

Uppsala Reports 27

UPPSALA REPORTS October 2004

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

New Herbal ATC guides

Profile: Bill Inman

Vigilance of HIV/AIDS drugs in Africa

WHO Programme reaches 75 members

New BCPNN application



DIRECTOR'S MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring Centre

In Shanghai, on the 18th September, a notable event occurred: the first meeting of the WHO World Alliance for Patient Safety. Lucien Leape of Harvard University, USA was a pioneer in pointing out how medical failures of one sort and another caused huge morbidity and mortality as well as costing money. The use of drugs was seen as a frequent cause of avoidable patient injury. Pharmacovigilance may have played an important role in finding new and rare adverse reactions, but it has had little impact on the known, day-by-day and avoidable damage caused by drug therapy. This will now change, and the Alliance will have impact on our work in pharmacovigilance (see page 13).

Both the WHO Programme for International Drug Monitoring and the International Society of Pharmacovigilance have just had their annual meetings, back-to-back, in Dublin. In both meetings the wider scope of pharmacovigilance was discussed. In the former meeting, the need for additional, focussed, surveillance methods was a major topic, ably introduced in a keynote address by David Coulter. More innovative analysis tools, particularly the use of data mining, was the topic of the first keynote speech in the ISoP meeting, given in grand style by Stephen Evans.

For me, though, the second keynote address by Sir Michael Rawlins, chairperson of the UK's National Institute for Clinical Excellence (NICE), summarised my own views and the tone of the two meetings. He said that drug regulation must become more open and focussed on the needs of patients and society. Good communication of knowledge was essential. He discussed the need for widening our views on evidence away from our concentration on p-values to a broad view on evidence of all sorts (he particularly mentioned Bayesian approaches!). Effectiveness and risk balance should become far more rigorous, moving away from just the consideration of efficacy in narrow clinical trials on the one hand, and solely qualitative judgements on the other. He also discussed the need for economic considerations in the distribution of equitable medical care.

These were two superb meetings. Niamh Arthur and her colleagues from the Irish Medicines Board set the highest standards for both organising the meetings and contributing to their content. I am very grateful for their huge efforts.

Linked with the above, I must also mention the very successful course on the pharmacovigilance, and management of ADRs, in the HIV/AIDS Programmes in Africa (also reported later in this issue, pages 8-9). The workshop, with representatives from 8 African countries, was over two weeks in September, in Pretoria, South Africa, and excellently supported by Mrs Precious Matsoso and her team, scientifically and organisationally.

If there was a theme for that workshop, it was that the successful management of patients with HIV and AIDS depended upon the skill in recognising known and new adverse reactions clinically and then managing them without any failure in compliance. To do this as more drugs become available, millions more patients are treated, and in such variable health care situations will demand all of the considerations mentioned from the meetings above. To fail to this well, is to lead to resistant AIDS and disaster. We, in pharmacovigilance, must play our part to the utmost to see that useful information on ADRs gets to treating doctors and patients promptly.

8 WHO training course in Pretoria targets programme managers for HIV/AIDS in southern African countries.



10 Bill Inman, one of the great pioneers of pharmacovigilance, is 75. We look back over his life and career.



14 the UMC has launched its Herbal ATC Index and Guidelines – two important publications for those working in drug registration and drug safety.



15 UMC staff visited Poznan to attend an international conference and present the latest UMC research, and to learn about Research Institute of Medicinal Plants' work in herbal medicines.



Nigeria and Malta join WHO Programme

We are pleased to report a further expansion of the WHO pharmacovigilance network. In September two more countries fulfilled the requirements for becoming full members of the WHO International Drug Monitoring Programme, Nigeria and Malta. They are member countries 74 and 75 in the Programme. The two countries are very different. Malta, a small island in the Mediterranean Sea, has a population of around 400,000 while Nigeria has a population of approximately 130 million.

The pharmacovigilance programme in Malta has developed through a twinning programme with the Irish Medicines Board. Head of the pharmacovigilance centre is Dr Patricia Vella Bonanno, Medicines Authority, No 198 Rue d'Argens, Gzira, Malta, Tel +356 23439110 / 112, Fax +356 23439161 / 158, e-mail address - patricia.vella@gov.mt. The technical contact person is Mr Michael Bonett, e-mail - michael.p.bonett@gov.mt.

Head of the new pharmacovigilance centre in Nigeria is Mrs Ijeoma Nnani, National Agency for Food and Drug Administration and Control (NAFDAC), Plot 2032, Olusegun Obasanjo Way, Wuse Zone 7, Abuja, Nigeria, Tel: +234-09-6702823, 234-09-5241108, Fax: +234-9-5240994, e-mail: ijeomannani@yahoo.com

See page 4 for more information about pharmacovigilance in Nigeria.

2	Director's Message
4	New Member Countries
5	Vigibase Online online
6	BCPNN applied to IMS data
7	Reports from Serbia and Mongolia
8-9	Training in Pretoria
10-11	Profile of Bill Inman
12	ICDRA report
13	WHO Global Alliance for Patient Safety
14	Herbal ATC guides
15	UMC herbals team visit Poland
16	Conference reports
17	Visitors
18	Products and Services
19	Conferences
20	the UMC team



Communications information

Postal Address:

the Uppsala Monitoring Centre,
Stora Torget 3,
S-753 20 Uppsala,
Sweden

Telephone: +46 18 65 60 60

Fax: +46 18 65 60 80

E-mail:

general enquiries: info@who-umc.org
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

Internet: www.who-umc.org

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

Uppsala Reports © the Uppsala Monitoring Centre 2004

ISSN 1651-9779



Africa's biggest country embraces pharmacovigilance



Inauguration of the Nigerian pharmacovigilance system, September 2004



Ralph Edwards as seen during his interview for Nigerian TV



Sten Olsson and Kayode Omotayo

After a long gestation period (see Reunion after 23 years) the Nigerian pharmacovigilance programme was officially born on 9 September 2004. The birth of the new baby was celebrated by a big meeting in the capital Abuja in the presence of the Minister of Health, Professor Eytayo Lambo, the Senate president Mr Adolphus Wabara, the head of the National Agency for Drug Administration and Control, NAFDAC, Dr Dora Akunyili and many other dignitaries. *the UMC* was represented by Ralph Edwards and Sten Olsson. Nigeria's first lady, Mrs Stella Obasanjo was unable to attend but sent a personal message to the meeting. The inauguration ceremony was heavily covered by local media.

In his opening speech Professor Lambo requested Nigerian medical, pharmacy and nursing schools to revise their curricula in order to provide proper training on assuring the safety of medicines and on the need for health professionals to contribute to the Nigerian pharmacovigilance programme. He also gave advice to pharmaceutical manufacturers marketing products in Nigeria as to the kind of safety information they are requested to submit to NAFDAC. He launched the pharmacovigilance programme by submitting a case report to UMC via the internet-based reporting system Vigibase Online. Nigeria thereby fulfilled the requirements for becoming the 74th member of the WHO Drug Monitoring Programme.

Dr Akunyili thought that the establishment of the national pharmacovigilance programme was long overdue. Nigeria, having the biggest black community in the world, cannot rely solely on drug safety information acquired in other countries. The country, its people and its healthcare system have unique features and the full benefit/harm assessment of medicines used can only be made with sufficient good quality local data. She emphasized the need for consumers to be involved and committed to the collection of information regarding drug safety.

The launch of the Nigerian pharmacovigilance programme was followed by a well-attended 3-day training programme for health professionals and regional healthcare administrators from all parts of the country. Tutors were recruited locally, including Professor Ambose Isah; from *the UMC*, India (Mr Brijesh Regal) and Ghana (Dr Alex Doodoo). The final day had a parallel training session for media representatives to which Alex Doodoo also contributed.

Ms Ijeoma Nnani, the head of the new pharmacovigilance unit of NAFDAC who organized the inauguration programme, was very happy with the outcome. She realizes that the pharmacovigilance

programme, after its flying start, needs to remain visible and provide support and guidelines for healthcare professionals around the country in order not to lose momentum. To this end Ralph Edwards, Brijesh Regal and Sten Olsson were brought to participate in a TV show to explain to Nigerian viewers what pharmacovigilance is about.

Reunion after 23 years

On the first page of *the UMC* visitors book there is the signature of Mr Kayode Omotayo from Nigeria. Mr Omotayo spent a month at the WHO Centre in 1981 at a time when only Marie Lindquist, Cecilia Biriell and Sten Olsson worked there. Although Mr Omotayo learned a lot about drug safety monitoring during his period in Uppsala, the time was not ripe for establishing an adverse reaction reporting system in Nigeria at his return. The contacts between Mr Omotayo and his friends in Uppsala got fewer and soon stopped completely.

In early 2004 Mr Omotayo, who is now Director of Food and Drug Services at the Federal Ministry of Health, visited the WHO Regional Office for Africa. While there he flicked through an issue of the WHO Pharmaceuticals Newsletter and found Sten Olsson's e-mail address. He decided to contact Sten to get an update of the current UMC situation. Sten was very happy with the re-established contact and could advise that he had been invited for the official inauguration of the Nigerian pharmacovigilance programme in September. Having arrived in the Nigerian capital Abuja, Sten Olsson and Kayode Omotayo could meet at the Ministry of Health (see picture). Mr Omotayo also participated in the inauguration ceremony for the pharmacovigilance programme and lectured about the need for a pharmacovigilance policy at the subsequent training course.

From *the UMC* perspective it is interesting to note that all pieces in the pharmacovigilance puzzle need to come together before a functional national system can be established. Mr Omotayo, who trained at *the UMC* in 1981, is now placed in the national policy-making circles. Dr Amrose Isah, who attended *the UMC* training course in 1996, has established an enthusiastic team at his university department in Benin City, responsible for the majority of present ADR reports in Nigeria. Ijeoma Nnani, who passed *the UMC* training course in 2003, is now heading the new pharmacovigilance department within the regulatory agency, NAFDAC. Many levels of the health-care society have to be co-ordinated, and the political climate needs to be right for important changes to be implemented.

Vigibase Online - up and running

Vigibase Online is now up and running for ADR report management and transmission to the WHO ADR database at *the* UMC.

Vigibase Online has been developed as a simple, secure solution for ADR reporting for regional and national pharmacovigilance centres and pharmaceutical companies. It is web-based and allows seamless electronic transmission of ADR reports in E2B format from healthcare professionals to their designated reporting centres and onwards to the WHO database, or other destinations such as EMEA or FDA.

New features and fine-tuning

Over the last few months some new features have been added - and others fine-tuned - including

- ♦ the possibility to produce feedback letters for reporters and paper reports
- ♦ a development of a search and statistic module is underway which will further increase the value of the program
- ♦ a complete audit trail can now be made accessible to users
- ♦ more general improvements for reporting speed in response to user demands
- ♦ improved procedures for submitting Vigibase Online reports to the WHO database.



Figure 1

Collaboration with Swiss

Swissmedic, the national pharmacovigilance system in Switzerland, has been the principle partner of *the* UMC in initiating this software system. Since the 1st July 2004, three regional centres have been using the system, in addition to the national centre (three

languages are available in the software: English, German and French). During August and September the rest of the Swiss Regional Centres have been introduced on the system, so that all are online by October 2004.



Figure 2

Ruedi Stoller, Head of the Swiss national pharmacovigilance centre has been pleased with the new system "Vigibase Online has strongly improved the speed and effectiveness of our reporting processes. It is well-adapted to the organisation of pharmacovigilance in our country which is based on 6 regional centres directly involved in data entry and it has significantly reduced administration and delays."

The reports start arriving

So far, over 250 reports have been submitted to the WHO database via Vigibase Online - the majority from Switzerland, but some also from Ghana and Morocco - all active members of the WHO Programme. South Africa, plus Lithuania, DR Congo, Zambia and Mozambique (only Associate members of the WHO Programme) are currently trying it out.

Vigibase Online

Vigibase Online offers significant benefits:

- No local software or hardware
- Unlimited number of users
- Simple, secure ADR reporting in E2B format
- Improvement of report quality
- Extensive optional data fields and free-text entries
- Live access to latest versions of terminologies (WHO-DD, MedDRA, WHO-ART)
- Streamlined reporting
- Report download for local storage
- Multilingual
- Built-in statistics and data retrieval
- Cost-effective and time-saving
- User guide and online help available

For more information do contact Magnus Wallberg or Sten Olsson at *the* UMC.

Figure 1
Vigibase Online - the case overview window

Figure 2
The first screen for entering data in Vigibase Online

UMC collaboration with IMS takes step forward

Jonathan Edwards reports

The Data-Mining group at *the* UMC recently had the opportunity to run BCPNN software on a new dataset. This opportunity came about when IMS Health in the UK showed interest in our techniques. A pilot study was set up with the goal of testing the feasibility of data-mining the IMS Disease Analyser dataset on a regular basis. The pilot study is now complete and has been a huge success! Further discussions are now taking place and we are looking forward to an ongoing collaboration with IMS Health in the exciting area of data-mining.

The 1-month pilot study began when we received a copy of the database in March. The data was imported and pre-processed using a dedicated Linux server. We then adapted our BCPNN tools so that we could run all the data-mining tasks via a secure web browser interface against the server.

The Disease Analyser dataset was an interesting challenge for us because it differs in a subtle but fundamental way from the WHO ADR database. In the WHO database, suspected associations between drugs and events are reported based on a clinical evaluation, while in Disease Analyser, all prescriptions and events (not just adverse events) are reported. This means that, using Disease Analyser, we can compare figures before and after drug prescription potentially giving us the following information:

- Signals of currently unknown side-effects of drugs
- Signals of likely future side-effects of drugs
- Signals of new information about adverse drug reactions - facilitating consideration of change in prescribing information to avoid further adverse effects
- Signals of unexpected positive outcomes of drug use, which might indicate possible new indications of a product
- Specific target groups of patients where the drug indication is most likely to work
- Comparisons of drugs where one drug seems to be less related to specific side-effects than its competitors
- Suggestions of risk/effectiveness balances

Various BCPNN tools have been implemented for producing hypothesis about the above, including a pattern recognition tool. All can be run via a secure, user-friendly web interface.

IMS Health and *the* UMC believe that routine data-mining of the IMS health database will be extremely interesting to both IMS and UMC customers.

New member country introduction: Colombia

Carlos Arbeláez of the Colombian pharmacovigilance team at INVIMA reports

INVIMA, the Drug regulatory agency of the Republic of Colombia, is an institute associated with Ministerio de la Protección Social (Colombian Health Ministry), which includes the National Pharmacovigilance Centre.

INVIMA began a pharmacovigilance programme in 1996 using the modality of spontaneous reporting because of the operative advantages of the method, and has adopted the CIOMS I format.

Eight years later, in 2003, INVIMA reviewed the concept and reasons of undertaking pharmacovigilance. We believe that drug safety is a global responsibility and that it is determined by factors depending on the host (patient), the drug (composition) and on drug use. This concept leads to the necessity of public health initiatives; it is a great benefit for Colombia to access information about safety related to drug products and early knowledge of drug alerts before public health is damaged.

As drug safety also depends on drug use unique to our local situation, the Colombian pharmacovigilance programme develops activities related to rational drug use and advises physicians to evaluate host-related aspects.

The actions developed since August 2003 to achieve our goals in drug safety are:

- Joining the WHO Programme
- To answer each ADR case report received from a health care professional
- To organize a national pharmacovigilance network with health care institutions as reporting centres
- Establishment of a national drug information service
- Editing 'Boletín Nacional de Farmacovigilancia y Tecnovigilancia' – our publication that has appeared every two months since January 2004
- Active search for international drug alerts in regulatory agency web pages
- Technical support from universities such as 'Universidad Nacional de Colombia'

The National Pharmacovigilance Network that has been developed will be inaugurated on October 31, 2004 in a forum with the participation of international experts.

Serbian update

Branka Terzic of the National Centre for Serbia and Montenegro has been very busy, organizing a specialization for hospital pharmacists. In addition, the Serbian parliament has passed a new law about medicinal products, (in line with European Union law). This should lead to the formation of drug agency in a very short time, which will give an additional boost to pharmacovigilance.

The expert group of the National Centre for Adverse Drug Reactions Monitoring (NC) organized its third scientific symposium on adverse drug reactions, on 29th April 2004 in Belgrade. The meeting covered the work of the National Centre during the last ten years and was aimed at the promotion of pharmacovigilance in Serbia. The symposium was divided into three sessions, through 21 selected topics. Dr Ronald Meyboom, Medical Adviser of *the* UMC and Senior Researcher of the Faculty of Pharmacy at the University of Utrecht, participated in this symposium and presented two interesting lectures in pharmacovigilance.

350 doctors and pharmacists from all around Serbia and Montenegro attended; representatives of pharmaceutical industry

were also present. The results of 10 years long adverse drug reactions monitoring in Serbia and Montenegro, and the accumulated knowledge in pharmacovigilance were presented and discussed.



*from left to right,
Ljiljana Pitic, MD, Clinical Pharmacologist until recently in Pfizer Belgrade,
Nada Djokanovic, MD, Clinical Pharmacologist, GALENIKA Ltd, Belgrade,
Ljiljana Djukic, pharmacist, M.Sc. active in pharmacovigilance at the Institute
of Pharmacy of Serbia, Milan Stanulovic and Ron Meyboom*

Research in Mongolia

Although not even yet an Associate Member of the WHO Programme, we are delighted to hear from *Tsogzolmaa Nanjaa* of first steps in starting a pharmacovigilance system in Mongolia:

"The last two years have seen official registration of ADR monitoring and pharmacovigilance in Mongolia. In toxicology too, drugs causing poisoning and their symptoms are now covered. Although laws on drugs and on appropriate usage of drugs have been passed, and have started being implemented in Mongolia, there are still problems of irrational usage and storage of drugs. To take appropriate measures of prevention and detection it's vital to determine causes of ADR and poisoning cases, so we have chosen to research this issue.

Our main objective of pharmacovigilance in Mongolia was to identify and evaluate the drugs that are causing ADRs and acute poisoning and determine the causes and symptoms as well as ways of preventing them."

The results of this research showed a range of ADRs such as anaphylactic reactions and skin eruptions from anti-microbial drugs and Parkinsonism and salivation from CNS drugs. Other drug groups were investigated; for example non-steroidal drugs, and traditional medicines. The main ADR for elders was caused by gentamicin and digoxin, which are in popular use in Mongolia.

In 2002-2003 156 reports were registered. CNS drugs were particularly noted. The most common ADRs to penicillin were allergic reactions and the number has increased during recent years. The main reason of mortality of ADR is anaphylactic reaction and there were 5 deaths of 7 anaphylactic reactions.

Monitoring anti-retrovirals in sub-Saharan Africa

Bruce Hugman reports on a major training initiative to enhance the safety of HIV/AIDS patients under treatment

Twenty-six representatives of eight African countries met in Pretoria, South Africa, from 1–10 September on a WHO-sponsored training course¹ to study how antiretroviral (ARV) therapy on the continent could be monitored for quality, safety and effectiveness. Countries represented were: Kenya, Malawi, Mozambique, Nigeria, South Africa, Uganda, United Republic of Tanzania, and Zambia. Teaching was provided by staff from WHO HQ, the UMC, a number of experts from around the world and by participants themselves. As HIV/AIDS treatment programmes roll out across Africa, and more and more patients gain access to ARVs, the need for post-marketing surveillance becomes ever more urgent. While much is already known about ARVs from the experience of developed countries, there is little data on patients from a wider ethnic spectrum, where the introduction of multi-source generics, as well as genetics, diet and other variables may influence the effectiveness and risks of ARVs.



Mary Couper, WHO; Ms Precious Matsoso, Cluster Manager and MCC Registrar, South Africa; Dr Linda Morfeldt, Karolinska University Hospital, Stockholm, Sweden; Dr Jens Lundgren, Copenhagen HIV Programme, Denmark

Host country

South Africa was chosen for the training course because of the high percentage of the nation's infected population and because considerable progress has been made in developing safety monitoring activities in the country.

During the course, participants attended the opening of the MEDUNSA² Pharmacovigilance Centre by the Minister of Health, The Hon Dr M E Tshabalala-Msimang. This brand-new facility will complement the existing ADR monitoring centre at Cape Town University and will give priority to monitoring of ARVs.



Ralph Edwards speaking to the group in Pretoria

A tough curriculum

The participants faced a packed, ten-day programme which covered the following major topics, amongst much else:

- Theory and practice of pharmacovigilance
- Establishing and running a pharmacovigilance centre
- The WHO 3 by 5 strategy³
- Risk evaluation and causality assessment
- Current knowledge about ARV therapy, toxicity, side-effects and prognosis
- Reporting, data collection and research methods
- Communications issues, including training skills, media relations and crisis management
- Development of an action plan for each country
- Plans for future networking and collaboration



Opening of the MEDUNSA Pharmacovigilance Centre. Ms Precious Matsoso, Cluster Manager and MCC Registrar, South Africa; The Hon Dr Tshabala-Msimang, Minister of Health, South Africa; Prof M F Ramashala, Vice-Chancellor and Principal of MEDUNSA, Director General, Department of Health, South Africa; Dr Henry Fomundam, Acting Director, MEDUNSA Pharmacovigilance Centre

Mary Couper, from the WHO Quality and Safety of Medicines team, who organised the course on behalf of the Essential Drugs and Medicines Policy division, commented on the quality of the participants and their work:

"As ever with limited time, the programme was very ambitious in terms of its scope and depth. However, any anxieties we may have had were swept away by the energy of the group and its evident hunger for knowledge. Particularly impressive was the way that the participants who were already experienced in drug safety issues took the opportunity to push the boundaries of their knowledge forward, and contributed generously to the group's learning."

The challenge of effective therapy

A major issue which became dramatically clear was the degree of attention that patients on ARVs need if they are to enjoy optimal benefits and quality of life. Adherence and tolerance of side-effects were two of the big issues in patient management.

No-one was left in any doubt that only meticulous management of patients and recording of every aspect of therapy and response, including side effects, would provide the best hope for the welfare of individuals and for the accumulation of knowledge that would lead to improved therapy in the future: access to ARVs was only a part of the story.



Ralph Edwards, Director, the UMC; Ms Precious Matsoso; Sten Olsson, Head, External Affairs, the UMC, at the MEDUNSA opening

The Future

Among participating countries, South Africa and Tanzania already have pharmacovigilance systems in place, while Mozambique and Zambia are in the early stages of development; Nigeria's was launched on 9 September, just as the course finished. Plans were made for following up countries' progress after the course, and for future collaboration. It was the hope of all that the importance of post-marketing surveillance of ARVs would become unconditionally accepted by the authorities, and that adequate, harmonised systems would soon be in place across the continent.

References

1. Financial contributions from the governments of Japan and Ireland and the European Commission made it possible to organise this workshop
2. Medical University of South Africa
3. The global objective of having three million patients in developing and middle income countries under ARV treatment by the year 2005



'3 by 5' is the WHO Programme to get three million people living with HIV/AIDS in developing and middle income countries on antiretroviral treatment by 2005. It is a step towards the goal of providing universal access to treatment for all who need it as a human right.

Zambia declares national emergency 15 September 2004

Zambia has declared HIV/AIDS a national emergency to drive HIV/AIDS treatment and prevention scale-up efforts and to start producing generic AIDS drugs locally. The emergency will be in force from August 2004 to July 2009 and local drugs manufacturers will be allowed to produce more affordable life-prolonging antiretroviral drugs for people living with HIV/AIDS in the country.

According to the latest UNAIDS/WHO estimates, up to 1.1 million people are currently living with HIV/AIDS in Zambia and 140,000 of these are in urgent need of antiretroviral therapy. In order to address this need, in the context of the global movement to increase access to antiretroviral treatment and the 3 by 5 target, the Zambian government has set a target to treat 100,000 people by the end of 2005.

YELLOW CARDS & GREEN FORMS

Dr Bill Inman, retired Professor of Pharmacoepidemiology, University of Southampton, UK, pioneered the system of spontaneous reporting of adverse drug reactions ('yellow card') and of prescription event monitoring.

To have developed the major form of ADR reporting might be considered a big enough achievement; to have also developed the largest prescription event monitoring programme is even more remarkable. The fact that Bill Inman did all this – and more – after having contracted polio at the age of 21 is amazing; Bill spent his clinical medical training and entire professional life in a wheelchair. His services to medicine and public health, in the face of disability and struggles with bureaucracy make a remarkable story.

Studies; getting into drug safety

Bill Inman graduated in medicine from Cambridge University in 1956, before the official founding of the University Medical School. After three years in hospital clinical medicine he worked as a medical adviser to ICI Pharmaceutical Division, then joined the UK Department of Health and Social Security in 1964. Following the thalidomide tragedy, Bill was invited by the Founder Chairman of the independent Committee on Safety of Drugs, Sir Derrick Dunlop to develop the spontaneous ADR reporting system that later became known internationally as the 'yellow card' system, and which was subsequently absorbed into the DHSS's licensing system. (The colour yellow was chosen for ADR reporting because during the war the colour had been used for warnings that could be picked out by hooded car lights driving in the 'blackout'.)

From 1965 to 1967 Bill Inman designed and directed studies on the role of oral contraceptives in thromboembolic disease. This led to his discovery of the relationship between oestrogen dose and risk of thrombosis – and the development of the 'mini-pill'. He was also involved in vital work on sudden asthma deaths, halothane and jaundice, and phenylbutazone and blood dyscrasias. After 1975 he drafted proposals for what he then termed 'Recorded Release', which eventually evolved into the post-marketing system used by the Drug Safety Research Unit (DSRU), which he founded independently in 1980, as the health department would not support the scheme.

International WHO meetings

As a consultant to the WHO from 1966 to 1980, Bill Inman attended many formative meetings including important ones in 1966 and 1968 at Alexandria, Virginia, USA. There, 12 experts from 10 countries, with little knowledge of computers (computers were then a rare, rigid and difficult to use novelty that most people knew little about), planned practically from scratch the ADR terminology and Drug Reference List. The basis for the WHO Adverse Reaction Terminology (WHO-ART) was created by Barbro Westerholm (Sweden), Bruce Royal (Australia / WHO Geneva) and Bill Inman. The pilot phase of the drug monitoring programme was positively evaluated by the World Health Assembly and became an on-going WHO Programme, based until 1978 in Geneva.

Event v Reaction

In 1977, in the aftermath of the Eraldin and Practolol scares, a conference was convened in Honolulu, presided over by Franz Gross of the University of Heidelberg. This significant meeting (proceedings of which were published) examined the shortcomings of spontaneous reporting systems – and the need for ADR data which includes a

numerator and denominator. This led Bill Inman to found the DSRU – an independent research institute funded by no-strings donations (particularly from the USA) and with links to the local university. The format of reporting for general practitioners was and is known as 'green forms'. At DSRU no member of staff was allowed to have a personal retainer or remuneration from a pharmaceutical company.



Bill Inman in his Skylark III around 1960

Next steps in pharmacovigilance

The fact that in the past forty years new therapies have mainly been developed and initiated by big companies and not by independent scientists has constituted a major change for the medical profession. Bill believes that there are currently too many drugs on the market. There is also the huge influence of industry on medical education in most countries. Within industry he perceived the tensions between the sales personnel and the medical staff.

Risk perception

Bill Inman contributed to a major initiative on risk management by Wolfson College Oxford in 1984. At an eight-speaker symposium, he outlined the problems of communicating risk perception, and demonstrated the vast differences in the views of medical personnel of risk in their own fields. (He notes with amused horror that in the 1980s, despite the high risks associated with smoking and low risks for use of oral contraceptives, official advice was given for smokers not to use the pill!) In his Wolfson lecture, he illustrated the comparative annual risk of doing something or being somebody. "A United States President had a one in forty-five record of assassination, about the same as matadors whose annual risk was one in fifty-nine, per year. Only these two were at greater risk than a person who smokes twenty or more cigarettes each day, whose annual risk of smoking-related death was one in two hundred..." By contrast, drug withdrawals after a single drug-related death of one in two million have occurred. In the last few years, we may have become better at calculating risk in medicine, but still struggle to communicate it successfully.

How should countries set up a monitoring system?

For countries setting up a pharmacovigilance system, Bill Inman has simple advice: "A system for spontaneous reporting should be tailored to the needs of the country and population (eg drugs against protozoal diseases such as malaria or amoebic dysentery). Use WHO distributed signals to stimulate research, or perhaps conduct a PEM study. Events must be recorded irrespective of cause. Use field-workers – possibly volunteers ('bare-foot doctors') for follow-up of reports." He also stresses his four points in chapter 12 of 'Don't Tell the Patient':

1. the need for independence (no contracts or interference)
2. the need for transparency (everything must be published)
3. consideration of relative efficacy as well as relative safety (relative efficacy is as important as safety) – all data from all patient records, but confidential
4. patients in prospective studies must be fully informed (and involved) volunteers.

Looking forward

Bill Inman has been away from direct contact with drug monitoring for ten years. However, as well as his four key points mentioned above, he still holds strong views such as the complete separation of monitoring from both Government and industry, and that medical evaluation be separate from the national licensing authority. Government interests in drug safety can sometimes lead to ridiculous situations, as in the 1960s, when the ministers in the upper and lower houses of the British parliament each gave completely divergent explanations about the potential problems with the pill, on the same day!

There is also a need for independent, anonymous discussions in a safe environment to find ways to tackle medical error.

Highs and lows

Bill's biggest disappointment is that (with a couple of exceptions) there are no national systems in place which might prevent another thalidomide tragedy – a database of pregnant women's drug histories is critical. The lack of medium-term and long-term (25 years) follow-up for cancer treatments is another concern – the WHO should be more active in this, he feels.

His greatest achievement? Discovering the link between the pill and death from thromboembolism – working with Vessey, Westerholm, and Engelund. The MRC asthma study (Adelstein and Inman) was another highpoint. And he was the first doctor to qualify from Cambridge University! He had "the good sense to marry the right girl" – June. They have three daughters and eight grandchildren.



Bill Inman's last flight, 1994

On the impact of ADR monitoring? "Not enough!" "Key signals from WHO could be regularly resumed in BMJ and JAMA – or via internet and responsible journalists. Although caution is needed, unusual reactions should be published as soon as possible."

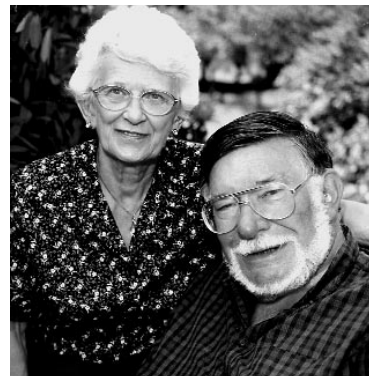
Another Bill Inman

There are more sides to Bill Inman. He won awards for gliding (after the onset of polio). When the Inmans lived at Hever in Kent he much enjoyed trout fishing, especially at Bewl Bridge (followed by a beer at the Henry

VIII pub). In his day, he was also a good shot and bagged many a pigeon. His musical prowess is more limited, although he claims to have filled pubs in Austria with his playing of the musical saw. Once a keen gardener, he still does what he can, including what he calls 'genetic experiments'; he recently "accidentally bonsaied a lettuce"! His children and grandchildren are close to him although none has ventured into medicine or medical science – quite the contrary. A man of great humour and positive outlook, he has completed his autobiography which he hopes to have published soon.

Bill Inman is a pioneer: one of the most eminent and principled of those who have worked in the field of drug safety. He achieved many things despite lack of funding, and lack of support from central bureaucracies. He realised working drug monitoring systems against opposition from all manner of interests.

At 75, Bill Inman can reflect on a life packed with achievements of the highest order in medicine and public health, which have had impact for every person in the United Kingdom, and for many all over the world. He has received no civilian state honour in the UK, but deserves the admiration and thanks of all who are aware of his work.



With June on his 70th birthday

For a full account of Bill Inman's work, his book 'Don't Tell the Patient – Behind the Drug Safety Net' or his forthcoming autobiography (yet to be published), make informative and often entertaining reading.

Selected references

1. Inman WHW. *Don't Tell the Patient – Behind the Drug Safety Net*. Highland Park Publications 1999. ISBN 0-9675812-0-6.
2. Inman WHW. The reporting of adverse reactions to drugs. Proceedings of the European Society for the Study of Drug Toxicity, 1966, 7:191. (Excerpta Medica International Congress. Series No 115.)
3. Medical Research Council. Risk of Thromboembolic Disease in women taking oral contraceptives. *BMJ*, 1967, 2:355.
4. Inman WHW, Vessey MP. Investigation of deaths from pulmonary coronary and cerebral thrombosis and embolism in women of child-bearing age. *BMJ*, 1968, 2:193.
5. Inman WHW, Adelstein AM. The rise and fall of asthma mortality in England and Wales in relation to the use of pressurised aerosols. *Lancet*, 1969, 2:279.
6. Inman WHW, Vessey MP, Westerholm B, Engelund A. Thromboembolic disease and the steroidal content of oral contraceptives. *BMJ*, 1970, 2:203.
7. Inman WHW, Mushin WW. Jaundice after halothane. *BMJ*, 1974, 1:220-221.
8. Gross FH, Inman WHW eds. *Drug Monitoring: Proceedings of an International Workshop in Honolulu*. London, New York, Academic Press, 1977.
9. Inman WHW. *Monitoring for drug safety*. Lancaster, MTP Press Ltd, 1980.
10. Inman WHW. Assessment of drug safety problems. In: Gent M and Shigematsu I, eds. *Epidemiological issues in reported drug-induced illnesses*. SMON and other examples, 17. Hamilton, Ontario, McMaster University Library Press.
11. Inman WHW. Prescription-Event Monitoring – A preliminary study of benoxaprofen and fenbrufen. In: *Symposium Drug Utilisation – Implications for Medical Care*; 7-10 June 1982, Stockholm. Acta Med Scand Supplement. 683, 119-126.
12. Inman WHW. Risks in medical intervention. In: Cooper MG, ed. *Risk: Man-made Hazards to Man* (Wolfson College Lecture January 1984). Oxford, Oxford University Press, 1985:35-53.
13. Inman WHW. Blood disorders and suicide in patients taking mianserin or amitriptyline. *Lancet*, 1988, July 9th.
14. Inman WHW, Pearce G. Prescriber profile and post-marketing surveillance. *Lancet*, 1993, 342:658-661
15. Inman WHW and others. PEM Reports 1-10. *Pharmacoepidemiology and Drug Safety* 2:4/5. 259-521 (1. Nicardipine, 2. Terodiline, 3. Fluconazole, 4. Ciprofloxacin, 5. Fluoxetine, 6. Paroxetine, 7. Itraconazole, 8. Cisapride, 9. Omeprazole, 10. Zopiclone.)

Pharmacovigilance discussions at ICDRA

Plenary 4 of the 11th International Conference of Drug Regulatory Authorities (ICDRA) in Madrid, Spain consisted of discussions on the approach of ICDRA to pharmacovigilance. We reproduce the main points here:

Pharmacovigilance Practices

Spontaneous reporting is the mechanism used for compiling adverse drug reaction reports and regulatory authorities take important decisions based on these data.

Pharmacovigilance is a broad concept, and also includes the re-evaluation of marketed drugs, risk management, communicating drug information, promoting rational drug use and crisis preparedness. It is becoming increasingly important to provide training in all of these activity areas and to carry out intensive monitoring of new drugs in order to evaluate the risk/benefit. Increasingly, medicines are being donated for off-label indications for specific public health needs and it is important that sufficient data is available to the national regulatory authority on safety, efficacy and quality.

Recommendations

- Member States should be encouraged to involve pharmacovigilance staff in public health risk assessment, management and communication for medicines safety activities including adverse reactions monitoring, medicines re-evaluation, drug information, rational drug use, lack of efficacy and crises preparedness.
- Increasingly, certain medicines are approved based on special conditions, such as finalization and reporting of Phase IV studies. National regulatory authorities should collaborate on harmonizing the terms of conditional approval, and develop systems to allow sharing of information on medicines in this category.
- All sponsors and donors of medicines should provide sufficient data to allow the national drug regulatory authority to be assured that the product being donated, or recommended for use, meets appropriate standards of safety, quality and efficacy. Obligations to conduct post-marketing surveillance as a public health protection measure should also lie with sponsors and donors, as appropriate. International agencies and aid programmes should make every effort to comply with these requirements and provide the necessary data.
- Members States should be encouraged to establish databases of clinical information suitable for epidemiological studies to examine and quantify signals of possible emerging risk. WHO should co-ordinate and develop training resources in pharmacovigilance and pharmacoepidemiology and expand its commitment to include training programmes in each of its

regions. WHO should provide, upon request, technical advice and support to Member States on the appropriateness of post-marketing surveillance plans submitted by sponsors when a medicine is being introduced to manage a specific public health campaign in that country.

- WHO should investigate the feasibility and potential utility of creating a database of 'recommendations for action' arising from evaluations made by national regulatory authorities of the periodic safety update reports (PSURs) in order to improve the usefulness of such information by making this generally available.
- ICDRA participants noted that strong international collaboration among regulatory authorities is needed to safeguard public health interests. Also stressed was the importance of government commitment to strengthening national regulatory systems and intensify international collaboration to improve access to safe and effective medicines of good quality.

The World Alliance for Patient Safety

The first Alliance Day for the WHO World Alliance for Patient Safety took place on 18th September in Shanghai, China, and was attended by Ralph Edwards, Director of *the UMC*. The Alliance will be formally launched on 27 October in Washington, led by the Director General WHO, Dr Lee Jong-Woo. *the UMC* has been a party to this development from the beginning, cooperating with the clusters Health Systems Policy and Operations and Quality and Safety of Medicines at WHO.

In November 2003, WHO collaborated with the United Kingdom to convene a meeting of senior policy-makers and international experts from all WHO regions to discuss future international collaboration on patient safety. An international alliance was proposed by Sir Liam Donaldson, UK's Chief Medical Officer, and now chairperson of the Alliance.

The proposal was unanimously supported and the meeting agreed that a number of working groups and activities should be established to consider the potential functions that the International Alliance for Patient Safety could deliver.

What will the Alliance do?

Six main arms have been identified for early attention and progress in some areas has already occurred in two working groups:

Reporting and Learning working group

- WHO is working with Professor Lucian Leape and others including *the UMC*, on draft guidelines for reporting and learning systems. An international consultation has followed, and will soon be finished. As part of this work an international survey on existing reporting systems is being conducted.
- The working group will focus on global reporting; this will mean the international sharing and pooling of data on specific issues not the creation of an international reporting system.
- The project will also consider the following issues:
 - ◆ the importance of a shared taxonomy
 - ◆ the capacity of countries, agencies, etc., to pool/share data
 - ◆ priorities – using global reporting only when it can add real value
 - ◆ centre of excellence approach – different centres taking the lead depending on the issues to be addressed
 - ◆ the existing international expertise in global reporting.

- It will also focus on:
 - ◆ International survey on reporting systems – feedback from Professor Lucian Leape
- Global reporting and data mining, in which *the UMC* is taking the major initiative.

Solutions working group

- The working group will conduct a scoping exercise in order to discuss activities that are taking place at country or agency level in relation to solution development. The National Patients Safety Agency in the UK, which is also Solutions working with *the UMC*, has agreed to undertake this on behalf of the group.
- The working group will focus on:
 - ◆ methodologies for solution development
 - ◆ sharing of solutions between countries and the adaptation of solutions to meet the needs of different health care economies
 - ◆ collaboration between countries in the development of new solutions.



Session at the Shanghai meeting

Impact on pharmacovigilance

The 'Reporting and Learning' is the area which will have most impact on pharmacovigilance. We know already that many adverse reactions are regarded as avoidable, and these will form a part of the work of the Alliance, though it is clear that taxonomy and solutions are also very close to the cause of drug safety. There are several more important strands to the work of the Alliance which is developing rapidly, such as 'Consumers for Patient Safety'.

Sir Liam has repeatedly shared with audiences the following thought "To err is human; to cover up is unforgivable; and to fail to learn is inexcusable."



Dr Shigeru Omi, Regional Director, WHO



Sir Liam Donaldson, Chairperson of the WHO World Alliance for Patient Safety. Director, WHO

For more information visit:
<http://www.who.int/patientsafety/news/establishment/en/>
and
<http://www.who.int/patientsafety/en/>

Patient safety perceptions

Perceptions of risk and safety Therapeutic Guidelines Limited have just published a 55-page paperback 'Health care and notions of risk' by an Australian medical scientist, Richard B Clark. It is based on his PhD thesis supported by the Commonwealth Department of Health and Ageing. Starting with a literature review 'understanding medical adverse events', it then recounts an Australian study of perceptions of patient safety, followed by a discussion of the implications for health professionals.

Please visit www.tg.com.au/home/hcanorf.html for further information.

Pharmacovigilance dictionary

Dictionary of Pharmacovigilance by Amer Alghabban, published by the Pharmaceutical Press (3,100 entries over 520 pages hardback) is "a new compilation which contains a comprehensive list of abbreviations, terms and phrases, giving definitions of commonly (and rarely) encountered pharmacovigilance terms. The author suggests that the book is "essential reference for a wide-ranging professional readership".

Herbal ATC guides

the UMC has just published two new guides on herbals: Guidelines for Herbal ATC Classification and Herbal ATC Index. To enable herbal drug utilisation research and safety monitoring, the existing systems for capture, storage and analysis of data need to be adapted to accommodate relevant information on herbal products; and the safety issues associated with the use of herbal products, and their public health impact, have to be evaluated and communicated.

Although the therapeutic value of many herbals may be well recognized, herbal medicinal products, are generally not part of the same regulatory framework as conventional medicinal products, and have not gone through the same rigorous scientific testing. With the growing awareness that herbal products may also cause harm, there is also a need for effective risk management strategies to cover herbal products.

The Herbal ATC system

The Herbal ATC system (HATC) provides a unique scientific framework for a harmonised, global nomenclature and therapeutic classification of herbal substances and combinations of them.

The Herbal ATC Guidelines contain a detailed description of classification principles and the nomenclature used, followed by a list of assigned HATC codes. The Herbal ATC Index lists all HATC codes for the preferred botanical names reported to the WHO ADR database. The Guidelines should be used as a terminology and a source of reference to the WHO Herbal ATC system. It is our hope that the benefits of using accepted botanical names will be recognised worldwide.

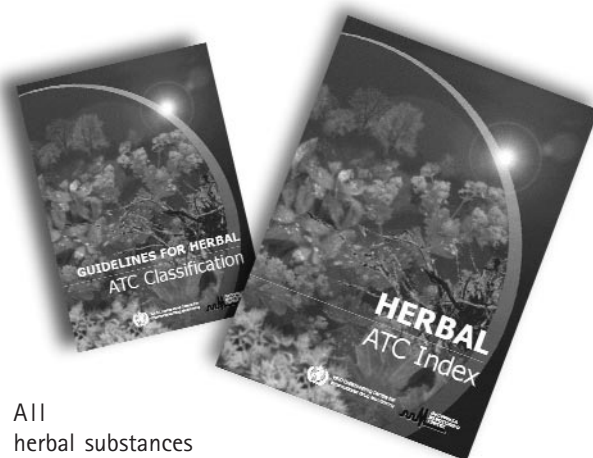
Implementation in your system

To take full advantage of the Herbal ATC system, it needs to be implemented as an integral part of existing information systems. When linked to a computerised medicinal product register or database, the hierarchical HATC structure supports both the broader overview, and in-depth analysis, by allowing grouping and aggregation of data at different level of specificity. Consistency of the quality of data is of utmost importance. This is achieved if herbal products are assigned HATC codes according to these guidelines. For single ingredient products, the assignment is straightforward so long as the correct botanical name of a particular substance is known.

Products containing several herbal ingredients present one difficulty, in that the link to the Herbal ATC may be tenuous in varying degrees. This is managed within the WHO Drug Dictionary (WHO-DD) and the WHO Adverse Drug Reaction database, by making links in a hierarchical way according to the precision of the

information available. Herbal ATC supporting international pharmacovigilance

By investigating groups of herbal drugs with similar therapeutic, pharmacological and chemical properties it is possible to find out if the adverse drug reaction is caused by a specific herbal product or if it is a group effect.



All herbal substances that are ingredients of recorded medicinal products in the WHO-DD have been assigned HATC codes. In addition, all new medicinal products entered into the system are assigned HATC codes on the product level. As a result of this work, all reports of safety problems involving herbal products can easily be retrieved and grouped using the pre-assigned HATC codes.

Since there is an extensive use of synonyms to herbal substance names, both other botanical names in Latin and vernacular (common) names, *the UMC* has produced a checklist linking all synonyms to the accepted botanical names entered in the WHO-DD. This checklist will be published in early 2005. The complete WHO Drug Dictionary is also available from *the UMC* in a computerised format.

It should be stressed that assignment of an HATC number to a herbal remedy is not an indication that the remedy has been proven effective and safe. Assignment of an HATC number indicates only that information about medical use has been found in the literature.

To obtain a copy of these contact UMC Products and Services, details on page 18. There is a discount for academic and non profit-making organisations.

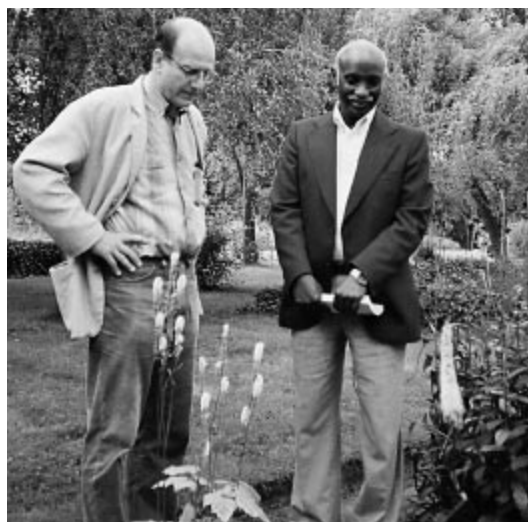
For general enquiries about herbals work at *the UMC*, please contact Mohamed Farah or Jenny Ericsson.

UMC Herbals team in Poland

Jenny Ericsson and Mohamed Farah recently attended the XV international Congress of the Polish Pharmacological Society in Poznan. They spoke on 'Herbal classification, interaction between herbal and conventional medicines'.

Varied programme

Under 'Interactions between herbal and synthetic drugs - advantages and risks', the meeting also heard presentations on 'Activity of international scientific network: Interactions between herbal and synthetic drugs - advantages and risks' by P.M. Mrozikiewicz - Director of the Research Institute of Medicinal Plants, Poznan and 'Drug-drug interactions: role in treatment', by J. Splawinski of the National Institute of Public Health, Warsaw.



Admiring the specimens at the Research Institute Gardens

Other presentations included: 'Information on interaction between herbal medicines and other medicinal products in Europe' (W. Dymowski, Office for registration of Medicinal Products, Medicinal Devices and Biocidal Products, Warsaw), 'Interaction between inhaled herbal medicines and synthetic drugs' (B. Kedzia, Research Institute of Medicinal Plants, Poznan), 'Risk assessment in the interactions between nutrition and drugs - study on selected group of patients' (K. Wolnicka - National Food and Nutrition Institute, Warsaw) and 'Interactions between St. John's wort and synthetic drugs' (M. Ozarowski - Research Institute of Medicinal Plants, Poznan).

Tour of Poznan Research Institute

Mohamed and Jenny also made a fact-finding trip to the Research Institute of Medicinal Plants in Poznan, their botanical garden, fields for cultivation and labs, where they were privileged to discuss issues of mutual interest with the friendly and knowledgeable staff.

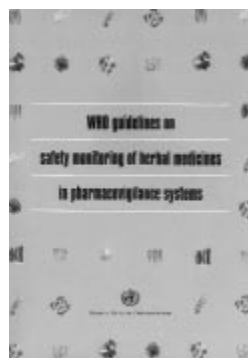


Mohamed Farah and staff from the Research Institute of Medicinal Plants in Poznan in their botanical garden

WHO Guidelines on safety monitoring of herbal medicines

Guidelines for safety monitoring of herbal medicines in pharmacovigilance systems were released by WHO in October 2004. They have come about through a collaboration between the Traditional Medicines team (TRM), the Quality and Safety: Medicines team (QSM) of WHO headquarters and the Uppsala Monitoring Centre. The text has been subjected to a series of international consultations, the concluding one in Vancouver, Canada, in February 2004.

The 70-page document covers general aspects of pharmacovigilance and also the specific considerations required when documenting and reporting unwanted medical events suspected to be associated with herbal products. The guidelines advocate monitoring of herbals to be integrated with the general pharmacovigilance activities in a country. Around the world there is a massive underreporting of suspected adverse reactions associated with herbal medicines. It is hoped that the new guidelines will contribute to a greater understanding of the need for better reporting overall and for the specific need of proper identification of the suspected plant, including the plant part and/or extract.



New Herbals Signal Reviewers

Dr Joanne Barnes is Lecturer in Phytopharmacy in the Centre for Pharmacognosy and Phytotherapy, at the School of Pharmacy, University of London. She was Research Fellow in Complementary Medicines at the University of Exeter, UK from 1996 to 1999, and has worked as a hospital clinical pharmacist, medicines information pharmacist in the pharmaceutical industry and in pharmaceutical publishing.

Her research interests include utilisation and pharmacovigilance of herbal medicines, including traditional Chinese medicines; the quality, efficacy and safety of herbal medicinal products; the pharmacist's role in effective use of herbal and complementary medicines; consumer and practitioner perspectives towards herbal and complementary medicines.

Tamás L Paál graduated in pharmacy, completed postgraduate studies in drug control and chemical engineering, then received his PhD in Budapest.

After 11 years working for the Hungarian pharma industry he joined the National Institute of Pharmacy, the Hungarian medicines regulatory agency. He was Director-General between 1984 and 2001 and again from 2002. He became a university professor in 1984. At present, he lectures at the Institute of Pharmacy Administration, Semmelweis University, Budapest and is Director of the Department of Drug Regulatory Affairs at the University of Szeged, Hungary.

Tamás Paál is, among others, a member of TOPRA, DIA and EFGCP as well as a holder of awards of RAPS, DIA and TOPRA. He has published more than 160 papers on medicine evaluation, analysis as well as on the Good Practices.

Recent publications from the Uppsala Monitoring Centre:

Articles:

Ståhl M, Lindquist M, Edwards IR and Brown EG. Introducing triage logic as a new strategy for the detection of signals in the WHO Drug Monitoring Database. *Pharmacoepidemiology and Drug Safety*, 2004, 13:355-363.

van Grootheest K, Olsson S, Couper M and de Jong-van den Berg L. Pharmacists' role in reporting adverse drug reactions in an international perspective. *Pharmacoepidemiology and Drug Safety*, 2004, 13:457-464.

Lindquist M. Data quality management in pharmacovigilance. *Drug Safety*, 2004, 27(12):857-870.

Book Review:

Edwards IR. Medicines out of control? - Antidepressants and the conspiracy of goodwill (C Medawar and A Hardon). *International Journal of Risk & Safety in Medicine*, 2004, 16:147-148.

Comment:

Edwards IR. Intuition, evidence and safety. *Lancet*, 2004, 364: 387

Signal meeting in Barcelona

Marie Lindquist participated in a course on 'Signal Identification in Pharmacovigilance' in Barcelona, Spain in July. She gave a presentation outlining the historic evolution of signal generation with special emphasis on the part played by the WHO Collaborating Centre for International Drug Monitoring in Uppsala.

The meeting was organised by Fundació ESAME (Escuela del Medicamento), and also included Ignacio Ayani (Head of Pharmacovigilance, Pfizer), Consuelo Pedrós from the pharmacovigilance centre for Catalunya, Emilio Sanz (Dep. Pharmacology, Laguna Univ., Tenerife and member of *the UMC* expert review panel), Javier Cid (Senior epidemiologist, Novartis), Mariano Madurga from the Spanish National Centre and Susana Pérez-Gutthann (President of ISPE).

ISPE in Bordeaux

A team from *the UMC* participated in the ISPE meeting in Bordeaux last August. Andrew Bate presented a poster on 'Pattern Recognition of celecoxib and rofecoxib in the WHO database'. Among highlights of the meeting were the session on 'SSRIs for Depression in Children: Efficacy, Safety and Policy Issues', where Lolkje van den Berg gave a wide-ranging overview of antidepressant use in US, Germany and Netherlands. David Healy from McGill, Canada talked about meta-analyses of randomized controlled trials (RCTs) and the final speaker was an American clinician, Adelaide Robb who described the criteria used for diagnosing a depression and referred to a study in JAMA which found that therapy alone was no more effective than placebo.

A small ISoP session: 'Breaking out of the Bubble: What have we learned about risk Communication?'



Andrew Bate talking to delegates in front of his poster at ISPE

presented views from Carmen Kreft, France - the authority view and Kasia Petchel, Head of Pfizer Safety Surveillance, New York, who gave an industry perspective using Viagra as an example of how difficult it had been for Pfizer to cope with excessive, negative, media attention. Frederic Bourdé, from the King's Centre for Risk Management gave a stimulating and enjoyable presentation on risk communication and risk perception 'How is the pharmaceuticals area seen by the media?'. He contended that industry is distrusted, pricing is questioned, the focus is on 'luxury' drugs, high profile recalls and litigation. He also emphasized that risk communication is not a new technique to 'educate' laymen, a substitute to the media, a marketing device or a PR exercise. He gave a useful checklist of risk perception drivers in pharmaceuticals, and discussed communication strategies which should be developed.

CPT in Brisbane

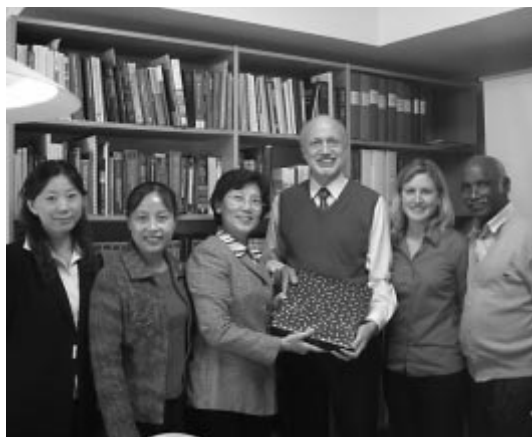
In August, Anne Kiuru from *the UMC* spoke at the Pharmacovigilance workshop at the 8th World Congress on Clinical Pharmacology & Therapeutics in Brisbane, Australia. Her topic was 'Data mining in the international WHO ADR database', which included a summary of *the UMC* signal detection process as well as a brief introduction on how to deal with the complexities of the database by using pattern recognition.

the UMC also displayed a poster at this meeting 'Bisphosphonates and ocular side effects' which was a WHO signal last year, and a collaboration between *the UMC* and one of our reviewers, Dr Rick Fraunfelder, an ophthalmologist of the Casey Eye Institute in USA.

A full report on the ISoP conference will follow in the next edition of Uppsala Reports.

Chinese National Pharmacovigilance staff in Europe

In the last week of September a delegation from the National Centre for ADR Monitoring in Beijing, PR China, visited Europe. Members of the delegation were Professor Li-ya Cao, Deputy Director, Ms Tian Chunhua, Programme Leader of National Centre for ADR Monitoring and Mr Huang Guo, Associate Director at the General Office, State Food and Drug Administration. The National Centre for ADR Monitoring belongs to the Centre for Drug Re-evaluation of the State Food and Drug Administration from China. The delegation spent a day at *the UMC* and then proceeded to the Spanish national centre in Madrid.



*from left:
Miss Xu Hongfei, Miss Tian Chunhua, Professor Li-ya
Cao, Sten Olsson, Annica Lundström and
Mohamed Farah*

The visit was of great significance for *the UMC* since the WHO database currently holds only a fraction of all Chinese ADR reports. The pharmacovigilance infrastructure in China has developed rapidly and currently all 31 provinces of the country have pharmacovigilance centres. Reporting to the national centre is carried out using an internet based system. As a consequence the rate of reporting has doubled every year for the last 3 years with a new record of 37,000 case reports being received in 2003. The trend is expected to continue.

For *the UMC* it is a top priority to solve the technical challenges involved in translating and transferring data from the national database to the WHO one. If the issues can be resolved China may become the biggest provider of ADR data to the WHO database within a few years. A part of the challenge is to include Chinese names of medicinal products, including herbals, in the WHO Drug Dictionary.

Chinese visit to Spanish Centre

On October 1st, (following on from their time in Sweden) the delegation from the National Centre for ADR Monitoring visited the Unit of Pharmacoepidemiology and Pharmacovigilance of the Spanish Agency of Medicines and Medical Devices (SAMMD).



*Miss Tian Chunhua, Professor Li-ya Cao, Mariano
Madurga at the Spanish National Centre in Madrid*

The delegation of Huang Guo, Li-ya Cao, and Tian Chunhua, were assisted by Xu Hongfei, a helpful translator. During the visit, Dolores Montero and Mariano Madurga explained the structure and functions of the Unit and of the Spanish Pharmacovigilance System. The latter is – as with the system in China – a decentralised system of 17 centres within the Regional Health Departments, co-ordinated by the Unit of Pharmacoepidemiology and Pharmacovigilance of the SAMMD.

Later this year, the Spanish pharmacovigilance system will celebrate its 20th Anniversary, in a symposium to be held in Barcelona, 12-13 November.



Buying UMC services online

the UMC's Products and Services website is not only up and running, but it is now possible to make the majority of orders via the webshop. As well as placing your order in the webshop, you can also calculate the cost and, where appropriate, generate a standard licence agreement. The website contains detailed guidance and downloads about WHO Drug Dictionary and other services.

In addition, we have started to develop user group areas so that customers will always have easy access to the information they need, on our website.



www.unc-products.com

Do explore www.unc-products.com, your partner in clinical trials or drug safety operations. Do also let us have any comments about the site and how it might best serve your and your organisation's needs!

Meet us there!

UMC staff are planning to attend the following conferences in the coming months:

- 14th Annual European Clinical Data Management Conference Amsterdam, 8-10th of November
- 1st DIA Multi-Track Meeting on Clinical Trials & Pharmacovigilance Paris, 29-30th of November

We look forward to seeing many of you at there; if you wish to arrange a meeting with us, please contact Mats Persson, e-mail mats.persson@unc-products.com.

Updates – 3rd Quarter 2004

The new versions of the computerised WHO Drug Dictionary (WHO-DD) and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 3rd quarter of 2004 are now available. These were sent to subscribers during October/November 2004. The WHO-DD pack contained the updated version of WHO-DD along with a wealth of background material.

Need help?

If you have any queries about the content of this package, or any detail of the DD itself, or need further information about your current subscription or how to upgrade it, do call the UMC Products & Services.

You can e-mail:

drugdictionary@unc-products.com for comments about the DD, corrections, additions, and

katarina.hansson@unc-products.com for queries about your subscription.

If you are a subscriber to either WHO DD or WHO-ART and have not yet received the update, please contact Katarina Hansson.

Data files for the 4th quarter of 2004 should be available during February 2005.

Have you moved?

If there is a mistake in our database, or you have changed your address, do please let us know as soon as possible. Please either log on to our web site www.unc-products.com to correct your address, or e-mail your correct address to us. We will then be able to update our address lists.

Thank you!

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
20-23 October 2004	Risk Management in Pharmacotherapy (33rd European Symposium on Clinical Pharmacy)	Prague, Czech Republic	ESCP Tel: +32 2 743 1540 Fax : +32 2 743 1584 E-mail : geraldine@associationhq.com www.escpweb.org
8-19 November 2004	UMC pharmacovigilance training course	Canberra, Australia	the UMC Tel: +46 18 65 60 60 E-mail : info@who-umc.org www.who-umc.org
8-10 November 2004	Three Worlds – One Voice (14th Annual European Clinical Data Management Conference)	Amsterdam, Netherlands	DIA Tel: +41 61 225 5151 E-mail: diaeurope@diaeurope.org www.diahome.org
9 November 2004	Pharmacovigilance Aspects of Licensing Agreements	London, UK	Management Forum Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 E-mail: info@management-forum.co.uk www.management-forum.co.uk
11-12 November 2004	Case Narrative Writing for Reporting Adverse Events	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
12-13 November 2004	V Jornadas de Farmacovigilancia	Barcelona, Spain	Institut Catala Farmacologia Tel: +34-93 428 3029 Fax: +34-93 489 4109 E-mail: xp@icf.uab.es
23-24 November 2004	European Drug Safety	Budapest, Hungary	IBC Life Sciences Fax: +44 (0)20 7017 5656 www.abc-lifesci.com/courses
24 November 2004	Data Safety Monitoring Boards & Data Review Committees	London, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
29-30 November 2004	Hot Topics in Pharmacovigilance	Paris, France	DIA Tel: +41 61 225 5151 E-mail: diaeurope@diaeurope.org www.diahome.org
8-9 December 2004	Introduction to Pharmacoepidemiology	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
22-23 January 2005	IV Annual Conference of Society of Pharmacovigilance, India (SOPI)	Bareilly (UP), India	SOPI 2004 Tel: +91 581- 2523745/2527900 E-mail : kamalbareilly@yahoo.co.in
26-28 January 2005	Medical Aspects of Adverse Drug Reactions	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
10-11 February 2005	New Challenges in Clinical Safety, Pharmacovigilance and Vaccine vigilance	Barcelona, Spain	ISoP Administration Tel/Fax: +44 (0)20 8286 1888 www.isoponline.org
7-9 March 2005	DIA Euro meeting	Lisbon, Portugal	DIA Tel: +41 61 225 5151 E-mail: diaeurope@diaeurope.org www.diahome.org
23 May - 3 June 2005	The 10th international training course 'Pharmacovigilance - The Study of Adverse Drug Reactions'	Uppsala, Sweden	the UMC Tel: +46 18 65 60 60 E-mail : info@who-umc.org www.who-umc.org
21-24 August 2005	The 21st International Conference on Pharmacoepidemiology Et Therapeutic Risk Management ISPE	Nashville Tennessee, USA	International Society for Pharmacoepidemiology Tel: +1 (301) 718 6500 Fax: +1 (301) 656 0989 E-mail: ispe@paimgmt.com
17-19 October 2005	ISoP Annual Scientific Meeting	Manila, the Philippines	ISoP Administration Tel/Fax: +44 (0)20 8286 1888 www.isoponline.org



Petteri Aalto Team Support, Internal Affairs
Ali Bahceci Network Technician, Internal Affairs
Andrew Bate Manager, Research & Development
Cecilia Biriell Senior Specialist, Head of Internal Affairs
Anna Blomquist Drug Dictionary Services
Geoffrey Bowring External Affairs Co-ordinator
Bill Dagerus Systems Developer
Ralph Edwards Professor in Medicine, Director
Jonathan Edwards Programme Leader, Data-Mining Development
Hannah Ericson Sales and Marketing Assistant
Jenny Ericsson Programme Leader, Traditional Medicines
Mohamed Farah Senior Specialist, Traditional Medicines
Inger Forsell Sales & Customer Relations Executive
William Frempong Signal Detection & Analysis
Helena Fucik Senior Specialist, External Affairs
Katarina Hansson Sales and Marketing Assistant
Anne Kiuru Signal Detection & Analysis
Anneli Lennartsson Team Support, Internal Affairs
Marjatta Leván Manager, Internal Affairs
Stefan Lewenfalk Systems Developer
Marie Lindquist General Manager, Head of Data Management & Research
Anna Lindquist Web Editor, External Affairs
Annica Lundström Data Management
Lars Magnusson Director of Products and Services
Jessica Nilsson Programme Leader, Data Management
Malin Nord Programme Leader, Drug Dictionary Services
Niklas Norén Data-Mining Research Engineer
Sten Olsson Manager External Affairs & Traditional Medicines, Head of External Affairs
Bo Östling Senior Systems Developer
Mats Persson Manager, Business Development
Monica Plöen Manager, Signal Detection & Analysis
Sven Purbe Senior Specialist, Research & Development
Helena Sjöström Data Management
Malin Ståhl Research & Development
Kristina Star Signal Detection & Analysis
Johanna Strandell Signal Detection & Analysis
Erik Swahn Data-Mining Developer
Daniel von Sydow Project Co-ordinator
Erica Walette Programme Leader, Database Services
Magnus Wallberg Manager, Data Manager & Systems Development
Annika Wallström Product Manager



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

Telephone: +46 18 65 60 60

Fax: +46 18 65 60 80

E-mail:

(general enquiries) info@who-umc.org

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

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

Internet: www.who-umc.org

Uppsala Reports ISSN 1651-9779

the Uppsala Team

