

Issue 9
April 1999

Published by *the*
Uppsala Monitoring
Centre 1999

Uppsala REPORTS

For everyone concerned with the issues of pharmacovigilance and toxicovigilance



- A special interview with Martijn ten Ham
- UMC involvements in Anti-Malaria Donation Programme
- Results from the questionnaire on Signals
- New e-mail addresses for *the* UMC team!



An anniversary celebration - then what?

Together with IIR Conferences, the Uppsala Monitoring Centre organized an anniversary symposium in Stockholm on: *The Current State of Pharmacovigilance - A Critical Examination*, 9-10 December 1998, followed by an IIR conference on *The Regulatory Perspective*, 11 December. The Symposium was attended by 250 people from all over the world.

(Deliberations of working group discussions held at the WHO Anniversary Symposium are also summarized on our Internet website: <http://www.who-umc.org> the UMC has also set up an e-mail discussion group to stimulate further exchange of ideas on how to improve our approaches to pharmacovigilance. If you wish to join this group, please contact Sten Olsson: sten.olsson@who-umc.org)

Ralph Edwards, the UMC Director, made the following closing statement:

“ It is ten years since I summarised the last anniversary symposium held in Sweden. On that occasion I concentrated on two main topics: risk-benefit approaches to our work and the need for more openness and better communication. These areas have been referred to several times during the current symposium, and there has clearly been progress. What I failed to predict ten years ago were the great developments in, and the enormous impact of, information technology on drug safety regulation.

EXCITING TIMES

From the presentations and discussion at this meeting, we seem to be on the brink of harvesting the results of the ICH efforts and the EU's Pharmacovigilance strategy. The pharmaceutical industry and its regulators have developed more harmonised approaches and there is much more dialogue between these players than before. Better ways of managing and searching data have already brought clarity to our work.

THE WAY FORWARD?

There are several lessons to be learned from points raised during this meeting. We need to:

- use the tools that we have in a more coordinated fashion. There is no single answer to pharmacovigilance
- stop talking about the draw-backs of spontaneous reporting, case control studies etc
- understand the characteristics of each tool and use them appropriately - 'a screwdriver for a screw and a hammer for a nail' - then we can see the gaps in our toolkit and fill them.

Furthermore, the integration of pharmacovigilance information with pheno-, genotype databases and other resources such as pregnancy

registers could and should enhance drug safety.

EVALUATING OUR WORK

It follows from the above that we must constantly re-assess the results of our endeavours. We learned, for example, that a questionnaire sent to 16 countries showed that they got no added value out of external industry case reports. How can we improve that situation? We also heard that there was general duplication of effort and duplication of case reports, so we obviously need to rationalise our work as much as possible.

Communication has been a large topic of the meeting. Suffice it to say that good communication between all players involved in drug safety is essential. This includes ensuring that communications are received, understood, acted upon and followed-up.

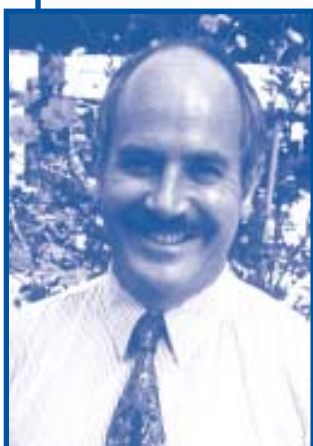
There are new drug issues which present specific challenges, such as the wider use of herbal medicines and drugs targeted to the human genome. New evaluation methods, particularly the development of large automated multi-purpose population based systems, need to be researched and developed to meet these challenges.

GLOBAL SOLIDARITY

We have been given the stark contrast between the activity in ICH countries and that in some other countries. The ICH has left the rest of the world aside, though with the understanding that WHO would act as a link. The problem is that WHO has lacked the finance and other resources to really be that link. There is a need for WHO to ensure that any advantages of ICH efforts are made available in the rest of the world and that other problems, which are greater in some of those countries (e.g. Drug fraud) are addressed.

It has been mentioned several times that pharmacovigilance is a worldwide endeavour. The World Health Organization, now being reorganised under a new Director General, is the only Organization with a truly global remit to harmonise healthcare. It is an inter-, not supra-governmental body, coordinating and not controlling national endeavours. WHO has provided guidelines and coordination in pharmacovigilance through the Programme of International Drug Monitoring.

CIOMS has brought together drug safety expert groups from industry and national regulatory authorities. the UMC has provided tools and scientific support for all of the WHO Programme's work. The work of all three bodies is having a major impact and needs your continuing support. ”



MESSAGE FROM RALPH EDWARDS, DIRECTOR

With the Millennium very much on everyone's mind, this really is a time to be thinking about the future of pharmacovigilance.

Our Anniversary Symposium in December brought experts from all over the world to examine what we do here at the UMC and to help us set a new agenda. There was no doubt how much there is to be done!

An issue of great importance - presented particularly by Andrew Herxheimer - is the need for a greater focus on the safety of drugs and on the funding of safety research. As drug companies search for the decade's great block-busting drugs; as the pressure for results leads to increasingly compressed development timescales; as more activities are outsourced; as the genome project takes us towards a greater understanding of the causes of disease, with the prospect of drugs which will work in a much more profound fashion; so, we must be absolutely clear how the benefit-risk balance is being affected and solidly confident about the data on which we make licensing and clinical decisions. We must also be sure that maximally useful information gets to prescribers and patients.

Co-ordination in this challenging field, and setting guidelines and standards are clearly among future tasks for WHO and the UMC.

Many positive changes are occurring in WHO which recognize drug-benefit and risk as a key part of health policy, but it is sad that these will take place without Martijn ten Ham and Juhana Idänpään-Heikkilä both of whom retire before the Millennium. Their work and experience will be missed, but we will build upon it.

Thanks to all of you who travelled to a chilly Stockholm for the Symposium; thanks to all of you who continue to support our work and collaborate with us - and here's hoping we shall see many of you at one or other of this year's significant meetings - at our own Annual Meeting in Ankara or elsewhere.

Best wishes,

I Ralph Edwards

A special interview with Martijn ten Ham

(conducted for Uppsala Reports by Ronnie Meyboom)

In December 1998, Dr Martijn ten Ham retired from his position as Chief of the Drug Safety Unit in the Division of Drug Management and Policies at WHO, Geneva. In recognition of his considerable influence on the WHO Drug Monitoring Programme for the last ten years (1989-1998), we asked him for his general thoughts about the present status of pharmacovigilance.



Martijn ten Ham

UR: *What are the main programmes you have been involved in during your time at WHO?*

The worldwide communication of data and knowledge relating to drug safety is a major responsibility of the Drug Safety Unit. For this purpose we produce the monthly Pharmaceuticals Newsletter and ad hoc Drug Safety Alerts, which are widely distributed throughout the world, to health authorities and to many non-governmental organizations. There is now a world-wide network of governmental drug information officers actively collaborating with the Unit: they ask questions, receive information and provide information on drug regulatory issues. Also, since 1989, I have been responsible for the management of the WHO Programme on International Drug Monitoring.

UR: *From a public health perspective, what do you think were the major advancements during your WHO career?*

During this period, the awareness of and commitment by governments (health authorities, drug regulators) to the safety of medical drugs has increased enormously. The number of countries participating in the WHO Programme has more than doubled to 54 countries. The database maintained by the WHO Collaborating Centre for International Drug Monitoring in Uppsala, Sweden, now contains almost two million reports received from those countries. National authorities are now obliged by the EC Guideline on Pharmacovigilance to submit reports of adverse drug reactions to this database. For much of the progress made we have to thank the WHO Collaborating Centres in Uppsala, Barcelona and Cape Town, as well as other international bodies, in particular CIOMS which has provided a valuable independent forum for discussions between regulators and industry.

UR: *Can you give examples of projects that have not, in your opinion, flourished as they should?*

Personally, I believe that the enormous importance for public health of medical drugs and their safety should justify even more attention within WHO in Geneva. More specifically WHO should invest in the development of new drugs and the establishment of efficient treatment schemes for tropical diseases, and the improvement of global vaccinations. The counterfeit drugs monitoring programme (which has now come to a halt, due to lack of funds) should also be continued.

Another point of concern is that not all new pharmacovigilance centres have developed successfully. In a number of countries an initiative has started enthusiastically but then has not succeeded in achieving and maintaining a steady stream of case reports. We have to find ways of helping new centres to be more successful.

UR: *What do you see as the main role of WHO in the drug safety area today and in the future?*

First and foremost, the provision of assistance and training in pharmacovigilance in developing countries. In addition, there is an important role for the WHO in communication and exchange of information, and in harmonisation and standardisation of methods and procedures. In this respect the Collaborating Centre in Uppsala is a powerful instrument.

UR: *Do you think there is a conflict of interest between WHO and other international initiatives like the ICH and European Union, setting up its EUDRAWATCH database?*

I don't think there is likely to be a conflict of interest. What we should prevent is a duplication of activities or, the contrary of harmonisation, the proliferation of procedures. We have to ensure that the costs of the technical requirements (e.g. soft and hardware and the associated maintenance service) are affordable for less affluent countries.

UR: *If WHO provided you with an additional annual budget of US \$5m for development of pharmacovigilance, how would you spend it?*

This is a truly large amount of money! In part, I would use it for training and education: more courses in pharmacovigilance, and the creation of more academic fellowships to enable the exchange of scholars. I would probably use the remainder of the money for further pharmacoepidemiologic/pharmacoeconomic studies, for signal testing and the collection of the information needed for a more rational use of drugs.

UR: *Do you think consumers of medicines can feel safer today than they could 15 years ago?*

Of course improvements can always be made, but I am confident that in most developed countries pharmacovigilance has been reasonably well organized and effective in detecting most if not all serious unexpected adverse drug reactions. This was probably not the case 25 years ago. With regard to the safe and rational use of drugs, on the other hand, there is still much to be improved, and we must continuously be vigilant with regard to the possible circulation of counterfeit drugs. This requires both alertness and infrastructure (e.g. for random testing of the pharmaceutical quality of drugs). Of particular importance is the early detection of batches of contaminated or adulterated drugs. We have to avoid disasters such as what happened recently in Haiti, and earlier in Bangladesh, India and Nigeria, where children died of kidney insufficiency due to ingestion of paracetamol syrup containing diethylene glycol.

UR: *What will you be doing in your new job for the Dutch Government?*

As Senior Advisor International Affairs at the Ministry of Public Health, my responsibilities are primarily concerned with international matters relating to medical drugs. Fields which capture my special interest include: quality assurance of starting materials; counterfeit drugs; and the sale of medical drugs via the Internet.

We wish Martijn every good fortune in his new life!



- **The Drug Information Association (DIA)** is organizing a conference entitled *Monitoring Drug Safety in "Third Party" Joint Projects* in London, 12-13 April 1999.
For more **information** please contact:
DIA European Office
tel: +41-61 386 9393 fax: +41-61 386 9390
e-mail: diaeurope@stepnet.de
- **Management Forum is holding** *A Workshop on Periodic Safety Reports* on 19 April 1999, and one on *MedDRA-Medical Dictionary for Regulatory Affairs* on 12 April, both in London.
For more **information** please contact:
Management Forum
tel: +44-1483 570 099 fax: +44-1483 536 424
e-mail: management_forum@psilink.co.uk
- **Royal College of Physicians and Surgeons of Glasgow** in association with the International Society for Pharmacoepidemiology (ISPE) is organizing a symposium on *Safety and Effectiveness of Drug Therapy* in Glasgow, Scotland, 23rd April 1999.
For more **information** please contact:
The Education Secretary
tel: +44-141 227 3236 or 141 221 6072
fax: +44-141 221 1804
e-mail: mgt.cooper@rcpsglasg.ac.uk
- **IIR is holding a conference** on 10-11 May 1999 in London entitled, *ADRs '99*.
For more **information** please contact:
IIR Ltd
tel: +44-171 915 5000 fax: +44-171 915 5001
- **The 35th Annual Meeting** of the Drug Information Association will be held in Baltimore, Maryland, USA, 27 June - 1 July 1999. One of the tracks is on *Clinical Safety/Pharmacovigilance*.
For more **information** please contact:
DIA
tel: +1-215 628 2288 fax: +1-215 641 1229
e-mail: dia@diahome.org
- **The 15th International Conference on Pharmacoepidemiology** will be held on 26-29 August 1999, Boston, MA, USA.
For more **information** please contact:
The International Society for Pharmacoepidemiology
att: Katrina Crist
tel: +1-202 416 1641 fax: +1-202 416 1744
e-mail: ISPE@slackinc.com
- **The 22nd Annual Meeting of Representatives of National Pharmacovigilance Centres** participating in the WHO Drug Monitoring Programme will take place in Ankara, Turkey, 20-22 September 1999
For more **information** please contact:
Dr Mary Couper, WHO Geneva
tel: +44-22 791 2111 fax: +44-22 791 4730
e-mail: couperm@who.ch
- **The European Society on Pharmacovigilance (ESOP)**, will have its 7th Annual Meeting in Ankara, Turkey, 23-24 September 1999 (*following the meeting of representatives of national centres participating in the WHO Programme*).
For more **information** please contact:
Sevgi Öksüz
tel +90-312 230 1674 fax +90-312 230 1610
e-mail: tadmer@iegm.gov.tr
- **The Medicines Control Agency (MCA) UK, will hold** *The Sue Wood Memorial Symposium - Pharmacovigilance into the new Millennium, on the 11 October 1999* at the Royal College of Physicians, London. For more information please contact:
Mick Foy
tel +44-171 273 0263 fax +44-171 273 0060
e-mail: m.foy@mca.gov.uk

NEW PUBLICATIONS FROM the UMC

The Erice Report

The International Conference on Developing Effective Communications in Pharmacovigilance was held in Erice, Sicily, 24-27 September 1997. It was attended by health professionals, researchers, academics, media writers, representatives of the pharmaceutical industry, drug regulators, patients, lawyers, consumers and international health organizations. The full report of the conference - *The Erice Report* - is now available from the UMC at a cost of 250 SEK. Please contact Inger Forsell at the UMC Sales & Marketing Department to get your own copy.

National Pharmacovigilance Systems, 2nd Edition

This publication offers the first and only detailed and comprehensive overview of national pharmacovigilance systems throughout the world. The first edition, published in 1997, covered 45 countries.

The second edition, published in March 1999, includes detailed descriptions of 57 national pharmacovigilance systems and 2 centres for vaccine monitoring. In the new edition, the content of each country profile has been updated and considerably extended, including information on the use made of CIOMS and ICH initiatives. The book also provides a comprehensive directory of names, addresses and communications details.

The second part of the book provides an overview of global pharmacovigilance practices, including a survey of the information required on 40 national adverse reaction reporting forms.

Customers are provided with annual updates, keeping national centre contact details up-to-date.

The price of the book is 5000 SEK per copy or 1500 SEK for public sector and academic organizations. Customers of the first edition will be given a favourable rate for an update.

NEW PUBLICATIONS

Scrip Reports has published its 1999 edition of *Global ADR Reporting Requirements* which covers regulations in 26 countries. It is written by Dr Barry Arnold, Head of Drug Safety and Epidemiology at Zeneca Pharmaceuticals. The publication may be obtained from Scrip Reports.
Price: £695 or \$1,460.

Fax: +44-181-332 8992; e-mail: phil@repsinfo.demon.co.uk

The 2nd enlarged edition of the book *Responsibility for Drug-Induced Injury*, with the subtitle *A Reference Book for Lawyers*, the Health Professions and Manufacturers, was published in 1998 by IOS Press, Amsterdam (ISBN No: 90 5199 3870). The authors are: Graham Dukes, Mark Mildred and Barbara Swartz. The book can be ordered by:
Fax: +31-20-6203419; or e-mailing: order@iospress.nl

RECENT CIOMS PUBLICATIONS

The document *Guidelines for Preparing Core Clinical-Safety Information on Drugs* written by CIOMS working group III has been published as a second edition with an edition on *New Proposals for Investigator Documents* from CIOMS working group V. A report by CIOMS working group IV which addresses benefit-risk evaluation is currently available.

At the end of 1999 CIOMS working group V will be ready to publish *Perspectives about 'good case management practices' in pharmacovigilance*.

These publications can be obtained from COIMS, c/o WHO, 1211 Geneva 27, Switzerland. They are also available from booksellers through the network of WHO sales agents, a list of which can be obtained from CIOMS.



TRAINING IN PHARMACOVIGILANCE

The Uppsala Training Course in Adverse Reactions and Adverse Reaction Monitoring; 31 May - 11 June, 1999

the UMC is organizing, for the fifth time, its two-week training course aimed at providing basic training for health professionals who have recently become engaged, or soon will become engaged, in the practical operation of programmes for spontaneous adverse reaction reporting. To satisfy the needs of healthcare professionals from different backgrounds the course is divided into three separate Sections:

Section I : Mechanisms and clinical manifestations of adverse drug reactions

Section II : Spontaneous adverse reaction reporting

Section III : Introduction to pharmacoepidemiology

Attendees may choose to follow two or three sections.

Section II is mandatory.

Theoretical and practical aspects of adverse reactions and adverse reaction monitoring will be covered. The theoretical parts will include lectures as well as group discussions. Practical sessions will include recording of case information and computerized retrieval of information from the database of the WHO Drug Monitoring Programme.

The course, designed for 25 students, will be held in English. Please contact Anna Lindquist (**e-mail: anna.lindquist@who-umc.org**) at the UMC to get the invitation brochure and an application form.



Prof K.C Singhal

Workshop on Adverse Drug Reactions, New Delhi, India 9-12 November, 1998

This workshop, organized by Professor K.C Singhal, Department of Pharmacology, Aligarh Muslim University, attracted 70 doctors and pharmacists from all over India. It was originally scheduled to be held in Aligarh but, due

to unforeseen last-minute circumstances, it was moved to New Delhi. Prominent Indian clinicians lectured about unfavourable drug effects which affect various body organ-systems. Methods of drug monitoring, individual case assessment, signal detection and follow-up were among the other topics covered in the work-shop. Reporting forms and study protocols for spontaneous reporting, case-control studies and cohort studies were designed during working group sessions.



Sten Olsson

Foreign participants included: Dr John Autian and Dr Peter Chyka, Tennessee, **USA**, Dr Ronnie Meyboom, **the Netherlands** and Sten Olsson, **the UMC**.

As a follow-on to the workshop, Professor K.C. Singhal is now in the process of establishing an *Indian Society of Pharmacovigilance*.

Extended Pharmacovigilance Training Programme carried out in Argentina

ANMAT (*the drug control authority in Argentina*), undertook a national pharmacovigilance training course between April and November 1998. The aim was to:

- provide a systematic capacity for healthcare professionals to detect, report and process adverse drug reactions and product quality defects
- enable the establishment of regional pharmacovigilance centres.

The course was divided into nine eight-hour modules. One module per month was taught for nine months. The thirty-five participants were provided with bibliographical material before each module, participated in working group sessions and carried out projects within each topic. Students were recruited from provincial health authorities, universities, hospitals, drug manufacturers, the national drug authority and from neighbouring Uruguay.

As a result of the course, two new regional pharmacovigilance centres have been established in Argentina. The existing centres have also been strengthened.

PRODUCT NEWS

The current versions of the computerized WHO Drug Dictionary (DD) and the WHO-Adverse Reaction Terminology (WHOART) as well as the software DDAccess-professional, contain information up to and including the fourth quarter of 1998.

Updated versions (December 1998), of the printed WHO-ART, English edition, and the software WHO-ARTAccess are currently available.

WHOART is now also available in an Italian version in paper print. Terms in Italian are also included in the computerized WHOART file. Also an updated edition of WHOART in German is now printed.

In May/June 1999 the computerized DD and WHOART 1999:1 will be available, as well as the paper print version of DD and the standard version of DDAccess. The 99:1 versions of the DD will have revised ATC-codes as decided by WHO.

Swedish Government Reviewing *the UMC*

The Swedish Government has decided to make an appraisal of the organizational aspects of *the UMC*, including questions relating to the agreement between WHO and Sweden and the Swedish financial support to the Centre. A two-person review committee was appointed to carry out the work. The committee members, Åsa Lidbäck and Lars Markstedt, started working in early February and will present their conclusions to the Government by 1 July, 1999.

The background to the review, as stated in the terms of reference for the committee, is the expansion of the WHO Drug Monitoring Programme and *the UMC* since the foundation was established in 1978 and the changed environment it is now operating in.

The review committee is mandated to analyse:

- the content, scope and financing of *the UMC's* operations in relation to the agreement with WHO
- changes in the outside world that could motivate alterations in the operation, organization or financing of the Centre
- potential for development of new activities or financing that were not foreseen in the original agreement with WHO.

The review will include an analysis of the outside view of *the UMC*, both from regulators and industry.



News from Around the

WORLD

United Kingdom

Dr Patrick Waller from the Medicines Control Agency (MCA), **UK**, has replaced the late Susan Wood as Chairman of the European Pharmacovigilance Working Party. The working party is a sub-committee of the Committee for Proprietary Medicinal Products (CPMP), of which Dr Waller is a new member.

Peru

In December 1998, a National Technical Pharmacovigilance Committee was created in **Peru** with the aim of establishing a national pharmacovigilance system. Chairman of the committee is **Susana Vasquez Lescano**, Ministry of Health, Peru. Her e-mail address is: SVASQUEZ@digemid.gob.pe

Fiji Islands

Fiji Islands has applied for membership to the WHO Drug Monitoring Programme and is in the process of submitting the first ADR reports to *the UMC*. **Abdul Ahjaz Azam** is our contact person at this new centre. He can be contacted at: Ministry of Health, G.P.O. Box 106, Suva, Fiji Islands, (tel: +679-315022; fax +679-304199; e-mail: aazam@health.gov.fj).

Malawi and Swaziland

Dr James Ndalama and Margareth Magagula from Queen Elisabeth Central Hospital, Blantyre, Malawi and Swaziland, studied pharmacovigilance techniques at the South African National Pharmacovigilance Centre in February 1999. Dr Ndalama also took part in the Regional Training Seminar on Pharmacovigilance in Kadoma, Zimbabwe, 3-6 August, 1998.

.....

France

Dr François Maignen has moved from the pharmacovigilance unit of the Medicines Agency in **France** to a post at the pharmacovigilance department of the European Agency for the Evaluation of Medicinal Products (EMA) in London.

Bulgaria

The **Bulgarian** Drug Control Institute has set up a new Internet website: <http://www.ndi.bg400.bg> which includes a pharmacovigilance section. The main part of the site is in English but the drug safety messages are still available only in Bulgarian.

Singapore

The Pharmaceutical Department, Ministry of Health, **Singapore**, released the first issue of its *Adverse Drug Reaction News* in January, 1999. If you would like to receive the newsletter and be included on the mailing list, please contact the chief editor: Ms Chan Cheng Leng. Fax: +65-3255448; e-mail: chan_cheng_leng@moh.gov.sg

China

On 23 December, 1998, the Shanghai Centre for Pharmacovigilance was inaugurated in the Hua Shan Hospital. General manager of the new regional centre in **China** is **Mr Wang Da-You**, who spent six months at *the UMC* on a WHO fellowship in 1993. He can be contacted by e-mail: dywang@shmu.edu.cn

New Zealand

The Ministry of Health, **New Zealand**, has set up a new Internet website: <http://www.medsafe.govt.nz/hprofs.htm> containing a lot of interesting material on the safety of medicines, published in the latest issue of *Prescriber Update*. You can also subscribe to monthly e-mail messages about new safety articles available on the Internet site. This electronic service will replace the printed *Prescriber Update*.

Philippines

Dr Kenneth-Hartigan Go, who has had the operational responsibility for the **Philippine** Pharmacovigilance Programme was recently appointed Deputy Bureau Director of the Food and Drug Administration in the Philippines.

Obituary ~ Dr Karl Kimbel

Karl Kimbel, who was the Director of the Drug Commission of the Association of German Physicians from 1972 to his retirement in 1989, died suddenly on 12 November, 1998, shortly before his 74th birthday.

Karl devoted a major part of his professional life to drug safety issues and was instrumental in developing a system for spontaneous reporting of adverse drug reactions in Germany from his platform at Association of German Physicians. He published numerous papers on drug safety, both regarding individual drug problems and on methodological, philosophical and ethical issues. They appeared in journals for German physicians and in the international press.

Karl Kimbel was an active discussant at meetings within the WHO Drug Monitoring Programme and he was also a member of the Advisory Group to the WHO Collaborating Centre in Uppsala, 1979 - 1980.



NEWS FROM *the* UPPSALA MONITORING CENTRE

We all have new e-mail addresses!

We are currently moving over to a new server for our e-mail and Internet services and all our e-mail addresses have been changed. There are now two general addresses:

- **info@who-umc.org** should be used for general enquiries/messages, or if you don't quite know to whom you should address your message
- **sales@who-umc.org** should be used for all enquiries regarding the sales and marketing of our products and services

*(Personal e-mail messages may be sent to any member of the UMC team by putting their name (e.g. ralph.edwards) in place of **info** or **sales** in the addresses above. Please start using these new addresses now since the old ones will only remain operational for a relatively short transition period.)*

World record for entries into Drug Dictionary

1998 saw a **world record** for entries into the Drug Dictionary - a staggering 2,700 entries now brings the total entries to 44,690. There are usually 1,500-2,000 new entries a year. *(There are also an increasing number of requests from users to include drug names they need to use.)*

Monitoring of herbal medicines - Mohamed's work continues

In Uppsala Reports 6 (March 1998) we reported on the project Mohamed Farah (scientist - traditional medicines) was under-

taking with herbals. The aim of *the* UMC is to achieve a global standardization for herbal medicines.

In 1998 there were 1,400 listed entries in the Drug Dictionary for herbal medicines. The enormous task of cross-checking and correctly classifying these entries is still underway. One of the most difficult problems Mohamed faces is the variety and inconsistency of information available for each and every herbal entry. One plant will have many names, different countries will favour certain names and there is a lot of misinformation in the public arena. Up until now there hasn't been one standard for the classification of herbals.

The process of gathering and checking information and achieving an acceptable classification is painstakingly slow, it requires an extraordinary meticulousness and dedication and there are many obstacles to overcome. So far Mohamed has recorded and classified 363 herbals. This tremendous work continues...

Ronnie Meyboom in Uppsala

Dr Ronnie Meyboom, who presented his PhD thesis in pharmacovigilance in October 1998, (see *Uppsala Reports* No 7) and normally works for the LAREB foundation in the Netherlands, spent a three week period at *the* UMC during January and February 1999. Ronnie is a member of *the* UMC signal review panel and he used a major part of his time in Uppsala working with the team developing a new procedure for identification and analysis of new ADR signals from the WHO database. Ronnie will come back to Uppsala later this year and he will also be a member of faculty of the ADR training course in Uppsala, 31 May - 11 June, 1999.

President of thalidomide victims association visits *the* UMC

On 23 February 1999, Rosangela Nascimento visited *the* Uppsala Monitoring Centre. She is the president of ABVT, the Brazilian Association of Thalidomide Victims. The main purpose of her visiting Europe was to investigate what social benefits are provided to thalidomide victims in other countries, with the aim of improving conditions for members of her association in Brazil.

ABVT currently has 600 members, who are all victims. The group is growing on a weekly basis, as unknown thalidomide victims are identified. The most recent new thalidomide baby was born in 1995.

Thalidomide has been available on the Brazilian market for approximately 40 years, now used primarily for the treatment of erythema nodosum secondary to leprosy. Rosangela expressed her worries about the lack of strict control on the use of thalidomide in Brazil and the risk of the drug becoming more widely spread because of recent use in HIV-positive patients. A proposed legislation, including controlling measures of the drug and financial contributions to ABVT, has been before the Brazilian congress for years without being passed. At the moment ABVT is totally dependent on voluntary contributions.

The present priorities of the organization are:

- 1. to improve the social situation for thalidomide victims**
- 2. to identify unrecognized thalidomide victims**
- 3. to engage in information campaigns**
- 4. to avoid unwarranted use of the drug.**

Rosangela would like to get in touch with other organizations of thalidomide victims or individuals who could contribute to her picture of the worldwide situation for persons affected by this drug. Her address is:

**Associação Brasileira das Vítimas da Talidomida,
Caixa Postal 1351-Ag. Aarão Reis,
CEP 30161-970-Belo Horizonte-
MG-Brazil.
Fax: +55-31-4921288**



Rosangela Nascimento



UMC INVOLVEMENT IN THE MALARONE DONATION PROGRAMME

- During 1996, **Glaxo Wellcome** announced the initiation of a controlled donation programme of up to one million treatment courses per year of the anti-malaria drug Malarone.
- **Malarone** is a fixed combination of atovaquone 250mg and proguanil hydrochloride 100 mg, developed for the treatment of acute, uncomplicated *P. falciparum* malaria. An independent Advisory Committee of experts was set up to provide guidance on technical and operational issues ensuring responsible use of the drug in a way that will maximize its public health benefits while minimizing the risks.
- **The Advisory Committee** has asked Ralph Edwards of *the UMC* and Hugh Tilson to assist in the development of systems to monitor the clinical safety of the drug. East Africa was selected as the initial focus for programme activity.
- As a consequence **the UMC** has provided some initial support for development of a drug monitoring programme in Kenya.

Results from the questionnaire on signals sent to National Centres in October 1998

The Combinations database is the result of a Bayesian Confidence Propagation Neural Network (BCPNN) scan of the WHO database. The scan generates counters and statistical measurements for each drug-ADR combination reported.

COMBINATIONS DATABASE

- The questionnaire was sent to 69 people in 62 countries. 47 replies were received from 43 countries
- A majority of the centres view the new statistical information to be useful or very useful and all but 5 fully agreed that the current material should be replaced with the new Combinations database
- A majority of the responding centres said they have the resources to further assess possible drug-ADR problems highlighted in the Combinations database. We are currently working on the production of the Combinations database quarter 98:4, together with guidelines for use and detailed field descriptions. We hope that the new searchable/sortable database can inspire and help centres to use the information from the WHO database more actively.

To make the Combinations database as useful as possible, we intend to optimise the contents and layout during a test period of about three quarters. Feedback from national centres during this period will play an important role in determining the final content of the database.

SIGNAL DOCUMENT

The Signal document contains summary information on evaluated drug-adverse reaction associations in the WHO database

- 42 centres say they make use of the information in the Signal document the way it is presented today. We also received some suggestions for improvements of the contents of Signal.
- 40 centres are prepared to give *the UMC* information on actions taken and outcomes in their country upon receipt of Signal.

Comments on the Signal document relevant to our expert review panel will be forwarded to the reviewers in the improved guidelines we are producing.

The information on actions taken by national centres and their outcomes will be included in the Signal follow-up database.

SERVICE TO INDUSTRY

- Providing excerpts from the Combinations database as a service to industry is acceptable to almost every centre.

The details of this new service are currently being explored in a pilot project.

the Uppsala Team



Director:
Manager (External Affairs):
Manager (Internal Affairs):
Manager (Marketing):
Manager (Research & Development):
Manager (Sales & Promotions):
Scientists:

Pharmacists:

External Affairs Assistant:
Internal Affairs Assistant:
Sales Assistant:

Professor Ralph Edwards
 Sten Olsson
 Cecilia Biriell
 Liza Storm
 Marie Lindquist
 Mats Persson
 Mohamed H. Farah (*Traditional Medicines*)
 Jonathan Edwards (*Information Systems*)
 Malin Ståhl (*Biomedical*)
 Andrew Bate (*Neural Network Methodology*)
 Helena Fucik, Monica Pettersson, Malin Zaar,
 Erica Walette, Anna-Karin Flygare
 Anna Lindquist
 Maria Bergström
 Inger Forsell

Communications information

Uppsala Reports © *the Uppsala Monitoring Centre* 1999

Postal Address: *the Uppsala Monitoring Centre*, Stora Torget 3, S-753 20 Uppsala, Sweden

Telephone: +46 18 65 60 60 **Fax:** +46 18 65 60 80

e-mail: (general enquiries) info@who-umc.org (sales & marketing enquiries) sales@who-umc.org

*Personal e-mail messages may be sent to any member of the team by putting their name (e.g. ralph.edwards) in place of **info** or **sales***

Internet: <http://www.who-umc.org>

Uppsala Reports is produced and published for *the Uppsala Monitoring Centre* by EQUUS, UK.

(Tel: +44 (0)171 274 8724; Fax: +44 (0)171 733 3600; e-mail: info@equus-group.com; internet: www.equus-group.com)