

UMC R43

UPPSALA REPORTS October 2008

For everyone concerned with the issues of pharmacovigilance

UMC course follow-up

Research presentations

New publications

Training in Western Pacific, Africa and Latin America

30th

UMC
Anniversary
Edition



DIRECTOR'S ANNIVERSARY MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring
Centre

Autumn is here in Sweden, the harvest almost in and the deciduous trees turning to yellow, gold, scarlet and brown. Soon the days will be short and the leaves: gone.

It was to have been the year of my retirement – my autumn, even winter, in *the UMC* but against all the odds, no new appointment has been made and I have been asked to continue for a further year. It does however prompt me to consider my 'harvest'.

When I came to Uppsala, *the UMC* had four staff, and very quickly I was confronted by a publicly-stated threat that no signals were found out of all the data collected¹. Our *Signal* and other publications gave easy demonstration that it was not so, and over the years we have proven the worth of *the UMC* in solid and continuous development and improvement in all areas. I am inordinately proud of the achievements of *the UMC* and our colleagues throughout the world in the WHO Programme; but I am not complacent!

What have we achieved by our 30th Anniversary year?

At the start, *the UMC's* only income was from the Swedish Government, and was on the basis of an Agreement with WHO which pledged funding '...at the 1977 level of operations'. This funding stopped in 2000 when it was found that *the UMC* could earn money by sales of the WHO Drug Dictionary.

Our main purpose has always been to aid national pharmacovigilance centres in the WHO Programme. Extraordinarily, this WHO Programme is funded almost entirely via the work of our sales of goods and services which are neutral to our core role in drug safety: finding signals. Moreover, we now provide support and services to over one hundred national centres either as full or associate members of the WHO Programme, with about 60 staff in Uppsala.

Over and above our support for the Programme, we are also justifiably proud of our data management and quality, our research track record and our other leading developmental roles. We have first publications in data mining, standards for signals, benefit/risk assessments, data quality, and the importance of communication. We have also been analysing longitudinal health care records for new signals for about five years, and have published on this topic².

I am immodest enough to say that I have seen, and foreseen, most of the faults and deficits in pharmacovigilance as well as the many opportunities for exciting improvements. Only by true independence of thought, could I hope to fulfil *the UMC's* global role in suggesting and supporting progress for all stakeholders, and to initiate the work mentioned in the previous paragraph. Yes, I can also claim some success in having an expanding, vibrant, friendly, motivated group here in Uppsala and similar colleagues throughout the world, making sure that we stand independent of regulatory and other pressures, and staying objective in our science and analyses.

Having said we have led many useful changes in pharmacovigilance, I have failed to achieve my main goal so far: our harvest of success in preventing or limiting damage to patients has yet to be gathered in. We do all kinds of studies and make changes, but we have no real evidence that we do any good to the patient. We talk about iatrogenic disease due to drugs as being a huge health burden, about half of it preventable. But the main audit on the pharmaceutical industry is the provision of their case safety reports, in a timely manner, to regulators – and we accept just the fact that they do it as some sign of success. We count drugs withdrawn for safety reasons as success; that we have much improved the 'Summary of product characteristics' – SPCs and 'Package insert leaflets' – PILs, as success; and indeed that we have a safety industry as success.

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There is little or no information about reducing the iatrogenic disease burden, and this is true globally. We must be responsible for the whole chain of events from signal to improved, safer therapy: we must make this part of our responsibility, not somebody else's. If we don't, nothing will happen.

In this Anniversary Year, this last year of my unexpected extension, and afterwards as a consultant, I intend to find out what really happens to patients and find out how we improve their chances of benefit to them and mitigate harm. That will indeed be a golden harvest.

1. Edwards IR. Drug safety monitoring in Europe. *Lancet*, 1992, 340(8831): 1355-6.
2. Norén GN, Bate A, Hopstadius J, Star K, and Edwards IR. Temporal pattern discovery for trends and transient effects: its application to patient records. In: *ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, 2008. Las Vegas, Nevada, USA: KDD '08, ACM.



The Uppsala Monitoring Centre (*the* UMC) is the field-name of the WHO Collaborating Centre for International Drug Monitoring, responsible for the management of the WHO Programme for International Drug Monitoring.

An independent centre of scientific excellence, *the* UMC offers products and services, derived from the WHO database of Adverse Drug Reactions (ADRs) reported from member countries of the WHO Programme.

With an independent and global perspective on drug safety, *the* UMC provides resources for regulatory agencies, health professionals, researchers and the pharmaceutical industry.

The UMC's important worldwide work is financed solely by the organisation itself, without support from WHO, the Swedish Government, member countries of the WHO Programme or any grant-making body.

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You go for a training course somewhere, listen to some nice speakers, meet colleagues from different places with problems – some similar, some different – perhaps make some good contacts and even new friendships. Then you return back to the office...

That's usually when the difficult part starts. Assimilating all the information you learnt, trying to square your changed perspectives with others who didn't go on the course, confronting day-to-day obstacles of resources, bureaucracy, communication and just keeping on top of your ordinary work-load.

We thought readers might be interested to hear some of the feed-back from participants in the 2007 Uppsala pharmacovigilance training course. After a year, all those who attended were asked to let us know how they were getting on; we are focussing here on the progress participants from Indonesia, Mexico and Nigeria made when the course was over.

Indonesia reports

Recent pharmacovigilance activities in Indonesia

Siti Asfijah Abdoellah

Indonesia is a big country in South East Asia, both in terms of population and land area, with more than 200 million people and 17,000 islands. These conditions are challenging for the National Agency of Drug and Food Control (NADFC), the Republic of Indonesia's drug regulatory authority. Although in place for many years, the importance of adverse reaction monitoring remains questioned, with a low reporting rate of ADRs, both in quantity and quality.

When I began in pharmacovigilance activities in September 2006, it was clear that much work and efforts were needed to increase the quality and quantity of ADR Reports. I was really pleased when I got the opportunity to attend *the* UMC two-week course last year. On completion of the course, we were all asked to draw up action plans.

Recognising that in Indonesia we rely on voluntary spontaneous reporting by health professionals, to increase the reporting rate we have to create a culture of ADR reporting. To do that, we have to make health professionals aware of and understand the pharmacovigilance programme in Indonesia. NADFC, as National Centre has responsibility to communicate with them. We therefore have a rolling programme of workshops for health professionals, especially in some large hospitals. In 2008, we have conducted a workshop in June in Dr Soetomo Hospital in Surabaya, East Java, involving physicians, specialists, pharmacists and nurses; and then in August, we conducted a similar workshop in Jogjakarta Province, in collaboration with Department of Pharmacology and Toxicology, Faculty of Medicine, University of Gajah Mada and Dr Sardjito Hospital. Next, we are planning a similar workshop in Dr Hasan Sadikin Hospital in Bandung, West Java.

Alongside workshops or seminars in hospitals, we encourage health professionals to report by sending them the Indonesian ADR Bulletin twice a year with blank yellow ADR reporting forms in it. For every report submitted, feedback or an acknowledgement will be sent back to the reporter. The bulletin consists of new information on drug safety, regulatory actions, labelling updates (if any) and also a sample of reported ADRs cases.

We cover a large area; Indonesia has 33 provinces and NADFC has 30 regional offices to function as NADFC representatives. Although our pharmacovigilance system is centralized, the regional offices in

provinces are important, especially to provide information for health professionals in remote areas. Starting in 2005, the national centre has continuously run workshops on the programme for regional officers: I went to Palu in Sulawesi (Celebes) in December 2007, and Medan in North Sumatra in May 2008, to provide such pharmacovigilance information.

To improve the handling of incoming reports, the national centre has developed a database for Indonesia. While the number of reports is still low, the database currently functions as a data storage program.



Sitting in front: Siti Asfijah Abdoellah, Dra Engko Sosialine M (Head for Sub Directorate of Surveillance and Risk Analysis of Therapeutic Products), Dra. Warta Ginting (Head for Section for Risk Analysis of Therapeutic Products). Standing: administrative staff –Melur Agustina SKM, Sugianto and Harini.

In November 2007, we invited 120 representatives from MAHs to a workshop in Jakarta on a pharmacovigilance scheme for them. We have done preliminary inspections at some MAHs, both multinational and local. This preliminary inspection was aimed at testing the inspection tool developed for pharmacovigilance systems in MAHs.

In promoting pharmacovigilance activities in the media, an article about 'Pharmacovigilance in Indonesia' was published in *Media Indonesia* on 18 June 2008, and we plan to routinely publish our activity in the future.

In November 2007, Dr Dina Pfeifer from WHO HQ visited, to look at how Indonesia is preparing for pandemic influenza, especially post-marketing surveillance as a part of NRA Pre-Assessment. From her visit, it was identified that capacity building of all key players on AEFIs needs addressing. So in March 2008, WHO conducted a training

workshop on 'Strengthening AEFI Monitoring and Causality Assessment' with participants from the national centre, the National Committee for AEFI, some provincial committees for AEFI, the EPI Programme and a vaccine manufacturer. We hope that similar training can be conducted in Indonesia for drug monitoring, with lecturers from UMC.

In March 2008, I attended the ISoP course on 'Basic Concepts in Pharmacovigilance' in Bangkok, Thailand and NADFC hope to participate in the WHO Annual Meeting this year, since we have been absent for several years.

In conclusion, we have identified problems to overcome:

Internal:

- a) Limited budget
- b) Limited personnel trained in pharmacovigilance
- c) Regulations to be strengthened.

External:

- a) inter-sectoral co-ordination with other stake holders in pharmacovigilance should be improved (including health professional associations, hospitals, academia, MAHs etc)
- b) professional gulf between physicians and pharmacists
- c) large coverage areas
- d) social economic conditions (reporting ADRs not a priority)
- e) fear of litigation.

We are hopeful to overcome these challenges over the coming years.

Pharmacovigilance, Mexico way

Alejandra Rosete

Mexico has been a member country of the WHO Programme since 1999. With a population of 106.5 million the National Pharmacovigilance Programme is growing. The Federal Commissioner for Health Risk Protection, the Commissioner for Evidence and Risk Management and the National Head of Pharmacovigilance, Carmen Becerril, are committed to evolve the programme. The UMC has helped Mexico with data capturing and the successful sending of reports to the WHO database. The goal for spontaneous reporting for 2008 is 16,500 notifications; the quality of information we are submitting in active reports to the WHO database is improving; 15–20% usually come from clinical trials; the rest are from day-to-day medications.

As Vice-President of the Mexican Pharmacovigilance Association (MPA), I had the opportunity to promote a joint initiative which resulted in Mexico's nomination as a 'National Chapter' during the 8th Annual Meeting of the International Society of Pharmacovigilance in Buenos Aires, Argentina. As such, we will be able to promote pharmacovigilance development and most importantly, to empower research and human resources training.

MPA and the National Pharmacovigilance Center are jointly organizing a national meeting in November 2008 with distinguished speakers from Europe and North America, to extend the interest in the field from different perspectives. This endeavour will cover a

proposal to develop a Latin American Collaborative Network for information and research, sharing successful strategies, for evaluation of regional policies and decision-making with our colleagues in Latin American countries. We are optimistic that there will be a positive outcome to this.



Alejandra Rosete during the 2007 UMC course

At a local level and as part of my job, Medica Sur Hospital (an academic private facility with 154 beds) achieved the nomination as an Institutional Center of Pharmacovigilance from the national health authorities on 4th December 2007, based on good performance. We reached 98 spontaneous reports in the first year of activities, with complete notification data and good quality information. By mid 2008 we had received 187 reports, all of them potential active reports for the WHO database regarding quality of information. We are the only healthcare institution in Mexico that is currently helping the National Centre in classifying causality of local reports, according to Naranjo's system. This model would be useful to decrease workload for the central system.

Rational use of medication. We conducted a retrospective study of a random sample with 327 cases which helped to identify systematic errors and particularly high alert medications. Actions are now being taken in order to improve safe and rational use of medications. Our results were submitted to a peer-reviewed journal for publication.

Academic institutional agreements. As a country, Mexico has very few clinical pharmacists and few hospitals have a pharmacist as part of the clinical team. We are working towards recognition as an academic hospital for clinical pharmacy and have trained four pharmacist bachelors in topics related to drug adverse reactions, detection of medication errors, their prevention through intervention during medical rounds and rational use of medications.

We would really appreciate to have follow-up programmes in collaboration with UMC, to share information with countries (such as Mexico) that need substantial improvement in pharmacovigilance, building databases for supporting decision-makers, health systems and policies, learning from each other's experiences and improvement strategies for motivating world-wide safe and rational use of medications. I particularly thank the huge support we have received from UMC/WHO team.

Nigerian Pharmacovigilance plan



Adeline I Osakwe

*Head and National Co-ordinator,
National Pharmacovigilance Centre (NPC),
Nigeria*

Following *the* UMC training course reinvigoration of the programme in Nigeria was aimed in several directions:

1. Use of VigiFlow to manage ADR case reports and build up national database on ADRs and other drug-related case reports.
2. Commencement of assessment of case reports at national level.
3. Collaboration with professionals in health institutions to conduct a drug use study to generate evidence-based arguments for pharmacovigilance.
4. Integration of pharmacovigilance into public health programmes on malaria, HIV/AIDS and tuberculosis/leprosy.
5. Build collaborative relationships with industry to sustain pharmacovigilance activity on their products.
6. Sustained awareness creation of pharmacovigilance through newsletters, group presentations, mass media campaign and one-to-one interaction.

Our achievements

The UMC training gave the unit a global perspective on the strategies for creating awareness on the need to detect and report adverse drug reactions and other drug-related problems. We received 156 ADR case reports from June 2007 to June 2008, and with the assistance of RaPID Pharmacovigilance we were able to improve our reporting rate to UMC through VigiFlow. ADR case reports were assessed at national level by the National Drug Advisory Committee before forwarding to UMC.

Pharmacovigilance guides for industry have been drafted and marketers are required to submit a pharmacovigilance plan to the NPC before their products can be evaluated.

Awareness creation has occurred through advertisements in professional newsletters and a poster on the pharmacovigilance programme distributed to healthcare delivery centres. A quarterly newsletter was disseminated to relevant healthcare professionals.

Pharmacovigilance has been integrated into public health programmes in malaria, HIV/AIDS and tuberculosis/leprosy; WHO facilitated training of NPC staff on malaria and HIV/AIDS. Cohort Event Monitoring on anti-malarials will commence in August 2008. Collaboration with public health programmes where ADR monitoring has been included is one of the indicators for monitoring the progress of such programmes.

Obstacles to achieving the goals set for my unit include poor internet speed which makes it difficult to send assessed reports to UMC, and the lack of a reporting culture. Direct funding for pharmacovigilance is not available so we have to work at the pace of the public health programme through which funds for the pharmacovigilance activity is extracted. Other constraints include under-detection and poor reporting by healthcare practitioners and pharmaceutical companies, poor reporting by healthcare practitioners involved in public health programmes, and practitioners feeling that reporting of ADRs might mean professional incompetence.

Absence of a binding policy

Presently, we do not have a policy document which makes it binding for healthcare practitioners to report ADRs. We are making efforts to overcome this obstacle through enactment of necessary legislation that will improve their commitment to ADR reporting and translate into improved quality and volume of ADRs received.

Practitioners in private practice

We have thousands of private hospitals, clinics and community pharmacies but very few ADR reports come from this vibrant health sector. Frequent pharmacovigilance detailing on the need to detect and report ADRs at conferences and mandatory continuous professional development fora is not yet yielding positive fruits.

International public health programmes

The NPC made advocacy visits to many international public health institutions (NGOs, etc) in the country to make ADR reporting an indicator in their routine work, and forward duplicates of such reports to NPC for documentation. Recognizing their role as an important stakeholder in ensuring patient safety, we have requested their active participation and commitment by forwarding reports on ADRs in their organizations to NPC.

Finally, the need for adequate funding cannot be overemphasized, especially given our population and area of coverage for pharmacovigilance activities. The National Agency for Food and Drug Administration and Control shoulders all the responsibilities on all pharmacovigilance activities. Our immediate needs are efficient internet facilities dedicated to NPC so as to forward ADRs electronically to *the* UMC. This would certainly improve our commitment to forwarding reports to UMC and at the same time strengthen our capacity for pharmacovigilance.

Sierra Leone ready to move forward

Mary Couper reports

Seven years after the war in Sierra Leone, many challenges remain. However, the country is making great strides in rebuilding itself. Nowhere is this more apparent than in the Pharmacy Board of Sierra Leone. Under the leadership of the acting Registrar Mr Wiltshire C N Johnson, the regulatory body is achieving its stated mission of assuring the safety, efficacy and quality of all drugs used in the country.



Staff of the Sierra Leone centre

It was my privilege to join with Dr Alex Dodoo, WHO Consultant from Ghana, Dr Jackson Sillah from WHO AFRO and Dr Monica Olewe, the focal person for malaria in WHO Sierra Leone, on a mission to provide technical support to review and strengthen the pharmacovigilance system in the country. The three days I spent in Sierra Leone, were action packed, exciting and exhilarating. The first day we paid visits to the Minister of Health, Dr Soccoh Kabia, the Chief Pharmacist, Mr H H Lawson, the programme managers of the malaria and HIV/AIDS programmes and the World Health Representative in Sierra Leone Dr W Alemu. We then spent a couple of hours in the Pharmacy Board finding out the strengths and weaknesses of the pharmacovigilance activities. It is headed by the acting Registrar and staffed by one full-time pharmacist, two interne pharmacists, two pharmacy technicians and one secretary. It is well equipped and has access to the internet. There is a database of all legally imported medicines but no database for ADRs. There are a total of 49 ADR reports in the system. These are assessed by a Committee that meets quarterly. An innovation is the presence of two billboards in the centre of town – one advertising the dangers of counterfeit medicines and another requesting health workers to report all ADRs.

Our next visit was to Connaught, the largest teaching hospital in Freetown. Much work needs to be done in that environment since neither the doctors nor the nurses consider it a part of their work to report ADRs.

The next day saw the start of a three-day workshop which was held with the aim of encouraging all the health workers both in the hospitals and the public health programmes to have a sense of ownership of the programme. The ultimate aim was to develop an action plan for the country in which all the stakeholders play a role. This workshop was opened by the Minister of Health.

Sierra Leone has all the correct infrastructure in place for a successful pharmacovigilance and furthermore has the all important political support. We should therefore be able to welcome the country as a full member of the WHO Programme very shortly.

Western Pacific focus on PV

Bruce Hugman reports from Manila

A pharmacovigilance training course for twenty-four representatives from eleven Western Pacific countries was held in Manila from 2-11 September.

In spite of the huge diversity in population, experience and maturity of ADR monitoring systems across the participants' countries, the common vision of improving patient safety united the group in ten days of intense study and discussion. While the scale and nature of concerns in an enormous country like China were different in many respects from small nations like Fiji or the Solomon Islands, the core issues were shared by everyone.



Participants from eleven countries and faculty members from six countries on the Manila pharmacovigilance training course

Countries participating in the course:

Brunei Darussalam	Cambodia
China	Fiji
Republic of Korea	Lao PDR
Mongolia	Papua New Guinea
The Philippines	Solomon Islands
Viet Nam	

Seeking a stable future

A common preoccupation was how to secure political, departmental and financial support on a continuing, stable basis. Several countries had long-established monitoring systems which had failed to achieve their aims because of changing political policies and priorities, reorganizations,

loss of personnel and a lack of departmental commitment. Many countries had only one or two designated staff in their monitoring centres, and some of those were expected to perform other duties as well. The priority of establishing the importance of pharmacovigilance in the minds of politicians and the public was felt by everyone.

Even in countries where there was a degree of stability and commitment, there remained the challenge of convincing health professionals of the importance of reporting. The participants spent some time debating methods for spreading the word, stimulating reporting and maintaining momentum and motivation.

Technical matters

The nature, significance and costs of ADRs, causality assessment, signal detection, database management, medication error, counterfeit drugs and other quality and regulatory issues were presented and discussed, with some workshop and hands-on activities too. There was a very interesting session of literature resources and the skills needed to make a critical assessment of published materials and research results.

Getting the message across

A good deal of time was spent on communication issues, including the promotion of ADR reporting, the design of reporting forms, techniques for educating professionals and the public about drug safety issues, crisis management, media relations and skills for training others in the science.

A fine environment for study

With the exception of one gigantic rainstorm (which flooded the streets of Manila) and a few showers, the City provided a comfortable and stimulating environment for the course. The hosts, the Philippine Bureau of Food and Drugs (BFAD) and the WHO Western Pacific Office, ensured that the participants enjoyed the best facilities and generous Filipino hospitality – including so much splendid food that everyone wondered how they would ever recover their normal body-weight afterwards.

A good team

The course faculty included people from WHO HQ, UMC, and BFAD, and other experts from the region. The participants themselves – a mature, active and lively group – contributed much to the learning and provided many insights into both problems and solutions which were helpful for everyone.

The last session was the presentation of each country's plans for the next twelve months. The real test of the effectiveness of the course will be how far participants can achieve their goals, and make significant progress in rooting pharmacovigilance in their healthcare systems.

News from FIP

The 68th World Congress of Pharmacy and Pharmaceutical Sciences (FIP) took place in Basel, Switzerland with over 3,000 attendees from 120 countries. The Congress which, took place from 29th August to 4th September 2008, had as its theme: 'Reengineering Pharmacy Practice in a Changing World'. It was opened by the President of the Swiss Federation Mr Pascal Couchepin, who offered praise for the role of the pharmacist in health care.



Alex Dodoo (right) with outgoing President of the FIP Pharmacy Information Section, Prof Han de Gier of the Netherlands

Significant events taking place at the meeting in relation to pharmacovigilance include:

Pharmacy Information Section Elections

The Pharmacy Information Section (PIS) is the Section that deals primarily with pharmacovigilance. In collaboration with *the* UMC, it organised two Satellite workshops in Cairo in 2005 and Beijing in 2006. Elections were held this year for a new Executive Committee for a four-year term starting in September 2008. Dr Alex Dodoo of Ghana was elected President with Ms Lindsay McClure (UK) as Secretary. The two become automatic members of the Board of Pharmacy Practice of FIP. In addition to Dr Dodoo, other pharmacovigilantes elected were Mr Graeme Vernon (Australia) and Mr. Carlos Vidotti (Brazil) who were elected as Executive Committee members to represent Asia/Pacific and The Americas respectively. The potential benefits of active collaboration between *the* UMC and PIS of FIP are enormous and will become evident in the coming years.

Policy Statements approved

The FIP Council approved three policy statements, on Control of Antimicrobial Medicines Resistance; Medicines Information for Patients; and Quality of Medicines Used for Children.

Full details of these are available from the FIP website at www.fip.org

Five countries join the Programme

Since our last edition of Uppsala Reports, more countries have made the transition from Associate member to Full member of the WHO Programme for International Drug Monitoring.

Both Kazakhstan and Barbados recently submitted ICSRs to VigiFlow and they now both meet the requirements to become Full member countries of the Programme. Helena Wilmar and Lovisa Sällstedt at the UMC helped to guide the Kazakhstan centre in managing VigiFlow, and Barbados managed through assistance from Naomi Jessurun in Suriname.

The responsible persons in the new centres are:

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Then, as we went to press, three more countries became Full members.

The national pharmacovigilance centre of Andorra, through VigiFlow, submitted its first 20 adverse drug reaction case reports to the WHO database. Head of the national pharmacovigilance centre is:

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The Safety Support and Services reporting team has noted that Sierra Leone and Ethiopia also managed to submit the stipulated number of ICSRs through VigiFlow.

The contact persons are:

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There are now 89 Full members of the WHO Programme. A more detailed description of each new national centre will appear in a future edition of Uppsala Reports.

International meetings imminent

As we prepare this issue of Uppsala Reports we are also in the final weeks before the 31st Annual Meeting of the WHO Programme, to be held in Uppsala from 20-23 October. We are expecting well over 100 representatives from more than 50 national centres, and hoping to see delegates not only from our more recent entrants to the Programme but also from all the ten original countries from 1968.

Full reports of the meetings in Uppsala will appear in the January 2009 Uppsala Reports.

Making Chinese ADR data available to the world

Sten Olsson

There has been a very positive development of adverse drug reaction reporting in PR China during the last few years. Reporting from the regional centres, of which there are now 31, to the National Centre for Adverse Reaction Monitoring in Beijing, has for some years doubled from one year to the next. Early in 2008 the Chinese national ADR database contained approximately 1.2 million individual case safety reports (ICSRs), and the addition of new reports this year may be as high as 500,000. Only a fraction of these reports is available in the WHO database (VigiBase), because the reports today need to be manually translated into English.



UMC and Chinese national centre staff after meetings at the Uppsala office

Although the Chinese national centre is very keen to contribute to the global pool of ADR information there are considerable technical challenges to overcome before this can happen. Case details are of course recorded in the national Chinese database using Chinese characters. Although VigiBase allows recording of Chinese characters there is a need for intelligent mapping of text and codes between the two databases to ensure that the information can be represented in a correct and meaningful manner in Latin characters in VigiBase. The UMC and the National Centre for Adverse Drug Reaction Monitoring (NCADRM) have decided to enter into a joint collaboration which, as its first major goal, has the adaptation of Chinese ICSRs to the international E2b format, used in VigiBase.

The UMC invited a project team from NCADRM to a first project meeting in Uppsala from 25–29 August 2008. The Chinese delegation, consisting of Mr Zhang Cheng Xu, Ms Chen Yixin, Ms Wu Gui Zhi, Ms Wang Ling and Mr Hou Young Fang spent some busy days at the UMC. After initial presentations of the status and expectations of

the two sides, discussions were held regarding the technical content, the process and the management of the collaboration that will be initiated. It was agreed that adaptation of the Chinese ICSR database to E2b will require detailed analysis regarding:

- Database structures
- ADR terminologies used
- Representation of Chinese drug names, including herbals, in the WHO Drug Dictionary
- Translation of free text.

Detailed project plans for the four areas will be further developed and agreed upon with the aim of commencing activities for implementation in early 2009.

It was further agreed during the meeting that the two parties will enter into a long-term collaboration for the development of methods for refinement of signal identification and analysis of drug safety data, including automatic quantitative approaches.

When our Chinese guests left we were all happy about a successful accomplishment of a project and optimistic about the long-term collaboration for which we had laid a first stable foundation. Once completed, the project will have a major impact on the content of VigiBase.

Latin American course

Mariano Madurga

A 40-hour course in Analysis and Risk Management of Medicines was held in Antigua, Guatemala, from 4–8 August 2008. Dr Francisco J de Abajo (director), Dr Miguel A Maciá, and Dr Mariano Madurga from the Spanish Medicines Agency were the trainers, while special help was received from Dr Julio Valdés, Regional Health Co-ordinator of SICA (*Sistema de Integración Centroamericana*).

The course was supported by the *Centro Iberoamericano de Formación (CIF)* of the Spanish Agency for International Co-operation on Development (AECID) in Antigua, Guatemala where the course took place. In this beautiful heritage village, 30 professionals (medical doctors, pharmacists, and nurses) from five Central American countries plus the Dominican Republic received training in risk



A big group for the training course in 'Analysis and Risk Management of Medicines' in Antigua, Guatemala

assessment of medicines, drug utilization studies, ineffectiveness and lack of efficacy, how to take regulatory decision and on safety communication.

Participants were professionals involved in regulatory affairs, monitoring and assessing ADRs, drug information centres, pharmacotherapy departments, pharmacovigilance departments, social health insurance systems departments, or from ministries of health. The course was also attended by investigators, clinicians, and professors.

During the course, students learnt basic knowledge on the epidemiological principles of the risk analysis, methods of drug utilization researches, pros and cons of spontaneous reporting, individual causality assessment, qualitative and quantitative signal analysis, data mining, bias, confounding, types of pharmaco-epidemiological studies, risk-benefit balance, regulatory measures, and risk communications. In workshops, practical cases were discussed regarding causality assessment, risk management, communication and how to take regulatory decisions.

During the last day a draft on a Regional Programme for Pharmacovigilance was distributed. The programme is aimed to harmonise activities within the Central American region, and agree on actions that will help those countries to initiate or further strengthen pharmacovigilance activities.

Those 30 professionals from five Central American countries (Costa Rica, El Salvador, Guatemala, Honduras, Panama) and Dominican Republic, received a unique opportunity to receive an in-depth training in pharmacovigilance.

A new initiative in India

Anna Celén reports

A 2-day workshop on drug safety was held in Hyderabad, India in September, organized by the Indian Medical Association (IMA) with support from Johnson & Johnson (J&J). The main co-ordinators of the event were S C L Gupta, joint secretary of IMA, and Vinod Elete, Medical Advisor at J&J. The 130 participants were mainly IMA leaders, aiming to learn more about pharmacovigilance in order to train another 100 physicians in their state hospitals within a year. The objectives were to understand the basics of pharmacovigilance, the identification of drug-related risks and practical reporting methods. The opening ceremony was visited by the health minister of the state of Andhra Pradesh; international speakers were John Knight and Carrie Corboy from J&J, and myself from *the UMC*.

The rationale for the workshop was that there is still no functional pharmacovigilance system implemented in India, although attempts have been made in the past. In 2004, the Drugs Controller General of India (DCGI) designed a pharmacovigilance network consisting of zonal, regional and peripheral centres, but the system has not been put into practice. Active pharmacovigilance centres do exist, but they are limited due to lack of funding, staff and resources. Although India became a member of the WHO Programme in 1998, currently no ADR reports are sent to *the UMC*.

In a press release, the IMA proposed to government that it is essential to develop a sustainable pharmacovigilance system. Since clinical trials are very common in India, the IMA wants to reassure patients that they are working with the government to establish patient safety. The IMA also requests that all pharmaceutical companies should have safety monitoring systems in place as well as risk management plans for all products. The IMA also states that ADR reporting should be actively encouraged and involve all stakeholders.



S C L Gupta addresses the Indian Medical Association meeting in Hyderabad, with VIPs and guests on the dais.

The workshop demonstrated the concern about drug safety among health professionals in India. The lack of reporting culture is evident and there is a great need for pharmacovigilance training and promotion. The participants claimed that they observe ADRs in their daily practice but until there is a pharmacovigilance network in place, there is no recipient for the reports. In connection with the conference, the IMA launched its National Pharmacovigilance Cell, headed by Dr Gupta. Physicians were encouraged to start reporting ADRs to the pharmacovigilance cell. The intention is to collect and process the data and submit it to the DCGI.

Statistics in China

Niklas Norén

The First International Symposium on Biopharmaceutical Statistics took place in Shanghai, China from June 30 to July 2, 2008. The meeting of around 450 participants consisted of both Chinese and foreign experts, mainly with an industry focus, but with some presence from the regulatory authorities as well as a few people from academia.

Among the invited keynote speakers at the meeting were Professor Jin Shaohong (Director of the Center for Drug Reevaluation at the Chinese sFDA), Hans-Georg Eichler (Senior Medical Officer at the EMEA), ShaAvhree Buckman (Acting Director for the Office of Translational Sciences, Center for Drug Evaluation and Research at the US FDA), and the heads of global biostatistics at several major pharmaceutical companies.

There was a strong focus on clinical trial methods in both invited and proffered papers. However, pharmacovigilance played a prominent role in several of the plenary talks, where Professor Eichler emphasized the need for statisticians' involvement in the analysis of pharmacovigilance data. Professor Shaohong discussed Chinese efforts in analyzing spontaneous reports, and underlined the Chinese sFDA's collaboration with the WHO Collaborating Centre in Uppsala. He also mentioned their on-going efforts to translate reports into English, saying that their commitment to the WHO International Drug Monitoring Programme made this essential.

Niklas Norén of *the UMC* gave an invited presentation on Statistical Methods for Knowledge Discovery in International Adverse Drug Reaction Surveillance in a session on Statistical Methods for Drug Safety Assessment. The session also included the presentation of a new Bayesian method for detecting potential safety issues in clinical trials by Dr Lawrence Gould of Merck, as well as a summarising view provided by invited discussant Dr Demissie Alemayehu of Pfizer.

UMC at ISPE in Copenhagen

Johanna Strandell

At this year's International Society for Pharmacoepidemiology (ISPE) conference in Copenhagen, Denmark, the Uppsala Monitoring Centre (UMC) was well represented with attendees: Ralph Edwards, Marie Lindquist, Annica Wallström, Richard Hill, Malin Jakobsson and myself. This presence was also apparent through the different areas which were tackled by *the UMC's* participants, including an introduction to the field of pharmacoepidemiology, decision-making, healthcare databases, vaccine vigilance and alternative uses for statistical analysis of ICSRs.

Ralph Edwards was involved in two sections in the pre-conference sections: 'Introduction to Pharmacoepidemiology' and 'Regulatory Epidemiology/Public Health Decision Making'. He also presented *the UMC's* current research within the symposium of 'Identifying Potential Safety Concerns in Claims and Electronic Health Records (EHR) Databases'. I gave a presentation regarding how a method primarily used for detecting drug-drug interactions screening of spontaneous reports can be useful to detect other three-way disproportionate reported patterns. Malin presented her Masters thesis concerning

vaccine vigilance; the poster showed comparisons between different vaccines which also the influence of stratified data when assessing vaccine reports. (This poster can be found on *the UMC's* homepage with other posters.) In addition to presentations/posters presented by UMC staff, Vigibase data was used in a presentation by Marianne Verdal from Utrecht 'Photochemical and other Molecular Characteristics and the risk of Drug Related Photosensitivity'.

John Karlsson from the Clinical Pharmacology unit at the University of Gothenburg presented a study on sudden death and new generation antipsychotic drugs based on Vigibase reports; Kristina Star at UMC's research unit is a co-author in this particular study. The importance of the spontaneous reporting system, in order to generate signals (with the WHO definition) was emphasised by the fact that the recent applied publication of 'Statins, neuromuscular degenerative disease and an amyotrophic lateral sclerosis-like syndrome: an analysis of individual case safety reports from Vigibase' (Drug Safety, 2007) by Ralph Edwards, Kristina Star and Anne Kiuru had been used as the trigger to investigate whether the prescription registers in the Nordic countries could be used to perform quick studies in order to respond to serious alarms.

14th ACM SIGKDD Conference

Ola Caster

'Knowledge Discovery and Data-mining' – or KDD – was a refreshing experience. This is the premier international forum for data-mining researchers and practitioners from academia, industry, and government to share their ideas, research results and experiences. Over 800 people gathered in a remote but luxurious hotel in the hot Nevada desert to exchange ideas. The most striking overall characteristic of the research presented was the pragmatic focus on solutions. This community acknowledges that any solution, even if it is not perfect, is better than no solution at all.

There was a clear emphasis on web and text applications, especially on social networks. It became evident that there is a great potential in discovering knowledge from unstructured sources using for example text mining, even though it is still a difficult task.

The UMC was delighted to again have a paper accepted for the conference; following on from our previous award-winning submission on duplicate detection in KDD2005 (see UR31 p14). Niklas Norén presented this paper entitled: *Temporal Pattern Discovery for Trends and Transient Effects: Its Application to Patient Records* in the main conference. This was one of 12 out of 87 submitted manuscripts accepted for presentation in the industry sessions.

I had a four-page paper in the workshop 'mining medical data' entitled *Large-Scale Regression-Based Pattern Discovery in International Adverse Drug Reaction Surveillance*.

Overall we are gratified that there was a considerable interest in our work, showing the relevance of our work beyond pharmacovigilance and healthcare.

ACM = Association for Computing Machinery; SIGKDD=Special interest group on knowledge discovery and data mining.

Global support for regional problems?

Alex Dodoo asks

The rapid development of pharmacovigilance in Africa over the past 10 years is testimony to the untiring efforts of the WHO and UMC who have expertly utilised public health programmes and the resources they bring to expand interest in pharmacovigilance. Since the meeting in Lusaka, Zambia in 2003 when the deployment of artemisinin-based combination therapies was used as a legitimate basis to introduce pharmacovigilance in Africa, other public health programmes, particularly HIV/AIDS Control Programmes, have used pharmacovigilance to establish local and/or national pharmaco-vigilance systems. This has seen the number of full and associate national pharmacovigilance centres in sub-Saharan Africa (The Africa Malaria Report, WHO (AFRO/EMRO, 2006)) increase tremendously though the number of countries at the Associate membership level is still too high. What has been the impact of these centres and how do they relate to global PV? The case of antimalarials in general and amodiaquine+artesunate in particular may shed some light.

Over the past five years, several countries in Africa have moved from the cheap but increasingly ineffective chloroquine to artemisinin-combination therapies for the management of uncomplicated malaria in adults and children. One of the recommended combinations is amodiaquine PLUS artesunate (ASAQ). Artemisinin products originate from China where they have been used for centuries for the treatment of malaria. Amodiaquine is a 4-aminoquinolone, similar in structure to chloroquine. It has been used for decades for treating malaria but, very significantly, was banned for the treatment of malaria in Europe and the USA due to its association with fatal agranulocytosis. Its widespread deployment as part of ASAQ in Ghana was associated with increased ADR reports and public anxiety leading to the withdrawal of specified brands, because the initial problems were suspected to be related to product quality. Since then, there have been safety concerns and anxieties in Sierra Leone, Kenya, Nigeria and Burundi amongst other countries. Since most of these countries are now developing capacity for pharmacovigilance, signal generation and public health action, the global pharmacovigilance community has a responsibility to ensure that the reported signs and symptoms as well as the anxieties and rumours are managed appropriately at both the local and international level. Ghana enjoyed WHO and UMC support in dealing with the ASAQ-associated problems it faced in December 2005 (<http://www.who.int/countries/gha/news/2006/anti.malaria.drug.policy/en/>). However the reports from other countries in addition to some reports in Ghana from GMP certified qualified products raises a few questions which require global consideration and solution including:

- the evidence base for the safety of amodiaquine
- the evidence base for the withdrawal of amodiaquine in some ICH countries
- the response that would have emanated from ICH countries had the events observed in Ghana (and later in other countries) been observed in the West
- the evidence needed to satisfy malaria endemic countries of the safety (or relative safety) of products recommended by global agencies.

Pharmacovigilantes and policy makers in Africa have huge and increasingly astute constituencies and publics to answer to. In cases like amodiaquine they need rigorous, scientific data to provide answers. They want to, and need to, be seen as concerned about the safety of their population as pharmacovigilantes and policy makers in ICH countries. They will soon be asked why a product withdrawn for safety concern in certain markets is being actively promoted for their use. The need for global support and collaboration with these countries to provide robust answers to their government and publics is obvious, urgent and important. Pharmacovigilance is global and requires global support.



Antimalarial
Combination Therapy

18th Meeting of the Global Advisory Committee on Vaccine Safety

The Global Advisory Committee on Vaccine Safety (GACVS), an expert clinical and scientific advisory body, was established by WHO in 1999 to respond promptly, efficiently and with scientific rigour to vaccine safety issues of potential global importance. Issues described by the Committee during its 18th meeting, held on 18-19 June in Geneva, Switzerland, included the safety of yellow fever vaccine, mitochondrial diseases and vaccination, and thiomersal.

Safety of yellow fever vaccine

The Committee was updated on evidence regarding the safety of 17D yellow fever vaccines. It focused primarily on four fatal cases and one non-fatal case of vaccine-associated viscerotropic disease (YEL-AVD) occurring among 63,174 individuals vaccinated in the Ica Region of Peru following a yellow fever vaccination campaign conducted in September-October 2007 after a major earthquake. All five cases received vaccine from the same lot. The incidence of YEL-AVD (estimated as 11.7/100 000 vaccinated based on the number of people receiving the vaccine lot or 7.9/100 000 based on all those vaccinated in the Ica Region) was noted to be more than 20 times higher than the risk previously associated with 17D vaccines in general.

Following review of the data collected during the investigation, the Committee concluded that the cause of the cluster of cases was not clear. One of the cases presented a known risk factor; a second case presented a potential risk factor. Tests showed that the lot administered met all quality specifications and the yellow fever virus isolated from three confirmed cases was consistent with the vaccine virus and did not appear to have mutated. Approximately 72 000 doses of the vaccine lot common to the YEL-AVD cases was confirmed to have been used elsewhere in Latin America without additional cases of YEL-AVD.

The GACVS reiterated the need to obtain better estimates of rates of serious adverse events and to be better able to predict which individuals are at risk for such events. Members indicated support for the initiatives of WHO and other global partners in these areas.

Mitochondrial diseases and vaccination

The GACVS reviewed the limited data on mitochondrial disorders and vaccination available from the United Kingdom and the United States. The Committee concluded that there is no convincing evidence to support an association between vaccination and deterioration of mitochondrial diseases (inherited disorders of energy metabolism that tend to affect tissues with high energy requirements such as the brain, heart and liver). The topic will be reviewed further if new findings become available. GACVS supports continued vaccination of children with mitochondrial diseases with the same vaccines as are given to healthy children.

Thiomersal

The Committee reviewed a recently-published pharmacokinetic study of mercury in premature and low-birth-weight infants who received a birth dose of hepatitis B vaccine containing thiomersal,

and the results of a study conducted in Italy that examined neuropsychological performance 10 years after immunization in infancy with thiomersal-containing vaccines.

On the basis of the presented data, GACVS remains of the view that there is no evidence to support a change in WHO's recommendations for thiomersal-containing vaccines and the vaccination of low-birth-weight infants, where indicated.

Other topics discussed during the meeting were: diphtheria-tetanus-pertussis (DTP) vaccine and asthma; non-specific effects of DTP vaccine on child mortality; and inadvertent administration of rubella vaccine to women shortly before or during pregnancy.

The report of the meeting was published in the WHO Weekly Epidemiological Record on 8 August and has been posted on the GACVS web site at http://www.who.int/vaccine_safety/en

Commonwealth Pharmacists to Discuss Pharmacovigilance

The 10th Commonwealth Pharmacists Association meeting is scheduled to take place in Accra, Ghana from 4th to 8th August 2008 under the theme: 'Managing threats and crises: the vital role of pharmacy in an unstable world'. Among the threats to be discussed is that of unsafe medicines. A plenary session has been planned specifically to look at pharmacovigilance in Commonwealth countries and the UMC and WHO are expected to be active participants at these. Full details of the CPA meeting can be found at www.psg.org/cpa.

LSHTM course – ten years on

by Ian Douglas

The Certificate course in Pharmacoepidemiology & Pharmacovigilance at London School of Hygiene & Tropical Medicine has been running for over 10 years. The 2007–2008 intake have (as I write) finished their projects and exams, and will be waiting (with excitement!) for their results to be made available in the next few weeks.

The course provides a strong foundation in the core elements of pharmacovigilance and pharmacoepidemiology, and covers a broad range of topics including general epidemiology, basic statistics, study design, spontaneous reporting, regulatory requirements, critical appraisal and research databases. There's an emphasis on understanding how studies of drug effects are designed, conducted and reported, allowing students to make a considered judgement of papers they are likely to come across in the literature.

The course keeps pace with the ever-changing world of drug safety and one of the most popular workshops this year had students tackling some of the issues involved with Risk Management Planning. Less well understood study designs and statistical techniques, such as the self-controlled case-series and propensity scores were also featured; they have gained in popularity in the field of pharmacoepidemiology over recent years and can seem baffling. Teaching focussed on understanding the fundamentals of these approaches, making sure that publications featuring their use are less daunting.

The affordability of medicines is becoming an increasingly important aspect of decision-making for health authorities. Students are introduced to the main concepts of health economics which underpin these decisions with a focus on the UK's National Institute of Clinical Excellence model for Technology Appraisal.

All students complete a written project on a subject selected by the course organisers. Past topics have included the debate around MMR and autism, the cardiovascular effects of COX-2 inhibitors and the HRT and osteoporosis controversy. The idea of producing a written report may seem intimidating to start with, but all relevant materials are provided and all students are matched with an academic advisor to provide guidance. Many students have commented that the project is one of the best ways to put into practice the various strands of teaching received on the course.

A third of the lectures and teaching sessions are given by staff from the London School of Hygiene & Tropical Medicine with broad experience in both pharmacoepidemiology and pharmacovigilance. Other sessions are led by experts from regulatory authorities, national public health bodies and industry, ensuring a wide range of perspectives are heard. Several past students, including Andrew Bate from *the UMC*, have even become lecturers on the short course!

One of the main strengths of the course is the diverse nature of the students – with scientists and physicians from several countries participating. Most come from regulatory authorities or industry, with a few independent healthcare practitioners ensuring a range of perspectives. This broad mix of participants stimulates lively

discussion and debate, particularly in the many workshops and round-table discussions featured on the course. All teaching is face-to-face at the School and is spread over three teaching blocks, totalling 12 days over 6 months.

Part of the University of London, the London School of Hygiene & Tropical Medicine is an internationally-recognized centre of excellence in public health, international health and tropical medicine and is one of the highest-rated research institutions in the UK. Students who successfully complete the course are awarded a certificate, making this course one of very few certificated courses in pharmacovigilance available. Students are often keen to pursue further study here at the School, and for them more advanced courses in medical statistics and epidemiology are available.



Certificate course students outside the School, in Bedford Square, London

A one-day conference is being planned for 2009, to mark the course running for over a decade. All former students will be invited and others with an interest in drug safety will be most welcome. Well-known speakers from the field of pharmacovigilance will look at recent developments in pharmacoepidemiology and, if previous experience is anything to go by, they are sure to stimulate some lively discussion.

Details of future courses can be found on the school website at www.lshtm.ac.uk/prospectus/short/index.html or by e-mail from Ann.Arcott@lshtm.ac.uk or Ian.Douglas@lshtm.ac.uk.

Richard Hill

introduces himself



I moved from Canberra, Australia to Uppsala in August to start work at *the UMC* as Medical Assessor in the signal detection team. My work involves, together with other members of the signal team, reviewing potential signals from the WHO Global ICSR database (Vigibase), liaising with external reviewers, and editing articles for publication in the Signal document. I will also be providing medical input for other areas of *the UMC*, such as the research and terminologies groups, and will be looking at ways to further develop our signal production and publication processes.

I graduated in medicine from the University of Melbourne, and worked for several years in hospital medicine before spending a year as a medical editor at Australian Medicines Handbook in Adelaide. In 1999 I moved to Canberra to work at the Therapeutic Goods Administration (TGA), Australia's medicines and medical devices regulator, as an evaluator for cardiovascular and analgesic medicines. From 2001 until this year, I was a medical officer in the Adverse Drug Reactions Unit at TGA; in 2004 to 2005 I spent a year on secondment to the Marketed Health Products Directorate, Health Canada, in Ottawa.

Also with me in Uppsala are my wife and two daughters (aged 8 and 3). Living in Uppsala has posed a number of interesting challenges – a different range of products to choose from in the local supermarket, learning how to use an ATM when the instructions are only in Swedish, and riding a bicycle (the common means of transport around Uppsala) for the first time in many years. Fortunately the staff at UMC have been extremely helpful whenever we have had questions or need translations (or even a live demonstration of an ATM). I have already been introduced to the Swedish sport of floorball, but miss the (somewhat less sweaty) weekly game of bridge a small group of us played at TGA. I have been impressed by the enthusiasm of all the staff here at UMC and the very friendly working environment, and am looking forward to working with everyone here.

UMC Director

During the early part of 2008, the Board of *the UMC* advertised for a replacement for Ralph Edwards, who was due to retire in late 2008. That recruitment was not conclusive, and Ralph has been asked to remain as Director until late 2009, while the recruitment process is brought to a successful close.

Other staff news

Niklas Norén has been appointed Adjoint associate professor at the Institution of Statistics and Mathematics, Stockholm University with effect from 1 January 2009.

Johanna Strandell will be a full-time PhD student in the Clinical Pharmacology Unit at the University of Gothenburg.

Miyuki Arnqvist started in August 2008 to work for a year at *the UMC*. She is from the Karolinska Institutet (Medical Informatics Program) in Stockholm, and has completed her Master's thesis at *the UMC*, on structuring Chinese Pharmaceutical terminologies data-modeling and systematic mapping in the WHO Drug Dictionary Enhanced.



The UMC staff recently went to a nearby village for a planning day in the countryside. The team can be seen between sessions taking the autumnal air.

Recent Visitors



UMC had the pleasure of **Dr David Coulter** from New Zealand working in the office on a project funded by WHO Headquarters for three months this year. The outlines of the project were to

- refine the structure of WHO-ART so that each term is placed in an appropriate clinical grouping within each system organ class (SOC).
- mapping the terms in the New Zealand Intensive Monitoring of Medicinal Products (IMMP) events dictionary to WHO-ART

the result is expected to be used in Cohort Event Monitoring projects in the future.

The UMC has also welcomed **Ruth Savage**, one of our signal reviewers, and a fairly regular visitor, although she comes all the way from New Zealand, and a student **Mirthe Pasmans** working with our regular collaborators in Utrecht.

News about UMC products and services

September release – WHO Drug Dictionary Enhanced

The September 1, 2008 version of the WHO Drug Dictionary Enhanced is now available, as well as the combination of WHO Drug Dictionary Enhanced and WHO Herbal Dictionary, and the subset of the dictionary called WHO Drug Dictionary. If you subscribe to this version you have received an e-mail with login details.

The latest statistics for the September 1 release with the number of unique names from 94 countries can be viewed on the website. As of September 2008 the dictionary contained:

- 194,885 unique names
- 1,472,631 different medicinal products, trade names with for example form and strength information added
- 10,049 different ingredients mentioned in these products

New drug names have been added in the September 1 release but no changes have been made to existing entries – changes are only made in the March 1 releases.

Try the Drug Dictionary Browser

Organizations can improve efficiency and productivity by using the WHO Drug Dictionary Browser, accessible online with a user-friendly interface. The latest version of the Browser allows users to filter their search results, to find generic and preferred names and to browse both the latest version of the Dictionary as well as previous versions.

CROs will also have the possibility to select which Dictionary to browse depending on the demand of their sponsors. Questions regarding the WHO Drug Dictionary Browser (or applications for a one week test account) may be sent to drugdictionary@umc-products.com

Meet us

Representatives from *the* Uppsala Monitoring Centre are scheduled to attend the following meetings:

Phase Forward User Group
San Francisco, CA, USA
28-30 October 2008

ERFA No 39
Steningevik, Sweden
28-30 October 2008

DIA Signal Detection Conference
Hyatt Regency on Capital Hill, Washington DC, USA
18-20 November 2008

You can subscribe to regular news about *the* UMC's products and services via the website. A newsletter is distributed periodically to a wide range of health care professionals, aiming to keep you up-to-date.

Recent UMC Papers

Intranasally administered corticosteroids and neuropsychiatric disturbances: a review of the International Pharmacovigilance Programme of the World Health Organization. *Ann Allergy Asthma Immunol*, 2008;101:67-73.

Jitka Pokladnikova, Ronald H. B. Meyboom, Jiri Vlcek, Ralph I. Edwards.

The systemic use of corticosteroids is connected with a variety of psychiatric and neurologic effects. An unexpected cluster of case reports of neuropsychiatric disorders during intranasal corticosteroid use was reported to the Uppsala Monitoring Centre. This paper looks at the possible connection between intranasal corticosteroid use and the development of neuropsychiatric disorders, as reported to the WHO Programme, covering a total of 429 reports from 16 countries.

Vigibase, the WHO Global ICSR Database System: Basic Facts. *Drug Information Journal*, 2008, 42:409-419.

Marie Lindquist

This article on Vigibase recently published in the *DIA* journal is a reference to *the* UMC database system and its associated tools, and is an ideal review for anyone wishing to find out about the background and working of much of *the* UMC's activity.

A statistical methodology for drug-drug interaction surveillance. *Statistics in Medicine*, 2008, DOI: 10.1002/sim.3247

Norén GN, Sundberg R, Bate A, Edwards IR.

In this paper, the authors implement and evaluate a shrinkage observed-to-expected ratio for exploratory analysis of suspected drug-drug interaction in ICSR data, based on comparison with an additive risk model. They argue that the limited success of previously proposed methods for drug-drug interaction detection based on ICSR data may be due to an underlying assumption that the absence of interaction is equivalent to having multiplicative risk factors.

UMC crisis publication proves popular

Expecting the Worst, the UMC's manual on anticipating, preventing and managing medicinal product crises, has been reprinted once and it is hoped that a second edition may be published in the future.

Readers of *Uppsala Reports* are warmly invited to submit their suggestions for improvements to the next edition, or their experiences or case histories in relation to crises they've been through.

Please send your contributions to sten.olsson@who-umc.org or mail@brucehugman.net



Dr Wang Gang, from the Chinese Ministry of Health, was so enthusiastic about UMC's publication *Expecting the Worst*, that he translated several chapters during the Manila pharmacovigilance training course (see page 7). He hopes to have the book published in China in due course. Here he is with Bruce Hugman, who wrote the original text for *the* UMC.

Drug Benefits and Risks

International Textbook of Clinical Pharmacology

Edited by: Chris Van Boxtel, Budiono Santoso and Ralph Edwards

Hardcover (revised 2nd edition) approx. 850 pp
ISBN:978-1-58603-880-9 Price: US\$290 / €200 / £150

This updated and revised 2nd edition of *Drug Benefits and Risks* is a comprehensive reference exploring the scientific basis and practice of drug therapy, focusing on the balance between the benefits and risks of drugs, while also highlighting the social impact which drugs have in modern societies.

Taking an evidence-based approach to the problem, the practice of clinical pharmacology and pharmacotherapy in the developing as well as the developed world is examined. The book covers general clinical pharmacology, pharmacology of various drug groups and the treatments specific to various diseases; the book gives guidance on how doctors should act so that drugs can be used effectively and safely; and it encourages the rational use of drugs in society.



COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
5-7 November 2008	DIA's 6th Canadian Annual Meeting: Benefit and Risk Management: An Evolution in Progress	Ottawa, Canada	DIA Tel: +1 (215) 442 6100 E-mail: dia@diahome.org www.diahome.org
5-7 November 2008	XIII Reunion Nacional y il Congreso de la Asociación Nacional de Farmacovigilancia	Acapulco, Mexico	Congresos, Incentivos y Convenciones Mundiales S.A. de C.V. Tel: (55) 5171-1380 www.cicmundiales.com.mx
12-13 November 2008	Case Narrative Writing For Reporting Adverse Events	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
17-18 November 2008	Adverse Event Reporting and Pharmacovigilance	London, UK	Customer Services - PTI Tel: +44 (0)20 7017 7481 E-mail: registration@pti-europe.co.uk www.iir-events.com
19-20 November 2008	Signal Detection and Data Mining: International Perspectives on Spontaneous Reports and Other Healthcare Data Sets	Washington, USA	DIA Tel: +1 (215) 442 6100 E-mail: dia@diahome.org www.diahome.org
24 November 2008	Pharmacovigilance Aspects of Licensing Agreements	London, UK	Management Forum Ltd Tel: +44 (0)1483 730071 Fax: +44 (0)1483 730008 www.management-forum.co.uk
26-27 November 2008	Clinical Pharmacology and Pharmacovigilance	Mexico	Mexican Association of Pharmacovigilance www.farmacovigilancia.org.mx/
8 December 2008	Essential Guide to Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730071 www.management-forum.co.uk
8-10 December 2008	Practical Guide for Pharmacovigilance: Clinical Trials and Post Marketing	Paris, France	DIA European Branch Office Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
11-12 December 2008	Advanced Workshop Et Round Table Meeting on Pharmacovigilance Planning and Risk Management	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org
15-17 December 2008	Basic Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730071 www.management-forum.co.uk
28-30 January 2009	Medical Aspects of Adverse Drug Reactions	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org
23-25 March 2009	DIA 21st Annual Euro Meeting	Berlin, Germany	DIA European Branch Office Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
9-11 April 2009	P2T – including Journées de Pharmacovigilance	Marseille, France	Société Française de Pharmacologie et de Thérapeutique http://www.congres-p2t.fr/
25 May-5 June 2009	Pharmacovigilance - The Study of Adverse Drug Reactions and Related Problems	Uppsala, Sweden	the Uppsala Monitoring Centre Tel: +46 18 65 60 60 E-mail: info@who-umc.org www.who-umc.org
6-9 October 2009	Annual Meeting of the International Society of Pharmacovigilance (ISoP)	Reims, France	ISoP www.isoponline.org/upcoming-meeting.html

the Uppsala Team

Director

Ralph Edwards, MB, ChB, FRCP (Lond), FRACP Professor in Medicine, **Director**

Deputy Director

Marie Lindquist, Dr Med Sc Chief Scientific Officer

Finance and Core Services

Birgitta Toreheim, CA **Manager, Chief Financial Officer**

Ali Bahceci **Network Technician**

Britt Gustavsson-McCurdy **Corporate Secretary**

Anneli Lennartsson **Economy Assistant**

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Safety Support and Services

Monica Plöen, BSc Pharm **Manager**

Jenny Bate, BSc Pharm **Signal Detection (on maternity leave)**

Cecilia Biriell, MSc Pharm **Senior Specialist, WHO-ART**

Mohamed Farah, Pharm D **Senior Specialist, Traditional Medicines**

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Helena Sköld, MSc Pharm **Signal Detection**

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