

Uppsala Reports 32

UPPSALA REPORTS January 2006

For everyone concerned with the issues of pharmacovigilance

Validating Vigibase Online

New countries join the Programme

Lapdap and The Constant Gardener

Conference reports from around the world

the UMC in Argentina and Venezuela



DIRECTOR'S MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring
Centre

I am almost continuously concerned that drug safety is not taken seriously. No, that is not quite true! Once something is 'proven' (usually by an epidemiological study) to be seriously harmful for a convincing number of people we do take the situation seriously, and even act very rapidly to take the drug off the market. The real problem is when 'doubt exists'.

'Doubt exists' even after epidemiological evidence is available: there is the probability based on numbers and the nature of the study done. But what concerns me most, is the effort needed to get to the point of performing any study at all. Any evidence from the laboratory or from less than immaculate case reports is relegated to a very lowly position as evidence, often too low to warrant the expense and trouble of supporting a study. So we wait: what for? More and better case reports to accrue, but don't we always say that numbers of reports do not tell us anything because of biases and because we don't know how much of the drug has been used?

Cisapride and cardiac arrhythmia are quoted as an example of an ADR signal that took years to 'confirm'⁽¹⁾. But there are two new situations where we needed, or need to have, a much more active attitude to determining safety, and communicating the results.

Original research on chlorproguanil/dapsone (Lapdap) as a combination to treat malaria in Africa was being undertaken from early 2000⁽²⁾ and it was launched throughout Africa in autumn 2003⁽³⁾. However, a WHO report on Lapdap safety has only just been issued (see p15). Both chlorproguanil and dapsone are relatively toxic, old compounds. The dangers of dapsone in those people with G6PD deficiency are well known, and a 'caution' or 'relative contraindication' to the use of dapsone in such patients is widely recommended. Such a statement is made in the package insert and product information for Lapdap. But it is easy to buy Lapdap from pharmacists in Africa with no advice on precautions for its use.

Therefore, this is one situation where evidence on safety in real life lags far behind what is necessary to protect patients. Undoubtedly, Lapdap has value in treating resistant malaria but surely the period between 2000 and the release of the report in 2005 is too long for there to remain any doubt over its safety in practice. Only if we know that the previously-documented safety concerns of this combination are unfounded is it possible to support its relatively uncontrolled use in a vulnerable population. This is particularly so when many who self-medicate with anti-malarials in Africa do not even have the disease!

A topical issue (writing in mid December 2005) is Tamiflu safety, because of deaths in children in Japan, which include suicide deaths. Oseltamivir (Tamiflu) has been widely promoted as an anti-viral medication with potential for use in the expected influenza pandemic to come from Asian avian influenza (H5N1) virus, and already there is a call to double the dose because of treatment failures and possible resistance⁽⁴⁾. Apparently 69 of the 135 known patients with avian influenza have died, some after anti-viral treatment, which gives the logic for the dose increase. The drug is currently recommended for influenza A and B, though there are some resistant strains of influenza A known.

Roche Product Information states "*the following adverse reactions have been identified during post-marketing use... because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to TAMIFLU exposure.*

General: Rash, swelling of the face or tongue, toxic epidermal necrolysis

Digestive: Hepatitis, liver function tests abnormal

Cardiac: Arrhythmia

Neurologic: Seizure, confusion

Metabolic: Aggravation of diabetes

The WHO database has reports on the above adverse reactions including some with hepatic necrosis, as well as other neuropsychiatric reactions. Apparently about 32 million people have been treated with Tamiflu, and the FDA Paediatric Advisory Committee has recently reviewed the product positively.⁽⁵⁾ However, only about 3,500 subjects (adolescents, healthy adults and elderly) were in phase III prophylaxis studies, and about 1,000 adults and 1,000 children in treatment studies have been evaluated using controls, according to the Roche information. These people had mostly minor adverse events. So there is the usual gap between the pre-marketing safety experience in relatively small numbers of people, thoroughly investigated, and the occurrence of more severe events in a much bigger uncontrolled clinical population which raise questions.

1. Olsson S, Edwards IR. Tachycardia during cisapride treatment. *BMJ* 1992; 305(6856):748-9.

2. <http://www.who.int/tdr/publications/tdrnews/news62/lapdap.htm>

3. <http://www.who.int/tdr/publications/tdrnews/news70/lapdap.htm>

4. <http://www.bloomberg.com/apps/news?pid=10000103&sid=aqouUiOj1Utk&refer=us>

5. <http://www.cnn.com/2005/HEALTH/conditions/11/18/fda.tamiflu.ap/?eref=yahoo>

Continued on page 3

CONTENTS

2 Director's Message

News from Around the World

4 Mozambique and Brunei

5 Argentina

6 Bhutan, Panama, Uganda

7 Classifications

8-9 Conference reports

10-11 Vigibase Online

12-13 WHO Programme map

14 News from Stora Torget

15 Malaria report

16 Film review

17 News from Geneva

18 Chinese meetings

19 UMC visitors

20 Bill Inman

21 News from Products & Services

22 New Books

23 Conferences

24 *the UMC team*

4-7

News from around the world

Two more countries join the WHO Programme – which now has 78 full members, and three new associate members are introduced on page 6



10-11

Validation at *the UMC*

Vigibase Online, the report management software from *the UMC* has been undergoing a validation process. We talk with the man behind this innovative software



17

WHO and drug safety

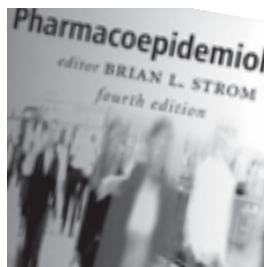
The close collaboration between the WHO's Quality Assurance and Safety of Medicines department and the WHO Collaborating Centre in Uppsala continues – with several features in this issue, including the latest WHO Advisory Committee on Safety of Medicinal Products meeting



20

New Books

Managing Safety Information from Clinical Trials from CIOMS, Strom's *Pharmacoepidemiology* is now in its 4th edition, *the UMC* and Adis revamp 'Pharmacovigilance in Focus'



Continued from page 2

In an H5N1 influenza pandemic we will need to be sure that the double dose recommended will really reduce the mortality of the disease and that the higher dose maintains a good effectiveness to risk balance. Moreover, one can expect that many people may take the drug who do not have the disease: what do we say of the effectiveness-risk in them!

How much time do we have to do this? The stockpiles are already out there and Tamiflu is a name known to those who access the public media. The public will need to have unambiguous, authoritative information about this product brought up-to-date all the time, if it is to be used effectively when the day comes. Where will they get this from?

Ralph Edwards



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](mailto:ralph.edwards@who-umc.org)) in place of info

Internet: www.who-umc.org

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

Uppsala Reports © *the Uppsala Monitoring Centre* 2006

ISSN 1651-9779



NEW MEMBER COUNTRIES

New country contacts



CIMed staff in Maputo with Dr Esperanca Sevene (centre)

Drug monitoring in Mozambique

Mozambique is a country of around 20 million people in south east Africa. The annual income per head in 2004 was US\$275; major industries include: prawns and fishing, and agriculture (cotton, cashew nuts, timber, sugar and copra). In September 2005 Mozambique joined the WHO Programme for International Drug Monitoring.

'CIMed' is a Drug Information Centre collaboration between the Eduardo Mondlane University, Faculty of Medicine and Ministry of Health (MoH) of Mozambique. Since 1999, CIMed has supported clinicians with therapeutic queries and the Pharmaceutical Department of the MoH with technical information about the use of medicines.

When CIMed started, pharmacovigilance was planned but not defined as a priority. The policy change for treatment of malaria and the introduction of new drugs (particularly the artemisinin-based combinations) for treatment of malaria provided an opportunity to establish a pharmacovigilance system in Mozambique.

In 2003, CIMed members participated with other African countries in the WHO training workshop on pharmacovigilance held in Zambia (see UR22 p5). The training was to introduce pharmacovigilance in malaria control programmes. To commit to the implementation of pharmacovigilance in Mozambique, CIMed presented a proposal to the MoH (Malaria Control Programme, Pharmaceutical Department and Institute of Health) which all these institutions approved.

Integration with public health

CIMed in its proposal suggested the implementation of the pharmacovigilance system step by step, starting with a pilot phase in two districts (Namaacha and Matutuine) where the introduction of the new malaria therapy was expected first.

Integrated with the training on introduction of the new anti-malarial policy, health professionals from pilot districts were educated in pharmacovigilance specific issues - particularly spontaneous reporting. The spontaneous reporting Adverse Drug Reaction (ADR) form and a guidebook were designed and adapted with collaboration of the health professionals during the training. Subsequently three other districts (Boane, Magude and Marraqene) were incorporated into the system.

While the basis for instigating pharmacovigilance was related to the introduction of new anti-malarial drug combinations, the aim of the system is to capture ADRs associated with all drugs, and not only anti-malarials. Collaboration with other disease control programmes, particularly the HIV/AIDS programme, was instigated,

and since 2005 pharmacovigilance has been integrated in a regular training course for the implementation of anti-retroviral therapy.

As a result of the CIMed activities, about 150 health professionals have received training in pharmacovigilance. A focal person in each district was nominated to coordinate the activities at district level and facilitate communication between CIMed and the health workers. About 95 ADR reports were received, the anti-malarials being the drugs most included in the reports, and skin reaction was the most reported term.

Next steps

With the experience acquired in the implementation pilot phase, CIMed is ready to go ahead with more activity in order to reach all the country. Therefore CIMed will concentrate on collaboration with other health programmes, particularly tuberculosis and vaccines. Promoting ADR reporting by health professionals will be the main activity.

CIMed staff

The staff of CIMed consists of five medical doctors, one pharmacist, and one administrative assistant. Apart from CIMed activities the five medical doctors are pharmacology lecturers.

Contact:

Dr Esperanca Julia Sevene
Drug Information Center (CIMed)
Av. Salvador Allende n. 702
MAPUTO
Mozambique
Tel: +258-1-32 52 27 / 32 42 10
Fax: +258-132 52 55
Email: esevene@health.uem.mz

Pharmacovigilance in Brunei Darussalam

Brunei Darussalam became the 78th member of the World Health Organisation International Drug Monitoring Programme on 28th September 2005, which was a much-anticipated moment for our country.

Membership of the Programme provides the opportunity for Brunei Darussalam to work more closely with WHO and other member countries in the monitoring of drug safety. It also enhances the development and further strengthens the pharmacovigilance programme in Brunei Darussalam.

The country in brief

Brunei Darussalam is an independent sovereign Sultanate located on the north-west coast of Borneo Island with a population of 350,000 people. The citizens of Brunei Darussalam enjoy free medical and health care which is provided by the Ministry of Health via



*Pharmacovigilance staff in Brunei Darussalam:
Ms Asma A'tiyah Haji Abdul Hamid
(in the centre) with Inpatient Pharmacists*

government hospitals, health centres and health clinics throughout the country.

National Programme History

The National Adverse Drug Reaction Monitoring Programme was implemented by the Ministry of Health in December 1998 to conduct pharmacovigilance activities. The Drug and Poison Information Section, under Department of Pharmaceutical Services, was appointed as the National Centre for co-ordinating this programme.

Similar to pharmacovigilance programmes in other countries, the objective of the National Adverse Drug Reaction Monitoring Programme is to detect any suspected adverse drug reaction at the earliest possible in order to protect other patients. At the same time it will promote proper, safe and rational use of drugs.

ADR Reporting

Healthcare professionals including doctors, pharmacists, pharmacy technicians and nurses are encouraged to report any adverse drug reactions using the Adverse Drug Reaction report form. Reports are either sent directly to the National Centre, or via pharmacies located at the different government health facilities that will subsequently forward the reports to the National Centre.

Activities

Over the years, various activities have been conducted to promote local adverse drug reaction reporting, which included:

- roadshows which were incorporated in the continuing education sessions of healthcare professionals such as doctors, nurses and pharmacy staff
- drug safety training courses for staff under the Department of Pharmaceutical Services in the four districts
- ADR lectures to medical undergraduates in the local university as part of their curriculum.

Staff

The National adverse drug Reaction centre is staffed by two pharmacists who are responsible for collecting, processing and evaluating the adverse drug reaction reports received and other pharmacovigilance activities, with the assistance of a clerical staff.

Future

The National Adverse Drug Reaction Monitoring Programme will continue pharmacovigilance efforts by conducting drug safety courses for healthcare professionals and building closer ties with other member countries in the exchange of drug safety information.

Contact:

Ms Asma A'tiyah Haji Abdul Hamid
Pharmaceutical Chemist
Drug and Poison Information Section
Department of Pharmaceutical Services
Ministry of Health
Brunei Darussalam
Tel/ Fax : + 673 2 242424 ext 569
Email: aatiyah@brunet.bn

Argentina back on track

Sten Olsson reports

Argentina was the first country in South America to formally join the WHO pharmacovigilance network. Already in 1994, when Argentina was admitted, the country had established a national pharmacovigilance network with electronic ADR reporting from peripheral centres to the national centre at ANMAT, the drug regulatory agency. Representatives from *the UMC* were invited to take part in training activities in Argentina twice in the 90s, the latest in 1997. Since then the country has lived through a very difficult period of financial hardship which affected also the pharmacovigilance network and international collaboration. With this background we were particularly pleased to again receive invitations this year to take part in pharmacovigilance events in Argentina.

A UMC delegation consisting of Sten Olsson and Anna Celén set out for a long journey from Uppsala to Argentina from 7 – 14 November, involving ten separate flights. The most important events during the trip were:

- Meeting with staff at the national pharmacovigilance centre at ANMAT notably the centre head Inés Bignone and Soledad Zanchi, responsible for submitting case reports to *the UMC*. Anna Celén is *the UMC* contact person for Latin American countries and she and Soledad had many issues to talk about, not only related to ADR reporting.
- A meeting with Manuel R Limeres, Director of ANMAT, at which the conditions for organizing an annual meeting for the WHO Programme in Buenos Aires were discussed. *the UMC* team was also requested to demonstrate the functionality of the Vigibase Online system for the processing of ADR case reports.
- 'Jornadas Regionales de Farmacovigilancia' was organized for two days by Mabel Valsecia in the north-eastern town of Corrientes. This regional centre is the most active of all Argentinean pharmacovigilance centres. The conference attracted almost 200 participants from six different provinces of Argentina and also from Uruguay and Paraguay.

UMC in Argentina



Sten Olsson, Inés Bignone, Soledad Zanchi and Anna Celén enjoying a tango evening in Buenos Aires



Mabel Valsecia, who arranged the conference in Corrientes. Inés Bignone, to the right



Anna Celén making her presentation in Corrientes

Continued on page 7

New Associate Members of the WHO Programme

Bhutan

A pharmacovigilance programme was initiated in Bhutan on 7 September 2005. Bhutan is a small country of 1 million inhabitants in the Himalayas bordering China and India. Two national pharmacovigilance centres have been established under the auspices of the Drug Regulatory Agency of Bhutan, one focusing on traditional medicines only. Ministry of Health of Bhutan have now also applied for membership in the WHO International Drug Monitoring Programme.

Contact details of the two centres are:

National Pharmacovigilance Centre
Pharmacy Department
JDWNR Hospital
Ministry of Health
Thimphu, Bhutan
Tel: +975-2-322420 (231) Fax: +975-2-325384
E-mail: npv@druknet.bt
Responsible officer: Mr Tashi Tobgay

Traditional Medicines Pharmacovigilance Centre
Pharmaceutical and Research Unit
Inst of Traditional Medicines Services
Department of Medical Services
Ministry of Health
Thimphu, Bhutan
Tel: +975-2-321686 Fax: +975-2-324215
E-mail: ntmpvc@druknet.bt
Responsible officers: Mr Ugyen Dendup and Mr Sherub Tenzin

Panama

In August last year *the* UMC received a visitor from Panama, Dr Hilda Acosta de Patiño, for a few hours only (UR31 p. 22). This first contact started a series of events that lead the Panamanian Ministry of Health to apply for membership in the WHO Programme for the national pharmacovigilance centre. This national centre was started in 2001 as a result of a governmental decree. At the time of application in October 2005, the Centre had received 428 case reports of suspected adverse drug reactions, although they have not yet been submitted to *the* UMC. Training activities in pharmacovigilance have been carried out.

The contact person at the national centre is:

Lic Indira I Credidio
Centro Nacional de Farmacovigilancia
Dirección Nacional de Farmacia y Drogas
2048 Panamá 1, Panama
Tel: +507-212-9162 Fax: +507-2129196
E-mail: fvigilancia@minsa.gob.pa or icredidio@minsa.gob.pa

Uganda

The National Drug Authority of Uganda is introducing pharmacovigilance into the health care agenda in collaboration with the national HIV/AIDS and malaria control programmes. This is a process initiated at a joint WHO/UMC training course carried out in Pretoria, South Africa in September 2004 (UR 27, p 8). The Uganda Ministry of Health has now applied for the new pharmacovigilance centre to be incorporated into the WHO network.

Contact person is:

Juliet Okecho
Drug Information Department
National Drug Authority
Plot 46-48 Lumumba Avenue
P.O. Box 23096
Kampala
Uganda
Tel: +256-41-347391 Fax: +256-41-255758
E-mail: oajuliet@yahoo.com

WHO Programme in Belgium in 2006

Liège in eastern Belgium will be the setting for the 29th Annual Meeting of National Centres participating in the WHO Programme for International Drug Monitoring from 9-11 October 2006.

A thousand year-old city, Liège possesses an exceptional cultural and architectural patrimony, highlighted in its museums. Theatres, music of all kinds, as well as cafés and restaurants enhance the warm nature of a welcoming city.



Place Saint Lambert in Liège by night

The meeting venue, the Palais des Congrès convention centre, is located in a pleasant park by the river Meuse, within walking distance of the historic centre and next to the Museum of Modern Art, which displays works of painters such as Picasso, Chagall, Gauguin, Monet and Utrillo.

Liège is easily accessible by train or shuttle bus from Brussels international airport and by high-speed trains from neighbouring countries.

The preliminary programme will be sent to National Centres soon, and we hope many representatives from the Programme will take part this year. More details will follow in the next Uppsala Reports.

ISoP's Annual Meeting will directly follow the National Centres' meeting, with a joint session on 11 October. The theme for the 6th ISoP Annual Meeting is 'Joining Forces for Managing Risks'. Courses entitled 'Introduction to pharmacovigilance' (half a day) and 'Risk Management Plans' (one and a half days) will take place before the main ISoP meeting.

Family of International Classifications

Marie Lindquist

There has been an ongoing dialogue for some time between *the* UMC and the co-ordinator of the WHO Family of International Classifications (FIC) network, Dr Bedirhan Üstün, head of the WHO Classification Assessment and Terminology (CAT) Team at WHO Headquarters.

The WHO FIC includes, in addition to the International Classification of Diseases (ICD) the International Classifications for Health Interventions (ICHI), and Functioning, Disabilities and Health (ICF), and a number of special ICD versions (country versions or for specialist clinical areas). A new classification for procedures is under discussion.

Possible collaboration

Dr Üstün and his colleague Dr Robert Jakob (Medical Officer) have expressed enthusiasm about the possibility of a collaboration with *the* UMC, including the linking of our terminologies with ICD and possible work towards a common strategy for all WHO classifications. Ralph Edwards and Marie Lindquist presented *the* UMC's thoughts on these issues to the annual WHO-FIC meeting in Tokyo, on 21-22 October to an audience which consisted of Centre Heads from many WHO Collaboration Centres on ICD Classification in different areas of the world, and other classification experts and terminologists.

Ralph gave a concise presentation of *the* UMC's functions and interest in joining the WHO-FIC network. He said that *the* UMC could contribute with classifications and terminologies in the drug safety area, plus expertise and experience in disseminating these products.

Marie provided a summarized description of WHO-DD and WHO-ART, and how they might be linked to ICD; WHO-ART as a sub-

classification for pharmacovigilance, and WHO-DD as the drug extension of the existing high-level ICD drug classification. The proposal is that ATC (Anatomical Therapeutic Chemical classification) upper levels should be implemented as part of ICD-11 (the book), and that WHO-DD would be a linked sub-classification for products and substances. This way there would be a low-cost publication available to everyone, and the possibility of add-ons on different levels for those who need them.

Moving terminologies forward

The FIC group strongly proposes that other terminologies in use around the world be linked to ICD, and that WHO should have a lead role in any standards development in the health care classifications area, ensuring that the best interests of all Member States are taken into account.

The group seemed to welcome *the* UMC proposals, and the meeting agreed to pursue the alignment of ICD and WHO-DD/WHO-ART. The minutes from the meeting will be made public on the WHO homepage.

<http://www.who.int/classifications/network/en/>

Argentina back on track, continued from page 5

Experiences from Uruguay were given by Carolina Seade, one of the directors of the national centre there. José-Luis Castro gave an update of pharmacovigilance activities carried out by the WHO Regional Office. Anna made her first two presentations to an international audience (she joined *the* UMC only 6 months ago).

- The V Argentinean Congress of Hospital Pharmacy was organized in Córdoba, the second largest city of Argentina, from 10 – 12 November. In this major congress three separate sessions were devoted to pharmacovigilance. Sten gave a UMC perspective on 'Current Trends in Pharmacovigilance', 'Good Communication Practice in Pharmacovigilance' and 'Patient Safety – the Role of the Hospital Pharmacist'. It was encouraging to note the active discussion that resulted in the audience following the presentations.

Many of the safety concerns that were brought up for discussion in Corrientes and Córdoba related to local conditions. Inés Bignone and other representatives of the national pharmacovigilance network were very active in discussing those issues with the health care practitioners. In this way these meetings provide important platforms for learning and exchange of views between authorities and health care practice.

From *the* UMC perspective it is encouraging to note that, as Argentina is finding its way out of its financial crisis, the pharmacovigilance system is also becoming more active. Inés Bignone was appointed head of the national centre in late 2004, in 2005 she attended the annual WHO meeting, and moreover ADR case reports are now being submitted to the WHO database on a weekly basis. We have great expectations for the future.

Faces at ISoP



Ken Hartigan-Go, local organizer in the successful International Society of Pharmacovigilance (ISoP) meeting



Mohamed Lakhali makes his presentation in Manila

ISoP in Manila

Marie Lindquist reports

A truly international programme and several inventive features marked ISoP's first venture to Asia for its Annual Meeting – in Manila from 16–19 October, superbly organized by Ken Hartigan-Go. With 380 participants, the networking and social aspects were fantastic; while what the scientific content perhaps lacked in hot topics and controversial discussions was made up for by sheer range of contributions.

Ecopharmacology

Klaus Kümmerer introduced the concept of ecopharmacology: the environmental aspects of the ever-increasing use of medical compounds. One key message was that high stability of a product, which on the whole is desirable for human use, is bad for the environment. What is needed are chemical compounds that are metabolized quickly to harmless substances after they are released in the environment (air, soil, water). This is a difficult equation!

Research and posters

Parallel sessions on pharmacovigilance education and training, and pharmacovigilance in rational drug use followed. I presented some work by Johanna Strandell and myself on how to use information on Cytochrome P-450 (CYP) enzymes (involved in the metabolism of many drugs) for the detection of possible drug-drug interactions. Other presentations were: the problem with counterfeit medicines in Argentina, new information about safety of the cholesterol-lowering statin drug group, a study on the Taiwanese medicines reimbursement database to identify possible cases of interactions involving thioridazine, and a short report on drug pharmacokinetics.

High-profile Keynote speaker

Day 2 started with a spectacular performance from former Philippines president Fidel Ramos. He cited *the UMC's 'Viewpoint'* and set out his views on drug safety, linking signal detection in pharmacovigilance to the signal detection that politicians must act upon, as exemplified by the current bird flu issue.

After this block-buster performance the morning included: Pharmacoepidemiology and Hot Topics including Ruth Savage (New Zealand), talking on rofecoxib and the relative risk/safety of NSAIDs. Saad Shakir of the DSRU, UK gave two presentations, and Misayoshi Harigai (Japan), spoke about a registry of Japanese rheumatoid arthritis (RA) patients. This is to study long-term effects of the relatively new anti-TNF drugs, and compare them with other drugs used for RA – worth keeping an eye on! The session concluded with Jörg Hasford (Germany), 'Hospital admissions caused by ADRs', and 'How to evaluate safety of OTCs', and

Nicholas Moore (France) on differential use of NSAIDs in the French population.

First pharmacovigilance Quiz Bowl

Quiz master (Bruce Hugman) and referees (Ralph Edwards and Ron Meyboom) had set the questions for this light-hearted competition – an idea of Ken Hartigan-Go. He put great enthusiasm into this endeavour, although it was not certain how it would be received. The 'Quiz Bowl' final was a plenary, and the teams showed great bravery – 'Amnesia': Xavier Kurz (Belgium) Sevgi Öksüz (Turkey), Pramote Tragulpiankit (Thailand) – the eventual winners, and 'Feeling Cool': Ulrich Hagemann (Germany), Richard Hill (Australia) and Herbert Ho (the Philippines). Although some of Ron Meyboom's trickier questions had been deleted (how many know of the link between mazindol and testicular pain?), it became obvious that what is well known to experts like Ralph and Ron with long experience (and memory!) is not always known by everybody in pharmacovigilance.

If this wasn't enough, another innovation was 'Adopt a delegate' – where foreign delegates were matched with local Filipinos and taken out for one night to experience sights, cuisine and to engage in discovering more about the country at a person level.

Herbal highlights

The Herbals session had a series of good quality presentations, given by Rachida Soulaymani (Morocco), J M Aggarwal (UK), Debbie Shaw (UK), Kiichiro Tsutani (Japan), and Albert Chan (Hong Kong). *the UMC* herbals team had prepared a presentation on the WHO herbal database and herbal ATC. Other plenaries included David Henry (Australia) on 'Quantifying alerts: the burden of ADRs to the individual and the society' and Saad Shakir 'Risk Management: theories and practice'.

The final day had two sessions: 'Pharmacoepidemiology', and 'Women and children safety issues'. The latter included interesting presentations on inhalation anaesthetic safety (Wen-Wen Chen, Taiwan), birth outcomes after in-utero exposure to oral hypoglycaemic drugs (Mohamed Lakhali, Tunisia), and intensive monitoring of adverse events during malaria treatment of women (Alex Doodoo, Ghana). *the UMC* signal team was represented: Anne Kiuru and I hoped that the title 'Why do boys stop crying' would be more intriguing than 'An overview of gender differences in ADR reporting' – the topic presented. The ensuing panel discussion was lively and raised a number of important real life safety problems.

After this taste of the Orient, next year ISoP will be organized in Liège, Belgium.

European Health Forum discusses safety

The Austrian Ministry of Health and Women and the Austrian Broadcasting Corporation organised the 8th European Health Forum in Bad Hofgastein, Austria from 5-8 October 2005. Part of the programme 'Risk and rewards: The safety of medicines', focussed on key challenges in present-day pharmacovigilance and reached several conclusions. The meeting was attended by Ralph Edwards and Mohamed Farah from *the UMC*.

Evolving surveillance

Delegates agreed on the need for more emphasis on post-approval surveillance, linked to risk management planning starting in the pre-marketing phase, to more systematically identify potential adverse effects, especially in view of initiatives around medication errors, drug interaction and the diagnosis of ADRs. With more people living with long-term conditions, taking combinations of drugs not tested in clinical trials, monitoring systems are important to prevent these adverse drug interactions.

Reporting and risk management

There was consensus that existing means of reporting and signal detection must become more pro-active - demanding more active involvement of stakeholders, patients in particular, perhaps through feedback systems. The need to develop effective tools to assess and communicate uncertainty and risk throughout a drug's life-cycle is also vital. Risk management strategy should include active co-operation with those who influence public perception of risks. On the monitoring of over-the-counter (OTC) drugs changes from prescription to OTC status of certain medicines have resulted in increased self-management of chronic conditions, underlining the need for effective monitoring.

Role of stakeholders

Lack of transparency, deficient risk communication, lack of access to relevant data and lack of phase IV studies were identified as problems of existing pharmacovigilance systems, potentially resulting in poor information for health care providers and patients. It was felt that ADR reporting through the medical profession needs to be strengthened - perhaps through feedback mechanisms. Reinforcing the role of community pharmacists and nurses in reporting was suggested, as they have expertise necessary to identify potential ADRs, and enjoy high levels of trust in most European countries. Nonetheless, active involvement of patients was seen as the key to improving existing pharmacovigilance, with systems to encourage patients to report on the concomitant use of OTCs or alternative medicines. Examples of active patient reporting were examined (eg The Netherlands' Digital Experience Dossier (DED), and pilots in Denmark and the UK); it was accepted that developing such systems needs to be facilitated, and that user feedback to encourage reporting is essential.

Wider vigilance

Present pharmacovigilance systems focus on conventional medicines, and systems for alternative, herbal and complimentary medicines need to be strengthened. Central to integrating alternative medicines into pharmacovigilance is their classification (eg *the Uppsala*

Monitoring Centre's classification system for herbal medicines), so as to facilitate this process. The group also acknowledged the EU's new Directive on traditional herbal medicines and Committee for Herbal Medicinal Products for registration of herbal medicines.

Venezuelan prospects

Ralph Edwards reports

A symposium on 'Intelligent use of Drugs' was held in Caracas, Venezuela, on 26-30 October 2005, and was very well attended by clinical pharmacologists and other health professionals in the South American region, about 400 delegates in all. The session was organised by Dr Luisa Helena Valdivieso and a colleague from the Ministry of Health, Dr Leopold Landaeta. There was also time for less formal interactions with Ministry staff and other health professionals with an interest in drug safety. The presentation I gave was on the 'Pharmacotherapeutic basis for benefits and risks in medicinal products'.

I was very impressed by the attendance and active participation in the session on drug safety issues. Luisa gave a powerful and most exquisitely illustrated talk on the general area of drug safety. The Symposium President was Prof Luigi Cubeddu, a clinical pharmacologist whom I knew from my time in New Zealand when one of my staff, Donald Ferry, spent some time with him on sabbatical leave, and which resulted in some joint laboratory work. Our professional world is indeed small and friendly!

Venezuela is a fascinating country, which I was able to spend only a day in appreciating. This was by a tour into a rural area and native forest, and greatly enhanced by a 2-hour taxi drive into the tour area and back. The drive was lovely, but the driver was really a disc jockey and boasted that he had two hard disks full of music, and had made many compilations for his work. In his car he had some hits from the sixties, so we had a great sing-along, particularly enjoyable when stuck in the traffic returning to Caracas!

I was struck by the national pride in Venezuela, indeed we were all given national flags at the conference dinner, and there was also a rally outside the hotel addressed by President Chaves. This is a country of great potential waiting to be fully realised. One can only hope that internal and external politics allow this to happen.

Introduction

Since the inception of international collaboration in safety monitoring of medicinal products there have been technical challenges in integrating information in national databases for adverse reactions reports with WHO's international database. Since 2001 the UMC has collaborated with the Swiss medicines agency, Swissmedic, on the challenge of improving ADR reporting and feedback in the age of the internet. When the Swiss national centre needed to upgrade their systems, instead of building something completely new, the UMC worked with them to develop a national ADR database parallel with the WHO database. This software, called Vigibase Online (VOL), has been made available from the UMC for other pharmacovigilance centres in need of a modern system for management of adverse reaction reports (there is a charge depending on Gross National Income and volume of reporting), and it is intended in the future that it will be suitable for others using drug information databases.

With the validation of VOL nearly complete, Uppsala Reports took the chance to chat to Magnus Wallberg, manager of the project.

Validating Vigibase Online

When the concept first emerged for storing national ADR reports directly in a UMC-structured database what were the key considerations for the planning team?

The collaborative thoughts from Swissmedic were, from the outset, to use UMC's analysis tools and structure. They saw the advantage of sharing our knowledge of handling large amounts of ADR data with their many years experience as a national centre. Swissmedic also had a commitment to improved speed and directness of reporting. As the WHO database is not 100% compatible with ICH-E2B specifications, a 'parallel' 100% E2B repository was created – a national database from which data is easily copied over to the WHO database. This solution allows for the specific requirements of Swissmedic and other organisations using VOL to be catered for. The import mechanism to the WHO database is the same as is already in place for other E2b, non VOL reports.



The chief designer of Vigibase Online in relaxed mode

What were the advantages for the national centre of using the WHO database architecture?

Analysis tools and methods already existed within the WHO database e.g. technical quality control, data-mining, and internet-based search facilities.

What are the incentives for pharmacovigilance centres to use Vigibase Online?

If internet connections are adequate there should be less time needed for input and checking reports – presumably releasing staff to undertake more assessment of data. The biggest gain would be for countries with regional networks since VOL supports the report processing at regional centres as well as data exchange between regional and national centres. There is the gain of better quality of reports, mandated by the rigour and processes of the software. All users will save time on extracting and sending case information to *the* UMC, and the fact that they don't need separate 'linking' software to *the* UMC. The E2b

format can be easily exported to any modern database. I certainly think that Vigibase Online is as attractive as any other option I am aware of, and the fact that users do not have to worry about installation consultants or the cost of future upgrades – or additional computer servers – are key incentives.

Why did you decide to have Vigibase Online validated, and what does the validation project require from *the* UMC?

We realised that *the* UMC has to prove that what we have been developing is a secure and tested package, and that it works as we say it will. Obviously the software has been properly documented during its stages of development, but pharmaceutical companies in particular who are expressing an interest in using VOL require a validation done known as GxP (see explanation in margin). Validation involves much more than producing a long list of Standard Operating Procedures – it is a full description of how our system works, together with evidence that we actually use it in the way we describe and that the system operates as specified. The other major requirement of validating VOL is to ensure that every modification in each upgrade is fully recorded. I wish to stress that the GxP system is not purely IT driven; it also examines how all users, from the originator to the end users, utilize the software.

We have engaged a validation consultant, Ms Marianne Rönnbäck of Litoda AB to coach us during the validation process. She has a lot of experience in software validation from the pharmaceutical and other industries. She is teaching us about the GxP requirements and has given us a lot of advice on how to reach our goal of working according to quality assured standards.



Marianne Rönnbäck

When will the validation finish and what will it mean to current and potential users of the software?

We plan to finish validating version 3.0 by the end of January 2006. Current users will not notice any real difference. There will be more controlled version handling – in other words the transition from one version to another will be clearer and smoother, probably with new versions installed less often. For potential users they have the reassurance that independent experts have concluded that we have control over the system and are working in a coherent way. The validation will not affect further development of the software or the flexibility which we are able to bring to it.

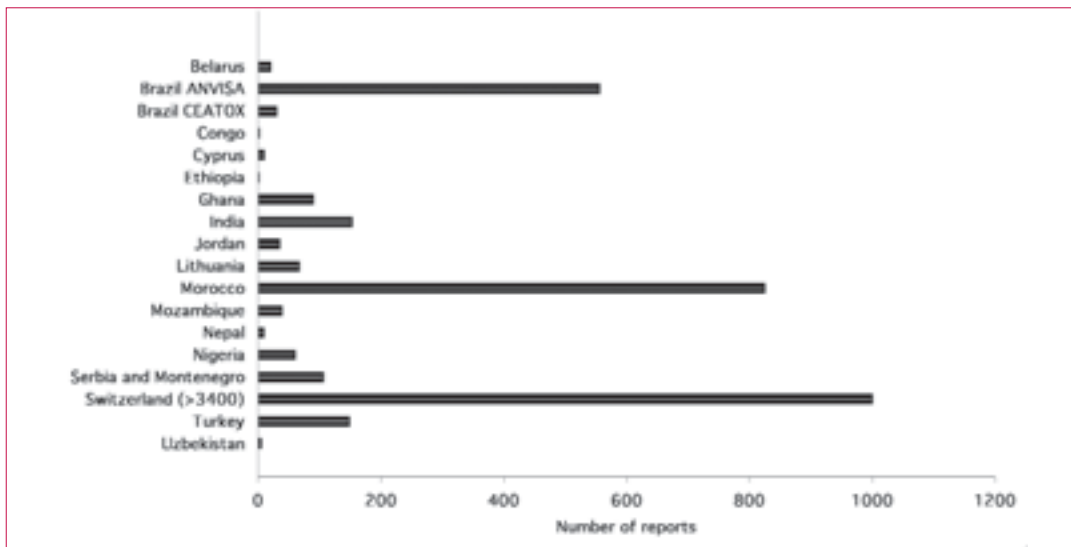


Figure 1: Vigibase Online statistics from different National Centres

What more's in the pipeline, short- and medium-term?

Existing national centre users are continuing to expand their usage, and new countries (most recently India and Turkey) are coming on board (see Fig 1 for current statistics on reports submitted via VOL). The main new features I am currently working on are direct E2b import from pharmaceutical companies to national pharmacovigilance centres, extending the search and statistical facilities, support for the primary notifier, and implementing the UMC's duplicate detection tool within Vigibase Online. The capacity to attach separate text files or image/photo files is something we are keen to finish. We are also getting very close to pharmaceutical companies having their own direct use and we're at the point of European companies actually doing so.



Figure 2: the search facility in Vigibase Online

Will it be easy to add on other functions on request from users?

That depends on how good an idea is! If a function is commonly requested, that would be fine, we can probably do it. Swissmedic required extracts to be

presentable in a particular spreadsheet program, for instance, which we created. If the requested function is very country-specific, the development cost would have to be borne by the national centre. But we are happy to look at new requests from users of Vigibase Online. More functions will be added as the system develops.

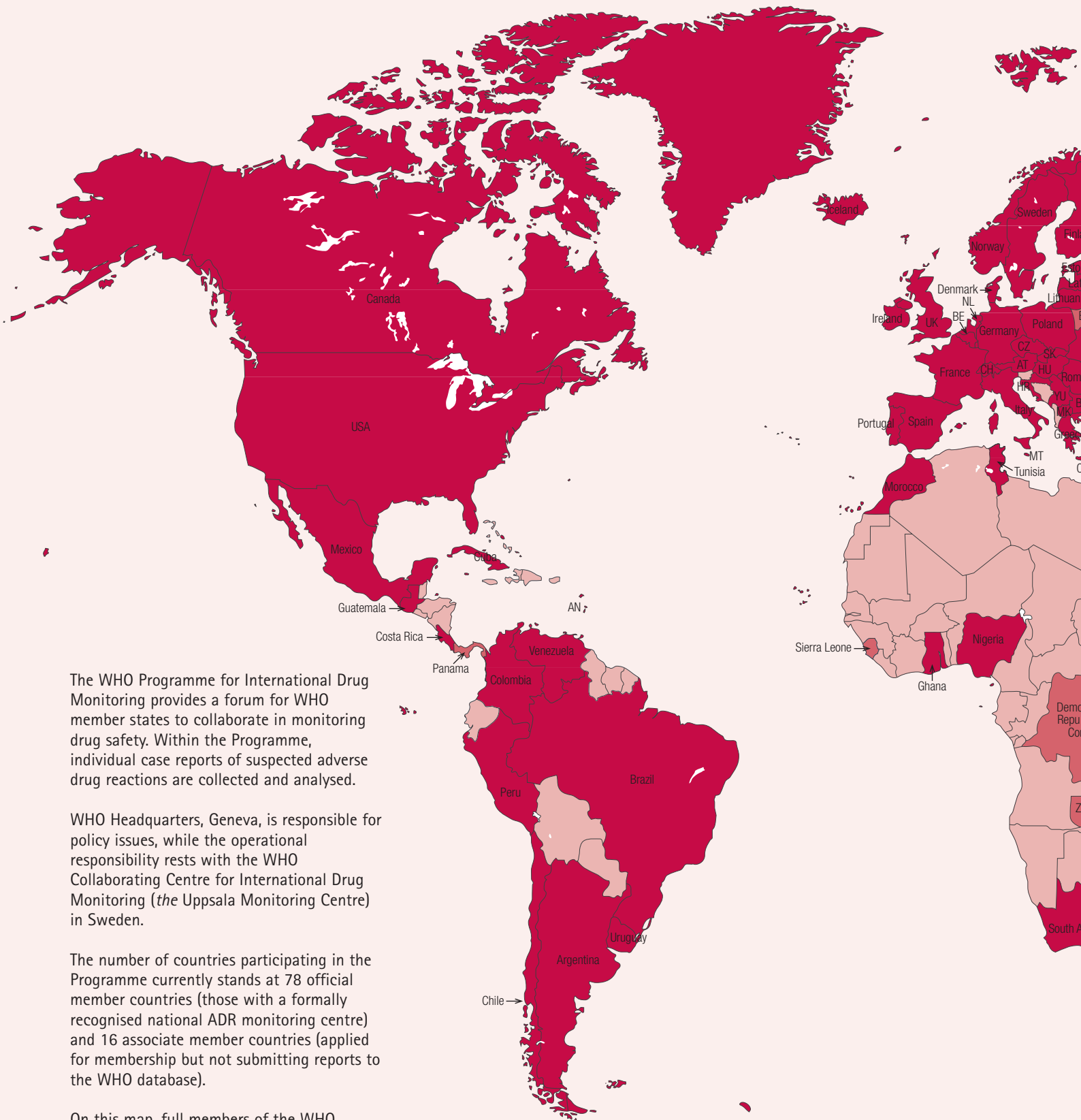
Any other comments?

I should like to thank in particular staff from Swissmedic who have collaborated with us on the project, especially those on their steering committee. The strength of Vigibase Online lies in the multi-disciplinary input to the software – from experienced UMC staff (pharmacists, scientific staff, and classification experts), our IT team with its huge experience of the WHO database and E2b format, as well of course as the Swiss and other national centre colleagues.

Good practice systems

GxP is the generic term for a set of 'good practice' requirements in widespread use in the pharmaceutical industry, eg Good Laboratory Practice, Good Clinical Practice, Good Manufacturing Practice, Good Distribution Practice. The key to validation under 'GxP' is documentation, so companies must prove that the software and systems they use work according to the specification needed and are used as such.

WHO PROGRAMME FOR






The WHO Programme for International Drug Monitoring provides a forum for WHO member states to collaborate in monitoring drug safety. Within the Programme, individual case reports of suspected adverse drug reactions are collected and analysed.

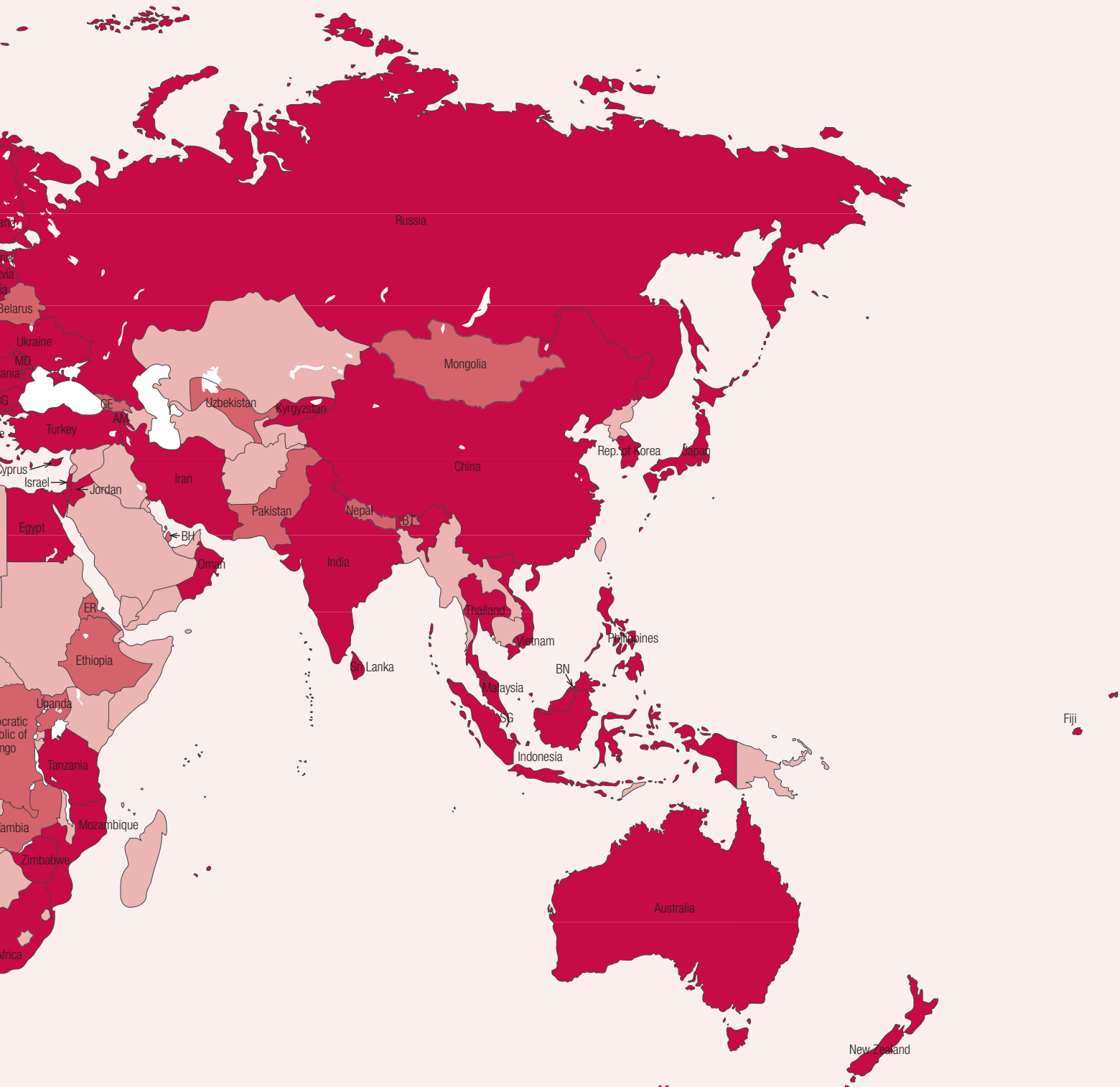
WHO Headquarters, Geneva, is responsible for policy issues, while the operational responsibility rests with the WHO Collaborating Centre for International Drug Monitoring (*the Uppsala Monitoring Centre*) in Sweden.

The number of countries participating in the Programme currently stands at 78 official member countries (those with a formally recognised national ADR monitoring centre) and 16 associate member countries (applied for membership but not submitting reports to the WHO database).

On this map, full members of the WHO Programme are shown in dark red associates in medium red

-  Full members of the WHO Programme
-  Associate members of the WHO Programme
-  Non members of the WHO Programme

INTERNATIONAL DRUG MONITORING



Key

AM	Armenia	HR	Croatia
AN	Netherlands Antilles	HU	Hungary
AT	Austria	MD	Moldova
BE	Belgium	MK	Former Yugoslav Republic Macedonia
BG	Bulgaria	MT	Malta
BH	Bahrain	NL	Netherlands
BN	Brunei Darussalam	SG	Singapore
BT	Bhutan	SK	Slovakia
CH	Switzerland	UK	United Kingdom
CZ	Czech Republic	YU	Yugoslavia
ER	Eritrea		
GE	Georgia		



Cecilia Biriell checking part of the major building work which took place at the UMC offices

Foreign reports in Vigibase

The WHO Adverse Reaction database (Vigibase) contains adverse reaction reports originating from all 78 members of the WHO Programme. It has now become apparent that, contrary to our intentions, it also includes a number of so-called 'foreign reports'. These are ADR case reports submitted from a country other than that where the reaction was first reported, and which bring a risk of duplications. We are now pleased to advise that we recently received a list of case identifiers for such foreign reports from the FDA in the USA.

From this list we identified 41,837 foreign cases which were present and active in Vigibase in a version submitted by the country of occurrence. Since *the* UMC has the policy that no foreign reports should be present, we have labelled all these foreign reports submitted from the USA as 'inactive'. This means that the reports will still be present in the WHO database but as they are not 'active', they will not be included in the normal searches or the signal detection process.

Renovation of UMC premises

The main part of *the* UMC is located in a building at Stora Torget, right in the middle of the centre of Uppsala, where we have welcomed many visitors over the years. The building dates from 1934, at that time in a modern style, which was very different to the other buildings around the main square. Before this, a house which was built in 1691 for Professor Olof Rudbeck, one of the great scientists of Uppsala, was situated here.

After seventy years, a renovation, mainly of the plumbing and electricity systems was necessary. Following any heavy rains, the people in the bank on the ground floor were not happy, and of course old



Work in progress - everything covered and sealed while the new pipes and services are put in all around us

electricity wiring is a safety hazard.

Parts of UMC's premises had to be closed at various times during the renovation, but work has been going on anyway. At times it has not been easy for the staff, without access to water, toilets or the coffee machine(!). However, with modern IT, it has been possible for many UMC staff to work at home and be hooked up to the internal network and the adverse reactions database.

Finally, after about 4 months we are through this difficult period and all the dust and hassle. The corridors and the coffee room are being painted in new nice colours. We hope that the renovation has not too much affected the service we give to our customers – we trust in fact that you won't have noticed at all!

Funding of *the* UMC

In response to regular requests for explanation or information about the funding arrangements for *the* Uppsala Monitoring Centre (and to correct any misunderstandings), a short statement has been prepared to explain simply the current position:

"the UMC receives no funding of any kind from any external source. The 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.

the UMC has been effective in funding itself, but at the cost of considerable resources needed to generate income, and without the long-term security which such a vital international enterprise might be expected to enjoy."

We will keep Uppsala Reports readers informed of any changes to this situation.

Expert committee issues recommendation on use of Lapdap in Africa

The Roll Back Malaria and Essential Drugs and Medicines Departments of WHO has issued its recommendations on the use of LAPDAP in malaria endemic countries following a technical consultation meeting held in Geneva in July 2004 to assess the risks and benefits in the use of chlorproguanil-dapsone (CPG-DDS) [LAPDAP] in Africa. Nine international experts from different fields participated, and following extensive review of available information and discussions with both the Medicines and Healthcare Products Regulatory Agency of the UK (which first approved the use of LAPDAP) and GlaxoSmithKline (the Marketing Authorisation Holder) provided recommendations to national health authorities on the use of this medicine in the treatment of uncomplicated falciparum malaria in Africa.

In-depth report issued

Their report, just published by the WHO, makes various recommendations about the use of LAPDAP noting that it is a drug with known risk of causing haemolysis in young children with malaria and in adults. The anaemia which may develop after treatment with LAPDAP could be severe and potentially life-threatening. Predisposing factors to severe anaemia after treatment with CPG-DDS include pre-existing anaemia, haemoglobinopathies, G6PD deficiency, and malnutrition. G6PD deficiency is a widespread genetic trait throughout Africa.

In addition, since there are known risks to the fetus of haemolysis and methaemoglobinaemia when the mother is treated with dapson (a component of LAPDAP), more information is needed on the use of the drug in pregnancy in order to assure its safety in pregnancy.

Key contraindications

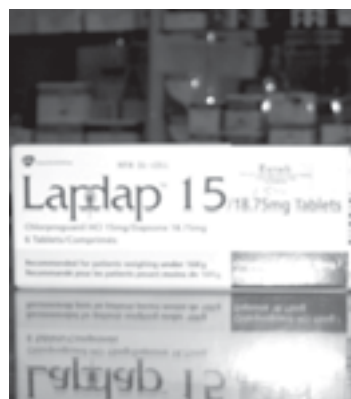
LAPDAP is contraindicated in patients with known hypersensitivity to sulphonamides and sulphones. Based on the known pharmacology of the components of LAPDAP (chlorproguanil and dapson), certain subpopulations may be at higher risk of serious adverse effects. Experience and information on the safety of this medicine is thus needed in particular in relation to:

- i) G6PD status
- ii) renal or hepatic diseases
- iii) pregnancy
- iv) HIV/AIDS
- v) elderly
- vi) malnutrition
- vii) haemoglobinopathies, and
- viii) specific Cyp450 polymorphisms and acetylator status.

In view of these, the experts are of the opinion that information on the safety of CPG-DDS is still too limited to warrant its widespread and unregulated use and more pharmacovigilance studies and post-marketing surveillance are needed.

Advice to African countries

In malaria endemic countries in Africa therefore, the experts recommend that LAPDAP should only be used if the diagnosis of malaria is confirmed and there are no contraindications to its use including pre-disposing factors to haemolytic adverse events. If it is not possible to have a reliable diagnosis of anaemia and a test for G6PD deficiency, a suitable alternative anti-malarial medicine should be used instead of LAPDAP. In pregnancy, LAPDAP should only be used as a last resort and only if the benefits of its usage far outweigh any potential risks.



The recommendations will be reconsidered when more data are available from pharmacovigilance and active post-marketing surveillance.

Priorities for further field research, with specific reference to phase IV studies and pharmacovigilance are safety and effectiveness studies, based on:

- appropriate protocols
- GCP standards
- use of an intention-to-treat analysis
- appropriate patient monitoring
- patient follow up to day 28
- rigorous recording of adverse events until resolved or outcome
- prospective study design, if possible, for patient populations that are at extra risk for adverse effects or insufficient efficacy.

The experts and authors of the report include

Prof Martin Danis (France),
 Prof Ralph Edwards (*the UMC*),
 Prof Mohammed Hassar (chairperson, Morocco),
 Prof Lucio Luzzatto (Italy),
 Dr Siddika Mithani (Canada),
 Dr Veronique Mugisha (Rwanda),
 Prof Olugbemi Sodeinde (Nigeria),
 Prof Frank Sullivan (UK),
 Prof Chris J. van Boxtel (rapporteur, Netherlands),
 and consultant, Prof Urban Hellgren (Sweden).

The report 'Review of the safety of chlorproguanil-dapsone in the treatment of uncomplicated falciparum malaria in Africa' is available from the WHO.

Profits, Patents and Patients

We asked a staff member of *the UMC* and a head of a pharmacovigilance centre in Africa to give their response to the film adaptation of *The Constant Gardener*

"The world is our clinic"

"Stop caring about Africa and start being loyal"

"Disposable drugs for disposable people"

These phrases from the film *The Constant Gardener* stuck with me after watching a multi-layered love story combined with a strong social message: drug companies and politicians not dealing properly with AIDS and tuberculosis in Africa. Two separate worlds presented by shots of garden parties, overcrowded shanty towns, beautiful, isolated landscapes, politics and golf, and the huge gap between rich and poor in Africa. The movie itself is slightly slow and long, but the excellent acting and the topic of political and financial gain at the expense of the African people, kept my interest. *The Constant Gardener* is a 'message movie' about how medicines are tested in developing nations without consideration of side effects, and how bad things happen when these trials are covered up.

A quiet, green-fingered British diplomat Justin Quayle (Ralph Fiennes) begins his own inquiries when his activist wife Tessa (Rachel Weisz), is killed and mutilated on the shore of a desolate lake, while on an aid mission. Allegedly the result of a bandit raid, Quayle suspects a cover-up. Tessa's idealism and outspoken criticism of the corrupt power structure had made her an embarrassment to the diplomatic community, and slowly but surely Quayle discovers that her secretly uncovered proof of a horrendous conspiracy lead to her death, this knowledge also putting him in danger.

The view of the greedy drug companies posing as altruistic, while viewing an epidemic as lucrative business, is disturbing and I wonder if I am naïve when I am not prepared to accept it? I don't want to believe that companies are driven by greed, corruption and conspiracies. I guess there are individuals with very perplexing views on human beings and human rights, but I also know that there are people who are passionate about keeping patients as safe as possible.

The movie left me disturbed and roused. The day after, back at my office I felt small, helpless and frustrated. Living in a safe world and not exposed to poverty, famine, terror and brutality, it is easy to retreat inside your comfort zone and pretend that your small contributions are worthless. I want to act! Maybe I should join 'Pharmaciens sans frontières', or sponsor a child? I know I can help by continuing my work in pharmacovigilance, playing my small part... we have to start somewhere.

Anne Kiuru

*Why should it surprise me? Drugs are the scandal of Africa. If anything denotes the Western indifference to African suffering, it's the miserable shortage of the right drugs, and the disgracefully high prices that the pharmaceutical firms have been exacting over the last thirty years".¹ *The Constant Gardener* brings to life the not-so-pleasant aspects of powerful pharma companies and spotlights the issues of clinical trials in deprived environments. Should a drug known to cause blindness and even death in pregnant women be marketed, even for a condition like multi-drug resistant tuberculosis for which options for cure are few? Can drug regulatory authorities in poor countries earn the trust placed in them to protect people by only allowing medicines of assured safety and quality to be supplied? What is the role of the ethical pharmaceutical industry in drug development and promotion in poor countries, and is the activity of industry based on profits alone, or is there an ethical and moral dimension? What about clinical trials in poor countries and informed consent in populations which can barely read – let alone understand the complex language on informed consent documents?*

*Dypraxa is a drug which does not exist, but John Le Carré's excellent book – now a film – on the release of a drug without adequate safety information on a poor population, and collusion of governments, regulatory authorities and marketing companies is familiar. Indeed, but for the fact that *The Constant Gardener* was written before 2001, the author could be accused of having eavesdropped on the National Centres meeting in Dunedin, as the issues raised were all tackled there! "[Dypraxa] was a good drug. With five more years' development they'd probably get there. You couldn't quarrel with the idea of the drug. It was short-course, cheap and patient-friendly. But they'd been too quick. ... They hadn't covered all the side effects."² How remarkably similar to contemporary issues on drug registration and withdrawals...*

*I hope that *The Constant Gardener* will be a source of comfort to pharmacovigilantes who often feel isolated and harassed. We too can raise our scientific, ethical and moral concerns, neatly summarised by Lara, who says "... *Dypraxa is a good drug. That is not the issue. The issue is threefold.... Issue one: the side-effects are being deliberately concealed in the interest of profit. Issue two: the world's poorest communities are used as guinea pigs by the world's richest. Issue three: legitimate scientific debate of these issues is stifled by corporate intimidation*".³*

Though the film of the book makes great viewing, my suggestion is to read the book once or maybe twice. The film compliments the book, so whatever you do, read the book: it is great!

Alex Dadoo

References

1. *The Constant Gardener* p169
2. *The Constant Gardener* p254
3. *The Constant Gardener* p383

The Constant Gardener by John le Carré (Hodder & Stoughton, 2001) is available in several translations (pages refer to 1st edition) and the film, based closely on the novel, was released in November 2005.

WHO Advisory Committee on Safety of Medicinal Products (ACSoMP)

Mary Couper reports

The WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) held its third meeting in December 2005. Constituted to provide advice on pharmacovigilance policy and issues related to the safety and effectiveness of medicinal products, the following are a few highlights from this meeting.

The WHO Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre)

Concern was raised that the UMC, in order to secure its financial viability, has been forced to spend much of its effort on providing services for the commercial sector and it was strongly suggested that a better budget allocation be obtained at the highest level of WHO.

Pharmacovigilance for antiretrovirals

A small working group was established to deliver a pharmacovigilance action plan for a pilot project in sub-Saharan Africa, working with the WHO HIV/AIDS programme to provide for strengthening spontaneous adverse drug reaction reporting, monitoring of specific toxicities and application of a pregnancy register. The HIV/AIDS programme in WHO will be consulted during the development of this plan which will include a proposed realistic budget.

Advocacy

At a political level and at a high level at WHO, discussions were proposed along with a proposal to the World Alliance for Patient Safety to integrate pharmacovigilance into the Alliance and adopt yearly themes, including a world pharmacovigilance day theme. WHO may have to make some high level endorsements to ministries of health so that pharmacovigilance centres can move forward to promote safety of medicines and find ways to integrate this in the health policy of the country.

Safety of medicines in children

The Advisory Committee has recommended that WHO address the issue of safety of medicines in children and that a guideline be prepared. The actions taken so far include approaching Karolinska Institute in Sweden to prepare the first draft manuscript. This project is currently in the development phase.

Report on kava

The Advisory Committee had commissioned an investigation on research into the safety of kava. The resulting report prepared by David Coulter contains extensive analysis of various available literature (case reports, clinical trials, etc). The conclusions and recommendations were presented for comments to this committee.

Safety of specific products

Oseltamivir Roche has pledged to provide WHO with three million treatment courses of the medicine oseltamivir to a WHO international antiviral stockpile. It is necessary therefore that the

efficacy and safety of this medicine is adequately documented both prior to and during the possible pandemic. Roche should be asked to share the methodology of active surveillance and assist countries which will be using oseltamivir as mass treatment during influenza pandemics. Particular attention should be given to pregnant women who take this drug. The risk of counterfeited products appearing on the market was noted.

Amodiaquine/artesunate Ghana has switched to using amodiaquine and artesunate combinations in the treatment of malaria in the light of resistance to chloroquine and sulfadoxine/pyrimethamine. Reports of ADRs to this combination are emerging from Ghana and also reports from Nigeria and Sierra Leone, including dystonic reactions. The reports should be investigated further. Risk minimization plans should be put in place in order not to negatively affect the malaria control programme.

Levamisole Concerns were raised by China that leukoencephalopathy followed use of levamisole. This had resulted in removal of this medicine from the national formulary by the government. Since this drug is on the WHO model formulary, and many countries have withdrawn levamisole, the overwhelming data on toxicity should be communicated to the Essential Medicines Programme.



Some of those involved in the ACSoMP relax in a Geneva café after work: (left to right) Murilo Freitas, Mary Couper, Gerald Dal Pan, David Coulter, Shanthi Pal, Sten Olsson

Safety monitoring of contraceptives in China

David Coulter reports

The National Population and Family Planning Commission in China is giving priority to safety. There are 250 million women using contraceptives in China and so safety, as well as efficacy, is very important. As part of a safety development programme, an ADR Monitoring Training Workshop for 10 of the 31 provinces was held in Nanjing, Jiangsu Province, 23-29 September. Along with Dr Michael Tatley, my successor as Head of the New Zealand Pharmacovigilance Centre, I was privileged to be invited to participate.

Nanjing is a former capital of China and the meeting was held at the International Conference Hotel in a beautiful area rich in history. It was organised by Professor Li Ying and her team. Professor Li is now Director of the Jiangsu Research Centre for Reproductive Health in Humans and has been doing some excellent pharmacoepidemiological research. One of the speakers was Dr Zhang Su-min from the National ADR Centre in Beijing and it was good to see this liaison.



Visit to the School of Public Health, Nanjing Medical University, where Professor Li conducts some of her pharmacoepidemiology research into CARs. From the right Prof Li Ying and Prof Chen Feng, Deputy Head of School of Public Health with staff and David Coulter.

The meeting covered a variety of interesting topics on the use of contraceptives in China and the development and status of Contraceptive Adverse Reaction (CAR) Monitoring. It fell to my lot to discuss International Pharmacovigilance, Communication and Risk Management and the methodology of the NZ Intensive Medicines Monitoring Programme (IMMP) together with its application to monitoring contraceptives. Dr Tatley spoke about Pharmacovigilance Systems and Methods and gave an introduction to Spontaneous ADR Reporting and the NZ Intensive Vaccine Monitoring Programme (IVMP) and its Electronic System.

Throughout the workshop the talks by the New Zealanders were translated into Chinese and, very courteously, the talks in Chinese were translated into English for the benefit of the two overseas guests. The translations were performed by Dr Zhou Lifeng who has previously worked in the IMMP.

The meeting was followed by a visit to the Consultation & Research Centre for Emergencies in Public Health at the Nanjing Medical University and a field visit to the network of CAR Monitoring in Taicang City. Altogether, it was wonderful to meet so many well-informed, dedicated and enthusiastic people.

Adverse reactions to contraceptives will go through a chain of assessment within the National Population and Family Planning Commission and will then importantly link with the National ADR Monitoring Programme. Since the meeting, it has been announced that the Center for Contraceptive Adverse Reaction Monitoring of China is to be established in Nanjing.



Main speakers at the Nanjing conference

Big drug safety focus in Shanghai

Bruce Hugman writes

22-24 October 2005 saw a great gathering of professionals from across China at two major meetings in Shanghai discussing pharmacoepidemiology, pharmacovigilance and clinical pharmacy. Senior officials, distinguished academics, researchers, clinicians, industry personnel and a group of foreign guests contributed to lively programmes enjoyed by large, national audiences. The main meeting was again organised by Dr Du Wenmin, of the Shanghai Centre for ADR monitoring. The annual national conference of clinical pharmacists also took place later the same week, organised by Professor Yongming Wang.

Among the distinguished contributors from China were Professor Fandian Zeng and Professor Jingbo Tang; international participants included: Frank May (University of Kentucky), Mitchell Levine (McMaster University), Chris van Boxtel (Netherlands), Bruce Hugman (UMC consultant), Duncan Topliss (ADR Advisory Committee, Australia).



Speakers, officials and participants in the 5th National Conference on Pharmacoepidemiology and Drug safety and the 2nd Shanghai International Congress of Drug Rational Use and Pharmacoepidemiology, Shanghai, October 2005

Czech pharmacists

the UMC is currently hosting two research fellows from Charles University's School of Pharmacy in Hradec Kralove, Czech Republic. Jitka Pokladnikova and Marcela Zemkova were awarded a competitive research fellowship by the EU 'Leonardo da Vinci' programme, and will each spend six months in Uppsala.

Marcela Zemkova graduated with MSc Pharm from the Charles University School of Pharmacy in 2001. She then joined the PhD study programme in clinical pharmacy – and started research on safety in patients with haematological malignancies and blood stem cell transplantation. "My research work focuses on targeted analyses of the drug safety issues with the aim of identifying the therapeutic value of the drugs used in haemato-oncology and identifying risk situations in blood stem cell transplantation patients or groups at risk. In my thesis I focus mainly on negative aspects of drug treatment and I try to put the knowledge of adverse effects into a patient safety context. I welcome the chance to collaborate on a scientific project related to the topic of my thesis.

I would like to use the skills and interests I developed during PhD studies, along with professional training as a clinical pharmacist, and to get hands-on experience of all aspects of UMC work."

Jitka Pokladnikova's research studies have focused on effectiveness, cost-effectiveness, safety and quality of life of treatment alternatives in patients with allergies, comparing different administration routes of specific allergen immunotherapy. She has also been involved in putting her knowledge to practice at the Drug Information Centre of the School of Pharmacy, where graduate students volunteer to provide health care professionals from all of the Czech Republic with drug information services.



Jitka and Marcela at the UMC Christmas lunch

Jitka has a certificate in homeopathy, and initiated her own research project investigating attitudes, knowledge and experience of pharmacy students and pharmacy professionals on complementary medicines. "Improvement of patients' quality of life requires pharmacy researchers and practitioners to be knowledgeable about other alternatives such as herbal medicine to help patients solve their unique health equation."

Her goal at *the UMC* is to extend her skills and knowledge on signal detection processes of conventional and herbal medicine at an international level both in theory and practice. Jitka has been enthused about working with her new colleagues "it has been great experience to work side by side with all the members of *the UMC* team" she says.

Jitka and Marcela would like to thank them all and especially Ronald Meyboom, Marie Lindquist and Ralph Edwards who made their stay at *the UMC* possible.

Uppsala dignitaries

Although *the UMC* has been active in Uppsala for almost 30 years it is very poorly known locally, both by people on the square outside the office and by politicians and local administrators. *the UMC* has not identified a need to promote itself in Uppsala since almost all UMC partners and customers are based in other parts of the world (except for the Swedish Medical Products Agency).



Jan Ask, vice-president, Lena Hartwig, president of the city council and Bengt Rinde, business relations

We were somewhat surprised and pleased to be contacted by the Uppsala City Council in October 2005. The president, vice-president of the City Council and a representative of the business secretariat wished to be briefed about *the UMC* activities. They spent half a day at *the UMC* office and the presentation resulted in interesting discussions on how the city may assist *the UMC* in networking and in administrative support. From *the UMC* side it was pointed out that the name of the Centre is a global promotion of the city and that we continuously bring employment and visitors to Uppsala.

Veronese visitor

During December 2005 *the UMC* welcomed Lara Magro from Verona, Italy. She works at the Clinical Pharmacology Unit, Veneto Region Pharmacovigilance Centre, and Reference Centre for Education and Communication within the WHO Programme for the International Drug Monitoring at the University of Verona.



Lara Magro

The aim of her two weeks at *the UMC* was to gain a better understanding of the WHO signal process; she worked closely with Johanna Strandell and others in the signals team. Lara wrote "I met nice people that made me feel at home and I have learnt a lot for my work back in Verona. It was really a great experience."



Bill Inman

Remembering a great pioneer

A tribute by Ronald Meyboom

In August 2004 when we visited Professor Bill Inman at his house in the English countryside close to Southampton, we found him in excellent spirits and reasonably good health and had a delightful discourse that resulted in the interview to celebrate his 75th birthday, which was published in October 2004 in Uppsala Reports 27.

Sadly we now have to report that Bill has died; the burden of the long-lasting confinement to a wheelchair and progressive illness finally took its toll.

With his death one of the first great pioneers of drug safety has gone. The first graduate in medicine from Cambridge University (1956) he joined the UK Department of Health and Social Security in 1964 and was asked to develop the ADR reporting system later known internationally as the 'yellow card' system. After 1975 he drafted proposals for what he termed 'Recorded Release', which eventually became the UK post-marketing monitoring system used by the Drug Safety Research Unit (DSRU) in 1980. He had a huge influence on drug safety from the 1960s through to the 1980s. The article in Uppsala Reports 27 (available to download from *the UMC website* or by post) lists his major publications.

In Bill's lifetime pharmacovigilance developed from something virtually non-existent into an established pharmacological profession and a new branch to the tree of medical science. To this nobody has contributed as much as he did. Bill's final work – an autobiography – entitled 'Feeling better doctor?' will be published by Highland Park (see the box below).

With the passing of Bill Inman and Beje Wiholm, 2005 has brought irreparable losses to pharmacovigilance. As can be seen for instance during recent meetings of National Centres participating in the WHO Programme, interest in *the UMC pharmacovigilance training courses* and the many professional meetings around the world organised by ISO, ISPE and others, a new generation of hundreds if not thousands of young scientists have chosen pharmacovigilance as their specialty and committed themselves to the evaluation of medicines and to their safe use, at regulatory agencies, regional centres, universities and pharmaceutical companies alike. All dedicated to sustain our young profession and to a better care of patients; all profiting from the achievements and sometimes hardships of pioneers such as Bill and Beje.

The introduction to 'Feeling Better Doctor' by Michael O'Donnell FRCGP, prepares the reader for "the story of a far from ordinary man who has lived a far from ordinary life. It is also a story played out against the background of the most dramatic changes in recorded history in the medicinal treatment and prevention of disease."

By the time these changes were taking place Bill Inman had, "with characteristic energy, started to fashion a career that would lead him to play a remarkable role, as monitor and restrainer, of the therapeutic revolution that accelerated though the next four decades. The scale of that revolution is taken for granted by a generation that assumes there is a pill for every ill."

Dr O'Donnell concludes that when the reader reaches the final pages "I suspect you will agree that their author has earned the accolade of one of those beastly people who are always bringing up awkward subjects and making respectable people feel uncomfortable".

'Feeling Better Doctor' will be published in February 2006 by Highland Park, South Croft House, Winchester Road, Botley, Hampshire, SO3 2BX, United Kingdom

E-mail highlandpp@aol.com

Price £9.99

More entries in WHO Drug Dictionary Enhanced

To be able to increase the coverage of Drug Dictionary data in a large number of countries and to get fast access to information about new drug product releases, the UMC has entered into collaboration with IMS Health. The result of this collaboration is called WHO Drug Dictionary Enhanced.

WHO Drug Dictionary Enhanced combines the unique structure of the WHO Drug Dictionary with the strength of the IMS Health's comprehensive product data.

The third release of the WHO Drug Dictionary Enhanced, released December 1 2005, has additional data from the USA, Canada, Mexico, Austria and Germany to complement the countries (Japan, United Kingdom, Finland, Poland, Latvia, Lithuania, Hungary, Estonia and Czech Republic) which have already had product information from IMS Health added.

This has resulted in the following statistics:

Country	# of Products from IMS Health	# of Unique Names from IMS Health	Total # of Medicinal Product entries (variation of MAH/Form/Strength) in WHO DDE
USA	36,300	5,600	70,600
Germany	14,400	10,600	37,000
Austria	4,700	3,050	8,600
Canada	3,900	2,200	10,100
Mexico	6,100	4,350	10,900

The WHO Drug Dictionary Enhanced statistics are now as follows:

Type/Format	# of Medicinal Products in C Format	# of Drug records in B.1 Format	# of Drug records in B.2 Format
WHO Drug Dictionary	142,209	117,996	60,252
WHO Drug Dictionary Enhanced including WHO DD	398,789	246,797	91,782

The next release of the WHO Drug Dictionary Enhanced, March 1, 2006, will include IMS Health product information from an additional 54 countries.

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.unc-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:



January 23-26

The 5th Annual DIA Workshop for Contemporary Pharmacovigilance and Risk Management Strategies, Washington, DC, USA

March 6-8

18th Annual DIA EuroMeeting, Le Palais des Congrès in Paris, France

March 26-29

21st Annual Clinical Data Management Symposium and Exhibition, Philadelphia, PA, USA

April 4-6

ICR 27th Annual Spring Conference and Exhibition, Manchester, UK

June 18-22

42nd DIA Annual Meeting, Philadelphia, PA, USA

August 24-27

22nd International Conference on Pharmacoepidemiology (ISPE) & Therapeutic Risk Management, Lisbon, Portugal

October 8-11

The Society for Clinical Data Management (SCDM), Wyndham Palace Resort & Spa, Orlando, Florida, USA

Need help?

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

You can e-mail:

drugdictionary@unc-products.com for comments about the WHO-DD, WHO-DD Enhanced, corrections and additions, and katarina.hansson@unc-products.com for queries about your subscription.

Managing Safety Information from Clinical Trials Report by CIOMS Working Group VI, Geneva, 2005

A Description of the Report by Arnold J Gordon, PhD

The CIOMS VI Working Group has developed proposals for harmonizing many aspects of the collection, monitoring, analysis, evaluation/interpretation, and communication to all relevant parties of clinical trial safety information. In so doing, it has developed an approach to 'good clinical trial safety practices' that embraces an overall safety surveillance/risk management program that links pre-marketing to post-marketing safety environments. Among the topic covered:

Terminology and definitions: What terms, definitions and categories are the best ones to use and from what sources (e.g., WHO, ICH, prior CIOMS groups, various regulatory authorities, and others)? An extensive Glossary is provided.

Ethical aspects of clinical trials: The latest requirements and thinking on the roles and responsibilities of all stakeholders, including new privacy and data confidentiality laws and other considerations affecting the rights and welfare of study subjects, are discussed.

Overall safety surveillance/risk management system: Guidance is provided on a pharmacovigilance/risk management process that can form the basis for any general or specific pharmacovigilance plans during drug development.

Collection and proper management of safety data: The report addresses details concerning the what, when, how and why of data collection, including the possible use of internationally standardized forms and the proper approaches for coding and managing AE/ADR data.

Evaluation of safety data: Many aspects of data analysis and assessment are covered: when, how often, and to what depth; individual cases versus aggregate data; blinded versus unblinded data; special sub-populations; and much more.

Statistical analysis of safety data: Use of statistics in analyzing clinical safety data is complicated and often performed incorrectly. The report covers in detail: 'intention-to-treat' analyses applied to safety data; impact of statistical power, multiplicity (multiple analyses) and time dependency on analysis and interpretation of data; one-sided versus two-sided testing; correct approaches to analysis of continuous data (e.g., laboratory chemistries) versus binary data (e.g., present/absent); use of survival analysis techniques; meta-analytic approaches for pooling study data; use of background data from non-trial sources.

Regulatory reporting and communication of safety information during clinical trials: What information should be communicated to whom, how should it be done, when and by whom? These and other issues are covered in detail along with some recommendations for new approaches that deviate from current regulatory requirements.

The Working Group hopes that their report will enhance awareness of the ethical and technical issues associated with safety in clinical trials; they point out the need for increased care and scrutiny in the conduct of research. They also hope their work will advance the methodology for collecting, analysing, evaluating and reporting information on product safety ascertained in clinical trials, and help to set standards in these areas. The report has implications for all stakeholders in clinical medicinal research: patients, investigators and their site staff, ethics review committees, data and safety monitoring boards, drug regulatory authorities and the public health community, and pharmaceutical companies and other clinical research sponsors. They explain that there is a need not only to incorporate newer approaches for managing safety information in the clinical trial setting, but also to adapt the methods and tools used in post-approval pharmacovigilance to the early and late stages of pre-approval development of medicinal products.



Copies of the report can be ordered via www.cioms.ch or from CIOMS, Avenue Appia, 1211, Geneva 27, Switzerland

Strom's Pharmacoepidemiology reaches 4th edition

Professor Brian Strom of Public Health and Preventive Medicine at the University of Pennsylvania has stuck with generally the same format for the new edition. Although its 860 pages compare almost exactly with the number of the 2000 3rd edition and the book adheres to similar sub-divisions, this new edition has several new chapters among the more general updates and an impressive list of contributors.



Pharmacoepidemiology. Strom BL (ed). John Wiley & Sons Ltd, Chichester, England. 2005.

Pharmacovigilance in Focus



An expanded and updated version of the reprint collection from Adis, consisting of articles in Drug Safety by UMC staff, is in press. Further details will appear on *the UMC website*.

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
25 January 2006	Drug Safety – Everyone's Business	Edinburgh, UK	Royal College of Physicians of Edinburgh Tel: +44 131 247 3636 Fax: +44 131 220 4393 www.rcpe.ac.uk/education/events/index.php
1-3 February 2006	Medical Aspects of Adverse Drug Reactions	Southampton, UK	DSRU Tel: +44 23 8040 8621 Fax: +44 23 8040 8605 E-mail: jan.phillips@dru.org
2-3 February 2006	Pharmacovigilance: Science and Regulation. Is this compatible? Assessment and Management of Drug Liver Toxicity & Coping with Audits and Inspections	Sevilla, Spain	ISO P Administration Tel/Fax: +44 20 8286 1888 www.isoponline.org
13-14 February 2006	Post-marketing studies	London, UK	CBI Research Tel: +1 781 939 2438 Fax: +1 781 939 2490 E-mail: cbireg@cbinet.com
21 February 2006	Pharmacovigilance – Compliance and Quality Assurance	London, UK	Management Forum Tel: +44 1483 570099 Fax: +44 1483 536424 E-mail: info@management-forum.co.uk www.management-forum.co.uk
22-23 February 2006	Monitoring Safety in Clinical Drug Development	Southampton, UK	DSRU Tel: +44 23 8040 8621 Fax: +44 23 8040 8605 E-mail: jan.phillips@dru.org
6-8 March 2006	18th Annual EuroMeeting	Paris, France	DIA Tel: +41 61 225 51 51 Fax : +41 61 225 51 52 www.diahome.org
30-31 March 2006	VI Jornadas de Farmacovigilancia	Madrid, Spain	Reg Cent of Community of Madrid & Spanish Medicines Agency Tel: +34 91 204 2600 Fax: +34 91 559 7411 E-mail: dccimad6@viajesece.es www.jfv2006.com
10-12 April 2006	27eme Journées de Pharmacovigilance	Montpellier, France	Secrétariat de la Société Française de Pharmacologie Tel: +33 2 35 14 86 04 Fax : +33 2 35 14 86 09 E-mail : secretariat@pharmacol-fr.org
24-25 April 2006	ISPE Mid-Year Meeting	Rockville, Maryland, USA	International Society for Pharmacoepidemiology Tel: +1 301 718 6500 Fax: +1 301 656 0989 E-mail: ispe@paimgmt.com
26-27 April 2006	Back to Basics in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 23 8040 8621 Fax: +44 23 8040 8605 E-mail: jan.phillips@dru.org www.dru.org
26-28 April 2006	2½ day International Symposium on Pharmacovigilance of Herbal Medicines: Current state and future directions	London UK	Dr John Clements, Science Secretary Royal Pharmaceutical Society of Great Britain Fax: +44 20 7572 2506 E-mail: science@rpsgb.org www.rpsgb.org.uk
18-22 June 2006	DIA 42nd Annual Meeting	Philadelphia, Pennsylvania, USA	DIA Fax : +1 215 442 6199 www.diahome.org
24-27 August 2006	22nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management	Lisbon, Portugal	International Society for Pharmacoepidemiology Tel: +1 301 718 6500 Fax: +1 301 656 0989 E-mail: ispe@paimgmt.com www.pharmacoepi.org
11-13 October 2006	International Society of Pharmacovigilance (ISO P) Annual Scientific Meeting. Pre-conference training courses.	Liège, Belgium	International Society of Pharmacovigilance E-mail: info@isop2006.org www.isop2006.org



the Uppsala Team

Director

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

Executive Group

Marie Lindquist, Dr Med Sc Deputy Director, General Manager, Science & Technology

Lars Magnusson General Manager, Products & Services

Administration

Marjatta Leván, BA Manager

Cecilia Biriell, MSc Pharm Senior Specialist, Head of Internal Affairs

Ali Bahceci Network Technician

Anneli Lennartsson Economy Assistant

Linda Wallin Team Support

Science and Technology

Safety Reporting Support & Service, and Systems Development

Magnus Wallberg, MSc Eng Phys Manager

Bill Dagérus Senior Systems Developer

Stefan Lewenfalk Systems Developer

Annica Lundström, BSc Pharm Data Management

Jessica Nilsson, BSc Pharm Programme Leader, Data Management

Helena Sjöström, Pharmacist, Data Management (on maternity leave)

Bo Östling Senior Systems Developer

External Affairs

Sten Olsson, MSc Pharm Manager, Head of External Affairs

Geoffrey Bowring, BA External Affairs Co-ordinator

Jenny Ericsson, BSc Pharm Programme Leader, Traditional Medicines

Mohamed Farah, Pharm D Senior Specialist, Traditional Medicines

Research & Development

Andrew Bate, MA (Oxon), PhD Manager

Jonathan Edwards Programme Leader, Data Mining Development

Niklas Norén, MSc Eng Phys Research Engineer

Malin Ståhl, MMedSc Research & Development (on maternity leave)

Erik Swahn, MA Data Mining Developer

Signal Detection & Analysis

Monica Plöen, BSc Pharm Manager

William Frempong, BSc Pharm Signal Detection & Analysis

Anne Kiuru, MSc Pharm Signal Detection & Analysis

Kristina Star, Registered Nurse Signal Detection & Analysis

Johanna Strandell, MSc Pharm Signal Detection & Analysis

Products and Services

Business & Product Development

Annika Wallström, MSc Pharm Product Manager

Daniel von Sydow, MSc Pharm Project Co-ordinator

Customer Support Services

Anna Blomquist, BSc Pharm Drug Dictionary Services (on external placement)

Kristina Johansson, MSc Pharm Database Services

Anna Mattsson, BSc Pharm Drug Dictionary Services

Nike Meder, Pharmacist Drug Dictionary Services

Erica Walette, BSc Pharm Programme Leader, Database Services (on study leave)

Malin Zaar Nord, Pharmacist, Programme Leader, Drug Dictionary Services

Production

Johanna Eriksson Manager

Björn Moberg Systems Developer

Sven Purbe, BA Senior Specialist

Sales & Marketing

Mats Persson, BA Manager, Business Development

Hannah Björn Sales and Marketing Assistant (on maternity leave)

Katarina Hansson Sales and Marketing Assistant

Åsa Lindeberg Web Editor, Products & Services



the Uppsala Monitoring Centre
Stora Target 3
S-753 20 Uppsala
Sweden

Telephone: +46 18 65 60 60

Fax: +46 18 65 60 80

E-mail:

(general enquiries) info@who-umc.org

(sales & marketing enquiries) info@umc-products.com

(Drug Dictionary enquires) drugdictionary@umc-products.com

Internet: www.who-umc.org

Uppsala Reports ISSN 1651-9779

