-marketing surveillance is important to permit detection of less common, but sometimes very serious ADRs.

Or, en RDC, les études indépendantes qui devraient être menées pendant la période de l’autorisation provisoire d’une année sont insuffisantes. Par exemple, les études toxicologiques s’arrêtent à la détermination de la DL50.

Therefore health professionals worldwide should report on ADRs as it can save lives of their patients and others.

**Why pharmacovigilance is needed in every country**

There are differences among countries (and even regions within countries) in the occurrence of ADRs and other drug-related problems. This may be due to differences in e.g.:

- diseases and prescribing practices;
- genetics, diet, traditions of the people;
drug manufacturing processes used which influence pharmaceutical quality and composition;
- drug distribution and use including indications, dose and availability;
- the use of traditional and complementary drugs (e.g. herbal remedies) which may pose specific toxicological problems, when used alone or in combination with other drugs.

*Ceci est en accord avec la situation de notre pays.*

Data derived from within the country or region may have greater relevance and educational value and may encourage national regulatory decision-making. Information obtained in one country (e.g. the country of origin of the drug) may not be relevant to other parts of the world, where circumstances may differ.

Therefore, drug monitoring is of tremendous value as a tool for detecting ADRs and specifically in relation to counterfeit and substandard quality products. ADR monitoring is to help ensure that patients obtain safe and efficacious products. The results of ADR monitoring have also a very important educational value.

**How to recognize ADRs**

Since ADRs may act through the same physiological and pathological pathways as different diseases, they are difficult and sometimes impossible to distinguish. However, the following step-wise approach may be helpful in assessing possible drug-related ADRs:

1. **Identifier le medicament incriminé (son nom déposé)**
2. Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised;
3. Verify that the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation made by the patient;
4. Determine the time interval between the beginning of drug treatment and the onset of the event;
5. Evaluate the suspected ADR after discontinuing the drugs or reducing the dose and monitor the patient’s status. If appropriate, restart the drug treatment and monitor recurrence of any adverse events.
6. Analyse the alternative causes (other than the drug) that could on their own have caused the reaction;
7. Use relevant up-to-date literature and personal experience as a health professional on drugs and their ADRs and verify if there are previous conclusive reports on this reaction. The National Pharmacovigilance Centre and Drug Information Centres are very important resources for obtaining information on ADR. The manufacturer of the drug can also be a resource to consult;
8. Report any suspected ADR to the person nominated for ADR reporting in the hospital or directly to the National ADR Centre.

**Why should I report?**

I can reduce the suffering and save thousands of patients lives by doing
one thing: Report suspected adverse drug reactions.

**What should be reported?**

- For “new” drugs - report all suspected reactions, including minor ones. (In many countries drugs are still considered “new” up to five years after marketing authorization);
- For established or well-known drugs - report all serious or unexpected (unusual) suspected ADRs;
- Report if an increased frequency of a given reaction is observed;
- Report all suspected ADRs associated with drug-drug, drug-food or drug-food supplements (including herbal and complementary products) interactions;
- Report ADRs in special fields of interest such as drug abuse and drug use in pregnancy and during lactation;
- Report when suspected ADRs are associated with drug withdrawals;
- Report ADRs occurring from overdose or medication error;
- Report when there is a lack of efficacy or when suspected pharmaceutical defects are observed.

**Thus, report all suspected adverse reactions that you consider of clinical importance as soon as possible!**

**Who should report and to whom?**

Weekly, in the first level of our system, leaders of community should report to the Focal Point of the Health District. In the Health facilities, careworkers such nurses and others, doctors, dentists, pharmacists should report to the Focal point of the Health District.

The Focal Point must report to the Central level (Pharmacovigilance National Centre). This report must include the proactive research of informations.

**How to report ? And in what time frame?**

The first level in community will use the Primary Case Report Forms (PCRF) which should be obtained from the Focal Point of the Health district. They must do so each week and transmit their forms to the Focal Point. In the Health facilities, reporter must use a Serious ADRs form and transmit it weekly to the Health District (Focal Point). We will used the model of the IDS which is functional in most parts of the country.

**How to complete the form ?**

We will use two forms, one for the community level and another for the health facilities.
The first form (PCRF) should have four sections:

1. Patient information:
   — patient (N°)
   — age at time of event or date of birth
   — gender
   — weight

2. Adverse event or product problem:
   — description of event or problem
   — date of event

3. Suspected medication(s):
   — name (INN and brand name)
   — color, taste, size, frequency & route used
   — therapy date

4. Reporter:
   — name, address and telephone number
   — speciality and occupation

The second form should report the serious ADRs and be completed by careworkers. It will contain seven sections:

1. Patient information:
   — N° of patient
   — age at time of event or date of birth
   — gender
   — weight

2. Reason of treatment

3. Suspected medication(s):
   — name (INN and brand name)
   — dose, frequency & route used
   — date started
   — date stopped
   — batch number
   — expiration date

4. Concomitant drugs (including self medication)
   — name (brand name)
   — daily dose
   — route
   — treatment dates
   — reasons (indications)

5. Adverse event or product problem:
   — description of event or problem
   — date of event
   — duration
6. Outcome
--- recovery from adverse reactions
--- treatment required
--- rechallenged or dechallenged
--- causality
--- if pregnant woman, gestational age and drug exposure

7. Reporter:
--- name, address and telephone number
--- speciality and occupation

The completed Case Report Form should be sent to the Focal point who will transmit it to National Pharmacovigilance Centre(NPVC).

When should it be investigated? By whom and how?

The ADR should be investigated when the National Pharmacovigilance Centre assessment presumed on the causality of the ADR. This investigation will be conducted by the Focal Point at the district level (community and health facilities). It should consist in a clinical observation of the ADR and the SADR form will be replaced by the medical and laboratory forms.

How do I manage an ADR?

*The community worker will be responsible to detect and report the ADR in their community. All ADR judged serious must be referred to the Health facilities where patients can find technical capacities for the follow up. Thus, two forms are expected, one for the community worker and another for the care workers.*

How do I prevent ADRs from occurring?

*This goal can be achieved if communication for change behavior is strengthened and the central level transferred their technicity to the lowest level. All these will improve the understand and the good use of the medecins in the community. Their involvement in the report process will be an indicator of their perception.*

*Practitioners must share informations with their colleagues and try to involve much more care workers.*

What happens to my ADR and investigation?

*These documents must be analysed and assessed by the National Pharmacovigilance Centre. The panel of the experts can be consulted for their advise before reaching the Regulatory authorities.*

Any negative consequences for me?

*No one, because the confidentiality will preserved and feed-back to improve our behavior and practices will provided.*

What are the benefits of reporting?

*First, the magnitude of the problem in our communities will be known. Second, patients can be treated and their follow-up conducted. Third, the prescriptors will improve their knowledge and provide efficient treatment to their patients. Fourth, the occurrence of all these reactions will prevent.*
# PRIMARY CASE REPORT FORM IN COMMUNITY

## Patient Particulars
Name:  
Ref No.:  
Address  
Age:  
Sex:  
Weight (kg):  
Height (m):  

<table>
<thead>
<tr>
<th>Date of Report:</th>
<th>Date of Reaction</th>
</tr>
</thead>
</table>

## Reaction Details:
Description  

### Suspected Drugs

<table>
<thead>
<tr>
<th>Name (Brand)</th>
<th>Color</th>
<th>Taste</th>
<th>Size</th>
<th>Date Started</th>
<th>Date stopped</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
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</tr>
</tbody>
</table>
| Other drugs used  
|              |       |       |      |              |              |           |

## Remarks  

### Reporter Details:
Name  
Title:  
Date:  
Address:  

**SERIOUS ADVERSE EVENTS REPORT FORM**

**PATIENT INFORMATION**

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Date of Birth</th>
</tr>
</thead>
<tbody>
<tr>
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</table>

**Sex**

- [ ] M
- [ ] F

<table>
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<tr>
<th>Patient's Address</th>
</tr>
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<tbody>
<tr>
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</table>

**Patient Record Number:** ______________

(If female) Is the patient Pregnant?

- [ ] Yes: If Yes; Date of Last Menstrual Period …/…/…
- [ ] No
- [ ] Not sure

<table>
<thead>
<tr>
<th>Weight</th>
<th>Height</th>
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</table>

**NATURE OF ADVERSE EVENT: (CROSS THOSE THAT APPLY)**

- [ ] Death
- [ ] Life threatening
- [ ] Hospitalisation
- [ ] Permanent Disability
- [ ] Congenital Anomaly
- [ ] Other: (specify)

**DATE OF OCCURRENCE** … /…../....

**DESCRIBE THE ADVERSE EVENT IN DETAIL (INCLUDE ALL RELEVANT LABORATORY RESULTS)**

**DESCRIBE HOW THE REACTION WAS TREATED:**

- [ ] Recovered completely
- [ ] Not yet recovered
- [ ] Recovered with long term consequences

<table>
<thead>
<tr>
<th>Outcome of reaction</th>
<th>Date of Recovery</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
</tbody>
</table>

**MEDICINES** (List the medicine suspected of causing the reaction as well as all concomitant medicines)

<table>
<thead>
<tr>
<th>Brand Name &amp; Batch No</th>
<th>Daily Dosage</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Reasons for use</th>
</tr>
</thead>
<tbody>
<tr>
<td>(List the suspected drug first)</td>
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COMMENTS: (e.g. Include Relevant medical history, Drug allergies, Previous exposure to similar drugs, other lab data)

REPORTING DOCTOR/PHARMACIST Etc:

NAME: ............................................................................................

QUALIFICATIONS: ..........................................................................

ADDRESS: ...................................................................................

...................................................................................................

SIGNATURE: .............................................................................

TEL: (.........)................................................................. Date
Drug Regulatory Authorities and other useful information can be found on the Website of the WHO Collaborating Centre for International Drug Monitoring (www.who-umc.org) or requested from this Centre by e-mail: info@who-umc.org; by Fax: +46 18 65 60 80 or by Tel.: +46 18 65 60 60).

References

Useful Websites
WHO
www.who.int/medicines/
Section: Quality Assurance and Safety: Medicines
WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre) www.who-umc.org
Acknowledgements

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