

Pharmacovigilance—Approach to Challenges with Use of Medicines



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Systems for Improved Access
to Pharmaceuticals and Services



**World Health
Organization**
REGIONAL OFFICE FOR **Europe**

Stop TB Partnership



Background—Development of Pharmacovigilance (1)

Growing market of pharmaceutical products

- 2011 global market of pharmaceutical products
- 2012—over 350,000

Growth in sales volume

2011—540 billion US dollars

http://www.export.by/?act=s_docs&mode=view&id=28417&doc=64

Number of diseases

Over 12,000 (WHO data)



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Background—Development of Pharmacovigilance (2)

When a pharmaceutical product first appears on the market, it is rarely used by more than 5,000 people, which is less than 0.1 % of the global population.

Pharmacovigilance: ensuring the safe use of medicines. WHO, 2004.



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Background—Development of Pharmacovigilance (3)

Pharmaceutical products approved for the use in extensive medical practice are properly studied which ensures their efficiency and safety.

Is it really true?



Need for Pharmacovigilance in Use of Medicines (1)

At the stage of development, rare and delayed side effects remain unnoticed.

Side effects (SE):

- Cause additional expenses for medical care
- Prevent compliance with the standards of care
- Decrease patients' adherence to treatment
- Lead to an increase in morbidity and mortality
- Promote the need for alternative ways which are often more costly

Lebega O., J. Nwokike, and H. Walkowiak. 2012. *Safety of Medicinal Products in Ukraine: Assessment of the Pharmacovigilance System and its Performance*. Submitted to the U.S. Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program. Arlington, VA: Management Sciences for Health



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Need for Pharmacovigilance in Use of Medicines (2)

- Over 50% of all drugs are not being prescribed or administered as intended
- 50% of patients make mistakes in taking prescribed medicines
- Over 10% of medicine side effects lead to hospitalization
- Drug side effects are ranked fourth to sixth in the world among the causes of death.
- Over 50% of side effects are preventable.

In 1968, the WHO Program for International Drug Monitoring was launched.

Pharmacovigilance: ensuring the safe use of medicines. WHO, 2004.

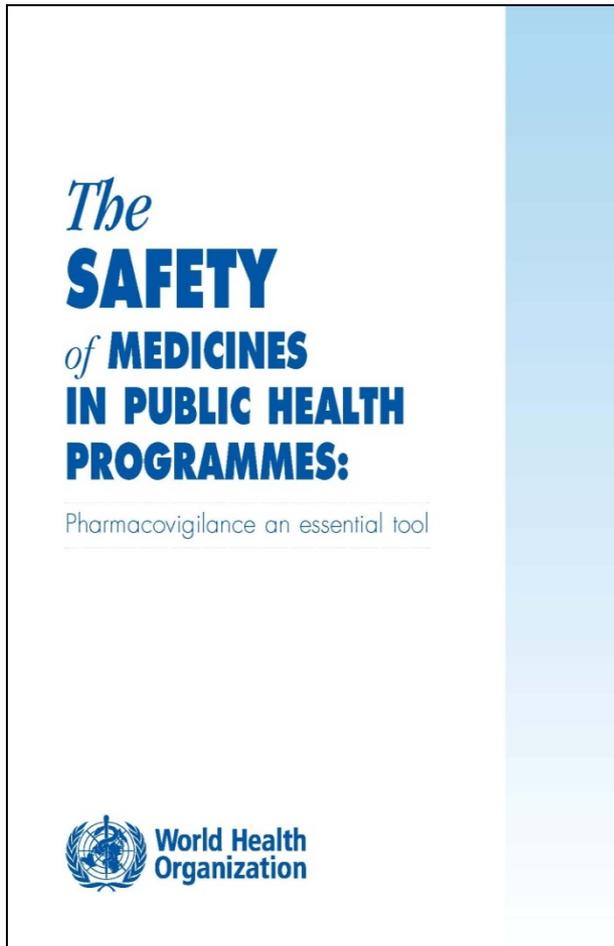
WHO Policy Perspectives on Medicines—Promoting Rational Use of Medicines: Core Components. <http://apps.who.int/medicinedocs/pdf/h3011e/h3011e.pdf>.



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What is Pharmacovigilance?



Pharmacovigilance or drug monitoring—is a set of scientific knowledge and activities related to identification, evaluation, analysis and prevention of drug side effects and any other adverse consequences of drug use in humans.



Functions of Pharmacovigilance

- To ensure rational and safe use of drugs
- To detection and examine side effects
- To assess the risk of drug use
- To assess drug efficiency
- To estimate ratio of benefit to harm
- To disseminate information on adverse drug events



Methods of Pharmacovigilance

- Passive pharmacovigilance/spontaneous reporting method
- Enhanced pharmacovigilance/targeted spontaneous reporting method
- Active pharmacovigilance/active monitoring of inpatient clinics



Passive Pharmacovigilance— Advantages

- Can be countrywide, able to generate signals
- Spontaneous reporting—the main source of information for the system of pharmacovigilance



Passive Pharmacovigilance— Disadvantages

- Problems related to the quality of information
- Insufficient motivation of physicians, lack of time, fear of punishment
- A lot of information remains unreported (about less than 5% of side effects are reported)
- Lack of information about the number of patients treated with the drug

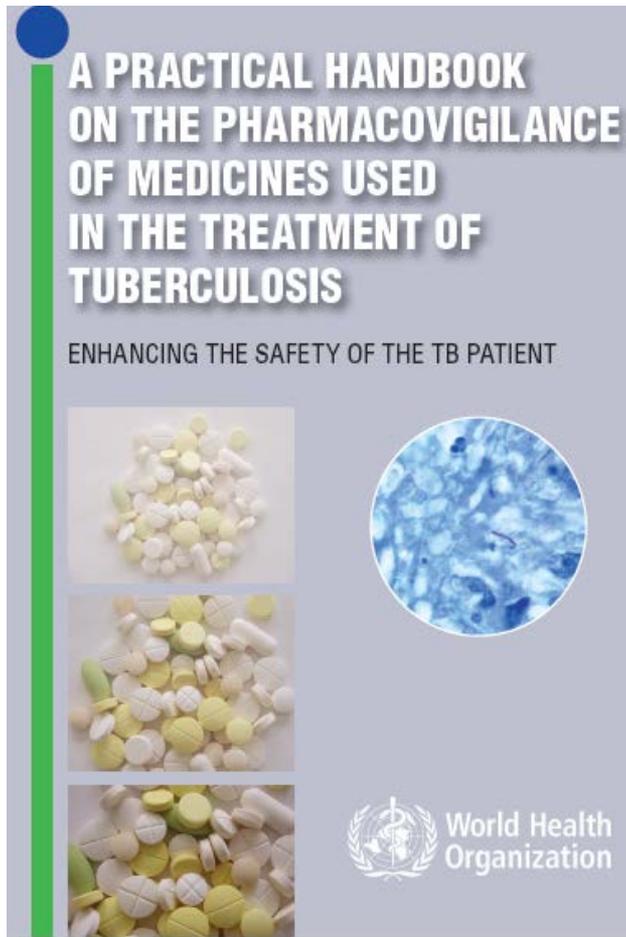


Methods of Pharmacovigilance— Active Pharmacovigilance

- Formal and ongoing monitoring aimed at evaluation and confirmation of signals or suggestions regarding the relationship between a drug and an adverse event(s).
- Examples:
 - Cohort studies
 - Retrospective studies
 - Prospective studies
 - Registers of patients on the same treatment

Pharmacovigilance in TB Control Programs

- Side effects of TB drugs are frequent and well known to TB specialists
- TB patients undergo long-term treatment
- Use of complex treatment regimens—drug interactions
- Increased probability of side effects occurring—the majority of DR-TB patients had one side effect and there is likelihood of major side effects
- High risk of DR-TB development (two-thirds of DR-TB patients being treated with at least one drug interrupted or completely stopped treatment because of side effects)



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WHO Recommends—

Make pharmacovigilance an integral part of all public health programs

The Global Fund recommends to countries applying for grants needed to support TB therapy to include pharmacovigilance as the main component in their TB prevention and treatment programs.

(WHO Policy Perspectives on Medicines—Promoting Rational Use of Medicines: Core Components. <http://apps.who.int/medicinedocs/pdf/h3011e/h3011e.pdf>);

World Health Organization “A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis” 2012;

World Health Organization and GFATM Meeting to Determine Minimum Requirements for Pharmacovigilance, Geneva, Switzerland, 14–15 January 2010 (www.who.int/medicines/areas/quality_safety/safety_efficacy/).



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Why is Pharmacovigilance Needed for TB Control Programs? (1)

It is difficult to measure a program's total benefit if problems related to medications are not considered, so the following are needed—

- Good program management for the implementation of treatment monitoring
- Well established practice of patient follow-up using the indicators

There is no tradition of monitoring the adverse reactions



Why is Pharmacovigilance Needed for TB Control Programs? (2)

- Problems related to the use of TB drugs are poorly reported and documented
- Health care workers need expert knowledge of adverse reactions to TB drugs, but there is a the lack of official information about the problems related to TB drugs:
 - Incidence
 - Mortality
 - Deterioration in quality of life



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Why is Pharmacovigilance Needed for TB Control Programs? (3)

Further enhancement of pharmacovigilance is governed by the credible factors—

- Use of more complex treatment regimens for DR-TB
- Use of antiretrovirals in patients with HIV-associated TB
- Inevitable emergence of new classes of TB drugs



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Bedaquiline—Pharmacovigilance, Good Management of Side Effects, and Prevention of Unwanted Drug Interactions

The use of bedaquiline in the treatment of multidrug-resistant tuberculosis

Interim policy guidance



- Bedaquiline—December 2012, based on IIB data, the drug was registered by US Food and Drug Administration
- Similar registration is being performed in the regulatory agencies all over the world
- Phase III of clinical trial is in progress
- There is no sufficient information on drug safety
- The policy guidance will be revised when the additional information on drug safety becomes available





Bedaquiline—Pharmacovigilance, Good Management of Side Effects, and Prevention of Unwanted Drug Interactions

Recommendations:

- Use of active methods of pharmacovigilance, “cohort monitoring of events,” to ensure early detection of side effects and timely reporting.
- Use of spontaneous information method—any adverse reactions to bedaquiline should be reported to the national pharmacological center
- Active participation of patients in monitoring all adverse events related to the drug use
- WHO strongly recommends speeding up phase III of the clinical trials to obtain more evidence for developing future recommendations on the use of bedaquiline



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