The IMPORTANCE *of* PHARMACOVIGILANCE

Safety Monitoring of medicinal products

World Health
Organization
2002

WHO Library Cataloguing-in-Publication Data

The Importance of Pharmacovigilance.

(Safety monitoring of medicinal products)

1. Drug monitoring
2. Pharmaceutical preparations - adverse effects
3. Adverse drug reaction reporting
4. Product surveillance, Postmarketing
5. Legislation, Drug I.Series

ISBN 92 4 159015 7 (NLM classification: QV 38)

Typeset and printed in the United Kingdom.

The IMPORTANCE *of* PHARMACOVIGILANCE

Safety Monitoring of medicinal products

World Health Organization
2002

the UPPSALA MONITORING CENTRE

WHO Collaborating Centre for
International Drug Monitoring

TABLE OF CONTENTS

PREFACE

The Quality Assurance and Safety: Medicines team in WHO aims to assure the safety of medicines by ensuring reliable and timely exchange of information on drug safety issues, promoting pharmacovigilance activities throughout the Organization and encouraging participation in the WHO Programme for International Drug Monitoring. This team is developing a series of publications on Safety Monitoring of Medicinal Products. This text was developed in consultation with the WHO Collaborating Centre for International Drug Monitoring and the national pharmacovigilance centres participating in the WHO Programme for International Drug Monitoring. The draft was widely circulated and discussed at two informal consultations with international experts in pharmacovigilance. The WHO Department of Essential Drugs and Medicines in Geneva held these consultations. Contributions were made by:

Ms N Arthur, Irish Medicines Board, Dublin, Ireland
Dr A Bentsi-Enchill, Vaccine Assessment and Monitoring, WHO, Geneva
Dr M R Couper, Quality Assurance and Safety: Medicines, WHO, Geneva
Dr P Duclos, Vaccine Assessment and Monitoring, WHO, Geneva
Dr I R Edwards, WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden
Mr T Fushimi, Ministry of Health, Labour and Welfare, Tokyo, Japan
Dr K Hartigan-Go, Makati City, Philippines
Dr P Folb, University of Cape Town, Cape Town, South Africa
Dr N A Kshirsagar, GS Medical College and KEM Hospital, Mumbai, India
Dr J K Lazdins-Helds, Product Research and Development, WHO, Geneva
Dr V Lepahkin, Quality Assurance and Safety: Medicines, WHO, Geneva
Dr Y Maruyama, Traditional Medicine, WHO, Geneva
Dr S Pal, Quality Assurance and Safety: Medicines, WHO, Geneva
Mr S Olsson, WHO Collaborating Centre for International Drug Monitoring, Uppsala, Sweden
Dr P Olumese, Roll Back Malaria, WHO, Geneva
Dr L Rägo, Quality Assurance and Safety: Medicines, WHO, Geneva
Mr B Rowsell, Ontario, Canada
Dr J S Schou, Charlottenlund, Denmark
Dr R Soulaymani-Bencheikh, Institut Nationale d'Hygiène, Rabat, Morocco
Dr K Tamiya, Quality Assurance and Safety: Medicines, WHO, Geneva

Special thanks go to Dr U Mehta, University of Cape Town, Cape Town, South Africa, who drafted the text and acted as rapporteur at the consultations. Thanks also to Mr B Hugman for his invaluable help in editing the document.

CHAPTER 1

INTRODUCTION

The purpose of this document is:

- to present the case for the importance of pharmacovigilance,
- to record its growth and potential as a significant discipline within medical science, and
- to describe its impact on patient welfare and public health.

It highlights the need for critical examination of the strengths and weaknesses of present pharmacovigilance systems in order to increase their impact. It anticipates developments necessary to meet the challenges of the next ten years. It argues that the distinctive approaches adopted by different countries in response to their individual needs should be supported and fostered. The document also highlights the importance of collaboration and communication at local, regional and international levels, to ensure pharmacovigilance delivers its full benefits.

Pharmacovigilance and all drug safety issues are relevant for everyone whose life is touched in any way by medical interventions. The document is intended for the following, wide-ranging readership:

- Policy makers at all levels of healthcare, particularly those concerned with drug policy
- Staff and consultants in national drug regulatory authorities
- Healthcare practitioners including doctors, nurses and pharmacists
- Pharmaceutical industry executives and scientists
- Professional staff in national pharmacovigilance centres
- Editors of medical and scientific journals
- Health epidemiologists
- Health economists
- Professional staff of poison and drug information centres
- Health administrators
- Consumer groups and patient support groups
- Legal advisors in health care
- Schools of health sciences, and
- The concerned layperson.

COMMON ABBREVIATIONS USED IN THIS DOCUMENT:

ADR	Adverse Drug Reaction
ICH	International Conference on Harmonization
UMC	*the* Uppsala Monitoring Centre (The WHO Collaborating Centre for International Drug Monitoring)
WHO	The World Health Organization

Other abbreviations and specialized terms appear in the Glossary.

CHAPTER 2

A SHORT HISTORY OF INVOLVEMENT IN DRUG SAFETY MONITORING BY WHO

This chapter introduces the events and ideas that have underpinned the foundation and early development of pharmacovigilance over the last thirty years under the aegis of the World Health Organization. In 2002, more than 65 countries have their own pharmacovigilance centres. Membership of the WHO Programme for International Drug Monitoring is co-ordinated by the WHO Collaborating Centre for International Drug Monitoring, known as *the* Uppsala Monitoring Centre (UMC).

The evolution of pharmacovigilance in recent years and its growing importance as a science critical to effective clinical practice and public health science are described. The national pharmacovigilance centres have become a significant influence on the drug regulatory authorities, at a time when drug safety concerns have become increasingly important in public health and clinical practice. Pharmacovigilance is now firmly based on sound scientific principles and is integral to effective clinical practice. The discipline needs to develop further to meet public expectations and the demands of modern public health.

Background

According to Article 2 of its constitution, the World Health Organization has a mandate from its Member States

> *to develop, establish, and promote international standards with respect to food, biological, pharmaceutical and similar products*

There is also provision made in Article 21 of the constitution of the World Health Assembly to adopt regulations concerning

> *standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce.*

It was not until the disaster caused by thalidomide in 1961 that the first systematic international efforts were initiated to address drug safety issues. At that time many thousands of congenitally deformed infants were born as the result of exposure in utero to an unsafe medicine promoted for use by pregnant mothers. The Sixteenth World Health Assembly (1963) adopted a resolution (WHA 16.36) [(1)] that reaffirmed the need for early action in regard to rapid dissemination of information on adverse drug reactions and led, later, to creation of the WHO Pilot Research Project for International Drug Monitoring in 1968. The purpose of this was to develop a system, applicable internationally, for detecting previously unknown or poorly understood adverse effects of medicines. A WHO technical report followed based on a consultation meeting held in 1971.[(2)]

From these beginnings emerged the practice and science of pharmacovigilance. Systems were developed in Member States for the collection of individual case histories of ADRs and evaluation of them. The collection of international ADR reports in a central database, would serve the important function of contributing to the work of national drug regulatory authorities, improve the safety profile of medicines, and help avoid further disasters.[(3)]

From pilot to permanence

The principal achievement of the 1971 WHO consultation meeting was:

- to advocate establishment of national centres for drug monitoring,
- to provide guidelines
- to identify the contribution that national centres might make to the international system.

In so doing, it was envisaged that the time necessary to recognize that a drug produces an adverse reaction might be reduced, and the importance of the reaction more readily assessed. It was noted that

- data collection from health practitioners,
- systematic monitoring of populations,
- review of health statistics and of drug utilization data, and
- effective analysis of input data

would be necessary for the objectives of pharmacovigilance to be achieved. Special attention would need to be paid to new drugs. Specialized reference centres would be required to provide additional data to National Centres and for investigation of particular drug safety problems.

Since the start of the International Programme in 1968 much has been accomplished:

- The pilot project has developed into the WHO Programme for International Drug Monitoring now co-ordinated by *the* Uppsala Monitoring Centre (UMC) in Uppsala, Sweden, with oversight by an international board
- The Programme has expanded to include more than sixty member countries
- In many countries, regional reporting centres, interest groups, dedicated internal medicine and pharmacology department units, drug and poison information centres and other non-governmental organizations have developed
- The idea that pharmacovigilance centres are a luxury, affordable only in the developed world, has been replaced by a realization that a reliable system of pharmacovigilance is necessary for public health and for the rational, safe and cost-effective use of medicines in all countries. Where no established regulatory infrastructure exists, a drug monitoring system is an effective and cost-efficient means of detecting and minimizing injury to patients and averting potential disaster.

Professional interest

The creation of the International Society of Pharmacoepidemiology (ISPE) in 1984 and of