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Profile

The Uppsala Monitoring Centre

Key points

The Uppsala Monitoring Centre is the field-name of the WHO Collaborating Centre for International Drug Monitoring.

The UMC is the principal, independent scientific group in the world concerned with the safer, more rational use of medicines and with broader issues of safety in healthcare.

The UMC's authority is based on more than thirty years of scientific research and achievement in collaboration with member countries of the WHO Programme for International Drug Monitoring.

The core activity of the UMC, worldwide pharmacovigilance, is the collecting, researching, assessing and evaluating of information on the adverse effects of medicines, biological products, herbals and traditional medicines with a view to identifying new information about hazards, and preventing harm to patients.

The growing WHO database of more than 3 million worldwide reports of adverse drug reactions (ADRs) is the basis for the UMC's scientific work and publications and the source of its several standard dictionaries, reference works, occasional papers and service to member countries.

A secondary high level priority is the promotion of effective education, training and communication about benefit, harm, effectiveness and risk in medicine in patient care and public health for all audiences.

Introduction

The work of international drug monitoring began in 1968 following the thalidomide disaster, and gave rise to the establishment of the the UMC, based in Uppsala, Sweden, in 1978.

The business of the UMC is to:

- co-ordinate the technical and scientific aspects of the WHO Programme for International Drug Monitoring and its member countries;
- collect, assess and communicate information from member countries about the benefit, harm, effectiveness and risk of medicinal drugs;
- alert the regulatory authorities of member countries to potential drug safety problems collaborate with member countries in the development and practice of pharmacovigilance.

Our vision is to support WHO's leadership in the field of world health by providing excellence

- in the science and concepts of all aspects of pharmacovigilance;
- to prevent harm to humans from the effects of medicines;
- to gather and share objective intelligence and opinion in the field of drug safety through open communication;

– to support the promotion of the rational use of drugs, and the achievement of improved patient therapy and public health;
– in global education and communications in benefit, harm, effectiveness and risk in medical therapy.

We will achieve this by:

– developing leading-edge systems and science for the identification and communication of safety hazards in medicines;
– carrying out research pushing forward the ethical, intellectual and scientific boundaries of theory and practice in pharmacovigilance;
– pursuing active collaboration and communication with all stakeholders;
– pursuing the goal of a single, global database for drug safety data.

The UMC has achieved a great deal in its more than twenty years in collaboration with the growing number of member countries in the Programme (currently 68, representing over one third of countries in the world), and with academic, scientific and medical experts and organisations throughout the world.

There is no other official body in the world which has a truly independent and global perspective on drug safety other than the WHO and its collaborating centre, the UMC. International harmonisation and standardisation are difficult to achieve without consensus. It is the WHO's general mandate to do this work, and the record of achievement in the field as a whole is substantial, authoritative and widely-recognised.

1. Activities, products and services

The WHO programme for international drug monitoring

There are now 68 members of the WHO Programme, and four associate members, with a number of new countries waiting to join. It is the UMC's responsibility to support them in their drug safety activities by providing the services described below, and to respond to their needs as new demands arise.

In collaboration with WHO HQ in Geneva, the UMC organises the annual meeting of member countries. This is an important forum for the debate of current issues of interest, presentation of the UMC's work and plans, and public exercise of its accountability to the membership.

The second edition of *National Pharmacovigilance Systems* provides extensive details of the operation of the pharmacovigilance systems of nearly sixty member countries and is a unique work of reference. A third edition is in preparation and will be available in electronic format, regularly updated.

The WHO ADR database

Maintenance of this unique resource involves the processing of over 200,000 reports submitted by member countries annually, including quality control and coding of information on drugs and reactions. There are currently 2,900,000 reports from 66 countries, collected since 1968.

The current version of the database is ICH (International Conference on Harmonization) E2B compatible and uses a drug file based on the CEN (European Committee for Standardisation) pre-standard.

Signal detection

A signal is an early concern or hypothesis about a possible drug safety problem. Detecting signals is one of the primary objectives of member countries of the WHO Programme. Providing them with reliable international scientific information to support their work is the core function of the UMC. Urgent concerns are published in a quarterly document called *Signal*, while other matters of scientific and broader interest appear in frequent papers in professional journals and presentations to scientific conferences.

A UMC review panel of around forty domain experts monitors and evaluates signals and signalling processes and assists in detecting and evaluating new drug safety concerns.

BCPNN

The Bayesian Confidence Propagation Neural Network (BCPNN) is the latest and most advanced of the tools developed by the UMC for automated signal detection in the WHO database. The technique uses a neural network architecture to search for dependencies in the data set. Such dependencies are quantified and have probability intervals attributed using the principles of Bayesian logic. The selected, non-biased, quantitative associations identified are then assessed clinically so that further action can be taken when appropriate.

Retrospective test-runs of the system have indicated that it is capable of generating signals some 2–4 years earlier than they were actually identified[1]

The WHO Drug Dictionary

The WHO Drug Dictionary is a unique and comprehensive record of all drugs and medicinal substances appearing in all international ADR reports submitted to the WHO Programme since 1968, along with others added on request: a total of 52,000 entries [March 2002]. It is the standard reference source for most regulatory authorities and pharmaceutical companies in the world.

It is an international classification of drugs providing proprietary names of medicinal products used in different countries, together with all active ingredients. The database also contains cross-references to pharmaceutical companies and reference sources. The database grows at a rate of about 2,000 entries annually.

WHO-ART

The WHO Adverse Reaction Terminology is a terminology for coding clinical information in relation to drug therapy, used worldwide by member countries and many others. It has been developed over more than thirty years to serve as the basis for international coding of adverse reaction terms.

The basic logic is a hierarchical structure starting with body system/organ level, within which there are grouping terms (general or high level), which are useful for the broader view of drug problems. Within these categories the specific *preferred terms* provide for precise identification. *Included terms* assist by pointing to the closest *preferred term* in the case of colloquial terms appearing in reports. Links with ICD versions 9 and 10 are already in place and will be enhanced.

Data searches

The database is consulted by national authorities and others in many different situations. It provides an invaluable source of information for assessment and decision-making, e.g., in circumstances such as the reporting of a single ADR or a cluster in one country or when a country is considering licensing a new drug. There is a direct-access, on-line facility; special searches may be carried out by UMC staff on request; and the ADRespherics service provides several levels of analysis of the database using the BCPNN (see above).

Vigimed

The UMC manages this email conferencing system which allows all member countries to discuss matters of interest and share concerns about emerging safety issues.

[1]European Journal of Clinical Pharmacology, 1998 #54: Bayesian Neural Network Method for Adverse Drug Reaction Signal Generation; pp. 315–321.

Traditional medicines

The emergence of ADRs associated with herbal remedies reflects the vast usage of them throughout the world. The UMC is active in extending all its activities to include traditional medicines. A single, worldwide herbals classification has been published, including a nomenclature for internationally recognised botanical names; the classification of all herbal product/ADR information in the WHO database has been revised; assignments of herbal ATC (Anatomical-Therapeutic-Chemical classification) categories is ongoing.

Education and training

Staff of the UMC are involved in frequent training activities in the theory and practice of pharmacovigilance for international participants. These courses are held in both Sweden and the regions of the world.

The UMC has been an active contributor to all the CIOMS initiatives in drug safety (except the first) and initiated and chaired the work on CIOMS 1A which was later the basis for the ICH E2B guideline on data transmission and storage.

Communications

The Uppsala Monitoring Centre has insisted for some years now that among the crucial issues to be addressed is the achievement of open and effective communication about benefit, harm, effectiveness and risk and about drug safety issues in general.

Technical and scientific issues clearly remain of fundamental importance, but unless healthcare professionals, patients, the public at large and journalists really understand the issues, and are much more critical and discriminating in their treatment of medical information, there will continue to be misunderstanding, mistrust, and crises which may damage patients and public health.

The *Erice Declaration* was an important statement of principle on these issues resulting from an international conference sponsored by the UMC and the Ettore Majorana Centre in Sicily in 1997. This and other UMC initiatives have placed effective communication firmly on the world agenda and pharmacovigilance is now rarely discussed without its inclusion.

The latest contribution is a major publication: *Dialogue in Pharmacovigilance: more effective communication*, authored by a group of international experts following the Erice initiative.

Spreading the word about drug safety

The publication of *Viewpoint* (Part 1) in 2002 represented a major commitment to accessible information about safety in medicine for a very wide audience. The 24-page booklet is packed with articles and information about drug safety in general; the concept of risk; the causes and costs of ADRs; regulation; the pharmaceutical industry; herbal medicines and much more. It is written in non-technical, everyday language and versions are also available in French and Spanish.

Conclusion

The UMC is unique in the breadth and depth of its authority in the field of safety in healthcare. In maintaining and developing the WHO ADR database it has not only a global perspective of safety issues, but also exceptional experience in the management and interpretation of very large data sets.

The staff of thirty or so professionals, along with their international experts and consultants, constitute a unique scientific resource.

As the concerns of the UMC have widened, particularly into the realm of the use and communication of safety information, the group has made a substantial contribution to theoretical and practical developments around the world.

Much has been achieved, but, undoubtedly, much remains to be done as the pace of activity in medical science accelerates and the pressure for quick returns affects every branch of science.

The Uppsala Monitoring Centre Overview

Activities, Products and Services
The WHO Programme for International Drug Monitoring,
The WHO ADR Database,
Signal Detection,
Bayesian Confidence Propagation Neural Network,
The WHO Drug Dictionary,
WHO Adverse Reaction Terminology (WHO-ART),
Data Searches,
Vigimed email,
Traditional Medicines,
Education and Training,
Communications,
Spreading the Word about Drug Safety.

Publications
The WHO Drug Dictionary,
WHO-ART,
Signal,
National Pharmacovigilance Systems,
Uppsala Reports,
The Erice Report,
Dialogue in Pharmacovigilance,
Guidelines for Herbal ATC classification,
The WHO Pharmaceuticals Newsletter (with WHO Geneva).

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