20 page issue

Issue 19
July 2002

Published by *the* Uppsala Monitoring Centre, 2002

Uppsala reports

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

MESSAGE FROM THE DIRECTOR

We are used to hard and tough stances being taken on the political stage, when opposing sides are deaf to arguments which challenge their views or in negotiations which require some openness to change. The same should not be true of science, where evidence, reason and balance are essential to progress, and where the acknowledgment of uncertainty is part of the description of truth.

Emotive issues such as the advertising of prescription medicines direct to consumers tend to polarise views and often lead to heated exchanges which do not really advance anyone's interests – least of all those of patients.

A group of clinical pharmacologists, physicians, industry representatives, journalists, communications professionals, and consumer advocates met in Erice, Italy, in May to discuss drug advertising to consumers. In this edition of *Uppsala Reports* we print the Erice Statement on Drug Advertising to Consumers. It is published with the support and respect of the whole working group behind it, even though it records a fundamental divergence of view: between those who believe that drug advertising to consumers should never be permitted, and those who believe cautious, experimental liberalisation should be allowed. Both sides have strong views of the nature of acceptable standards of communication in medicine, but agreement on the basic issue is unlikely to happen.

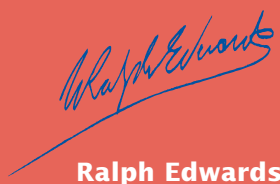
The divide in Erice seemed to be philosophical: is the partial nature of advertising so bad and are medicinal products so special that prohibition is justified? On one side, the insecurity of control measures, the largely commercial bias of direct-to-consumer advertising, together with the possible resulting distortion of priorities in public health and prescribing were cited.

The more permissive group thought that commercial interest and public health may not always conflict, and that more insidious biases can underlie other advertising and information in the health area. They considered the best way forward was in strict guidelines and monitoring, in line with advertising of other products in some countries.

There was no doubt among any of the participants that inducements and incentives which might distort the prescribing process and possibly harm patients, were entirely unacceptable.

Metamizole has also recently sparked something of a war of words. The argument has come mainly from those that believe that it should be banned because of the risk of agranulocytosis, despite the high rate of morbidity and mortality from cheaply available NSAIDs and paracetamol, which would be the likely substitutes. There are those who will not, in any circumstances review their positions, examine new evidence, or give credit to those who believe differently from them.

W B Yeats reminds us of what happens when disorder prevails: *The best lack all conviction, while the worst/Are full of passionate intensity.** I would like to see a greater conviction that we must often live with uncertainty and a measure of acceptable risk; and rather less intransigence in scientific debate.



Ralph Edwards

* W.B. Yeats, The Second Coming (1921)

Contributions wanted!

We aim to make Uppsala Reports an interesting and valuable communication for anyone working in or interested by drug safety issues and the WHO Programme for International Drug Monitoring.

If you would like to contribute news or a longer article or feature to Uppsala Reports, please do get in touch with Sten Olsson or Geoffrey Bowring (e-mail instructions below, or full address on back cover). We are always happy to hear from readers wherever you are in the world and whatever your part in safety of medicines or public health.

Get on the mailing list

If you do not receive a copy of Uppsala Reports directly, but would like your own personal copy, please send your name, position, organisation, full postal address and e-mail/phone to *the* UMC (address on back cover).

sten.olsson@who-umc.org or geoffrey.bowring@who-umc.org

Major upgrade for WHO ADR database

Vigibase comes on line

After nearly a quarter of a century it's time for INTDIS – the WHO ADR database to be upgraded. It has served reliably over the years, but it was essential to design a new format that can accompany us into the future of pharmacovigilance. 'Vigibase' is the new database; it is E2B compatible, but can still capture reports submitted in the old INTDIS format, as well as all old data.

- Vigibase - from E2B initiative
- Daily updates
- More information 'captured'
- Web search tool on the way

Hardware changes have enabled the upgrading as well: we are now able to capture and handle vastly more material than when INTDIS, one of the first - if not the first - large scale relational databases worldwide, was created. Also, the science of pharmacovigilance has developed and is now regarded as a necessary tool to achieve safer use of medicines. A lot of work has been done to harmonise and facilitate the sharing of collected information. The E2B standard for electronic transfer of ADR data was agreed upon under the umbrella of CIOMS, which *the* UMC initiated. So Vigibase has actually sprung out of the E2B initiative. The E2B recommendations have been adopted and made mandatory by regulators in the countries within the International Conference of Harmonisation (ICH) - countries who are also part of the WHO International Drug Monitoring Programme. It is heart-warming that our ideas were given such credence and we are now happy that all countries participating in the WHO Programme will get the advantages of using this harmonised system for information sharing which we started to develop 10 years ago.

All INTDIS reports have been converted into the new structure. By running the two databases in parallel until all quality checks were completed we have been able to receive reports without interruption during this merger.

The switch to Vigibase will not affect those who wish to continue submitting reports to *the* UMC in the old format. However, it will allow countries who have been forced to 'downgrade' their reports to INTDIS format for submission to resend the complete reports to capture as much information as possible in Vigibase (including free text).

When INTDIS closes down (by 31 August 2002) it's not only the launch of a new database, but a whole new system for handling the flow of reports into the database. One advantage is that Vigibase will be updated every night and thus all correct reports will be entered within 24 hours of receipt by *the* UMC. Another feature is that incompatible reports will be stored as a searchable subset of the database in the same structure as the correct ones. The report handling system has built-in features to speed up corrections, keeping the same high quality standard.

A web-based search tool for countries participating in the WHO Programme will be introduced over the summer. We are also developing a new web-based tool for ADR reporting for National Centres that do not have their own ADR database or do not wish to continue double entry of reports by using the INTDIS compatible WHOADR software for transfer of reports to *the* UMC.

The Vigibase system also includes new features of the WHO Drug Dictionary, for possible entry of more detailed information about each drug name. The WHO ADR terminology (WHOART) will still be maintained and used within the WHO Programme. However, since Vigibase is constructed to be able to capture reports in E2B format, and the ICH has declared it mandatory to use MedDRA terms, Vigibase is also compatible with these.

Enquiries
If you have any enquires about the new database, the new search tool or the new reporting tool, please contact Daniel von Sydow or Helena Fucik – or e-mail info@who-umc.org

THE MIND BEHIND THE MINING

Uppsala Reports talks to Dr Roland Orre

One of the primary aims of *the* UMC is to detect signals in the WHO database, which are followed up on a regular quarterly basis. *the* UMC constantly strives to improve the signal detection techniques used. To this end a Bayesian Confidence Propagation Neural Network (BCPNN) has been developed for data-mining the WHO database. This tool uses Bayesian theory to quantify the degree to which a specific drug-ADR combination is different from a background (in this case the whole of the WHO database), and a confidence interval is calculated for each combination. By implementing the theory in a neural network all drug-ADR associations in the database can be analysed quickly and automatically. Those highlighted associations can then be subjected to rigorous clinical assessment. The BCPNN is also being used to look at the strength of associations for combinations of several variables. Much of the work for the WHO Programme is carried out by **Dr Roland Orre** at the University of Stockholm. Roland, together with Erik Swahn and Jonathan Edwards are based in the Mathematical Statistics department, and work closely with Andrew Bate and others at *the* UMC. Roland spoke to Uppsala Reports about his vision and his work.

Uppsala Reports: * When you meet someone socially, how do you explain what you do?

Roland Orre: I usually start by saying that I'm working with data-mining of adverse drug reactions for WHO. From there on it's quite easy to continue in either a technical statistical or a general drug safety medical track depending on the background of the person. People generally grasp the issue about adverse drug reactions and often also know about the WHO database, but data-mining most people haven't heard about.

**** Is the WHO International Programme particularly important to you?***

I always wanted to work with some important issue helping humanity. The WHO Programme is perfect, as it's also a non-commercial project, which guarantees that the effort is aimed at the important issues instead of making profit for a company. Some years ago I was offered a job by a software company who said that they would pay me a huge salary. I didn't accept the offer even though I didn't have a contract with WHO at that time. No normal job can compete with being involved in a project like the WHO Programme, whatever the salary.

**** What is a typical day like in your team?***

In the morning we usually start by just saying "good morning", then we fetch some coffee and bring it to the desk and after this we work silently, each one focused on their problems. Occasionally Erik and Jon have some issue they want to discuss, otherwise I ask them after a couple of hours how they are doing, and now and then they have collected some issues that we need to discuss. After this we are all working silently until lunch. Often we eat lunch at our desks, but now and then, we go out to have lunch in the sun instead. The team I'm working with now is very focused and disciplined and it's a joy working with Erik and Jon. After lunch we may discuss the more visionary aspects for a while, touching on the future potential of our project. After this we continue working, focused and silent until the end of the day.

Erik Swahn, Roland Orre, Jonathan Edwards

**** Who in the field of data-mining (dead or alive) do you admire?***

Well, I'm not very much of an admirer of specific people as such; I prefer ideas and as such admire all people working for these ideas, but anyway, I'll mention a few names. Even if he is long dead I want to mention reverend and mathematician Thomas Bayes, who invented the Bayesian statistics with his posthumously published paper in 1763. The Bayesian statistics is fundamental for much of the data-mining issues of today. Of course, we also have to mention Pierre-Simon Laplace who reinvented the Bayesian statistics and also showed its usefulness. Among the living of today I'm more restrictive but there are a few, like the people from the old Bayesian group at NASA: David Heckerman, now working for Microsoft and Peter Cheeseman and John Stutz, still at NASA. There is Padhraic Smyth at the Jet Propulsion Laboratory and many others; also of course Usama M Fayyad who has done a lot to spread the ideas about data mining.

**** What makes you such a strong believer in BCPNN?***

BCPNN is intuitive, logical and simple. It's based upon strict mathematical and statistical principles dealing with plausibilities in the continuous range false to true. Add consistency and common sense to this and it follows that any valid way to reason about plausibilities requires a Bayesian analysis. BCPNN can solve both hard classification problems as well as tough pattern recognition problems, and do it much quicker than other methods. In the way it's used for adverse reaction signalling it also relates to information theory in a nice and simple way. As a computational model it's also excellent for the parallel machines being developed to increase computational power. It's also not too hard to imagine how artificial brains can be built with BCPNN modules.

**** How much do those reporting ADRs or working in drug safety need to understand about BCPNN?***

They don't need to understand the intrinsics about BCPNN but I think it's useful if they have a grasp of conditional probabilities and that they have an intuitive understanding about the IC (information component). The simple principle that the IC is a measure which gets stronger for events occurring together more often than expected and that it has a distribution, which makes it possible to calculate a credibility of the measure, based upon the number of reports we get. This, I would say, is essential. This helps in understanding why it's important that every suspected adverse reaction is reported.

**** Do you ever have inspiration in strange places?***

Usually I'm inspired by debating and discussing with people, but also by visionary writers. It happens though that unusual places can trigger me as well. When I was at the top of the cathedral in Firenze I got a transcendental feeling and at that time solved an intrinsic problem of our coming BCPNN package. When I sat on a park bench outside our institute, looking at a tree, I realized why software patents are limiting the technical development and I later got a fundamental idea for the next generation data-mining algorithm while I was meditating about it on my sofa at home.

**** Are you willing to risk a prediction of where BCPNN, and artificial intelligence in general, will lead - both for good and bad?***

My wife and I have two pet cats. When we finally have created an artificial intelligence I want to be loved by it like I love my cats. Regarding the predictions for BCPNN it's quite easy to say something. BCPNN combined with new technologies for patient / doctor / computer interaction gives a potential for instantaneous predictions of specific adverse reactions for this specific patient. With the new techniques for complex pattern findings we may catch drug-induced syndromes long before they are even known. Further some years into the future the genome for every person on earth may be known, allowing techniques like BCPNN to be able to condition drug prescriptions for the specific genome combination of this specific patient in the most safe way.
To come back to the issue about artificial intelligence it is very hard to predict what may come. I'm confident that we will create artificial intelligence some day, not too far into the future but how far is only speculation.
Artificial intelligence set up in the right way may give us utopia one day, but this is only one possibility of other much less attractive scenarios. For the well-being and safety of people on earth I consider it important that both research and development about artificial intelligence and nano technology are kept open to the public, and it's important that software and ideas are not allowed to be patented.

Reference:
Bate A, Lindquist M, Edwards IR, Olsson S, Orre R, Lansner A, De Freitas RM. *Pharmacoepidemiology and prescription*: A Bayesian neural network method for adverse drug reaction signal generation. European Journal of Clinical Pharmacology: 54: 4 (1998) pp 315-321.

Thomas Bayes was born in London in 1702, and died in 1761 in Tunbridge Wells. Bayes was a Presbyterian minister who first used probability inductively and established a mathematical basis for probability inference. His theories were published posthumously in 'Essay Towards Solving a Problem in the Doctrine of Chances' (1763), in ***Philosophical Transactions of the Royal Society of London*** 53, p 370-418.

Pierre-Simon Laplace was born in Beaumont-en-Auge, Normandy, France in 1749, son of parents in the cider trade and farming, and died in Paris in 1827. His original research in astronomy was produced from 1771-1787, but the first edition of ***Théorie Analytique des Probabilités,*** published in 1812 contains Laplace's definition of probability, Bayes's rule.

UPDATE FROM EASTERN EUROPE

In Uppsala Reports 16 there was a description of a project to develop pharmacovigilance systems in eight newly independent states (NIS) in eastern Europe. The project "Implementation and Development of National and Regional Systems of Pharmacovigilance in NIS" was clearly a powerful engine for change, as three more countries have now taken big steps forward.

Along with Armenia (also featured in UR16), these countries prove what a valuable initiative this project has been.

Ukraine: 68th member of the Programme

Our network continues to grow. Ukraine has now fulfilled our criteria for becoming a full member of the WHO Programme. Ukraine is the third new member country this year, which means that we now have 68 full members in the International Programme.

Contact person is:

Dr Marina Sharayeva
State Pharmacological Center
Ministry of Health of Ukraine
8 Hrushevsky Str.
KIEV
Ukraine
E-mail: vigilance@pharma-center.kiev.ua

Moldova, new Associate Member

An application for membership of the WHO Programme has been received from the Minster of Health, Republic of Moldova. The letter describes the National Centre for Adverse Reaction Monitoring, headed by V I Ghicavîi, which has been established within the National Institute of Pharmacy. The Republic of Moldova therefore becomes an Associate Member of the Programme.

Stop Press: Kyrgyz Republic

Just as we were going to press, an application was received in WHO-HQ Geneva from the Minister of Health of the Kyrgyz Republic. This easternmost country of the former Soviet Union has applied for Associate Membership of the WHO Programme. The monitoring function will be carried out within the Drug Information Centre of the Department of Pharmaceutical Provision and Medical Equipment.

Clinical Pharmacy in Slovenia

Portorož, the 'Port of Roses', in Slovenia, played host to the 3rd Spring Conference of the European Society of Clinical Pharmacy (ESCP).

Sessions included:
Hospital – primary care networks and disease management
The hospital – primary care continuum and the role of pharmacists, and
Pharmacovigilance in the hospital – primary care continuum.

Marie Lindquist from *the* UMC presented a paper in the last session entitled 'Practical problems in detection and classification of adverse drug reactions'. In this she spoke of some of the challenges and potentials of global pharmacovigilance. She discussed:

- Diagnosis and causality assessment of individual reactions. Under-reporting and limited information to help clinicians in drug safety are long-standing problems to be remedied.
- Coding and data transfer. Clinical information must be accurately coded in ways which make the retrieval of useful information easy for the end-user. Developments in terminologies and IT systems must be critically evaluated.
- International collaboration. To detect rare but serious adverse reactions, use of global data is mandatory. Local initiatives may compromise the existing system pioneered by WHO.

She concluded by stating that a major challenge for the future is to improve the interplay and communication of experience and knowledge between all stakeholders in drug safety. Regulatory and IT developments can both work as advantages and dangers in pharmacovigilance.

The next meetings of the ESCP will take place in Florence from 30 October to 2 November and Lisbon from 14-17 May 2003.

Latvia

Inese Studere describes the progress for ADR monitoring in Latvia

Latvia is one of the three Baltic States that re-established their independence in 1991. Although the health care system had been well developed before 1991 there were no traditions of ADR monitoring. In 1996 a State Agency of Medicines (SAM) was established. One of its functions is the authorization process of medicines and maintenance of the drug registry.

Setting up the Unit

Soon after regaining independence, the government started harmonization process of the legislation with regulations of the European Union. Pharmaceutical legislation is one of the spheres of the harmonization and covers the area of pharmacovigilance. The SAM was appointed to become the host for an ADR monitoring unit. The first activities for monitoring ADRs were started in 1999. One full time worker was engaged to start the work. The first corresponding professional knowledge was obtained at *the* Uppsala Monitoring Centre Training Course for Adverse Reactions and ADR Monitoring, held in 1999. We then designed an ADR reporting form, which was published in professional media and later on was approved by the Minister of Welfare. Since 2001 a Latvian government edict obliges doctors and pharmacists to report all serious and unexpected ADRs to the SAM.

Functions of ADR Unit

Now the ADR monitoring unit of the SAM exercises an increasing number of functions:

- It runs the ADR database where the reports by health professionals and manufacturers are registered. We acknowledge the receipt of the reports by a personal letter. If appropriate we provide feedback in the form of thematic articles in our professional journals. We have sent our ADR information to *the* UMC and during 2002 Latvia was accepted as the 66th participant in the WHO International Drug Monitoring Programme

Inese Studere at her desk

- We perform the functions of the international contact point for pharmacovigilance. For two years our delegate has participated at European Medicines Evaluation Agency Pharmacovigilance Working Party activities as an observer
- The unit contributes to the drug authorization and authorization renewal process
- Informative materials about the significance and aims of pharmacovigilance have been published in the professional and mass media. We have taken part in several initiatives for doctors and pharmacists to promote ADR reporting. To inform more doctors the SAM has sent personal letters to all certified specialists calling on them to report ADRs, explaining the reporting form and the terms of reporting
- An ADR Surveillance Advisory Board has been established at the SAM. Representatives of the university, professional societies of doctors and pharmacists as well as clinicians have been involved there. The main task of the Board is scientific assessment of the safety of drugs in case of the change of benefit/risk ratio, and advising the General Director of the SAM about the actions that should be taken to decrease the risk of adverse drug reactions. The establishment of our Advisory Board is also an attempt to unite doctors and pharmacists in the common activity of pharmacovigilance.

Still more work to be done

Our ADR Monitoring unit is working, but the number of spontaneous reports is not high. Development of effective pharmacovigilance system needs much more time. Contribution by other health authorities, professional groups and organizations and particularly from professional educational establishments is needed. We consider that in introducing a culture of ADR monitoring much depends on continuous patient educational and informative activities, which should be carried out by all the involved parties.

Inese Studere is Head, Department of Adverse Drug Monitoring in Latvia

Ghana

Pharmacovigilance in West Africa

Dr. Alex Dodoo reports

A year is a long time in pharmacovigilance. When the Ghana National Centre for Pharmacovigilance was launched on 11th June 2001, the fanfare and publicity attached to it suggested that hope had been born in West Africa. Hope in the midst of civil and political strife, which had decimated communities, upset health delivery services and impoverished whole generations. At the launching ceremony of the Ghana Centre, the Country Representative of the WHO, Dr Melville George called on the Centre to be active in all aspects of medicine use in the sub-region, since medicines, like illnesses, need no visas to cross borders.

Current position in the sub-region

West Africa (including Nigeria with its 100 million+) has over 250 million inhabitants in total. Together they speak over 200 different languages (note: languages, not dialects) but this does not pose a problem as each of the countries has an 'official' language, which essentially is the language of the colonial power. Thus one country has Portuguese as the official language, five use English and the rest speak French. Health systems and health practices vary widely, as do the channels and procedures for procuring and using medicines. Drug use patterns in the region are difficult to define. What is obvious though is the lack of access to conventional medicines. At least 50% of the inhabitants of this region have no access to orthodox healthcare and rely on traditional medicines. Where orthodox health facilities exist, their activities are challenged by several difficulties. There is the low remuneration of serving health workers, and the consequent brain drain of highly qualified health professionals to Europe and the Americas to seek greener pastures. In addition, lack of facilities and irregular and unpredictable supply of pharmaceuticals are major problems. With such challenges and threats, it is often easy to give up hope. But West Africa, like all of Africa, is full of paradoxes. Paradoxes of hope in the midst of despair, prosperity in the midst of poverty, excellence in the midst of mediocrity, and health in the midst of illness.

The Ghana National Centre became a full member of the WHO Programme for International Drug Monitoring in December 2001. By this admission, Ghana gained the singular honour of being the only country in the sub-region to belong to the WHO Programme. There is no other country in the sub-region in the Programme – either as associate members or full members.

from left to right Dr Alex Dodoo, Co-ordinator, National Centre for Pharmacovigilance, Ghana, Dr Jeremy Labadie, Regional Officer, LAREB, Dr Kees van Grootheest, Director, LAREB, Dr Sackey, Head of Disease Control Unit, Ministry of Health, Ghana

Challenges or Opportunities?

The spontaneous reporting system in Ghana is currently going well. Reports have been trickling in and there has been excellent acceptance of the programme by prescribers, dispensers and the general public. Invitations to deliver lectures on the safety of medicines are regularly received from hospitals and from churches. The message of drug safety is thus preached to both professionals, lay persons and the media. Pharmacovigilance in the sub-region is different. It has to be different. It is involved not only in spontaneous-reporting and signal generation. It has to deal with product quality, treatment failure, and rational use of drugs. It is also concerned with interactions between allopathic and herbal medicines and interactions between traditional medicine practices and orthodox medicine. This wider remit provides huge opportunities and these are being systematically exploited by the Ghana Centre, for the benefit of the sub-region.

Currently, the Ghana Centre is actively influencing its neighbours to join the WHO Programme. La Cote d'Ivoire has started a system for drug safety monitoring, and sent officers to the last ISoP Annual Meeting in Tunis. Nigeria has made overtures to *the* UMC. Ghana intends to bring together all these fledgling initiatives into something concrete by organizing a West African regional workshop on pharmacovigilance in November 2002.

Pharmacovigilance in West Africa is certainly still in its infancy but the challenges of medicine in the sub-region and the opportunities they afford mean that the sub-region is likely to see the most active and exciting initiatives in pharmacovigilance in the very near future.

Training workshop on Adverse Events Following Immunization

An intensive training workshop on Adverse Events Following Immunization (AEFI) was held in Kumasi, Ghana from 2nd – 5th June 2002. Dr Kees van Grootheest and Dr Jerry Labadie of the Netherlands Pharmacovigilance Foundation LAREB were resource persons for the workshop – a sign of increasing collaboration among member countries of the WHO Programme. Dr Alex Dodoo also gave lectures. The workshop brought together over 50 staff working in public health, reproductive and child health, disease control and health education from all ten regions of Ghana.

The programme was extremely successful and participants agreed to incorporate AEFI monitoring into the national Extended Programme on Immunization (EPI). The format of reporting forms for reporting AEFI under the EPI was agreed upon though some practitioners are allowed to continue to use the general ADR forms for AEFIs.

Visitors who attended the opening ceremony or the programme itself included Mr E K Agyarko, Chief Executive of the Food and Drugs Board, Dr Appiah Denkyira, Ashanti Regional Director of Health Services and Dr Ahadzi, Director of the National Surveillance Unit. Dr S Sackey, Head of Disease Control, Ghana Ministry of Health was the workshop moderator, ably assisted by Dr Mercy Ahun, Head of the EPI.

Zambia

We have made some progress here in our effort to start some ADR activities writes *Oscar Simooya*. The Director General of Health in Zambia has responded to my letter of intention and acknowledged the urgent need for Zambia to participate in the global monitoring of the adverse effects of drugs. My application was forwarded to the Pharmacy Board who have the mandate to initiate the programme. I had the chance to meet with the Registrar of the Pharmacy Board who expressed delight at my interest in starting a programme in Zambia. She regretted that there was as yet no post-marketing surveillance in Zambia and looked forward to us being involved in the WHO programme. The proposal has since been sent to USAID who are the major funders of the health sector in Zambia. It is hoped that funding for our activities can be mobilised from this source. I will be checking again with the Board soon on this important issue and keep you informed on our progress in Zambia.

Dr Oscar O Simooya
Copperbelt University Health Services

Uganda

Dr Winnie Tumwikirize from Makerere University, Uganda visited *the* UMC on 24 May, 2002. Dr Tumwikirize is embarking on an ambitious project to set up a Drug Information Service in Uganda and to monitor whether this intervention may decrease the burden of adverse drug reactions in the serviced hospitals. The rationale is that most adverse drug reactions are being caused by irrational drug use. If a Drug Information Service can have a solid impact to improve drug use, it should be possible to measure a decreased frequency of adverse reactions among hospitalized patients. Dr Tumwikirize's project is registered for a PhD in Clinical Pharmacology with the Makerere University in Kampala and the Karolinska Institute in Stockholm, Sweden.

Dr Winnie Tumwikirize (right) with Malin Nord at the UMC

Ethiopia

The Drug Administration and Control Authority (DACA) embarked on a restructuring programme two years ago and has moved into a new office building. Now they are settled in they have turned their attention to continuing the process of establishing an ADR monitoring system in Ethiopia. A division responsible for handling ADRs matters has been formed within the organizational structure of DACA (headed by a general manager Mr Haileselassie Bihon). This division falls under the Planning and Drug Information Department, Drug Administration and Control Authority, whose head is Abraham Gebregiorgis.

In May, an orientation programme was given to staff of the Drug Information and Registration departments. The programme covered:

- what pharmacovigilance is, and why ADRs monitoring is important and relevant to the daily medical practice
- initiatives and activities undertaken so far;
- sources of information
- the need to communicate with *the* UMC.

This will help them to continue with their professional development.

Canada

Health Canada Santé Canada

The Health Products and Food Branch of Health Canada/Santé Canada have announced the formation of a new body responsible for post-marketing surveillance: Marketed Health Products Directorate. The activities of this Directorate include:

- monitoring and collecting adverse reaction and medication incident data
- reviewing marketed health product safety data
- conducting risk/benefit assessments
- communicating product-related risks to health professionals and the public
- overview of regulatory advertising activities
- active surveillance and drug effectiveness projects.

The initial workforce of this Directorate will be 35 scientific staff with 15 support staff; the acting Director General is Dr Christopher Turner.

The contacts are as follows:
Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Room D-162, 1st Floor, Finance Building
Tunney's Pasture, AL 0201C1
Ottawa, Ontario K1A 1B9
tel: +1 613 954 6522
fax: +1 613 952 7738
e-mail: cadrmp@hc-sc.gc.ca
web: http://www.hc-sc.gc.ca

Bangladesh

The Directorate of Drug Administration (DDA) under the Ministry of Health and Family Welfare in Bangladesh has just published its first National Formulary. The formulary contains a section on 'Adverse Drug Reactions Monitoring' by Dr A A Salim Barami, (who sent in this report). In regard to safety and efficacy of drugs particularly those concerning ADRs in Bangladesh, much still remains to be done, due to lack of a systematic mechanism of monitoring.

Under the guidance of WHO, a cell has been established in Directorate of Drug Administration (DDA) in 1996. Initially the cell circulated posters, bearing awareness slogans of drug use throughout the country, organised awareness meetings among chemists in different areas and also published awareness instructions in the daily newspapers and broadcasted these awareness slogans on Radio Bangladesh. The cell is trying to introduce a systematic mechanism for ADR monitoring program in Bangladesh for collection, analysis and compilation of ADRs which will be spontaneously reported by the medical and pharmaceutical professionals.

The Ministry of Health and Family Welfare formed a ten member ADR Advisory Committee on 6 July 1997 to evaluate, analyse and make recommendations for solving problems of medicinal hazards due to ADRs. From 2000, the DDA organised ADR monitoring workshops/ meetings in five Medical Colleges and Hospitals of the country and distributed printed ADR reporting forms for spontaneous reports. A blue reporting card is bound in the back of the Formulary, or available from Dr A A Salim Barami, Superintendent of Drug Directorate of Drug Administration, 105-106 Motijheel C-A, Dhaka, Bangladesh (drugs@bdonline.com)

Dr Barami also reports that the DDA has a new Director, Professor Abdul Gani, who is taking a keen interest in ADR monitoring in Bangladesh. Who knows, this may lead to application for membership of the International Programme?

Networking in Malaysia

At the invitation of Dr Mohammed Zin Che Awang, the Pharmaceutical Services Division of the Ministry of Health in Malaysia organised a major conference for 50 Drug Information Pharmacists from all regions of Malaysia from 20-22 May in Subang Jaya, Kuala Lumpur. The Chair of the meeting was Mr Hj Mohammed Hatta Ahmad.

The objectives of the meeting were:

- To provide an understanding of local and global perspectives of drug safety monitoring, its impact and implications
- To explore methods and programs to expand and improve drug safety monitoring in Malaysia in general and hospitals in particular
- To introduce the concept of a virtual drug information networking service

Helena Fucik from *the* UMC was among the Faculty and gave four lectures on 'The Need for Pharmacovigilnace', 'The WHO International Programme', 'The decentralised model', and 'Sources of ADR information'.

Group at Malaysian training meeting: Mr Wong, Mr Normal Sharif, Dr Lian, Mrs Hasiah, Dr Irma Makalinao, Ms Helena Fucik, Mr Mohd Zin, Mrs Hasnah, Mrs Abida, Mrs Norlina, Dr Rahmat, Mr Mohd Hatta

The conference was very successful in promoting the vision of networking with the Drug Information Centres of regional hospitals in Malaysia, for the benefit of improved ADR reporting.

After the conference, Helena Fucik visited the Malaysian National Centre and held discussions with Abida Haq of the National Pharmaceutical Control Bureau. Discussions covered reporting to the WHO database and the monitoring of traditional medicines in Malaysia.

7th International UMC training course in Australia

Details are now available about the training course 'Pharmacovigilance – The Study of Adverse Drug Reactions', to be held from 4-15 November 2002 in Canberra, Australia.

The course is for health care professionals who have recently become engaged in the practical operation of programmes for spontaneous adverse reaction reporting in a hospital, regulatory or industry setting.

Theoretical and practical aspects of adverse drug reactions and pharmacovigilance are covered. Theoretical parts include lectures, group discussions and poster presentations.; practical sessions include recording of case information and computerised retrieval of information from the database of the WHO Drug Monitoring Programme.

The course language will be English; *the* UMC is running it in collaboration with the Therapeutic Goods Administration, Australia – the first time the course has been held away from Uppsala.
For a full course programme and application form, please apply to:

Mrs Anneli Lennartsson
the Uppsala Monitoring Centre
Stora Torget 3
S 753-20 Uppsala
Sweden

Fax +46 18 65 60 80
e-mail info@who-umc.org
or download from the 'Promotion and Training' section on *the* UMC website.

25th Annual Meeting of National Centres: Agenda agreed

The silver jubilee meeting of the WHO Drug Monitoring Programme will take place at the Royal Tropical Institute, Amsterdam, the Netherlands 14 - 16 October 2002.

Main points of the agenda will be:

1. Combining toxicovigilance with pharmacovigilance
2. Pharmacovigilance and the Essential Drugs Concept
3. Pharmacovigilance and public health
4. Items of international significance (MedDRA, CIOMS VI, ICDRA, EU)
5. Dutch profile issues
6. Drugs of current interest
7. Development projects at the UMC
8. Follow-up from working groups at the 2001 meeting

There will also be working group sessions on monitoring of herbal medicines, vaccines and reasons for drug withdrawals.

National Centre delegates should register their participation with Dr Mary Couper at WHO, Geneva (couperm@who.int) and arrange for accommodation through the information web site www.isop2002.org

Do you understand me?

A New Zealand survey* conducted to determine the level of understanding of some common medicine-related terms found that many people do not know the meaning of words such as hypertension and decongestant. The scope of understanding varied according to ethnic group, gender and education status. Health professionals have an obligation to ensure that consumers understand the information given to them. The results of this survey illustrate how and why misunderstandings can arise in regard to health information.
Dr Pauline Norris (from the University of Otago, New Zealand) and colleagues asked people to define words such as allergic, orally, cough suppressant, antibiotic, hypertension, and decongestant. Although half of respondents gave a correct definition of the first three words above, over a third of respondents gave an incorrect definition of the last three. Over half of respondents could offer no definition of antihistamine, diuretic and decongestant.
The authors comment, "many of these medicine-related terms are frequently used on the presumption that all consumers comprehend their true meaning". This study, and others in similar vein, should inspire all working in medicine to make communications in all forms as comprehensible as possible, in order to achieve active patient participation and informed consent in treatment.

*Prescriber Update published the article 'Talking the Talk'
(http://www.medsafe.govt.nz/Profs/PUarticles/talk.hm)

THE ERICE STATEMENT ON DRUG ADVERTISING TO CONSUMERS

A group of clinical pharmacologists, physicians, pharmaceutical industry representatives, medical and general journalists, communications professionals, and consumer advocates met in Erice, Italy, on May 9-13, 2002 to discuss drug advertising to consumers.

The meeting was triggered by proposed changes to European Union legislation on the advertising of prescription medicines to the public. Its purpose was to consider the wider implications of direct-to-consumer prescription medicine advertising and its relationship to the information needs of the public and of patients, throughout the world.

Summary

Everyone agreed on the fundamental need for high quality medicines information, but participants differed in their view on advertising of prescription medicines to consumers. Some wanted to maintain the present prohibition of direct-to-consumer advertising; others would allow advertising subject to strict control by an independent, non-commercial, multi-representative statutory body, affiliated to the Regulatory Authority or the Ministry of Health. The arguments supporting each of these views are summarized below.

BACKGROUND

Relationship between promotion, advertising and information

The World Health Organization defines drug promotion as all informational and persuasive activities by manufacturers and their agents, the effect of which is to induce the prescription, supply, purchase and/or use of medicinal drugs.[1]

Advertising is one form of promotion, partial in its selection of information, usually with commercial benefit to the promoter as its sole or principal intent. It is important to distinguish these forms of communication from information that aims to educate and/or inform.

The need for good quality information

Personal health care involves choices among many possible treatments. Although the use of a prescription medicine is mediated by a health professional, patients need relevant information of good quality on benefits and harms related to the available options, presented in a way that enables them to choose appropriate treatment together with the doctor, and to manage their treatment subsequently.

The information must be scientifically valid, up-to-date and balanced. It should allow comparisons between drug and non-drug treatments, and the option of no treatment. Facts, hypotheses and conclusions should be distinguished, uncertainty acknowledged. Sources of information, and their particular bias should be identified, including all potential conflicts of interest.[2]

Education on the appropriate use of drugs, including the interpretation of safety information, is essential for the public as well as for patients. Such education requires commitment and targeted resources.

Drug information directed to the public, in whatever form, should be balanced in its account of benefits and harms. Trustworthy sources should be mandated to provide balanced information about all healthcare options in a readily accessible and understandable form. Such information should aim to support good doctor-patient interactions.

All the evidence needed to understand benefits and harms, including comparative information, must be openly available to the public. Vested interests and any other constraints on communicating parties that hinder their ability to meet this goal must be identified and understood.

Information of any kind must never damage, distort or subvert the true interest of public health, or the essential needs of individual welfare.

SHOULD DIRECT-TO-CONSUMER PRESCRIPTION DRUG ADVERTISING BE ALLOWED?

Arguments against legislative changes to allow such advertising

Medicines sold directly to the public are used for self-diagnosed conditions and can be self-prescribed, but prescription medicines require professional knowledge and understanding for safe and appropriate use.

1) Advertising and other forms of drug promotion aim to increase sales and cannot meet the criteria of quality information as described above, even when they are disease-oriented. Promotional information distorts the interaction between doctor and patient by focusing on the advertised treatment rather than on the necessary diagnostic and therapeutic decisions.

2) Experience in the United States and New Zealand has shown that direct-to-consumer advertising of prescription medicines has repeatedly misinformed the public.[3] It has increased prescribing of the advertised drugs[4], leading to unnecessary increases in drug expenditure.[5]

3) Prohibitions on prescription drug advertising to the public are consistent with the WHO Ethical Criteria for Medicinal Drug Promotion and the EU Precautionary Principle. The latter supports action, "where preliminary objective scientific evaluation indicates that there are reasonable grounds for concern about potentially dangerous effects on the environment, human, animal or plant health…".

4) These considerations lead to rejection of changes to EU pharmaceutical advertising regulations[6], as well as similar proposed changes in other countries. Liberalisation is likely to have a profound negative impact, not only in Europe but throughout the world, in reducing the appropriateness and safety of medicine use.

Arguments in favour of cautious, controlled approaches to the introduction of prescription medicine advertising:

1) The aims of commercial and non-commercial promotion can coincide. When this is the case, commercial promotion may be in the interest of public health. However, each case must be considered individually, and the motivation and biases need to be transparently described.

2) A recent review of some experience on direct to consumer advertising in the United States drew the conclusion that there was little impact on the doctor-patient relationship.[7] The data was also interpreted as suggesting a positive association between advertising and compliance with the use of a medicine, which may in turn lead to health benefits and reduced wastage.[8] These references are however preliminary and not peer reviewed.

3) Research into the impact of general ethical promotion of prescription medicines should be permitted under the following experimental conditions:

- The evaluation of positive and negative effects under strict experimental protocols
- The promotion of medicines only after sufficient patient exposure to ensure reliable knowledge of their effectiveness-harm profile
- The promotion of appropriate use
- The provision of information about the medicine which is factual, balanced and fair
- The inclusion of appropriate warnings and cautions and encouragement to patients to consult their doctor
- Before it is used all such promotional material should be reviewed by an independent, statutory body, affiliated to the Regulatory Authority or the Ministry of Health
- Clear ethical and practical guidelines should be developed by this body and strict adherence to them ensured by regular monitoring and evaluation of promotional materials.

Vittorio Bertelè, Riccardo Braglia, Achille Caputi, Ralph Edwards, Margaret Ewen, Jackie Glatter, Andrew Herxheimer, Bruce Hugman, Thomas Henry Lee, David McNamee, Barbara Mintzes, Giovanni Polimeni, Franca Porciani, Giuseppe Recchia, Jane Smith, Cinzia Tromba, Giampaolo Velo, Massimo Vergnano, Anthony Wong, Alex Wyke.

The Workshop was organized by:

- the Ettore Majorana Centre for Scientific Culture, Erice, Italy
- the Verona Reference Centre for Education and Communication within the WHO Programme for International Drug Monitoring
- the International Association for Clinical Pharmacology and Therapeutics

Further information from:
Giampaolo Velo:
gpvelo@sfm.univr.it

Ralph Edwards:
ralph.edwards@who-umc.org

[1] World Health Organization's Ethical Criteria for Medicinal Drug Promotion (1988)

[2] "A competing interest exists when professional judgment concerning a primary interest (such as patients' welfare or the validity of research) may be influenced by a secondary interest (such as financial gain or personal rivalry). It may arise for the referees of a BMJ article when they have a financial interest that may influence-probably without their knowing-their interpretation of an article."

[3] Koerner C. US FDA. Division of Drug Marketing, Advertising and Communications. The Regulation of Direct-to-Consumer Promotion of Prescription Drugs. Presentation at Health Canada Multi-Stakeholders' Consultation on Direct-to-Consumer Advertising. Aylmer, Québec. April 14, 1999; Pratt P. Assessment of Regulatory Compliance for Medicines Advertised Direct to Consumer. Medsafe. New Zealand Ministry of Health. Wellington, 2000; Bell RA, Wilkes MS, Kravitz RL. The educational value of consumer-targeted prescription drug print advertising. Journal of Family Practice 2000; 49(12): 1092-1098

[4] Mintzes et al. The influence of direct to consumer pharmaceutical advertising and patient requests on prescribing decisions: two-site cross-sectional survey. BMJ 2002;324:278-279

[5] Findlay S. Prescription Drugs and Mass Media Advertising, 2000. National Institute of Health Care Management. Washington DC: 2001. www.nihcm.org. Also see www.nihcm.org for 1999 and 2000 reports.

[6] Articles 86-88 of Community Directive 2001/83/EC. The key proposed changes are to Article 88 (2), which currently forbids all advertising of prescription medicines to the public. They include introduction of a clause allowing advertising of drugs for AIDS, diabetes and asthma, and deletion of a clause forbidding advertising of treatments to the public for a specified list of serious diseases.

[7] Aikin K. J., Division of Drug Marketing and Communication, FDA. 2002 DTC Advertising of Prescription Drugs: Preliminary Survey Results.

[8] Ostrove N., Division of Drug Marketing, Advertising and Communication, FDA. Comments on Prevention Magazine Study on the Effects of DTC (May 4, 2002)

Behind the scenes at

by Rosie Stather, Consulting Editor, *Reactions Weekly*

Reactions Weekly began back in 1980 and is produced by a dedicated editorial team in the offices of Adis International Ltd, in Auckland, New Zealand. The publication is available in a variety of formats, but the one users are most familiar with is the A4 pink newsletter. As *Reactions Weekly* is used by many of the readers of Uppsala Reports we thought it would be helpful to describe how it is put together.

Team members

The *Reactions Weekly* team consists of the Editor, Associate Editor and a Medical Writer. The team can also call upon the help of experienced freelance medical writers and there is a Consulting Editor who acts as a link between *Reactions Weekly* and Drug Safety, the Adis International review and research journal that focuses on the latest trends in pharmacovigilance, pharmacoepidemiology and benefit-risk assessment.

Marie, Rachel (sitting), Helen

Obtaining material

Content for *Reactions Weekly* comes from the systematic monitoring of over 1,600 biomedical journals. Additional material is sourced from the Internet (such as press releases, information for healthcare professionals and online publications) and from National Centre newsletters and alerts. The staff of various editorial departments scan journal articles identifying material for consideration in all of Adis's Business Intelligence and Newsletter products, including *Reactions Weekly* . This material is copied and sent to the Editor, who uses rigorous criteria to select the material that is summarised and published.

The Editor will select all case reports of adverse drug reactions (including overdoses, drug interactions and cases of abuse) for inclusion. Where the original report is a non-English paper, only first reports will be summarised in full; the remaining reports are included as citations only. For case reports presented as abstracts (in meeting proceedings/supplements), only first reports are included. Other material (clinical studies, incidence studies, etc) is selected on the basis of its importance to our readers ('newsworthiness').

Classification

For easy reader access, material is assigned to one of the following sections: *Pharmacovigilance and Regulatory News* (includes news from National Centre newsletters and alerts, information from 'Dear Health Professional' letters, etc); *Current Issues and Opinions* (from media releases, journal letter sections and review articles, etc); *Adverse Drug Reaction* Research (clinical studies, postmarketing surveillance studies, toxicology studies, etc); and *Adverse Reaction Case Reports*.

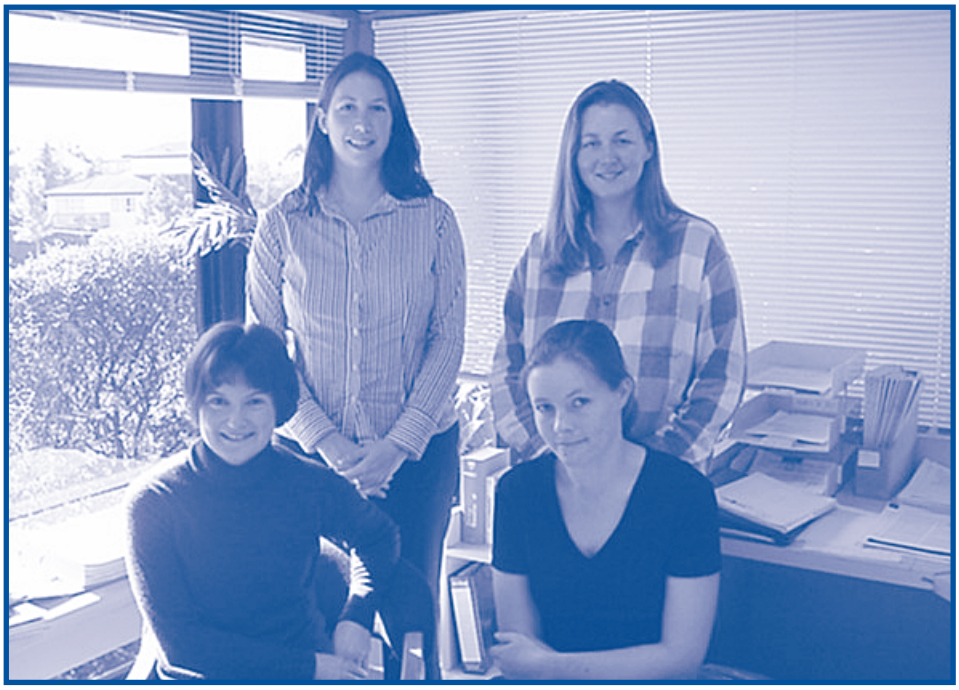
The writing

The newsletters at Adis are produced using a customised editorial tool. As each summary is written it is stored on a database and is identified by a unique number (seen in print after the citation details of the source article). The writer assigns indexing terms ('descriptors') to each summary allowing it to be retrieved from the database using standard search terms. After editing and proofing the summary is then 'released for publication'. It is then available through a number of

Reactions Weekly

online delivery channels and is ready to be assigned to a print issue.

For case reports the writer has a number of assessments to make. The case must be classified as serious or not; we currently use the US Food and Drug Administration MedWatch definition and this is published in each issue. The writer also verifies if a case report is the first published case report of the adverse effect/drug combination. This is done by searching the database of *Reactions Weekly* summaries and through a search of Medline (including PreMedline to ensure that the search is as comprehensive as possible). When a case report is confirmed as being a first literature report, the writer contacts *the* UMC with details of the report. *the* UMC then does a search of their database for reports of the same adverse effect/drug combination and this information is included in the published summary. For each case report the writer includes the following information (or highlights its absence): the country in which the case occurred; patient age and gender; drug name and daily dosage; time from commencement of the drug to the appearance of the reaction; a description of the reaction; and patient outcome. Thus, the case report summaries in *Reactions Weekly* provide the information necessary for cases presented as line listings for inclusion in Periodic Safety Update Reports. Case report summaries also include information, where provided, on treatment of the adverse effect, causality, concomitant medications and dechallenge/rechallenge.



back row: left - Reactions Editor: Rachel McLeay; right – Reactions Associate Editor: Helen Robinson front row: left - Reactions Consulting Editor: Rosie Stather; right - Reactions Medical Writer: Marie Le Fevre

Getting it into print

Each week, the print version of *Reactions Weekly* is put together. The process currently starts on Tuesday lunchtime with 'pasteup'. Material for inclusion in the week's issue is selected from that 'released for publication' (some copy might be 'overset' to the following week). Layout is done using a page makeup system and the pages are proofed, contents are generated and the whole issue is complete and sent to print by early afternoon on Wednesday. Shortly, the current page layout system will be replaced by a more automated batch composition system, thus streamlining production of the print product.

The issue is printed in Auckland using a docutech machine on the Wednesday night and is dispatched from the office by air on Thursday night to reach subscribers approximately 48 hours later.

Reactions Weekly is published weekly, 50 times a year with 2 quarterly indexes, a 6-monthly index and an annual cumulated index. It is available online through Dialog and DataStar and from 2002, with the aim of increasing timeliness, via a new service, PharmaNewsFeed, which pushes selected material direct to a subscriber's desktop via e-mail. It is also available on the Internet on Ingenta and on CD-ROM from SilverPlatter. Shortly, ***Reactions Weekly*** will also be available via Databases@Ovid.

the UPPSALA MONITORING CENTRE

News *from the* Uppsala

Drug Dictionary Developments

As a reference for all those working in pharmacology and drug safety, the WHO Drug Dictionary (WHO-DD) has been the international de facto standard for over 20 years. Drugs have been entered into the WHO Adverse Reactions Database since 1968 as part of the WHO Programme of International Drug Monitoring. Drugs recorded are those which have occurred in adverse reaction reports, but as all drugs taken by patients are included (whether or not they are suspected of having caused the reaction), the database covers a majority of drugs used in countries participating in the Programme. The data is taken from official data from drug regulators, national drug compendia or other trustworthy sources. An increasing number of DD entries are entered on request by companies and regulators when products are launched on the market, which means that the entries get into the dictionary faster. The WHO-DD is a vital tool for coding drug safety information, both pre and post marketing. However, the Drug Dictionary does not remain static; it has evolved to meet the needs of users: National Centres, pharmaceutical manufacturers, pharmacists and regulatory authorities. A vast majority of the top 100 pharmaceutical companies, major international CROs and regulatory authorities use the tool on a daily basis.

43,659 different drug trade names
9,098 chemical substances
2,400 new drug names/year
(December 2001)

Latest features of the WHO Drug dictionary

The main feature of the latest version of the database is its structure. It is now possible to register more country-specific information, including the name of the market authorisation holder as well as the manufacturer, and the pharmaceutical forms and strengths available in each country. The latest format also allows us to enter name-form-strength information for each product.
In the Drug Dictionary each entry has a unique ID field, separate from the drug record number field. If a product is reclassified with different ingredients, the ID stays the same; only the record number field (which is not part of the key) is changed. This greatly assists version handling and tracking.

New features that were introduced at the last version include:

- New data fields
- Dosage form and Strength
- Product Type. Medicinal/Herbal etc
- Market Authorisation Holder Company responsible for marketing
- Country
- Date of last change
- Full integration with the Anatomical Therapeutic Chemical classification (ATC)

Herbals

In recent years, *the* UMC has done extensive work in the area of classification of herbal substances. The WHO-DD already contains information on commonly used herbals, but the coverage of traditional medicines and herbal substances will improve considerably both in terms of quantity and quality in the new database.

Classification

Anatomical Therapeutic Chemical (ATC) classification is an integrated part of the WHO-DD. The ATC classification is a hierarchical classification which facilitates browsing in the dictionary and, more importantly, aggregation of statistical data for improved analysis of captured data. *the* UMC continues to collaborate closely with the ATC centre in Oslo, Norway. All drugs in WHO-DD are assigned therapeutic group codes according to the ATC classification. Products are coded with ATC codes approved for their *generic group* (Preferred Name). In addition to this, the new format makes it possible for us to code each *product* with the ATC code of its most common use. This allows a more flexible analysis and comparison of the drugs using the ATC classification.

Product grouping

A new feature in the current WHO-DD is the Product Group. Often a product is manufactured by the same company but marketed under different trade names in different countries. Grouping of these trade names is possible in the Product Group field, which consists of all products with the same ingredient(s) and the same manufacturer.

Medicinal Product and Pharmaceutical Product

The WHO-DD format allows for the use of a two-level structure of the product information. Some pharmaceutical products contain more than one dosage form, or more than one type of the same dosage form. For example: a suppository packaged together with a cream; oral contraceptives with three different types of tablets. The two level structure makes it possible to record both the Medicinal Product – the product name, manufacturer etc, and the Pharmaceutical Products with their individual ingredients.

Transition and growth

The WHO Drug Dictionary is backward compatible, that is, the new database retains the current fields which are mapped to the new structure and, particularly, the current drug record number system is retained in the new database structure.

There is currently a transition period where the previous version of WHO-DD is fully superseded by this more detailed version.

The Drug Dictionary grows at the rate of more than 2,000 entries each year. *the* UMC also provides an on-line tutorial/course on how to use the Drug Dictionary and a program 'DD History' which allows users trace all changes that have been made in the Drug Dictionary, from the first quarter of 1992.

Monitoring Centre

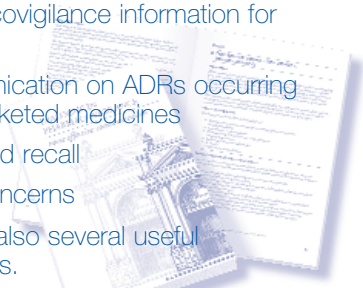
Dialogue in Pharmacovigilance *more effective communication*

New publication

the UMC is publishing a collection of writings about communication entitled **Dialogue in Pharmacovigilance *more effective communication.*** This 140-page book contains a wealth of material to anyone interested in how to improve the current state of communications in pharmacovigilance. The sections are:

- Principles in good communications in pharmacovigilance: the major issues
- Description of players – their activities, interests and needs
- The role of the mass media in public drug education
- Academic journals
- General public drug education
- Professional education
- Prescribing information
- Pharmacovigilance information for patients
- Communication on ADRs occurring with marketed medicines
- Crisis and recall
- Legal concerns

There are also several useful appendices.



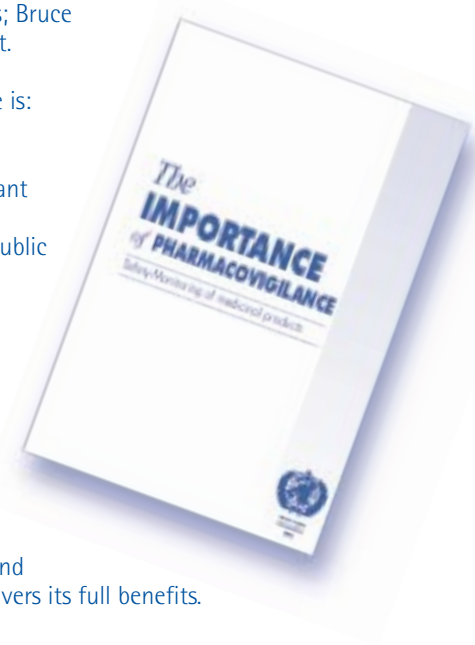
The monograph authors express the wish that this work can be part of the general debate on these issues, and welcome comments as a start of future activity.

Dialogue in Pharmacovigilance *more effective communication* may be obtained from *the* UMC for US$130 including postage (30% discount for non commercial organisations).

Payment should be sent to:
the Uppsala Monitoring Centre, Stora Torget 3, S-753 20 Uppsala, Sweden

The IMPORTANCE *of* PHARMACOVIGILANCE

This text was developed by WHO in consultation with the WHO Collaborating Centre for International Drug Monitoring and the National Centres participating in the WHO Programme for International Drug Monitoring. The draft was circulated and discussed at two informal consultations with international experts in pharmacovigilance. The WHO Department of Essential Drugs and Medicines in Geneva hosted these consultations. Dr U Mehta, University of Cape Town, Cape Town, South Africa, drafted the text and acted as rapporteur at the consultations; Bruce Hugman did invaluable work in editing the document.



The purpose of The Importance of Pharmacovigilance 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.

Availability details:
The Importance of Pharmacovigilance is being sent to all National Centres. Copies may be obtained from *the* UMC; please apply to the address on the back of Uppsala Reports.

New publications from *the* UMC

An article in which Andy Bate and Marie Lindquist are co-authors has been published in Pharmacoepidemiology & Drug Safely together with colleagues in the Netherlands.

A comparison of measures of disproportionality for signal detection in spontaneous reporting systems for adverse drug reactions
Eugéne P van Puijenbroek, Andrew Bate, Hubert G M Leufkens, Marie Lindquist, Roland Orre, Antoine C G Egberts Pharmacoepidemiology and Drug Safety 2002; Volume 11(1) pp 3-10.

and the following is now in press:

Bate A, Lindquist M, Orre R, Edwards IR, Meyboom RHB Data mining analyses of pharmacovigilance signals in relation to relevant comparison drugs. European Journal of Clinical Pharmacology.

Product and Marketing News

from Mats Persson

Trying to keep in touch...

We hope that our customers and contacts have received the plain colour cards sent out over the last couple of months. We do need to know if your address and other contact details are Right or Wrong.

If you have already replied to the card, you'll have received another acknowledgement card from us – we are very grateful for your help.

And for anyone who is just finding out about the services *the* UMC can offer, the yellow 'One Step Ahead' card tells you we are ready to start sending up-to-date information on our products and services.

We need to keep our database in top condition, so do let us know if you haven't received post you are expecting from us, or if there is anything wrong with our labels.

'No drug is 100% safe for all people in all circumstances'

The issues and questions surrounding the safety of drugs are the subject of *the* UMC's recent publication Viewpoint, where they are discussed in an accessible way for both general and specialist readers.

In an attempt to attract a wider audience to the subject, *the* UMC is now preparing slightly abridged versions in other languages, to be available this autumn. If you would like more information on non-English versions, please contact us at info@who-umc.org.

The full English language version of Viewpoint is available in Adobe Acrobat format and can be downloaded from the UMC website. However, the file is large (3.1 Mb) and may take a long time to download. If you would prefer a printed copy, or wish to place a bulk order, please contact us.

A summary of the Viewpoint content is also available in Adobe Acrobat format from our website. This summary may be used without any restrictions by media and other interested parties.

Maria moves to new desk

Since April 2002, Maria Bergström has changed her role within *the* UMC. She is now working as Sales Assistant in the Sales and Marketing Department, executing orders, providing general assistance to Inger Forsell, as well as being involved in the marketing campaigns.

Updates

1st Quarter 2002 Update

The new versions of the computerised WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 1st quarter of 2002 are now available. These were sent to subscribers during May 2002.

If you are a subscriber to either WHO DD or WHO-ART and have not yet received the update, please contact Inger Forsell (inger.forsell@who-umc.org).

Data files for the 2nd quarter of 2002 should be available by August 2002.

ADRespherics

If you are interested in starting using or subscribing to the commercial version of the BCPNN - ADRespherics please contact Mats Persson (mats.persson@who-umc.org) to set up a telephone conference to discuss more about ADRespherics and what it could do for you and your organisation. You can find out more at http://www.who-umc.org/adrespherics/default.htm (or via the UMC home page).

Come and meet us!

UMC staff will be attending the following conferences in the next few months:

- 18th ISPE Annual Meeting, Edinburgh, Scotland, 17-21 August
- The Management of Adverse Drug Experiences, New Orleans, USA, 6-9 October

We look forward to meeting many of you at these events; if you wish to arrange a meeting with us at one of them, please contact Mats Persson.

Forthcoming Courses and Conferences

Date	Title	Place	Organiser / Contact
19-20 Sept 2002	Adverse Event Reporting and Pharmacovigilance	London, UK	Contact: International Pharmaceutical Training Tel +44 (0)20 7915 5055 Fax +44 7915 5056 registration@iir-conferences.com
19-20 Sept 2002	Medical Aspects of Drug Safety and Pharmacovigilance	London, UK	Mangement Forum Fax +44 (0) 1483 536 424 registrations@management-forum.co.uk
2-3 Oct 2002	"Interpretation and Application of Pharmacoepidemiological Data"	Southampton, UK	Contact: Jan Phillips, Drug Safety Research Unit Tel 44 (0)23 8040 8621 Email: jan.phillips@dsru.org www.dsru.org
16-19 Oct 2002	ISoP Annual Meeting	Amsterdam, The Netherlands	Secretariat: Tel +31 73 6469 704 Fax +31 73 6426 136 www.isop2002.org
20-23 Oct 2002	New Safe Medicines Faster (EUFEPS)	Stockholm, Sweden	Contact: Congrex Sweden AB Tel +46 8 4596600 Fax +46 8 6619125 eufeps2002@congrex.se
21-22 Oct 2002	Medical Approach in Diagnosis and Management of ADRs Training Course	Hotel Sofitel Paris Forum Paris, France	DIA European Office Tel +41 61 386 9393 Fax +41 61 386 9390 e-mail: diaeurope@diaeurope.org
25-26 Oct 2002	III Jornadas de Farmacovigilancia 'La Farmacovigilancia en al sociedad de la información'.	Toledo, Spain	Centro de Farmacovigilancia de Castilla La-Mancha, Direccion General de Salud Publica y Participación Fax + 34 925 26 71 58 e-mail: farmacovigilancia@jccm.es web: http://www.jccm.es
30 Oct–1 Nov 2002	Drug Safety Surveillance & Epidemiology Training Course	Hyatt Regency Penn's Landing Philadelphia, PA, USA	Contact: Training Administrator Tel +1 215 628 2288
3-5 Nov 2002	5th European Congress "Workshop on Case Narrative Writing"	Rotterdam, The Netherlands	ISPOR Phone: (609) 219-0773 Fax: (609) 219-0774
5-6 Nov 2002	Electronic submission of individual case safety reports in the EU	London, UK	DIA European Office Tel +41 61 386 9393 Fax +41 61 386 9390 e-mail: diaeurope@diaeurope.org

Sally joins the team

Sally Eriksson has recently joined *the* UMC. As Team Support, she is responsible for the Centre's telephone services, mailings and general correspondence, along with assistance with maintenance of premises and office equipment and meeting arrangements. Sally was born in North Carolina, USA and brought up in New York City. She has previously worked as an IT- instructor, School Secretary, and Airline reservationist. As someone with many outside interests - photography, gardening, music, handcrafts – she is already organising social activities at *the* UMC. Welcome, Sally.

Help around the office

One member of the Uppsala team who has never been properly introduced to the outside world is Simson. Many visitors to the Centre will have met him over the years and we feel now is the opportunity to introduce him to the wider audience of Uppsala Reports readers.

How long have you been at the UMC?
Well, I first started at the Centre on 1st March 1998. It was quite a surprise at first to be in this environment, but I settled in fairly quickly. I work most closely with Inger, of course, but also Maria and Daniel.

You must have seen many changes in your time?
There have been many developments, most of them extremely welcome. There was the closer relationship with WHO Headquarters, which is so important for the flourishing of the International Programme. My role continues to develop with BCPNN (Barking Canine Provokes Noxious Notification) which has been such a major advance in the generation of signals. However, I spend most of my time in the Sales and Marketing department.

How do you see your role developing, particularly in view of new member countries in the WHO Programme?
I think the demand *for* UMC services and products will continue, so I am sure I will still be needed around the place! I'd like to see the WHO Programme have a higher profile, and I think with the wealth of new outreach activities, this can be achieved. Internally, I will retain responsibility for welcoming guests and for security, checking visitors, and so on.

Where do you stand on the MedDRA / WHO-ART debate?
Well, for a start that subject needs a whole article to itself. However, it's also one area where I think I'd prefer to leave it to the experts. There are strong feelings on both sides of the argument, but from our perspective WHO-ART remains an essential tool for many National Centres.

Do you find meetings stimulating at the UMC?
I do my best to provide some light relief at meetings when things get heavy – you could say I have a nose for a laugh. People are very generous with sharing of biscuits, but they also know I can't resist a carrot. You might say it was a 'carrot-and-stick approach' without the stick (laughs).

What do you think of the premises?
I must say I preferred the previous place close to the forest - there were many more trees around.

the Uppsala Team

Communications information

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

Ralph Edwards
Professor in Medicine, Director

Sten Olsson
Head of External Affairs

Cecilia Biriell
Head of Internal Affairs

Marie Lindquist
Head of Data Management & Research, General Manager

Mats Persson
Head of Marketing & Sales, Business Development Manager

Mohamed Farah
Programme Leader, Traditional Medicines

Malin Ståhl
Programme Leader, Signal Detection

Andrew Bate
Programme Leader, Signal Research Methodology

Helena Fucik
Data Processing Co-ordinator

Monica Pettersson
Programme Leader, Signal Analysis

Malin Nord
Programme leader, Database Products

William Frempong
Data Management

Annica Lundström
Data Management

Erica Walette
Programme Leader, Database Services

Anna-Karin Flygare
Medical Terminologies

Jenny Ericsson
Data Management

Jessica Nilsson
Data Management

Anne Kiuru
Signal Detection & Analysis

Helena Sjöström
Data Management

Daniel von Sydow
Project Co-ordinator

Sven Purbe
Data Management & Quality Assurance Co-ordinator

Anna Lindquist
Team Support, Web Editor

Inger Forsell
Sales & Customer Relations Executive

Maria Bergström
Team Support, Internal Affairs & Sales Assistant

Anneli Lennartsson
Team Support, Internal Affairs

Sally Eriksson
Team Support

Geoffrey Bowring
External Affairs Co-ordinator