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Safety of Medicines

A guide to detecting and reporting adverse drug reactions

Why health professionals need to take action

World Health Organization
Geneva 2002

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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]

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'.

   In this description it is of importance that it concerns the response of a patient, in which individual factors may play an important role, and that the phenomenon is noxious (an unexpected therapeutic response, for example, may be a side effect but not an adverse reaction).

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'.

   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.

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
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.

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,[2]. 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% [3], [4], [5].

Norway	11.5%
France	13.0%
UK	16.0%

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[6].

Beside ADRs, medicine-related problems include also – drug abuse, misuse, poisoning, therapeutic failure and medication errors.

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[7];
- 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.

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