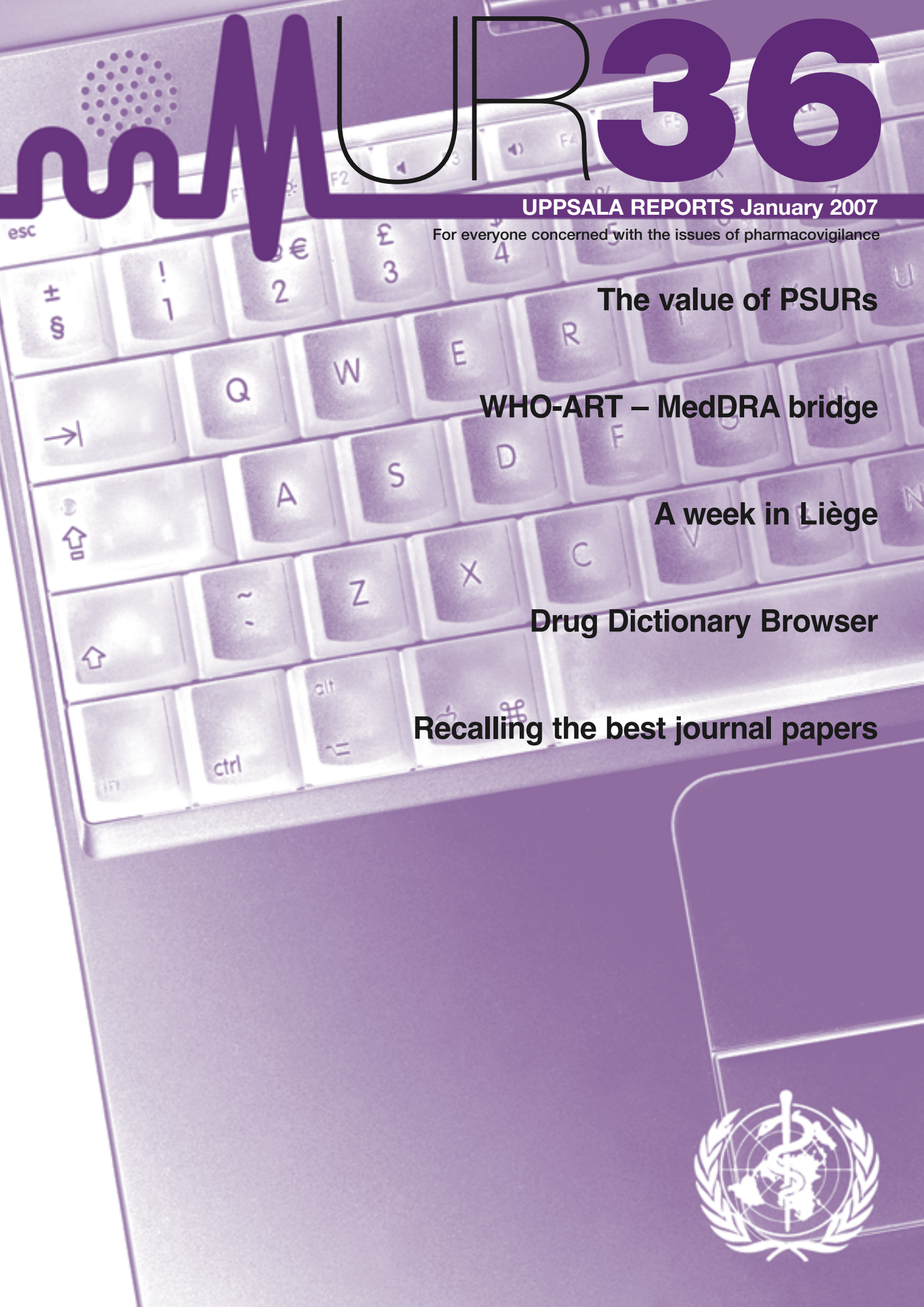

UMR 36

UPPSALA REPORTS January 2007

For everyone concerned with the issues of pharmacovigilance

The value of PSURs

WHO-ART – MedDRA bridge

A week in Liège

Drug Dictionary Browser

Recalling the best journal papers

DIRECTOR'S MESSAGE

Ralph Edwards
Director
the Uppsala Monitoring Centre

In considering the future of pharmacovigilance, almost invariably, the discussions at meetings end with a plea for better education of both health professionals and patients about the benefits and risks of drugs, and of course their appropriate use.

In thinking around this, I am still dismayed that the real, day-to-day prescribers, dispensers and users of drugs are often not represented at such meetings. But as important is our failure to grapple with the realities of health professional education.

For some years now, I have been an external examiner in pharmacology at the University of the Witwatersrand in South Africa each November. This outstanding Department runs courses in pharmacology for dental, pharmacy, nursing, physiotherapy, and science students and is fully involved in problem-based learning for medical students. They do this with four full-time and four part-time staff. Their resources have been much reduced over the last few years, but they still manage to run some post-graduate research, as well as teaching in seminars for graduate health professionals. It is obvious that contact time with students is limited, and there are no margins for staff sickness etc.

Wits Medical School (as it is often called) is not that unusual in its limitations, nor in its high ambitions. I hear from around the world that departments of pharmacology want to do much more in ensuring that students really know about safe prescribing, the practical importance of kinetics, drug interactions etc, as well as the essentials of basic and clinical pharmacology.

I am also told that the contact time with students in medical schools is about one month: is that sufficient to learn how to use the main tool of the health professional's trade? I don't think so. My view of essential activities, taking two professions as examples, would be as follows. ALL practising doctors must absolutely be able to do two things: make diagnoses, and provide treatment, usually drugs. ALL practising nurses must directly manage patients, including the administration of drugs, and make primary clinical observations, including adverse reactions. Teaching these core duties has been submerged in recent years by pressure to make doctors better managers and to understand their role in society better. This has been reflected in the curricula around the world.

The result of current health care education is that more topics are added to the curricula (such as management) at the expense of the core skills mentioned above, but external pressures are put upon doctors to perform their basic tasks with ever more cost/time effectiveness by the ever-increasing numbers of managers and bureaucrats.

Succinctly put, health professionals have less training in core skills and more demands on them to use those skills in ever more limited consultation time, with increased technical complexity of therapies, and under management pressures, – result: medical error and reduced patient safety.

While educating the health professionals of the future we mustn't lose sight of the ever-growing body of existing research. On page 10 we feature the first of what we hope to be a regular slot where a distinguished expert makes their personal choice of five important pharmacovigilance papers. And on page 20 we introduce a reprint collection of papers by one of the modern pharmacovigilance pioneers, Professor David Finney, whose publications from the 1960s onwards demonstrate the time it sometimes takes to develop ideas on issues in medicines safety, many of them timeless issues still debated today.

CONTENTS

the UPPSALA MONITORING CENTRE

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.

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

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

Sales & marketing enquiries: info@umc-products.com

Internet: www.who-umc.org

Editors: Sten Olsson and Geoffrey Bowring

ISSN 1651-9779

Belgium hosts 29th meeting of member countries

Over a hundred people representing 43 countries attended this year's meeting in Liège from 8-11 October. Major plenary topics included pharmacovigilance planning and its implications for developing countries; information sharing between national pharmacovigilance centres, and an evaluation of PSURs. *(See pages 12-13.)*

The Palais des Congres in Liège alongside the River Meuse

Two sets of workshops examined a wide range of issues, including types of monitoring required when new medicines are introduced in resource-limited and developed countries; safety monitoring for pandemic flu-vaccines and emergencies; global networking; collaborations with vaccine programmes; and several aspects of patient safety. A more detailed account of the working group sessions and recommendations made by them is available in the WHO Pharmaceuticals Newsletter No 6, 2006 p7–10.

There were updates on the WHO consultation on global monitoring of adverse events following vaccination; the WHO-ART – MedDRA collaboration; and the Programme's pilot patient safety project, currently getting underway in seven participating countries.Twenty 'Drugs of Current Interest', grouped in three sessions, were presented by participants and discussed by the audience.

In her report from WHO HQ, Mary Couper spoke of the new full and associate member countries which have joined the WHO Programme since the 2005 annual meeting, making the total membership 81. Her division had had an active year:

- Many publications, including the Pharmaceuticals Newsletter and guidelines for safe practice in public health programmes and clinical research
- Safety reviews and/or pharmacovigilance guidelines for specific products, such as kava, anti-retrovirals and the amodiaquine/artemisin combination
- Participation in global meetings such as ICDRA, ICH, ISO and the Advisory Committee on Medicines and Vaccines
- Organisation of training in pharmacovigilance itself and in relation to HIV/AIDS
- Involvement in developing vaccine pharmacovigilance and the pilot patient safety project.

It was clear that many organisations were keen to pursue goals which have long been advocated by the WHO Programme and *the* UMC, notably the improvement of information and communications throughout the whole area of medicinal safety, and in the refinement of signal detection methods.

Ralph Edwards highlighted the dilemma of *the* UMC as the organisation continues to survive without external funding of any kind and must divert a portion of its resources to income-generation. He emphasised *the* UMC's commitment to the welfare of those damaged by medicines, and to the prevention of such damage, as well as the preservation of useful medicines for the majority. In this sense, *the* UMC does not share the same over-riding public health perspective of other bodies – part of its uniquely important function. Patient safety remains its core focus.

The local host was Thierry Roisin from the Directorate-General Public Health Protection: Medicinal Products in Belgium, and he and his team provided a very effective venue for the meeting (the Palais des Congrès by the river Meuse), and a splendid gala dinner in the magnificent Palais des Princes-Evêques.

Bruce Hugman, Mary Couper and Thierry Roisin on the platform in Liège

The meeting was busy, but informal and friendly, and everyone appeared to have a good time. That impression was confirmed by the post-meeting evaluations which were very positive, while as usual providing suggestions for future improvements.

2007 venue announced

The 30th meeting will be held in Buenos Aires, capital of Argentina, at the invitation of the Administración Nacional de Medicamentos, Alimentos y Technología Médica (ANMAT), from 11-13 October 2007 (proposed dates). This will be the first time the WHO Annual Meeting has taken place in South America.

Satisfying ISoP

The 6th ISoP Annual Meeting which followed (with a joint symposium in common with the WHO delegates) had not only a heavy programme of plenary lectures across the breadth of drug safety, but an impressive assembly of posters. Over 180 abstracts were listed with the DSRU and the Moroccan and Tunisian pharmacovigilance centres prominent among them.

A slimmed-down ISoP Executive is now headed by President Nicholas Moore. In 2007 the Society goes to Bournemouth on the south coast of England from 21st–24th October. Marie Lindquist of *the* UMC is one of the new members of the ISoP Executive Committee.

ISoP posters

The ISoP poster committee (Professor Jean-Marie Maloteaux, Belgium and Drs Michael Tatley, New Zealand and Ronald Meyboom, the Netherlands) had an exciting experience progressing through almost 200 diverse posters, all interesting, many very valuable. It was practically impossible to decide which posters were better or best.

The first prize was awarded to Dr Jimmy Jose and the team of the Manipal College of Pharmaceutical Sciences in Karnataka, India, for their intensive hospital study of the adverse reactions to fluoroquinolone derivatives. Hospital and regional pharmacovigilance centres around the world have in recent years become powerful sources of real-life drug safety information and the judges were equally pleased with this well-organised, comprehensive and long-lasting study.

The two second prizes went to posters on the prevention of adverse drug reactions. Dr Loubna Alj and co-workers at the Moroccan Pharmacovigilance Centre studied the preventability of adverse reactions, and Dr Roberto Leone (Verona) and his colleagues of the multi-regional GIF database presented the prevailing causes of fatal adverse reactions in Italy.

The two third prize winners were studies on drug prescription data as a source of information. Dr Sequira and co-workers from Bahrein, on the dangerous prescribing of topical corticosteroids to children, and Dr Marianna Alacqua and her colleagues from Messina and Caserta in Sicily, concerning the changes in prescribing in osteoarthrosis after the sudden withdrawal of rofecoxib.

Posters involving the UMC at ISoP 2006

Beta-2 Adrenoceptor agonists and nocturnal enuresis (oral)
RH Meyboom, J Pokladnikova, M Plöen

Can WHO-database of suspected ADRs be used to support existing information on pharmacokinetic drug interactions?
J Strandell, A Bate, B Eiermann, M Lindquist, IR Edwards

Concomitant use of glucosamine potentiates the effect of warfarin.
Q-Y Yue, J Strandell, O Myrberg

Hypersensitivity reactions to Umckaloabo (Pelargonium sidoides DC and P reniforme Curtis)
H De Boer, U Hagemann, J Bate, RH Meyboom

Intranasal corticosteroids and psychiatric disorders
J Pokladnikova, RH Meyboom, J Vlcek, IR Edwards

Pulmonary fibrosis reported with statins
A Kiuru, Q-Y Yue, RH Meyboom

Readers are referred to *the* UMC website (Publications > Posters) for pdf files of the posters, or to *Drug Safety* 2006(29) 10:911-1010 for the full abstracts of all posters presented at the ISoP Liège meeting.

Nepal joins Programme

The Nepal Department of Drug Administration (DDA), the national drug regulatory authority, was established in 1979, to assure safety, efficacy and quality of medicines available in Nepal. On the basis of data from other countries, the DDA has in the past banned several drugs, and registration of some products reported to be unsafe (such as cox-2-inhibitor, gatifloxacin) has been refused. However, no system existed to collect ADRs within the country.

In October 2004, the Government of Nepal nominated the DDA as the focal point (National Centre) to liaison with the WHO Collaborating Centre for International Drug Monitoring in Sweden and start collection of adverse drug reactions; Nepal became a WHO Programme member in July 2006. The DDA acts as national centre for ADR monitoring and regional centres operate under the DDA. Three meetings were held with central government hospitals and medical teaching hospitals management personnel to initiate ADR reporting and for finalization of an ADR reporting form.

Pharmacovigilance staff outside the DIPC in Pokhara

At present, only one centre in Nepal is active in the ADR monitoring programme, and others are yet to start activities. This centre is located at the Manipal Teaching Hospital (MTH), Pokhara, a 700-bed tertiary care teaching hospital in western Nepal. This centre has taken the initiative in establishing pharmacovigilance activities.

ADR reporting forms are placed in the wards and outpatient departments of the hospital. When ADRs are reported, the concerned healthcare professionals (doctors, nurses, pharmacists, medical interns, postgraduate pharmacology students) report the ADR to the pharmacovigilance cell of the Drug Information and Pharmacovigilance Centre (DIPC). The centre normally works from 9am to 5pm during working days, but is contactable 24 hours a day for information in emergency cases, even during holidays. Pharmacists attending the ward rounds also report ADRs to the centre. Since the centre is attached with the DIPC, it has access to updated sources of drug information such as Micromedex, British National Formulary, Meyler's etc.

The centre has received 150 ADR reports from the various hospital departments since its inception and has published a few interesting case reports in journals as a part of its dissemination activities. The centre is also involved in research activities related to drug safety and

Continued on page 6

Continued from page 5

publishes a quarterly bulletin 'Vigil', which shares the experiences of spontaneous reporting with other healthcare professionals. The bulletin also publishes a few case reports that have clinical significance.

The centre has plans to convert the spontaneous reporting programme to a fully-fledged pharmacovigilance programme. The centre is also in the process of setting up community based pharmacovigilance in the Western region of Nepal. The DDA is organizing an awareness programme in December 2006 for hospitals, where ADR reporting forms will also be disseminated.

Contact persons for Nepal are:
Mr Bhupendra Bahadur Thapa, Director
Mr Gajendra Bahadur Bhuju, Drug Administrator
Department of Drug Administration
Ministry of Health and Population
Government of Nepal
Tel: + 977-1-4780432/4780227
Fax: + 977-1-4780572
E-mail: dda@healthnet.org.np Web: www.dda.gov.np

Anti-retroviral adverse events

Prospective intensive monitoring of the safety of ARVs

The benefits of anti-retroviral therapy in prolonging the lives of people living with HIV/AIDS (PLWHA) are clearly established, but their utility can be greatly reduced if patients do not adhere to treatment. Several factors including treatment-induced adverse reactions are known to reduce adherence to treatment and these may compromise the effectiveness of these medicines, most of which are expected to be taken on a long-term basis.

There is very little information on the safety of anti-retroviral drugs (ARVs) in Ghanaians (or indeed sub-Saharan Africans in general). Whilst toxicity of ARVs has been shown to lead to missed doses and reduced adherence to therapy, identification and proper communication of expected side effects of ARVs to patients has also been shown to lead to increased adherence. Ignorance of the toxicity profile of commonly-used ARVs may compromise the quality of care if practitioners are unaware of both common and rare side effects, the types of patients likely to suffer particular reactions and options for managing these reactions. Where toxicity is unexplainably high, patients may not derive the proven benefits from anti-retroviral therapy and may refuse to adhere to treatment. Physicians may also needlessly switch patients from one treatment regimen to the other at great financial cost to the National AIDS Control Programme.

A project being launched in Ghana aims to create an intensive pharmacovigilance and safety surveillance programme for ARVs. The specific objectives are:

1. To monitor suspected adverse drug reactions (ADRs) and adverse events (AEs) to all anti-retroviral drugs in Ghana
2. To record AEs and ADRs to ARVs
3. To perform case-causality assessment of serious reported serious adverse events (SAEs)
4. To calculate the incidence of ADRs and AEs to specific ARVs
5. To characterise the types of ADRs to specific anti-retroviral drugs
6. To develop a manual for the clinical management of ARV-induced ADRs and AEs
7. To educate health professionals on the identification, reporting and management of ARV-induced ADRs and AEs.

This study, the first of its kind in Ghana, will be an open label, prospective, non-randomised intensive monitoring of the safety of ARVs to establish the types and rates of adverse reactions to ARV in Ghana. The study population will be all consenting patients on anti-retroviral therapy in the four pilot sites. This focused surveillance method of soliciting for adverse events will permit calculation of incidence rates, since the crude denominator values will be available. For active post-marketing safety surveillance of medicines in specific identifiable populations focused surveillance has advantages over spontaneous reporting, the cheaper and more common method employed in routine pharmacovigilance.

Korle-Bu Fevers Unit, one of the four pilot sites for ART delivery.

Case-causality assessment on all serious adverse events (SAEs) will be carried out using standard WHO criteria and any risk factors predictive of adverse drug reactions will be noted bearing in mind the technical challenges of assigning causality to drugs used regularly in combination. Interventions for the management of observed adverse events will be developed and healthcare workers dealing directly with PLWHA in the four sites will be trained formally on the identification, reporting and clinical management of adverse events to anti-retroviral drugs.

All ADR/SAE reports will be maintained on VigiFlow, an E2B-compliant web-based secure database for the management of adverse drug reactions data. Data is entered and stored anonymously and the database is maintained and serviced regularly by *the* Uppsala Monitoring Centre.

It is hoped that this project will sensitise patients and health workers in this resource-limited country on the importance of regular safety monitoring of drugs for diseases of public health importance. It will give policy makers evidence on which to base treatment guidelines and protocols and provide patients and health professionals with information that will encourage adherence to treatment and promote the rational use of medicines.

The project team will include Dr Margaret Lartey (Physician in charge of the biggest ARV pilot site), Prof David Ofori-Adjei (a member of the UMC Signal Review Team) and Prof K K Adjapon-Yamoah (Physician and Clinical Pharmacologist) who will all be involved in case-causality assessment of SAEs and participate in writing the manual for clinical management of ADRs to ARVs. Pharmacists Augustina Appiah-Danquah, Jerry Nee-Whang and Ofori Tenkorang will be responsible for the day to day running of the project. The Principal investigator is Dr Alex Dodoo, Senior Research Fellow and Ag. Director of the Centre for Tropical Clinical Pharmacology & Therapeutics, University of Ghana Medical School.

Teaching hospital pharmacovigilance

The Indian Council of Medical Research (ICMR) has sanctioned 2.7 million Indian rupees (around 20,000 euros) for a 3 year project to establish ADR reporting and monitoring in five hospitals in the southern Indian state of Karnataka. The project aims at establishing or strengthening a pharmacovigilance programme in five teaching hospitals. Principal Investigator of the project is Dr G Parthasarathi, Professor and Head, Department of Pharmacy Practice, JSS College of Pharmacy and Head of the Department of Clinical Pharmacy, JSS Medical College Hospital in Mysore. He has the responsibility of co-ordinating the work with these institutions. Five senior research fellows will be working on this project at different centres possibly leading to the award of PhD degree in the area of pharmacovigilance.

Co-ordinators from different centres: Sitting L to R: Dr P A Patil (Belagaum) Dr Padma Rao (Manipal), Dr Shoba Guido (Bangalore) Standing L to R: Mr Ganachari (Belagaum) Dr G Parthasarathi and Dr M Ramesh (Mysore)

This is a worthy reward to Professor Parthasarathi's department and recognition of their work in the area of pharmacovigilance. It appears that this is the first time the ICMR has sanctioned this kind of a project to a principal investigator from a non-medical background. As one of the first institutions to show that a trained pharmacist can contribute to a great extent in the area of ADRs, this is recognition for clinical pharmacy programmes in India.

the UMC has had good contacts with Mysore for several years (Dr Parthasarathi attended *the* UMC course in 1999) and has offered basic training, encouragement and support for their pharmacovigilance programme.

Senegal

Senegal in west Africa has seen several initiatives over the last year to introduce pharmacovigilance of anti-malarials, *reports Rachida Soulaymani Bencheikh.*

A collaboration involving the WHO Region Office for Africa and country representatives in Morocco and Senegal is seeking to use the prescription of new combination therapies as a springboard for a Senegalese drug monitoring system.

Rachida Soulaymani Bencheikh and delegates at the Training meeting in Senegal

A workshop in Mbodiène in August 2006 brought together various players in the medicines field along with governmental and public health representatives to draw up an action plan. Discussion sessions, guided towards methods already proven internationally, lead to a detailed plan with deadlines. The key aim is to ensure that the national 'Roll Back Malaria' actions propel the development of full pharmacovigilance activities, particularly through capacity-building. A national pharmacovigilance centre, possibly incorporating other functions, will be necessary to co-ordinate and evaluate the planned activities. Support for the project activities has also come from the Global Fund.

New WHO DG

On 4th of January 2007 Dr Margaret Chan (PR China) became Director-General of the World Health Organizaztion.

From 1994 she was Director of Health of Hong Kong, moving to the WHO in 2003 to become Director of the Department for Protection of the Human Environment, and in 2005 Director, Communicable Diseases Surveillance and Response, WHO Representative of the Director-General for Pandemic Influenza, WHO.

Essential Medicines Policies

WHO-HQ regularly holds a seminar for staff from WHO Programmes, Collaborating Centres and others. Helena Sjöström from the UMC reports on the September 2006 week, which she attended with delegates from 20 other countries.

The sessions covered:

- Developing National Drug Policies
- Selection of Essential Medicines
- Access to Medicines
- Impact of Globalization
- Trade Agreements
- Drug Regulation
- Quality Assurance
- Procurement and Supply Systems
- Promoting Rational use of Medicines
- UN Pre-qualification Programme.

Main Challenges

Essential Medicines are defined by the WHO Expert Committee in April 2002 as "Essential medicines are those that satisfy the priority health care needs of the population".

- 33% of the world has no regular access to essential medicines
- Substandard and counterfeit medicines are widespread
- Irrational use leads to suboptimal treatment and waste.

Medicines work is often undervalued and underfunded, but medicines standards are essential for all Member States, and for most WHO Programmes.

Selection of Essential Medicines

Essential medicines are selected with regard to disease prevalence, evidence on efficacy and safety, and comparative cost-effectiveness. The WHO Model List of Essential Drugs began with around 200 active substances but as of 2006 there are 316 included, with a Core list (the minimum medicines needs) and a Complementary list (specialized).

Quality Assurance and Safety: Medicines

Areas of activity of this Unit at WHO (the one most closely associated with *the* UMC, and which controls the WHO Programme) are:

- Nomenclature
- Quality norms and standards
- Drug safety and information
- Pre-qualification' of Priority Medicines
- International harmonization.

One of the strategic directions of the WHO is to expand work on drug safety and rational use, with focus on pharmacovigilance in resource-poor settings, chronic treatments and containing antimicrobial resistance. Priorities for the near future include counterfeit medicines, pre-qualification of priority medicines and essential medicines for children.

Counterfeiting

The types of counterfeit products vary between developed countries (hormones, steroids) and developing countries (antibiotics, anti-malarials). The targets of counterfeiters tend to be expensive drugs, and those with a high volume or consumption. Currently 10% of the global medicines trade is counterfeit, equivalent to around 1% in Europe; 10-30% in parts of Asia, Africa and parts of Latin America; over 20% in Former Soviet republics, and over 50% via the internet.

IMPACT
International Medical Products Anti-Counterfeiting Taskforce

An International Medical Products Anti-Counterfeiting Taskforce (IMPACT) has been established. It will use a web-based system for tracking the activities of drug cheats and work with regulators to develop guidance for pharmacovigilance systems to include reporting and investigating suspected cases of counterfeit drugs.

The need for 'Pre-qualification'

This UN project managed by WHO aims to ensure quality and standards in medicines within a rigorous but efficient process. A manufacturer must apply for assessment and GMP inspections, after which innovator products with current authorization have fast-track process for listing (2 months from application). With substandard or counterfeit products it should eliminate or reduce the risks of sourcing drugs. Manufacturers can thus comply with international standards and participate in solving health emergencies. This will benefit millions of people with HIV/AIDS, tuberculosis or malaria who also have limited access to treatment.

Outcomes of Pre-qualification

The result are likely to be public lists of products and manufacturing units that meet international standards on quality, safety and efficacy. There should also be capacity-building for countries to produce good-quality ARVs (antiretrovirals) and on-going quality monitoring of pre-qualified products and quality control laboratories.

Children

Children are therapeutic orphans: there is a lack of appropriate clinical trials, a lack of licensed medicines and formulations, as well as a lack of information and access. Initiatives so far have concentrated on developed country regulatory structures (eg FDA, EMEA) and drug information (eg British National Formulary for Children), but these initiatives do not improve access to child-appropriate formulations of essential medicines.

A WHO/UNICEF Expert Consultation in August 2006 added respiratory tract infections and diarrhoea to the other priority disease areas (Malaria, HIV and Tuberculosis). ADR information is essential to support safe use of medicines. Risk factors with ADRs include young age, continuous changes of drugs, polypharmacy, unlicensed and off-label medicines, poor nutritional status and medication error. There is an urgent need to develop a system for enhancing safety monitoring of medicines in children.

My understanding of the concept on how to improve Access, Quality and Rational use of Essential Medicines has increased enormously and is now of great value in my daily work with ADRs at *the* UMC.

First steps in Kenya

Dr Jayesh M Pandit writes:

The first Stakeholders Workshop on Pharmacovigilance was held from 27-28 November 2006 in Nairobi. Organised by the Department of Pharmacovigilance and Post-Market Surveillance, the Pharmacy and Poisons Board, the workshop examined all aspects of implementing an appropriate pharmacovigilance reporting and monitoring system in Kenya. The stakeholder group comprised governmental and non-governmental organizations active in Pharmaceutical and health sector reform programmes, academics and WHO Technical advisers and field staff.

Objectives

The main objectives of the workshop were to:

1. Review and agree an Adverse Drug Reaction (ADR) reporting form
2. Develop and agree on other tools
3. Define a National Pharmacovigilance System
4. Suggest an appropriate Implementation Strategy for the Pharmacovigilance system.

Discussions

The workshop was opened by Dr F M Siyoi, Chief Pharmacist, Ministry of Health, who set the climate on what was expected over the next two days. Detailed presentations followed, all informative in aspects of educating participants on what pharmacovigilance is about, the perspective and experience from regional countries and the WHO's approach and requirements for pharmacovigilance in any country. In working groups, participants discussed the draft tools and financial implications, and proposed implementation strategies.

Recommendations

The groups presented their proposals in plenary, where they were discussed in detail by all participants. The recommendations that emerged were indeed very appropriate bearing in mind the current scenario of medicine use in Kenya. For the 'ADR reporting form' and the 'Alert card', it was proposed that there should be one, simple and easy to fill 'ADR reporting form' used to generate reports and detect any signals, if present; and another 'ADR documentation form' for investigating specific reports. The 'ADR reporting form' should be accessible to all health professionals, and be made available at all levels.

It was proposed that all activities pertaining to this be located at the Department of Pharmacovigilance and Post-Market Surveillance, Pharmacy and Poisons Board. Ideally it is hoped to cover the entire country at all levels, but if limitation of resources is a key issue countrywide, then a pilot survey can be carried out.

The WHO data collection software 'VigiFlow' would be evaluated to confirm if it can capture all the information required in Kenya, or an appropriate database should be designed. Field-testing at sentinel sites should be carried out as the earliest with the aim of a roll out in April 2007.

On training, an advocacy meeting was proposed to ensure commitment from stakeholders followed by a continuous training for clinicians, pharmacists, pharmaceutical technologists, nurses, and clinical officers. Pharmacovigilance training should be inculcated into university curricula.

News from Malaysia

Abida Haq is well-known to many throughout the WHO Programme 'family' is moving on from her current post to take on another job within the Malaysian regulatory agency. Her successor, Mrs Tan Lie Sie, has experience in drug regulation, having been in the drug evaluation division for many years.

Togo Training

The Moroccan Pharmacovigilance Centre has been asked by WHO Africa Region Office to help develop and set-up a pharmacovigilance system in Togo. A mission was undertaken by Dr Amina Tebaa in Lomé at the WHO office from 27th November to 8th December 2006.

Training course in Togo; Dr Amina Tebaa (front row, centre), on her right Dr Adjogble Kokou (Assistant of the General Director of health ministry), on her left WHO representatives in Togo, Dr Nyansa Atany (drug regulatory director) and Dr Morgah Kodjo (National anti-malarial programme co-ordinator).

The aims were:

- to review the pharmacovigilance system in place for drugs in general and anti-malarial drugs in particular
- to review the drugs regulation procedures and make recommendations as needed
- to train health workers at the national level in pharmacovigilance
- to develop a pharmacovigilance implementation plan for 2007.

My Top Five Papers

We asked an experienced person in the world of pharmacovigilance with wide knowledge of the discipline and its history to choose the five scientific papers they consider to be most important, interesting or influential.. Here, ***David Coulter*** *introduces his own 'top five' papers; we hope readers will be encouraged to seek out and explore his chosen articles.*

It has been fascinating going back to old papers that guided me in my early days in pharma-covigilance. There are insights that have set the foundation for our work today. There are insights that we are still talking about as though they were new and still we have not come to grips with them. There are few ideas, which are now not so important or no longer apply because we live in changed days. Here are my top five, in date order.

David Coulter

Graduated in medicine 1959 at Otago University, Dunedin, New Zealand. After two years internship, he worked as a sole practitioner in an isolated rural group of islands in the New Hebrides (now Vanuatu). Diploma in Tropical Medicine & Hygiene Sydney University 1964. After 11 years he returned to New Zealand and entered general practice with a part time appointment in rheumatology. In 1977 he was recruited to initiate a new programme in the Adverse Reactions Centre, Department of Pharmacology, Otago Medical School. This was the Intensive Medicines Monitoring Programme (IMMP). Initially a one tenth appointment, it gradually expanded to full time in 1995. Worked with Professor Garth McQueen (an early mover in international collaboration) and Professor Ralph Edwards. As well as being director of the IMMP, he later became head of the New Zealand Pharmacovigilance Centre and Research Associate Professor. Retired in 2004 and has since become a consultant and advisor to WHO on the safety of medicines.

Finney DJ. The design and logic of a monitor of drug use. *J Chron Dis*, 1965, 18:77-98.

A foundation document for pharmacovigilance. Over 40 years ago, in response to the thalidomide disaster, David Finney designed a monitoring system for the early identification of previously unrecognized adverse reactions and their characterization. There is much in it that we have done, some that has been adapted and much that very few have done and need to do.

Some quotes:

The purpose of monitoring is "to ensure that observations on a large number of persons who receive a new drug are collated and used effectively; only so can a warning of any untoward consequences be given as early as possible."

"...a reporter is not required to judge whether an event was drug-induced, though he may usefully express an opinion." A reporter's job is to report!

"The quality of results coming out of a computer cannot be higher than the quality of the records put in. Limited but conscientiously compiled records will always be preferable to an indiscriminate mixture of sound information and garbage."

He emphasizes the importance of "a skilled medical scrutineer at the centre" in identifying new ADRs.

"Any reasonable estimate of cost... [in setting up and running a centre] will surely be a small figure relative to the potential savings."

"WHO should assume responsibility" for an international database compiled from international collaboration – and it has.

He also recommended establishing a standard terminology and defined adverse events.

Karch FE, Lasagna L. Adverse Reactions. A critical review. *JAMA*, 1975, 234:1236-1241.

From the abstract: "The data on [spontaneously reported] ADRs are incomplete, unrepresentative, uncontrolled... No quantitative conclusions can be drawn from the reported data in regard to morbidity, mortality, or the underlying causes of ADRs, and attempts to extrapolate the available data to the general population would be invalid and perhaps misleading... studies on the benefits of drug use are needed to provide perspective on the risk-benefit." Have we become lulled into the belief that spontaneous reporting alone is adequate?

Karch and Lasagna present the categories of cause-effect relationship that we use as standard today: definite, probable, possible, conditional and doubtful. We should all re-read the 'conditional' category. It is promoted as a temporary classification for those cases that may be manifesting an as yet undescribed ADR. This category would prevent the loss of previously unsuspected adverse reactions, and help identify new ADRs. They deplore the inclusion in analyses of large numbers of unassessed events, without evidence of any relationship to a drug; we still suffer from this problem with the largest contributor to the WHO database sending reports that are still largely unassessed. I like the expression, "firmness of the link" when referring to the cause-effect relationship, which, confusingly, we normally refer to as 'causality'.

Skegg DCG, Doll R. Frequency of eye complaints and rashes among patients receiving practolol and propranolol. *Lancet*, 1977, ii:475-478.

A report of an epidemiological study investigating possible early events that might be related to the serious oculomucocutaneous syndrome with practolol. In principle, there are two things of great value:

a) The patients are used as their own controls with equal periods being examined before and after first administration of the drug. This is a very underutilized method of study in spite of the fact that we frequently bemoan the absence of a good control group.

b) This was one of the early studies using event recording, rather than that of suspected reactions. Minor events seemingly related to the serious practolol problem were common and were observed, but not linked to the drug. It also demonstrates that the recording of non-serious events has the potential for alerting to an ADR which may prove to be serious. Recording of all events early in the post-marketing phase could have averted the practolol-related tragedy for a significant proportion of the affected patients. 30 years on, few have acted on this principle in post-marketing surveillance.

Venning GR. Identification of adverse reactions to new drugs. *BMJ*
Part I. What have been the important adverse reactions since thalidomide? BMJ, 1983, 286:199-202.
Part II. How were 18 important adverse reactions to new drugs discovered and with what delays? BMJ, 1983, 286:289-292 and 365-368.
Part III. Alerting processes and early warning systems. BMJ, 1983, 286:458-460.
Part IV. Verification of suspected adverse reactions. BMJ, 1983, 286:544-547.

On the basis of a survey of UK physicians and regulatory authorities internationally, Venning selected what seemed to be the most important reactions identified post-thalidomide up until 1982. He evaluates the processes of alerting and verification of reactions and delays to regulatory action. Many things have changed since this series was published, but the discussion on the means of verifying alerts (signals) remains extremely valuable. Using patients as their own controls is promoted, thus avoiding biases in the selection of control groups.

Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients. A meta-analysis of prospective studies. *JAMA*, 1998, 279:1200-1205.
A landmark study highlighting the cost of adverse reactions (only) in hospitalized patients in the USA. A very good prospective study in the UK by Pirmohamed et al (BMJ 2004; 329:15-19) reinforces these findings. What does it take for governments to note these data and for them to fund monitoring systems adequately? We need to keep repeating these messages in the highest forums where policy is made and to stimulate ourselves with the reminder of the importance of our work.

Medicines for Children: Everything to do!

At the 9th European Health Forum at Bad Gastein in Austria, a panel of international experts brought together by IMS Health, the Pharmaceutical Group of the EU and the Task Force for Drug Development in the Young (TEDDY) welcomed a new EU Regulation on Paediatric Medicines but outlined further work that needs to be done. This includes:

- The workings of the Paediatric Use Marketing Authorisation needs to be clarified if financial opportunities are to outweigh the risks
- More co-ordination of research is essential if the potential of cross country studies is to be realised
- The development of longitudinal databases is essential to the safe use of drugs; this means greater use of computerisation in health care systems
- Consistency in interpretation of the Data Protection Directive across the EU is essential if sufficient ADR information is to be gathered
- A practical approach is needed to ensure a common understanding between patients, researchers, policy makers and health professionals of research and appropriate disease management
- This information, tailored in particular to the needs of the patient, should harness the power of the media to develop trust and thus effective treatment and clinical trial recruitment
- Health professionals should collaborate in multidisciplinary clinical teams and this requires a more structured approach to training and practice.

Ralph Edwards demonstrated that as well as under-reporting of side effects in regulatory databases, there were particular challenges affecting paediatric pharmacovigilance, not least the possibility of biasing by gender. He urged greater collaboration between regulators and database operators, leading to the development of new, more accurate signal generation techniques.

Children are not small adults pharmacologically and this poses particular challenges for pharmacovigilance. Developmental changes also mean that stratification is needed by relatively narrow age bands, so making it more difficult to find signals. Paediatric drugs require special attention as the types of drugs most commonly associated with side effects (notably vaccines) are not commonly used or associated with side effects in adults.

The panel was chaired by John Chave, Secretary General, PGEU and consisted of Professor Ian Wong, Professor Ralph Edwards, Dr Patricia Hamilton, Dr Tsveta Schyns, Ema Paulino, and Peter Stephens, Vice President of Public Health, IMS Health.

For further information, contact:
Peter Stephens, IMS Health: Tel:+44 (20) 7393 5323
John Chave, PGEU: Tel: +32 2 238 08 18

Are PSURs worthwhile?

Ralph Edwards, Mira Harrison-Woolrych, Marie Lindquist

At the October 2006 Annual Meeting of the WHO Programme members in Liège there was a plenary discussion about the value of Periodic Safety Update Reports (PSURs). Whilst members from some countries believe that PSURs are worthwhile, other countries question their value as a pharmacovigilance tool; whether the resources required to assess PSURs justify the outputs from these documents. Some regulatory authorities are therefore considering to what extent the evaluation of PSURs should be included in their pharmacovigilance processes. It is now timely to ask the question: 'Do PSURs do anything valuable enough to justify the work involved?'

Why were PSURs introduced?

In 1992, only the USA had a form of periodic review of products, but then the final report of CIOMS Working Group II[1] launched the idea of PSURs internationally. The need was precipitated by a discussion between the late Dr Bengt-Erik Wiholm and one of us (Ralph Edwards) after the introduction of mandatory reporting by industry of international suspected ADRs. Sweden and New Zealand were being swamped by case reports from industry sources. There was a considerable challenge of checking quality and duplications against the international data held by the WHO Programme for International Drug Monitoring. Then, industry had broadly defined responsibility to alert the health authorities, via the regulatory agencies, of any safety concern involving their products. The sending of countless single reports was an industry way of avoiding the responsibility for their internal scrutiny of data and for taking the difficult decisions over safety issues.

The purpose of the PSURs is clearly stated in the Introduction to CIOMS II, as
"Such summaries could fulfil the needs of countries that lack the capacity to handle single cases of ADR appearing in foreign countries…",
and,
"…for companies to report safety information to regulatory bodies, and to elaborate uniform procedures that should meet most existing and future needs…".
The CIOMS II concepts and procedures were tested with real-life data in a pilot study involving 10 companies: this was no trivial exercise for the companies, and shows the rigour of the initial work, but all involved thought it was a worthwhile and essential task for industry. Pilot companies had relevant data in many places within their organisations and it was a challenge to get them together.

On the output side it was agreed that the essence of the report should be in the companies' summaries, which should represent their legally-binding opinion of the safety situation regarding their product during the relevant time period. All other sections should be a compilation of the information which supported the conclusions in their summaries.

A fictitious example of a report on 'Queasytrol' was included as an appendix to the Report. It was often reiterated during many meetings that the reports should be as concise as possible, and Queasytrol was only 29 pages long.

Current PSURs

Since this glorious (and naïve?) vision, ICH has expanded the provisions for PSURs (as ICH E2C), and led them to be included in regulations in the ICH countries (Europe, Japan and the USA), as well as others.

Far from being simple, the PSURs now contain huge amounts of information and all the case reports for the period. We presume that the driving forces behind these developments are the industry's legal considerations that to leave anything out at all will lead to potential negative audit and punitive legal action, or at least to regulatory problems over their product. Some or several regulators may well compound this by asking for information, on a routine basis, in excess of what was first envisaged. This latter practice tends to increase work for all regulators because of a reasonable industry view that they should send the same thing to every regulator, whether or not they ask for it.

So, far from being a way to rationalise and simplify periodic safety reviews of products, files build up in small regulatory agencies which they have no chance of properly reviewing. They are then at risk of being taken to task when a safety issue arises, and industry defends its situation by pointing out that all their relevant data was sent to the regulator. Exactly the problem we wished to avoid in the first place!

In 'Dialogue in Pharmacovigilance'[2] there is a discussion, related to product information, on 'over-warning' which can take the forms of overload (too many outcomes presented) and clutter (too much information in one warning). Both are dangerous in obscuring the main, and perhaps critical, message; it seems that the PSUR has become an increasingly problematic example of clutter.

Debate on the content of PSURs

In an interesting review on the web[3], Dr Ernst Weidmann (a member of the CIOMS II Working Group) argues for a return to the original concepts, and that company processes to generate PSURs need to be continuous in data collection and optimised for efficiency within the company. He also says, "…we must make them digestible for agencies who have to assess thousands of reports for the accuracy of safety data." The website also contains a US FDA comment that current PSURs are, "Often not very thoughtful documents… often little more than data dumps."

Dr Weidmann also raises another important topic which is debated; consistency. Despite the best efforts of first CIOMS and then ICH, PSURs vary in their structure, type of content and approach. This variation is probably linked to a desire by industry to change things for some individual product situations and for regulators to ask for additional information sometimes.

Mention of the US FDA and Bayer is particularly pertinent because the latter has just been criticised by the FDA for failure to disclose data from a study on its drug Trasylol, which the company considered was preliminary. Whilst the context of this 'failure' seems to have been different from a standard PSUR submission, it is a specific of the problem of when a company should present what data to the regulators.

There is a clear potential for this Trasylol example to be considered in the PSUR context. Now the FDA E2C Guidance for Industry states, in relation to studies, "Only those company-sponsored studies and published safety studies, including epidemiology studies, that produce findings with potential impact on product safety information should be included with a discussion of any final or interim results. The MAH should not routinely catalogue or describe all the studies." Is this not a great temptation for industry to be defensive and send study data as it comes out and before analysis, particularly under 'interim results'? Indeed are 'interim results', data, some incomplete analysis, results of calculations which have not been checked, or draft findings which need further work, or any of those?

Value of PSURs as a pharmacovigilance tool

Another part of the debate going on concerns the ability of PSURs to find new signals, and many point out that there is little or no evidence that PSURs are useful in this context. In one way this may be irrelevant to the original thinking regarding the purpose of PSURs. The approach taken by CIOMS II was that PSURs would be, "...routine compilations needed so that manufacturers and regulators can be reassured that pertinent safety data available to the manufacturers are systematically reviewed." This is reinforced by the US FDA Guidance: "The PSUR is a practical and achievable mechanism for summarizing interval safety data, especially covering short periods (eg, 6 months or 1 year), and for conducting an overall safety evaluation. It is a tool for marketing authorization holders (MAHs) to conduct systematic analyses of safety data on a regular basis. In addition to covering ongoing safety issues, the PSUR should also include updates on emerging and/or urgent safety issues, and major signal detection and evaluation that are addressed in other documents." In other words, PSURs are a quality assurance and/or a fail-safe mechanism, and urgent, new signals should perhaps be dealt with by other mechanisms.

However, we believe we should also now question the value of systematically reviewing and summarizing the safety data on a product. Should it be just a bureaucratic exercise to ensure the completeness of the MAH's safety data, or should both the company and the regulator be assessing and analysing these data with the aim of identifying potential new safety issues? In either case the cost effectiveness should be reviewed.

The Way Forward

Can we conclude anything from the above to add to the current thinking? We believe that the following are now essential:

- Evidence for the value (and the fitness-for-purpose) of PSURs in adding to the usage and safety of medicinal products should be assembled as soon as possible
- Regulators should perform a cost–benefit analysis, where the value of PSURs is carefully weighed against the resources required to assess them
- If it is considered that PSURs should continue as a quality assurance mechanism for the industry in collecting and analyzing safety data, then the issue of data overload versus competent analysis and focused, précised information must be addressed.

There is a broad issue involved in all the above discussion: trust. The public and regulators must decide clearly

i) what they want in the way of data
ii) how much analysis is required by the MAH before sharing conclusions
iii) What the regulator will do with the information.

If this is the way to go, then punitive actions against companies must be limited only to the situations of withholding critical data, not to concentrate on minor infringements that have no public health consequence.

In Uppsala Reports 35, John Ruskin was quoted: "You must either make a tool of the creature or a man of him. You cannot make both". The dilemma of provision of analysed information versus the provision of data in a PSUR is another example. Do we expect industry professionals to make any decisions? And do we harass them over detail and miss the main issues?

References

1. *International Reporting of Periodic Drug Safety Update Summaries - Final Report of CIOMS Working Group II.* Geneva, CIOMS, 1992.
2. Dialogue in Pharmacovigilance – more effective communication. Uppsala, Uppsala Monitoring Centre, 2002; p97-101.
3. http://www.samedanltd.com/members/archives/EBR/Winter2001/periodicSafety.asp. Accessed 20th December 2006.

Linking WHO-ART to MedDRA

The WHO terminology

The WHO Adverse Reaction Terminology (WHO-ART), first issued in 1968, was created mainly to serve as a basis for rational coding of adverse reaction terms within the WHO Programme for International Drug Monitoring and is widely-used by both regulatory agencies and by pharmaceutical manufacturers. Change in the terminology is driven by the needs of users and aims to meet those needs as fast and completely as possible. WHO-ART is maintained by *the* UMC.

MedDRA

The Medical Dictionary for Regulatory Activities (MedDRA) covering the same area as WHO-ART but with more details was developed by the International Conference on Harmonisation (ICH) in 1994 with a fully implementable version (version 2.0) in 1997. The MedDRA Maintenance and Support Services Organization (MSSO) provides and maintains MedDRA. Within the pharmaceutical regulatory environment in ICH, MedDRA is applicable to all phases of drug development except animal toxicology. It is intended for use in all regulatory activities.

Since the introduction of MedDRA, pharmaceutical companies and national pharmacovigilance departments have been requesting a 'link' between the two terminologies to assist in their work.

Mapping Agreement

Following extensive discussions over the last year, representatives of *the* UMC and MSSO have now agreed on the mapping of the two pharmacovigilance terminologies. This agreement will enable users of WHO-ART to map their ADR reports to MedDRA.

The mapping will be made on the WHO-ART Preferred term level and will include the fields:

- WHO-ART Preferred Term (PT) text
- WHO-ART PT code
- MedDRA Lower level term (LLT) text
- MedDRA LLT code
- MedDRA PT text
- MedDRA PT code

Release of the mapping

The initial version of the mapping will be made available to both WHO-ART and MedDRA users by 15 March each year with the first version on 15 March 2007 based on WHO-ART 2007/Q1 and MedDRA 10.0.

After the initial release each organization will make mappings available for users based on several versions of the two terminologies.

The WHO-ART – MedDRA mapping will be released free of charge to WHO-ART and MedDRA customers.

Any enquiries about WHO-ART and the new mapping should be addressed to
Cecilia Biriell on cecilia.biriell@who-umc.org or
by phone +46 18 65 60 73.

The MedDRA website is
www.meddramsso.com/MSSOWeb/index.htm

Training with China continues

Sten Olsson reports

Intensive programme

For the second consecutive year *the* UMC welcomed representatives of the pharmacovigilance network of PR China for a one week's training in Uppsala. The second course with 25 participants was carried out on 6 – 10 November 2006. Delegation leader was Dr Xu Jia Qi, Deputy Director General, Department of Drug Safety & Inspection, State Food and Drug Administration. The tight programme covered important aspects from definitions, data collection, management, causality assessment, signal identification to decision-making and communications with stakeholders. We were happy to be able to offer a Chinese speaking tutor, Dr Qun-Ying Yue from the Swedish Medical Products Agency; most sessions however were translated between English and Chinese. In all, *the* UMC has now provided basic pharmacovigilance training to 45 professionals representing most of the 31 regions of China.

Course participants and UMC staff pose for the group photo

Qun-Ying Yue teaching during the course

Case report boom

Discussions during the sessions gave UMC staff a good understanding of the particular challenges involved in developing an effective pharmacovigilance programme in a huge country like China. In the last few years reporting has grown exponentially and from January to October 2006 approximately 200,000 case reports were sent to the national centre. Unfortunately only a small fraction of these reports currently reach Vigibase, the WHO database, because of lack of resources for translation.

Macau Launch

New reporting system

The Department of Health in Macau SAR (Special Administrative Region) organized a pharmacovigilance seminar and workshop on 9 December 2006. Foreign contributors to the programme were John McEwen, Australia, Yan Min, PR China and Sten Olsson, *the* UMC. There were some 250 health professionals in the audience; physicians, pharmacists, nurses and health administrators. The new reporting system in Macau and the reporting forms for ADRs and drug quality problems was presented by Ng Kuok Leong, Chief of the Division of Pharmacovigilance and Pharmacoeconomics at the Department of Pharmaceutical Affairs.

Staff from the Macau Department of Health and conference organisers

Push for public sector

Macau is a small country of some 450,000 inhabitants with healthcare being provided by both public and private institutions. The initial focus of the new pharmacovigilance programme is to engage professionals in the public sector. Since the administrative infrastructure is well-developed they can easily be reached with campaign material and follow-ups.

Yan Min speaking in Macau

Patient safety focus

An important background to the Macau seminar is that Beatrice Young from the Macau Department of Pharmaceutical Affairs attended *the* UMC/TGA pharmacovigilance training course in Canberra, Australia in 2002. Since then the Macau authorities have been preparing for this launch of the pharmacovigilance programme. Although the absolute number of case reports received is not likely to be high, the programme will help focusing the attention of the health care professionals on patient safety issues.

In the shadow of the Hapsburgs

Clinical pharmacists gather in force in Vienna

Bruce Hugman reports

The glorious city of Vienna was the setting for the 35th European Symposium of the European Society of Clinical Pharmacy, held on 18-21 October, 2006. The year's topic was: The role of communication in patient safety and pharmacotherapy effectiveness.

Bruce Hugman and Ralph Edwards at the ESCP conference.

Some eight hundred participants from all over the continent signed up for the intense and interesting programme. The opening plenary was given by Florian Metz, Professor of Applied Linguistics at the University of Vienna, the kind of expert voice rarely heard in medical and pharmacy circles, but making eloquently clear the insights his specialism can bring, amongst much else, to understanding patient expectations and the ways in which they are often frustrated, to the detriment of therapy. Rob Horne (UK) described research in patients' medicines-related behaviour, and how such knowledge can improve the efficacy of clinical pharmacy and patient outcomes. Such was the novelty and seriousness of many of the presentations, strongly demonstrating the truth of the message that without effective communications, therapeutic outcomes are likely to be compromised.

The Hofburg and Heroes' Square (Heldenplatz) in front.
Residence of the Hapsburgs for seven centuries, one amongst many of the overwhelming legacies of the imperial dynasty in this astonishing city.

There was a rich programme of workshops, oral presentations and posters. While the enthusiasm of the participants was beyond doubt, and the range of work being done in the area was impressive, it was still clear that bringing expert communications into the very heart of medical, nursing and pharmacy practice remained an uphill struggle in many places.

the UMC was represented by Director Ralph Edwards and Bruce Hugman, who ran three workshops on communications knowledge and skills, with particular emphasis on the transformation of information into useful material for decision-making between healthcare professionals and patients, and on ways in which spontaneous reporting can become a richer source of intelligence about the concerns of patients and physicians about all aspects of therapy.

The Ethics of Genetic and Medical Information

Ralph Edwards reports on a meeting of the NordForsk Research Network hosted by the University of Iceland in Reykjavík on the 11 November 2006.

This meeting was introduced by Donald Singer (University of Warwick Medical School) giving a broad view of what personalised medicine might offer. There is more to pharmacogenomics/ pharmacogenetics (the group debated whether they were the same thing!) than just DNA testing. There is a need to show that there is a true benefit to individuals and a cost benefit to society. The latter prompted a debate that continued throughout the meeting: what is the limit to the benefit to a few versus the cost to society of research, development and delivery of medical care based on such work? It is now well recognised that gene expression is a complex issue, and much work needs to be done before society will have much benefit in respect of individually-tailored drug therapy.

Ethical issues of privacy and access to sensitive information were clearly major issues. It was agreed that genetic data should be treated as any other sensitive personal information. But there are special issues such as:

- Lack of participant's understanding
- Impossible to give full information about the use to which DNA samples may be put
- 'Leakage' of genetic data – resulting in social or financial stigmatisation

On the latter point there was much discussion about who might benefit or be harmed by genomic research. For example, insurance companies might weigh policies based on the results. There is also a major challenge in respect to the communication of information to health care professionals, to make the best use of knowledge in this area.

More information is needed about the details of phenotypic variation, both of diseases and positive and negative responses to drugs. Monitoring of individual adverse reactions to drugs and of health care databases, using knowledge detection, were examples of how this information may be collected, but better documentation

is needed, and the link between phenotypic and genotypic information made.

Much mention was made about commercial use of genetic information. Two major areas were defined; diagnostic testing to identify patients who may be at risk from, or respond best to, specific drugs, and drugs developed for gene targets. Ethics and regulation in these areas was extensively discussed, and one presentation drew attention to the difficulties of reconciling the business and commercial paradigm with one that was altruistic and healthcare based.

Iceland in early winter

Judging from the discussions, formal and informal, the participants went away both excited and thoughtful, but certainly not subdued even by an uncommonly stormy Icelandic weekend

Nations come together in China

Bruce Hugman reports

The first Asian ISPE conference and the third China Shanghai international conference on rational drug use and pharmacoepidemiology brought together a host of experts from China, the Asian region and the rest of the world to share and discuss the latest developments in pharmacoepidemiology, pharmacovigilance, risk management and communications. It was held in late September, in Shanghai and in the mountain province of JiangXi.

The line-up of professorial stars was impressive, including: Yongming Wang and Dayou Wang (China); B J Park (Korea); Kiyoshi Kubota (Japan); Yea-Huei Kao Yang (Taiwan); Brian Strom, Stanley Edlavitch and Sean Hennessy (US); Frank May (Australia and US); and Songlin Xue (US) one of the several luminaries from ISPE, celebrating their first Asian meeting. *the* UMC was represented by Ronald Meyboom and Bruce Hugman.

There was a wonderful location for the final three days of the meeting: the magical environment of Lushan Mountain in JiangXi Province, which has inspired poets and artists for centuries. It also attracted Chiang Kai Chek and Chairman Mao, both of whom spent much time in the area during their periods of power.

A group of participants from the meeting rest at the Chairman Mao monument in JiangXi province, after a strenuous afternoon's exploration of the magical, classic Chinese landscape of Lu Mountain. (On the wall at the top of the steps, written in Mao's hand, is a poem to his wife.)

The meeting's objectives of:

- building relationships among regulators, researchers and industry globally
- promoting better practice and research in drug safety monitoring and risk management, and
- increasing scientific collaboration across the world,

were well served by the very stimulating and intelligent programme, with a hundred or so local and international guests participating. The occasion was characterised by typical Chinese efficiency and generous hospitality.

Particular gratitude is due to the tireless organising genius behind the meeting, Dr Du Wenmin (Shanghai Centre for ADR Monitoring), and his unsuspecting wife who was co-opted into the support team; and to Zhu Chouwen (Fudan University, professor and gastroenterologist) whose talent and endurance as a simultaneous interpreter, working for impossibly long shifts, are unparalleled.

Introducing new UMC staff

Welcome to staff who recently began working at the UMC

Anders Viklund

Anders Viklund, working in Information Retrieval in the Safety Support and Services department, comes from Piteå, a small town at the bend of the Gulf of Bothnia, just below the Arctic Circle.

After graduating with an MSc Pharm from Uppsala University, he worked at the hospital pharmacy in Sundsvall. "My particular role was to keep the staff updated in new pharmacy training areas. My present position at *the* UMC includes information retrieval from databases, mostly Vigibase."

In his spare time he likes to attend courses – which have included Lindy Hop, Salsa and Thai cooking, with perhaps German studies, crawl (swimming) to come. A more long-term commitment is as a member of one of the student male choirs in Uppsala.

"When I started working at *the* UMC I was surprised and happy to find the warm and encouraging spirit among colleagues. Another bonus was the close collaboration with health professionals from different countries and the opportunity to get familiar with new cultures."

Ulrika Rydberg

Ulrika grew up in Uppsala, although she also spent some of her childhood in Märsta (between Uppsala and Stockholm) and in New Haven, Connecticut, USA.

Annika Wallström, the Marketing department manager at *the* UMC, 'head-hunted' Ulrika when they were taking horse riding lessons together. Before joining *the* UMC Ulrika was at the Swedish Board of Agriculture, and also studied Science Communication at Uppsala University. She has two degrees, a BSc in Biology from the University of Gothenburg and a PhLic in Molecular Cell Biology from the Swedish University of Agricultural Sciences.

Besides horse riding, she reads a lot, does crochet and hikes in the forests around Uppsala. She says "I appreciate the combination of front line science, international contacts and positive atmosphere at *the* UMC".

She is Quality Co-ordinator in the Production, Development and Quality department.

Birgitta Toreheim

The new manager of Finance and Core Services at *the* UMC was brought up in Uppsala, although she studied Economics at Lund University in the far south of Sweden. "After graduation I have worked as a Public Certified Auditor (Ernst & Young), Chief Financial Officer (SYSteam Udac) and as Accounting Director (Fresenius Kabi).

"I played a lot of football when I was young and now again I've found out what fun it is and have even joined a team myself; I am also one of two leaders for my oldest daughter's football team. I play 'floorball' (innebandy) just for fun."

Birgitta knew nothing about *the* UMC when she first applied to the organisation. "I've found it differs to my previous jobs in that it's very open-minded, and I like to be in an organisation with different nationalities, competences and ages."

Elki Sollenbring

Elki grew up in Guancaste, Costa Rica, and moved to Uppsala in 1998 to start a new life 10,000 km from home after marrying Inge, from Sweden. "Anna Mattsson and I were classmates at Uppsala University and in 2005 she told me that *the* UMC needed a pharmacist. So while I did my Masters I worked part-time at *the* UMC."

Before coming to Sweden Elki worked as ceramist and in different pharmacies while studying pharmacy at the Universidad de Costa Rica. "For a time I was an au pair in Washington DC and the experience of meeting other cultures helped me to feel good here, because the differences in culture, food, and people between Costa Rica and Sweden are big."

"My pastimes are being with my 5 year-old daughter Isabella and Inge, and going to church. I also love to dance salsa and merengue, and make and paint pottery."

Farewell

We said "goodbye and good luck" in the autumn to Jonathan Edwards, who took a new position at an IT company in Stockholm to provide developmental and strategic expertise to customers.

Marjatta Leván and Kristina Johansson left us at the end of 2006 and we wish them the very best for the future.

Recent visitors at *the* UMC

From time to time *the* UMC has the pleasure of receiving guests from national pharmacovigilance programmes or from academic institutions interested in learning more about the activities of the Centre and of the WHO International Pharmacovigilance Programme.

Members of the Norwegian pharmacovigilance network in a seminar at the UMC in November.

Norway

A delegation of 12 representatives of the Norwegian pharmacovigilance network spent all of 17 November 2006 with UMC staff in Uppsala.

Sweden

Similarly, professionals recently joining the pharmacovigilance section of the Swedish Medical Products Agency visited *the* UMC on 6 December. After a general overview of the activities of the WHO Programme, the schedule for the delegations focused on processes for signal identification, strengthening and analysis. UMC staff demonstrated the functionality of the various tools developed by *the* UMC and how national centres can best benefit from using them.

Taiwan

On 15 December *the* UMC welcomed two visitors from Taiwan; Churn-Shiouh Gau, Centre for Drug Evaluation, and Hsiang-Yin Chen, Taipei Medical University. Discussions were held about the conditions for future collaboration between *the* UMC and the Taiwanese pharmacovigilance programme.

2007 training course

the Uppsala Monitoring Centre has announced its eleventh international pharmacovigilance training course, to take place in Uppsala, Sweden from 14-26 May 2007. The previous courses from 1993 to 2005 were attended by participants from all parts of the world, representing over 90 countries in total. The primary aim of the course is to support the development of programmes for spontaneous adverse reaction reporting.

Target audience

Health professionals, e.g. physicians, pharmacists, nurses, who have recently or soon will become engaged in the practical operation of pharmacovigilance programmes should apply. The course is limited to 25 participants, and the aim is to allow representatives of as many countries as possible and from different organizational set-ups to take part.

Outline

To meet the requirements of professionals with different needs, the course is divided into two modules, with an option for the second module:

Module I:

Introduction to ADRs
Spontaneous adverse reaction reporting

Module II:

a) Introduction to pharmacoepidemiology, or
b) Effective Communications in pharmacovigilance

Theoretical and practical aspects are covered: the theoretical parts include lectures, group discussions and poster presentations by course participants. Practical sessions include recording of case information and computerised retrieval of information from the WHO database.

Bruce Hugman teaching students on the 2005 course

Faculty

Staff of *the* Uppsala Monitoring Centre, the Swedish National Adverse Reaction Monitoring Centre and other international pharmacovigilance experts will act as lecturers, instructors and discussion leaders throughout.

Application

The course application form is also available from www.who-umc.org > Promotion and Training. Applications should be submitted before 23 February 2007.

Writings on Pharmacovigilance

In Uppsala Reports 21 there was a feature on Professor David Finney, one of the early pioneers of pharmacovigilance. Both the activities of the WHO Programme for International Drug Monitoring, and of many other experts in drug safety world-wide, have developed from original ideas and work of David Finney and his contemporaries. The progress in semi-automated signal detection, in recognizing broader patient safety matters, development of terminology and post-marketing surveillance are among many examples.

the UMC has decided to re-publish the key ideas and thoughts of David Finney in a volume of 23 papers published over 40 years, tracing Professor Finney's involvement with ADR monitoring and the growth of pharmacovigilance.

Recently he has described his personal involvement in pharmacovigilance over the years (Finney 2003), the final paper in this collection. In it he mentions other pioneers in the field including Garth McQueen and Bill Inman, who in the late 1970s were involved in developing cohort monitoring for the safety of new drugs, one of David Finney's ideas. Elsewhere he points out, "... A modern computer will have no difficulty in checking the value of the chosen measure after each new case enters the data-base; output of a signal, however, is not in itself proof of an adverse reaction to a drug, only a warning that an association merits further study."

The off-prints, originating from a range of different publications over a 40-year period (one is in French), vary greatly in size and print quality, however, these variations can be overlooked in view of the importance of the content of the articles.

Finney DJ, 2003. From thalidomide to pharma-covigilance: a personal account. In: Aronson JK, editor. Side Effects of Drugs, Annual 26: Amsterdam, Elsevier Science BV. p xxv-xxxii.

Writing on Pharmacovigilance – Selected articles by David J Finney is available from the UMC. There is a small charge to cover postage and packing.

Keeping disaster at bay

Reprint of the UMC's crisis management manual

Preventing and managing medicinal product crises was the subject of Expecting the Worst, *the* UMC's popular manual, published in 2003. Demand for the book had exhausted stocks, and now a reprint, with a short update supplement, is available.

The Asian tsunami and hurricane Katrina reminded the world just how ill-prepared for crisis we often are, and how we fail to act on known risks, when planning might mitigate the impact of crises when they occur, or prevent them entirely.

Vioxx, TGN1412 and avian 'flu are amongst the recent high-profile disasters and potential disasters in medicine, and they demonstrate how vital crisis planning and management are, if damage to patients and public health, commercial and economic interests, reputations and the credibility of science are to be avoided.

But less dramatic crises happen every day: a serious new ADR, doubts about the safety of a class of drugs or a vaccination, a death in surgery, a contaminated batch of tablets, counterfeit medicines – requiring immediate and effective action. Do you have a plan in the event of the death of your senior management team in a road or air accident? For a fire which destroys your stock or your server or your records? For a major public complaint or the threat of litigation?

Expecting the Worst provides detailed guidance for all stages of crisis planning including crisis preparedness, risk assessment and evaluation, and crisis communications. It examines the 'smouldering' crisis, which awareness and action can identify and resolve before it erupts, as well as the process for anticipating and managing sudden, unexpected crises – the risk of which may be small, but which is permanent and real for every organisation.

Expecting the Worst (paperback, 120 pages) is available from *the* UMC, price 525 SEK. Please see the website or contacts on the back page of Uppsala Reports.

Meyler's – cornerstone of the pharmacovigilance library

Jeffrey K Aronson
Reader in Clinical Pharmacology,
Radcliffe Infirmary, Oxford, UK

Since the publication of a slim volume entitled Schadelijke Nevenwerkingen van Geneesmiddelen (van Gorcum, 1951), by Leopold Meyler, the book that we now call Meyler's Side Effects of Drugs: An International Encyclopedia of Adverse Drug Reactions and Interactions (colloquially known as 'Meyler') has become the standard reference source in the field. Accompanied by its annual updates, the Side Effects of Drugs Annuals (SEDA – 29 issues so far), it covers the entire published literature on adverse drug reactions, from anecdotes to systematic reviews, and discusses it critically.

History

Leopold Meyler was a physician who caught tuberculosis in the 1940s, received medication, and experienced adverse effects. He discovered that there was no single text that prescribers could consult for information about unwanted effects of medications; Louis Lewin's text Die Nebenwirkungen der Arzneimittel of 1881 had long been out of print[1]. Meyler therefore wrote a book, in Dutch, 192 pages long, entirely devoted to descriptions of the adverse effects that drugs could cause[2]. The Elsevier Publishing Company, as it was then called, published an English translation, Side Effects of Drugs, in 1952.

The book was a great success, and Meyler then published what he called surveys of unwanted effects of drugs, each volume covering a period of two to four years[3]. After Volume IV he could no longer handle the task alone and recruited collaborators, notably Andrew Herxheimer. In September 1973 Meyler died unexpectedly, and Elsevier invited Graham Dukes to edit Volume VIII.

Dukes persuaded Elsevier that the published literature was too extensive to be comfortably encompassed in a four-yearly cycle, and they agreed to produce the surveys annually instead; the first Side Effects of Drugs Annual appeared in 1977. A complementary critical encyclopaedic survey of the entire field, Meyler's Side Effects of Drugs, appeared in 1980, labelled the 9th edition; after that a new encyclopaedic edition appeared every four years, until 2000. I started to contribute a regular chapter to the Annuals in 1978 and became editor in 1991. I joined Graham Dukes as co-editor of the 14th edition of the encyclopaedia (2000). The complete list of contributors to all volumes of Meyler and the SEDAs is at Elsevier's website[3].

The fifteenth edition

Had the previous cycle been adhered to, the 15th edition of Meyler would have appeared in 2004. However, over successive editions the quantity and nature of the information in Meyler's Side Effects of Drugs has changed. For the 15th edition, of which I was sole editor, a completely new format was clearly necessary.

For some years Elsevier had planned to make the complete text of the encyclopaedia available electronically, but difficulties in writing software suitable for the conversion had delayed the process. After the publication of the 14th edition we decided to make a concerted attack on the problem. I first devised a structure for the text that would be both reader-friendly and capable of being easily converted to electronic format, helped by Dieke van Wijnen and her colleagues at Elsevier. This dictated the conversion of Meyler's chapters into monographs, which also solved the problem that in previous editions some of the information about individual drugs had been scattered over different chapters (lidocaine, for example, in Chapters 11 and 17). Each drug or groups of drugs now has its own monograph, within which the material is arranged in the same logical order as in the Annuals.

The next step was to convert the existing material (Meyler 14 plus Annuals 23–27) into searchable text, using bespoke software. The conversion was done by University of Utrecht pharmacy students, guided by Joke Zwetsloot of Elsevier and with the kind permission of Professor Leufkens. I then edited the text into monographs, which contributors to previous editions of Meyler checked.

Tova at the UMC looks up Meyler's

Breadth and depth

Meyler 15 contains nearly 1,500 monographs dealing with about 1,800 drugs. It covers not only the vast majority of prescription drugs, old and new, but also non-prescribed substances (eg antiseptics and anaesthetics), herbal medicines, devices (blood glucose meters), and methods in alternative and complementary medicine. I also restored entries on some substances that had been regarded as obsolete, such as thalidomide and smallpox vaccine.

As Graham Dukes writes in his foreword, "There is nothing else like it, nor need there be; across the world, Meyler has become a pillar of responsible medical care." This was reflected in the number of enquiries I received about progress of the 15th edition while it was being prepared – all from users anxious to obtain the new edition. We have come a long way since Meyler published his first account. I think that he would have approved of the latest edition.

References

1. Aronson JK. Louis Lewin—Meyler's predecessor. In: Aronson JK, editor. *Side effects of drugs, Annual 27*. Amsterdam: Elsevier, 2005: xxv-xxix.
2. Meyler L. *Die Nebenwirkungen der Arzneimittel*. Amsterdam: van Gorcum, 1951.
3. www.elsevier.com/wps/find/bookseriesdescription.cws_home/BS_SED/description.

Increased efficiency and productivity with the WHO DD Browser

the UMC has recently created a WHO Drug Dictionary Browser. The browser, with its user-friendly interface gives Drug Dictionaries users direct access to the dictionary data and all useful features of the dictionary.

The Browser, and its interface is available over the internet, enabling immediate access when users start a subscription. This allows users to work via the Browser as their sole route to the data in the WHO Drug Dictionaries.

It may also be used to supplement any existing system which does not have the search capabilities to fully utilize the functionalities offered in our WHO Drug Dictionaries. For example, simply by entering text verbatim using the browser it is possible to search for the entries needed. Both straightforward and more complicated searches are simplified using our Drug Dictionary Browser.

When faced with a complicated search problem, the Browser will help find and select a particular product, for example:

- Find same name drugs with different ingredients-listed with a code added to the name in the dictionary B-2 format. Then the Browser helps you code the correct entry.
- Search on the active ingredients of concomitant drugs for generic and trade names.

When a user has found what they are looking for in the Browser, they can use it to:

- Code clinical data or case reports
- Understand the active ingredients of the particular product being investigated
- Understand what the ATC codes mean and differentiate between products that have several codes in the interactive tree within the ATC hierarchy.

The tool can help new customers get started quickly, but also help old customers find the correct codes for e.g. non-unique names.

Please visit the WHO DD Browser web page (http://www.umc-products.com/DynPage.aspx?id=38426) to learn more and go to *the* UMC web shop to get a license for the WHO Drug Dictionary Browser.

User Group

We are planning two stand-alone User Group meetings during April and May, one in Europe and one in the USA. The exact dates and venues will be announced on the User Group portal on *the* UMC Products and Services website www.umc-products.com. The User Group Portal assists both new customers and experienced users. The portal contains a library of articles and documents related to the User Group, advertises forthcoming User Group Meetings and has a discussion forum (you will need a password to register).

Meet the team

Staff from Products and Services are planning to be present at the following conferences during the coming year:

March 26-28
19th Annual DIA EuroMeeting, Austria Center, Vienna, Austria

March 26-29
22nd Annual Clinical Data Management Symposium and Exhibition, Lake Buena Vista, FL, USA

June 17-21
43rd DIA Annual Meeting, Georgia World Congress Center, Atlanta, GA, USA

August 24-27
23rd International Conference on Pharmacoepidemiology (ISPE) & Therapeutic Risk Management, Quebec City, Quebec, Canada

September 16-19
The Society for Clinical Data Management (SCDM), Hyatt Regency, Chicago, Illinois, USA

Need help?

If you have any queries about WHO-Drug Dictionary, or need further information about your current subscription or how to upgrade it, do contact *the* UMC Products & Services.

You can e-mail:
drugdictionary@umc-products.com for comments about the WHO-DD, WHO-DD Enhanced, corrections and additions, and katarina.hansson@umc-products.com for queries about your subscription.

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
26 January 2007	An essential guide to Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 www.management-forum.co.uk
29 January 2007	Periodic Safety Update Reports	London, UK	Management Forum Ltd Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 www.management-forum.co.uk
29-31 January 2007	ADRs, successfully managing adverse drug reactions	Amsterdam, Netherlands	Contact Simon Lau Tel: +44 (0)20 7915 5608 E-mail: slau@iirltd.co.uk
February - July 2007	Certificate in Pharmacoepidemiology & Pharmacovigilance (20-week course)	London, UK	London School of Hygiene and Tropical Medicine Tel: +44 (0)20 7299 4646 Fax: +44 (0)20 7323 0638 E-mail: registry@lshtm.ac.uk www.lshtm.ac.uk/
28 Feb–1 March 2007	Monitoring Safety in Clinical Trials and Drug Development	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
14-15 March 2007	Back to Basics in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
21-23 March 2007	Advanced Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 570099 www.management-forum.co.uk
22-23 March 2007	VII Jornadas de Farmacovigilancia	Cáceres, Spain	Spanish Pharmacovigilance System Tel: +34 927 214 321 E-mail: farmacovigilancia@orexco.net www.farmacovigilancia2007.com
22-23 March 2007	Safety of immunotherapy development and patient care	Budapest, Hungary	International Society of Pharmacovigilance Tel/Fax: +44 (0)20 3256 0027 www.isoponline.org
11-13 April 2007	28ème journées de pharmacovigilance	Toulouse, France	Secrétariat de la Société Française de Pharmacologie et de Thérapeutique Tel: +33 2 35 14 86 04 Fax : +33 2 35 14 86 09 E-mail : secretariat@pharmacol-fr.org
21-23 April 2007	ISPE Mid-Year Meeting	Amsterdam, Netherlands	International Society for Pharmacoepidemiology Tel: +1 (301) 718 6500 Fax: +1 (301) 656 0989 E-mail: ispe@paimgmt.com
14-26 May 2007	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
17-18 May 2007	Compliance in Pharmacovigilance and the role of the EU qualified person	London, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
27-28 June 2007	Periodic Safety Update Reports (PSURs)	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
4-5 July 2007	Introduction to Pharmacoepidemiology	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
21-24 October	7th Annual Meeting of ISoP	Bournemouth, UK	Hampton Medical Conferences Ltd Tel: +44 (0)20 8979 8300 Fax: +44 (0)20 8979 6700 E-mail: isop2007@hamptonmedical.com www.isop2007.org

the Uppsala Team

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

Deputy Directors
Marie Lindquist, Dr Med Sc **Chief Scientific Officer**
Lars Magnusson BA **General Manager**

Finance and Core Services
Birgitta Toreheim CA **Manager, Chief Financial Officer**
Ali Bahceci **Network Technician**
Cecilia Biriell, MSc Pharm **Senior Specialist**
Anneli Lennartsson **Economy Assistant**
Maja Östling **Administration Assistant**

Safety Support and Services
Monica Plöen, BSc Pharm **Manager**
Jenny Bate, BSc Pharm **Signal Detection**
Anna Celén, MSc Pharm **Safety Reporting**
Jeanette Johansson, BA, BSc Pharm **Drug Dictionaries**
Anne Kiuru, MSc Pharm **Signal Detection**
Anna Mattsson, BSc Pharm **WHO Drug Dictionaries**
Helena Sjöström, Pharmacist **Safety Reporting**
Elki Sollenbring, MSc Pharm **WHO Drug Dictionaries**
Anders Viklund, MSc Pharm **Information Retrieval**
Erica Walette, BSc Pharm **Information Retrieval** *(on maternity leave)*
Malin Zaar, Pharmacist **WHO Drug Dictionaries** *(on maternity leave)*

Marketing
Annika Wallström, MSc Pharm **Chief Marketing Officer**
Beatrice Allansson, BA **Sales and Marketing Assistant**
Hannah Björn **Sales and Marketing Assistant** *(on maternity leave)*
Katarina Hansson **Sales and Marketing Assistant**
Åsa Lindeberg BA **Project Manager**
Mats Persson, BA **Head of Sales and Marketing**
Daniel von Sydow, MSc Pharm **Product Manager**

External Affairs
Sten Olsson, MSc Pharm **Manager, Chief WHO Programme Officer**
Geoffrey Bowring, BA **External Affairs Co-ordinator**
Mohamed Farah, Pharm D **Specialist, Traditional Medicines**
William Frempong, MSc Pharm **Traditional Medicines and Terminologies**

Research
Andrew Bate, MA (Oxon), PhD **Manager**
Johan Hopstadius **Research Engineer**
Niklas Norén, MSc Eng Phys, PhLic **Research Engineer**
Kristina Star, Registered Nurse **Signal Detection & Analysis**
Johanna Strandell, MSc Pharm **Signal Detection & Analysis**

Production, Development & Quality
Johanna Eriksson **Manager**
Bill Dagérus **Senior Systems Developer**
Stefan Lewenfalk **Systems Developer**
Annica Lundström, BSc Pharm **Data Management**
Nike Meder, Pharmacist **Production Leader**
Björn Moberg **Systems Developer**
Jessica Nilsson, BSc Pharm **Data Management** *(on maternity leave)*
Bo Östling **Senior Systems Developer**
Sven Purbe, BA **Senior Specialist**
Ulrika Rydberg, BSc Biol, PhLic **Quality Co-ordinator**
Magnus Wallberg, MSc Eng Phys **Senior Systems Architect**

Want a personal copy?

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 below.

Prefer to get the electronic version?

If you currently receive a paper version of Uppsala Reports, but would be happy to get the pdf version from *the* UMC website every quarter, please let us know the e-mail to which we should send it. That will save paper and stamps! Do let us know, and we will arrange it.

the UPPSALA MONITORING CENTRE

the Uppsala Monitoring Centre
Stora Torget 3
SE-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) info@umc-products.com
(Drug Dictionary enquires) drugdictionary@umc-products.com

Internet: www.who-umc.org

Uppsala Reports ISSN 1651-9779