

# Uppsala Reports 34

**UPPSALA REPORTS July 2006**

For everyone concerned with the issues of pharmacovigilance

**Combinations in depth**

**ISO and drug safety**

**Erice's emerging legacy**

**Forward to Liège**

**Drug Dictionary web course launched**



# DIRECTOR'S MESSAGE



Ralph Edwards  
Director  
the Uppsala Monitoring  
Centre

I was fixing an electrical failure on an old car's headlights (it's one way to fill in spare time). I traced the fault methodically, as one should, and found that a relay was badly corroded. I fixed that, and one headlight bulb lit; the other did not. I thought there might be another fault in the circuit; perhaps I had put the wiring back incorrectly. After spending a good deal of effort, I tested the unlit bulb as opposed to visually checking that it seemed fine. The bulb was burnt out.

It reminded me of a previous occasion when both accessory (fog) lights on a car stopped working. They had a circuit and fuse of their own, which I checked diligently. I could find no problems at all. In the end I found that both bulbs had failed at the same time. They were replaced and all is still well.

Lessons for drug safety? Yes, I think so.

The first is an example of finding an obvious solution to a problem which on testing proves not to be the whole truth. How often do we say that we have the answer to a drug safety problem? If there is 'obvious confounding' we often stop there, and do not consider the possibility of a much less obvious and smaller drug-related effect that might occur as well.

The second example is a classic: assuming that rare chance does not occur at all. It is often deemed that individual case safety reports (ICSRs – much better than 'spontaneous reports'!) are proved 'wrong' by epidemiological results. This is not necessarily so: they may be reports of the human equivalent of the rare chance of two bulbs failing together which would be outside the power of many studies. Failure to evaluate ICSRs on a case-by-case basis might miss an important signal and perhaps a rare mechanism which produces a serious result.

There is also a third lesson. I found the solutions to the problems, eventually, by a combination of procedures. I used a learned, methodical approach, tracing and checking each wire and component (I thought my level of visual inspection for faults was good, but not good enough!) I then used experience and double checked components known to fail more commonly, and also used a multimeter for final testing and confirmation. The final check was to repair the likely problem and be sure that it was rectified.

We use standard operating procedures (methodical approaches) widely in pharmacovigilance. We also have audits and double checks of some of the pharmacovigilance processes. But do we have checks on the whole pharmacovigilance process through to providing solutions in a useful and timely way? Do we make sure that the problem is rectified (measure impact) of our activities? I certainly do not think we do, and it is even more important to do these checks in pharmacovigilance because the level of certainty that something is actually wrong is so very much lower with drug safety signals than car lights. We can easily do what garages do when faced with the intermittent fault which is so annoying on cars: either expensively take the car apart (so it seems!) and rebuild it, or say that you will have to 'live with it'. There are certainly analogies there to what we do in pharmacovigilance!

The above does not mean that we should spend all our time looking for the extremely rare – on the contrary. However, pharmacovigilance does not deal with truly common events. Risks of serious problems in less than 1:1000 are usually seen in clinical trials. I wonder what the chance is of two bulbs failing together? I also wonder whether the latest rebuild of pharmacovigilance after Vioxx will solve our problems? It will certainly cost more.

A handwritten signature in black ink that reads "Ralph Edwards". The signature is written in a cursive style and is positioned above a thin horizontal line.

# CONTENTS

2 Director's Message

News from Around the World

4 Sweden, USA, Austria, Germany

5 WHO Annual meeting

6-7 China, Madagascar

8-9 Lareb Intensive Monitoring

10 Anti-malarials meeting in Kenya

11 Pharmacovigilance of Herbal Medicines

12-13 After Erice

14-15 Combinations explained

16-17 Courses and education

18 News from Around the World

19 UMC Visitors' Book

20 ISO and medicines

21 Book reviews

22 UMC Products & Services

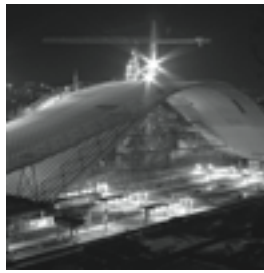
23 Conferences

24 *the* UMC team

5

## En route to the 2006 Annual Meeting

The WHO Programme and the International Society of Pharmacovigilance head for Liège in Belgium this October for their annual gatherings.



6-7

## Chinese developments

Marie Lindquist reports from the fast-expanding national centre in Beijing.



12-13

## Communications in pharmacovigilance

Bruce Hugman reflects on what has been happening since the Erice Declaration on Communicating Drug Safety in 1997.



16

## Education in pharmacovigilance

We focus on the well-established pharmacovigilance and pharmacoepidemiology course of the London School of Hygiene and Tropical Medicine.



## 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](mailto: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](http://www.who-umc.org)

Sales & marketing enquiries: [info@umc-products.com](mailto:info@umc-products.com)

Uppsala Reports © *the* Uppsala Monitoring Centre 2006

ISSN 1651-9779



## Erice Report Offer

Effective Communications in Pharmacovigilance - The Erice Report was published in 1998 to present the discussions and conclusions of the international conference held in Erice, Sicily in September 1997. As a complement to the review by Bruce Hugman of progress since the Erice Declaration, *the* UMC is making the report available at a reduced price of 150 Swedish Kronor. The conference report contains over 80 pages with extended abstracts of presentations, extracts of discussions, as well as the Declaration itself.

The quickest and easiest way to obtain this special offer is via <http://www.umc-products.com/DynPage.aspx> - or send an e-mail to [info@umc-products.com](mailto:info@umc-products.com)



## Sweden and USA to share information

The Food and Drug Administration (FDA) in the USA and the Medical Products Agency (MPA) of Sweden signed a mutual Confidentiality Arrangement in April 2006. The Arrangement allows the two agencies to share certain non-public information, including law enforcement information and internal pre-decisional information.

This important development was precipitated by the events around the time of the 'Vioxx' withdrawal in September 2004. The announcement of the withdrawal of this drug by the company (Merck) during the morning in the USA, had been notified in advance to FDA, but not to regulatory agencies in Europe, which meant that when the news was out towards the close of the day, they had little time to prepare their own statements for patients and prescribers, or to respond to media enquiries.

Given the importance of decisions taken in the USA, the MPA felt that in future they had to be aware in advance of issues such as this, to enable them to plan an orderly response. It took about a year to compile the agreement and have it checked by both sides, including the legal teams.

Thomas Kühler, Director of Operations at the MPA stressed "We are extremely happy with this agreement with FDA – when it comes to sharing drug safety data potentially resulting in regulatory action we should be working together internationally. Simultaneous risk communications, due to the time-difference between North America and Europe have been alleviated."

The FDA is also happy with this Arrangement with the MPA. In the media statement on the MPA's website, Acting FDA Commissioner Andrew C von Eschenbach, states that the FDA is eager to work with regulatory colleagues to establish mechanisms for sharing of important public health information.

With drug approval processes and drug safety monitoring a truly global endeavour, information-sharing is essential and it is possible other countries will follow this example and make similar bi-lateral agreements in the future. There will be an item on the agenda for the Liège meeting of national centre representatives in October at which means of exchanging information before formal decisions are made will be discussed.

## Structural changes at the FDA

The USA national centre has recently implemented several changes in its organizational structure. The Office of Drug Safety changed its name to the Office of Surveillance and Epidemiology in mid May, now reporting directly to the Director of the FDA Center for Drug Evaluation and Research Steven Galson.

Gerald Dal Pan becomes Director of the Office of Surveillance and Epidemiology, while a new section in the CDER Director's Office called Safety Policy and Communication is headed up by Associate Director Paul Seligman.

## Reorganisation in Austria

A new competent authority for all operative tasks in the field of medicines and medical devices has taken over in Austria from the Federal Ministry of Health and Women and the former Federal Control Institutes.

Amendments to various national laws on medicines, medical devices and blood safety were the basis for the establishment of the Austrian Federal Agency for Safety in Health Care (Bundesamt für Sicherheit im Gesundheitswesen, BASG) and the Austrian Medicines and Medical Devices Agency (AGES PharmMed).

The AGES PharmMed is the operative agency of the BASG. The BASG consists of a chairman, Dr Hubert Hrabcik, from the Federal Ministry of Health and Women, an executive member, Professor Marcus Müllner, director of the operative agency AGES PharmMed, and the third member Dr Johann Kurz, from the Federal Ministry of Health and Women. The BASG is located in the operative Austrian Medicines and Medical Devices Agency (AGES PharmMed, Schnirchgasse 9, A-1030 Wien, Austria) and the website is [www.ages.at](http://www.ages.at)

## German vaccines reporting

For many years *the* UMC has had intermittent contacts with the Paul-Ehrlich Institute (PEI) in Germany. The Institute is the German regulatory agency for vaccines, monoclonal anti-bodies, blood, plasma products and allergens and is, among other things, responsible for safety monitoring of such products in the country. *the* UMC has been of the impression several times that we were close to receiving case report submissions from PEI but our hopes have been frustrated. Now it has finally happened. Dr Dirk Mentzer, Head of the Pharmacovigilance Unit at the PEI has submitted close to 6,000 case reports in E2b format dating from October 2003 to December 2005. He hopes to have data sent quarterly from now on. This will be an important contribution to Vigibase and at *the* UMC we are very pleased about this development. We welcome the PEI as a national centre in our network.

Contact details :

Dr Dirk Mentzer, Head  
Pharmacovigilance Unit  
Paul Ehrlich Institut  
Bundesamt für Sera und Impfstoffe  
D-66235 LANGEN  
Germany  
Tel: +49-6103771011 Email: [mendi@pei.de](mailto:mendi@pei.de)

## Plans for Liège meeting forge ahead

The preliminary programme for the Annual Meeting of the WHO Programme for International Drug Monitoring, in Liège, Belgium has been circulated to national centres.

There will be a tutorial for those who are newcomers to the WHO Pharmacovigilance Programme on Sunday 8 October at 14.00, including a session on how to use and interpret data in the UMC Combinations database. The tutorial will be followed by a drinks reception. The meeting itself starts on Monday 9 October.

### Programme

After the Official Opening there will be reports from WHO HQ and the Uppsala Monitoring Centre, and feedback from the 2005 meeting held in Geneva. A talk about 'Pharmacovigilance planning in practice' will be followed by working groups looking at:

- Evidence of the need for pharmacovigilance: developing a standardized simple protocol
- Types of monitoring required when new medicines are introduced (a) in resource-limited countries (b) in developed countries
- Types of monitoring required in emergency situations, eg flu vaccine pandemic.

On Tuesday, sessions include:

- Information sharing between centres
- PSUR evaluation
- Updates on WHO Consultation on Global monitoring of Adverse Events following Immunization (AEFI), and Patient Safety.

There are also to be discussion groups covering:

- Global networking
- Reviewing and evaluating PSURs
- Collaborating with vaccine and blood product programmes
- Patient safety monitoring project.

Wednesday morning has a presentation of drug safety in Belgium, feedback from working groups and the announcement of the host for the 2007 Annual Meeting. As ever, Drugs of Current Interest will be a key part of the agenda.



The new rail station in Liège, designed by Santiago Calatrava, under construction.

Photos on pages 3 & 5 by kind permission of Jacques Renier.

### The ISoP meeting also covers:

- Hospital pharmacovigilance
- Contribution of spontaneous reporting to drug safety
- Paediatric pharmacovigilance
- Independence of post-marketing surveillance
- Pharmacogenomics, gene therapy and genetic resistance
- Risk perception and risk management
- Hepatotoxicity
- Hot topics in drug safety
- Safety of old and new antipsychotics
- Vaccine risk assessment
- Metabolic aspects of drug safety
- Pharmacovigilance of biologicals
- Epidemiological aspects of drug safety

### 6th Annual ISoP Meeting

From lunchtime on Wednesday, delegates at the ISoP conference arrive and come together with the WHO meeting for a 'Joint ISoP/WHO Symposium'. This includes 'Joining forces for managing risks', 'Pharmacovigilance planning for developing countries: how this relates to WHO Public Health Programmes', 'Risk perception in developing countries: the example of chlorproguanil/dapsone and amodiquine/artesunate', 'Genetic prediction of adverse drug reactions', 'Pharmacovigilance in the future: predictive pharmacology?'

The full ISoP programme may be downloaded as a pdf from [www.isop2006.org/programme.htm](http://www.isop2006.org/programme.htm)

### Come to Liège!

The city of Liège possesses an exceptional cultural and architectural patrimony, mainly in its museums, but also with theatres, Opera, Philharmonic Orchestra, which with the cafés and restaurants enhance the character of a welcoming city. October in Liège tends to be cool, and sometimes rainy – a raincoat or umbrella could be handy.

### Getting there

About 100 kilometres east of Brussels, Liège is easily accessible by train from Brussels National Airport and Brussels South Airport. High-speed trains from Paris, Frankfurt, Köln and London are another option. A variety of hotels are offered by the organisers and blocks of rooms in various price categories have been reserved at an attractive group rate. To get these reduced rates, please specify with your booking that you are coming for the WHO and/or ISoP meeting. You can book a hotel yourself or book it online with the conference registration form via [www.isop2006.org](http://www.isop2006.org) website.

For other hotels in Liège, go to [www.liege.be](http://www.liege.be).

### The venue

The Palais des Congrès ([www.palaisdescongresliege.be](http://www.palaisdescongresliege.be)), the meeting venue, is set in a pleasant park alongside the river Meuse, within walking distance from the centre of the city and next to the Museum of Modern Art. A welcome reception and gala dinner are planned for both the WHO and the ISoP meetings.

We look forward to meeting many of you in Liège in October!

## Chinese National Centre

Marie Lindquist recalls her visit in April 2006

### Impressions and reflections

Dr Guizi Wu and 'Eric' (Le Yang) met me at Beijing airport coming from the ISO meeting in Korea for a formal meeting with the Chinese national centre. Regrettably, I cannot speak any Chinese, but fortunately for me, my hosts have excellent language skills so we had no conversation problems.

The next day at the SFDA offices I was greeted by the Director of the National ADR Monitoring Centre Professor Shaohang Jin, and after an introductory conversation with him and the Deputy Directors Cheng Xu Zhang and Zhi Ang Wu, we moved to the conference room with the whole centre staff. I gave an overview presentation of our signal detection process and the data-mining methodology and answered a lot of questions. The group was also interested in the more theoretical aspects of data-mining.

### ADR database

The Chinese database entry is web-based (available from [www.adr.gov.cn](http://www.adr.gov.cn)). There are five main menu choices; the first is for national ADR centre staff report tools. Reporting by pharmaceutical companies and hospitals/regional centres can also be done through this site. Consumers/patients need to send paper report forms to regional centres who forward them to the national centre. So far, only a very small amount of reports are received from patients.

The report tools include data entry/correction, searches, statistics, and a log of reports to be sent to the WHO database. The reporting form is based on the WHO/INTDIS data fields, and includes a free text commentary to each case.

The Chinese database contains around 300,000 reports. Only 'serious' and 'new' reports are sent to the WHO database, the selection of what is 'serious' is done manually. Reports sent to WHO are translated manually. Some of the data fields are based on controlled vocabularies, and can thus be translated automatically (e.g. gender, causality). The main problem when it comes to translation to English is the drug names and ADR terms. Although the reporter can search the ADR term database and select an existing term (WHO-ART translated to Chinese) and do the same with the drug database for names of products to report, it is also possible to type in any text in these fields. The lack of standardised coded data entry causes great problems when sending reports to the WHO database, since each report must be translated manually.

### Herbals/traditional medicines

For many years the traditional Chinese medical system has been built on herbal practitioners, who give each patient an individual treatment composed of a mixture of different plants/plant components, prescribed specifically for the person treated. More recently, fixed-dose herbal medicines have been introduced, manufactured by companies, with a registration and approval process. I had brought a copy of *the UMC's* new book on herbal synonyms which was immediately scrutinized by Li Zhang, with a promise to come back to us with comments.

### Review panel participation

I also set out the function of *the UMC* signal review panel, that this is voluntary work done by experts from different countries. Although we have guidelines for reviewers, the conclusions of the reviews to a large extent depend on the individual reviewer. I encouraged the group to volunteer to become reviewers for us, including the herbal review work.

### WHO-ART

WHO-ART is the terminology used by the National ADR centre. *the UMC* is working with the MedDRA maintenance organization MSSO on a WHO-ART-MedDRA bridge on the preferred term level, which will allow for interoperability between WHO-ART and MedDRA codes.

### Critical terms

There were questions about the definition and use of critical terms. After showing how the critical terms are flagged in the electronic version of WHO-ART, and the meaning of a critical term (and the difference between critical terms and the 'serious' concept), the group was very keen to use critical terms for signal detection purposes.



Marie Lindquist and staff of the Chinese national centre

### Drug classification

The Chinese ADR database holds a limited data set on drug products and their ingredients. For some entries only the product name is available – the SFDA website or the Chinese pharmacopoeia is used to look up ingredients, e.g. when there is a signal. In principle INN names are used for western-type medicines, but the database is not fully updated. A new Chinese pharmacopoeia had just been released and I was taken by Le Yang to the biggest bookshop in Beijing and was lucky to be able to buy the only copy they had in stock.

### ADR monitoring problems

Like in all countries, the task of educating doctors about ADRs and the importance of reporting ADRs is a big challenge. In China, the doctors are responsible to the Ministry of Health, whereas the ADR

monitoring run by the SFDA is organizationally separate from this ministry and therefore has no direct and formal influence on doctors. Guizi Wu wanted to know how other countries' systems work, and if there are similar problems in making doctors understand the importance of adverse drug reactions. My answer was that this is something all national ADR centres struggle with.

Much of the afternoon was spent with questions and answers from both sides, and towards the end of the day Yang Le showed me the facilities available on their website, which includes report entry, searches and statistics. We talked about the difficulties to get through to prescribers. Apparently, traditional healers now quite commonly 'prescribe' antibiotics along with their own cures, and antibiotic resistance is a growing problem. It is very difficult to control whether the prescription regulations are being followed.

### The informal discussions

After the day at the centre, I was transported to an elegant restaurant for dinner. The Director-General of the SFDA Department of Drug Safety & Inspection Zhen Jia Bian gave an introductory speech, in which he particularly expressed a wish that *the UMC* may host the (postponed) training course for regional centre staff some time this year\*.

In reply I thanked my hosts for being so generous taking their time discussing matters of mutual interest. I said I hoped that we would continue the good collaboration between *the UMC* and the Chinese centre, and that by meeting in person we would also become good personal friends. After the formalities we enjoyed a splendid meal, with lots of formal toasting. The Peking Duck (yes, it is still called the old name) was accompanied by all sorts of food.

### ... and relaxation to follow

The next day Eric kindly accompanied me to the Badaling part of the Great Wall. Pre-warned that it would be cold, I was prepared with about five layers of clothing. Eric and I started the climb – a serious climbing effort – and I soon got warm, under all my layers! Half way up the top I had to take some garments off and when we'd reached the summit I had most of the stuff in the bag again! The wind was strong and cold, but the sun and the climb had the opposite effect. The views from the wall are quite staggering, with rugged mountains in every direction.

The final day I enjoyed the company of Guizi Wu and Le Yang at a guided tour of the Forbidden City. A splendid and educative end to my stay in Beijing!

*\*now to take place in Uppsala on 6–10 November 2006*

## From one edge of Africa to another...

Following the Antananarivo workshop for setting-up pharmacovigilance in Madagascar, (see UR33 April 2006), Dr Jean René Randriasamimanana (Director) and Dr Donat Racotomanana (Head of Pharmacovigilance department) from the Agence du médicament de Madagascar (AMM) visited the Moroccan Pharmacovigilance centre to observe the work of a well-established pharmacovigilance centre. The visit took place in Rabat from 24 March to 4 April 2006 with financial support from USAID.

The programme was diverse both in content and style of training (lectures, practical training on assessment, Vigibase Online, WHO-ART, site visits), and all the Moroccan national centre team was involved.

Included in the programme were participation at a pharmacovigilance technical committee meeting, working discussion group on causality assessment, a presentation on phytovigilance, vaccines, and observing a session introducing hospital-based health professionals to principles of drug safety. A valuable experience for the new Associate member of the WHO Programme.



*Dr Raja Benkirane (3rd from left), Dr Donat Racotomanana (4th left), Dr Rachida Soulaymani (5th left) and Dr Jean René Randriasamimanana (6th left) with staff of the Moroccan national centre.*

## Lareb Intensive Monitoring

Kees van Grootheest MD PhD writes

This year the Netherlands Pharmacovigilance Centre Lareb will start a web-based intensive monitoring program in order to receive earlier information about the safety of new drugs.

Intensive monitoring programs are observational cohort studies, investigating specific (new) drugs. These programs are used in some countries as part of the national pharmacovigilance system. The New Zealand Intensive Medicines Monitoring Programme (IMMP) was established in 1977<sup>1</sup>. Since 1980, the United Kingdom uses a form of intensive monitoring called *Prescription Event Monitoring* (PEM)<sup>2</sup>. In both systems questionnaires about the investigated drugs are sent directly to the prescribing physician, two to six months after the first prescription. Cohorts vary between 10,000 and 50,000 patients.

### Intensive Monitoring at Lareb

Lareb Intensive Monitoring (LIM) is based on two pilot studies, carried out in the Netherlands in 1995 and 2001<sup>3,4</sup>. In the first study, the questionnaires were given directly to the patients. In the second study they were sent by the pharmacist to the prescribing physician. Those studies showed that the first prescription signal in the pharmacy computer system provides a valuable tool for an early detection of patients who start with a new drug.

For Lareb Intensive Monitoring we have developed a website-based system, which automatically generates questionnaires. The electronic forms are sent directly to the users of a new drug.

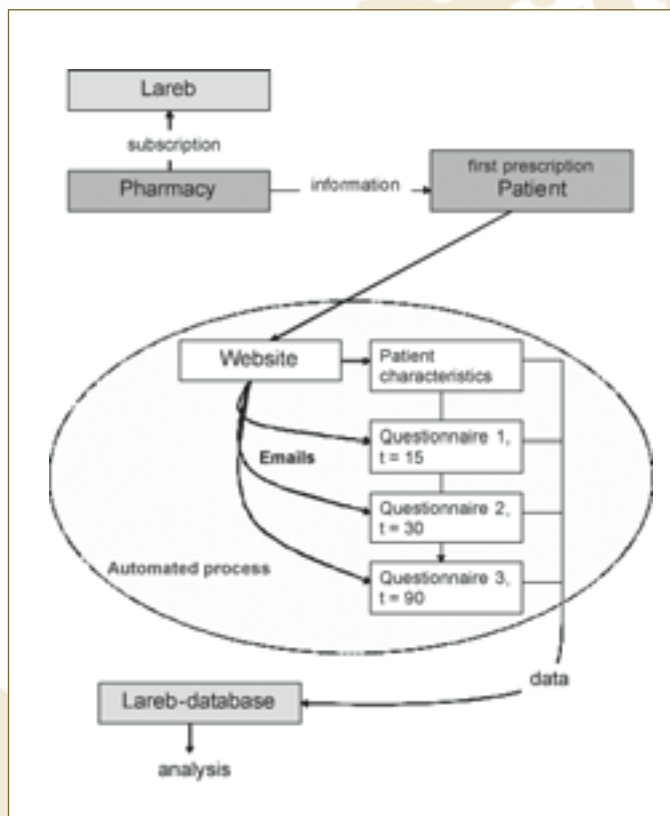
The choice for such a system is an obvious consequence of earlier changes in our organization. Since 2003 patients can report adverse events directly to Lareb. A first analysis shows that these consumer reports are reasonably well documented and can contribute to the generating of new signals<sup>5</sup>. For this reason we chose a direct patient approach in our intensive monitoring system. The second project which led to the design of the system was our 'transparency website', started in 2005. On this website we made all ADR reports and publications accessible for everybody. The good experiences with the development of such internet technology resulted in the website based approach of Lareb Intensive Monitoring.

### How does it work?

Patients who start for the first time with a new drug are selected in their own pharmacy using the first prescription signal. The pharmacist asks if the patient has internet access and would like to participate in a nationwide study concerning new drugs. The patient receives, together with his drugs, information about the intensive monitoring system and a pharmacy-unique login code. With this code, the patient can register himself on our website as a participant in Lareb Intensive Monitoring. Two weeks after starting the new drug, the patient receives his first electronic questionnaire by e-mail. As long as he continues the use of his drug, follow-up questionnaires will be sent automatically at several specific points in time. These moments can vary between the monitored drugs. In addition to questions about adverse drug reactions and drug use, it

is possible to add extra questions to every questionnaire for each specific drug. All answers are stored in a central database, separate from our regular reports.

We do not send direct feedback to the participating patients, but we inform their pharmacists about general (preliminary) results. Each pharmacist receives a private account on our website where they can see which patients from their pharmacy participate in the intensive monitoring program.



### Co-operation

The Dutch Medicines Evaluation Board (MEB) will fund the Lareb Intensive Monitoring system for the next three years. The choice for the monitored drugs will be made in close co-operation with the MEB. When there are safety issues, for example in a European context, the MEB can ask for specific analysis. Because the role of the pharmacist is crucial in this form of intensive monitoring we co-operate with several pharmacy organizations. The Royal Dutch Pharmaceutical Society (KNMP) is an official partner. In addition we get the support of several large collectives of pharmacies.

### Potential benefits

With Lareb Intensive Monitoring we monitor the first users of a new drug, directly from the first intake. This facilitates an early finding of unexpected adverse drug reactions. Because we receive our information directly from the drug users, also associations which



are at first sight not pharmacologically plausible will be reported; there is no 'professional filter'.

All kind of adverse events will be reported, known and unknown, serious and non-serious. This generates a broad overview of the ADR profile of the monitored drug. In addition we have the possibility to investigate other topics, because we can add additional questions to each questionnaire.

At this moment we are performing a short study in 20 pharmacies, to collect experiences with the system from patients and pharmacists. We will start to monitor the first drugs in summer 2006. From that moment all Dutch pharmacies can participate in the Lareb Intensive Monitoring program.

## References:

1. Coulter DM. The New Zealand Intensive Medicines Monitoring Programme. *Pharmacoepidemiol Drug Saf*, 1998, 7(2):79-90.
2. Mann RD. Prescription-event monitoring-recent progress and future horizons. *Br J Clin Pharmacol*, 1998, 46(3):195-201.
3. van Puijnenbroek EP, Amerongen CA. Is het eerste-uitgiftesignaal van nut voor postmarketing surveillance? *Pharm Weekbl*, 1996, 131(16):459-462.
4. van Grootheest AC, Grootte JK, de Jong-van den Berg LT. Intensive monitoring of new drugs based on first prescription signals from pharmacists: a pilot study. *Pharmacoepidemiol Drug Saf*, 2003, 12(6):475-81.
5. van Grootheest AC, Passier JL, van Puijnenbroek EP. Meldingen van bijwerkingen rechtstreeks door patiënten: gunstige ervaringen van het eerste jaar. *Ned Tijdschr Geneesk*, 2005, 149(10):529-33.

## Uzbekistan – first course on pharmacovigilance and patient safety

A partnership between two health consumer organizations DrugInfo Moldova and the Consumer Institute 'Kilen' in Sweden, financially supported by the Swedish aid organization Sida, has resulted in a series of conferences in Eastern Europe and Central Asia about patient safety in general and people living with HIV/AIDS and TB in particular. The UMC was involved in a pharmacovigilance training course in Chisinau, Moldova in April 2004 (see UR 30); as it was considered successful and useful it was followed by a similar training workshop in Tashkent, Uzbekistan, on 28 to 31 March this year.



*Dr H K Jalilov, head of the drug control agency, addressing the workshop.*

The first day plenary lectures were held in the offices of Ministry of Health. The following days were devoted to working group sessions and discussions held at the Department of Drug and Medical Equipment Quality Control which is the drug regulatory authority of Uzbekistan. Participants represented all significant partners involved in the health care and pharmaceutical supply system in Uzbekistan, most of them from the Tashkent area. Teaching institutions were also involved. Presentations were made by Uzbek experts, by representatives of the Moldovan and Swedish organizers, and by Sten Olsson from UMC, representing the WHO Pharmacovigilance Programme.



*Dr B Sh Shaislamov, chairman of the pharmacological committee, head of the pharmacovigilance centre*

The presentations stimulated lively discussions among the course participants who, towards the end of the week, changed the planned course programme. It was felt essential that the meeting should result in tangible recommendations for managers of various sectors of the Uzbek health care system to particularly address patient safety issues during drug therapy. A series of recommendations were agreed upon by the course participants. They were submitted to the Department of Drug and Medical Equipment Quality Control for consideration and action. Kilen and DrugInfo Moldova organized a meeting also in Samarqand, on 3 to 5 April, at which the recommendations were discussed. The drug control agency later circulated the recommendations to relevant parties in other parts of Uzbekistan to solicit a broad acceptance of measures needed to improve pharmacovigilance and patient safety in the country. Since the recommendations are still not available in English they unfortunately cannot yet be quoted here.

## African action on anti-malarials

### *Mohamed Farah reports*

A major meeting to drive forward use of artemisia-based anti-malarials in Africa took place in Kenya last March. The aim was to share information on current and future use of plant products in the control of malaria as well as plan strategies for ensuring safety, efficacy and standardization of herbal formulations in the control of malaria in Africa.

Malaria is endemic in over 100 developing tropical countries, infecting 200–450 million people annually and causing up to 2.7 million deaths. Enormous efforts and huge amounts of funding are now going in to finding anti-malarial drugs.

One of the most effective new drugs to emerge is based on an ancient Chinese herbal remedy, artemisia, but the actual number of authorised drugs on the market is insufficient to meet the needs of those who suffer from malaria. The same is true of public and private investment in the cultivation, processing, marketing and distribution of appropriate products throughout Africa. African people themselves have had little opportunity for input into malaria research and development strategy, nor to share their views and knowledge.

the UMC's concern is about the safety, efficacy and standards of these medicinal formulations. With increased resistance to conventional medicine by the malaria parasite, it is important to ensure that the right herbal formulations and dosages are safely administered if herbal medicine is to cause an impact in the disease control.



*Congress participants in Nairobi*

The Centre for Development Enterprise (CDE EU) and the World Agroforestry Centre (ICRAF) with support from other partners organized the Africa Herbal Anti Malaria Congress (AAHMC), held at the ICRAF Campus in Nairobi from 20th to 22nd March 2006. The meeting brought together expertise in various fields related to herbal medicine including plant specialists, herbal medicine practitioners, herbal medicine researchers, public health system specialists and biomedical practitioners. Institutions represented included donors, government departments, research institutions, conservation bodies, NGOs and the private sector. Delegates were from eleven countries around Africa, China and Vietnam, and Europe.

A 'Gigiri Declaration' from participants at the meeting makes powerful calls for a comprehensive and integrated approach to malarial treatment by the international health care community. The declaration covers policy and practice in several areas, such as Policy and Regulation, which specifies:

- (1) National health and drug policies to include of traditional medicines and traditional practitioners
- (2) Better recognition, certification and legal protection of traditional practitioners
- (3) Support for more clinical and genotoxicity trials for promising African anti-malarials
- (4) Safety recommendations for herbal anti-malarials and ensure adequate pharmacovigilance at national level
- (5) Fast track registration of proven herbal anti-malarials
- (6) Initiate, review and update inventories and profiles of herbal anti-malarials.

There are also recommendations under the headings of 'Cultivation and Harvesting' and 'Manufacturing and Processing'.

The declaration also states "to ensure that malaria deaths are drastically reduced and people have access to affordable treatments" participants call upon:

- Governments to accelerate policy reforms and establish appropriate regulatory frameworks
- Medical researchers to expand toxicological and clinical trials of herbal anti-malarials
- Traditional healers to share knowledge to enable clinical trials to be undertaken
- Botanists and biochemists to step up screening and development of plants for anti-malarial activity.

Participants are creating an Africa Herbal Anti-malaria Consortium (AHAC) to finance, develop and share knowledge and products associated with herbal anti-malarials. There is to be further CDE support for a number of private sector projects to grow and process artemisia in Uganda, Kenya and Madagascar.

Plans are also in place to raise funds to conduct an evaluation including clinical trials concerning the safety and efficacy of artemisia tea with technical advice from UMC.

Further work on identifying promising African herbal anti-malarials will be fast tracked by a number of agencies, while creation of the permanent forum AHAC for further lobbying and project implementation is being championed by ICRAF with support from many other organisations that attended the meeting.

### **For more information, contact:**

Walter Vanopzeeland (ICRAF)  
wvanopzeeland@cgiar.org  
+254-20-722 41 32 (Direct)  
+254-20-722 40 00 (Operator)  
+254-(0)720-65 04 86 (Mobile)

# Current state and future directions

*Joanne Barnes and Jenny Bate report*

Trees covered in blossom and pleasant spring weather greeted 200 delegates at the end of April arriving at the Royal College of Obstetricians and Gynaecologists, by Regent's Park in London, for two and a half days of intense examination of the current position of monitoring the safety of herbal medicines around the world. The conference attendees came from all continents (apart from south America) and all sectors: academia, industry, regulatory bodies. The principal organiser was Joanne Barnes, one of UMC's herbal reviewers and associate professor in Herbal Medicines at the University of Auckland.



*Alumni of the London School of Pharmacy helped organise the London meeting*

## Risk

Sessions on risk management, risk minimisation and risk modification for herbal medicinal products (HMPs), had presentations from Phil Routledge, chairman of the new Herbal Medicines Advisory Committee in the UK, and Peter de Smet (Scientific Association of Dutch Pharmacists, Netherlands). June Raine and Linda Anderson, from the UK's MHRA, discussed regulatory pharmacovigilance and its relevance to HMPs and how the UK is playing an active role in the new EU regulatory framework, and regulation of herbal medicine practitioners in the UK.

## Quality issues

Mohamed Farah (WHO-UMC) – talking about the Herbal Anatomical Therapeutic Chemical classification system and the new 'Accepted Scientific Names for therapeutic herbs and their synonyms' book – and Robert Allkin from the Royal Botanic Gardens (RBG) in Kew, London emphasised the need for an internationally accepted directory of botanical names. Dr Allkin explained that there are >1.5 million scientific names published – more than the number of existing plants! He argued that the use of improper names leads to meaningless publications, failure to find all relevant information, false conclusions, waste of time and effort. Monique Simmonds, also from RBG, gave a presentation on authenticating Chinese medicinal plants on the UK market and an initiative between RBG and the Institute of Medicinal Plant Development in Beijing to create a reference source for Chinese medicinal material and use this to identify the ingredients of products sold in the West. Arnold Vlietinck (University of Antwerp) described implications of quality of HMPs with respect to safety and efficacy.

## Proffered papers

Oral presentations of submitted abstracts included results of a cross-sectional study of the herbal pharmacovigilance activities of National Pharmacovigilance Centres (Anjana Aggarwal, School of Pharmacy, University of London and J Barnes) and an assessment of the quality of published reports of suspected adverse drug reactions associated with HMPs (T Wegener, Germany). Other presentations included views on effectiveness and safety of traditional Chinese herbal medicines where shop employees had been interviewed on the products' safety and effectiveness.

Alison Broughton, a herbal practitioner and director of research at the National Institute of Medical Herbalists (NIMH), and Chinese TRM practitioner and President of the Register of Chinese Herbal Medicine Tony Booker both talked about spontaneous reporting schemes. Alex Doodoo (National Pharmacovigilance Centre, Ghana) presented the traditional healers' perspective on herbal safety. Other perspectives discussed in this session included ESCOP (Simon Mills) which has produced 80 monographs which are submitted to EMEA to provide basis for European core data sheets, the herbals industry (Stephen Köhler, Schwabe Pharmaceuticals, Germany), the pharmaceutical industry (R Tiner, Association of the British Pharmaceutical Industry) and consumers (J Barnes).

## Tools

Moving on to tools and techniques in herbal pharmacovigilance Ralph Edwards (UMC) showed how the WHO database has been structured to better deal with herbal reporting and herbal signal detection, citing a recent herbal signal. Alex Doodoo from Ghana and Professor Yixin Chen from the National Pharmacovigilance Centre in China followed, setting out the situation in countries where a large proportion of the population uses traditional medicines. The challenges in the analysis and identification of the causes of the ADRs relates to different preparation forms, adulteration, use of the wrong species etc. Head of the Pharmacovigilance Division of BfArM in Germany, Ulrich Hagemann talked about spontaneous reporting and challenges in risk to benefit assessment.

Several speakers discussed the potential of observational data in herbal pharmacovigilance. John Parkinson (General Practice Research Database, UK) explored how the GPRD could be used in herbal safety investigations, and others described practitioner-prescription-based models for monitoring safety of HMPs (Deborah Layton, DSRU, UK; Marion Schaefer, Berlin).

This superbly rewarding meeting was organised by the Royal Pharmaceutical Society of Great Britain, in conjunction with the UMC, ISO, the Gesellschaft für Arzneipflanzenforschung, the ESCOP, the School of Pharmacy University of London, the School of Pharmacy University of Auckland, New Zealand and the Academy of Pharmaceutical Sciences (UK).

For more information about the presentations, abstracts are presented in *Drug Safety*, 2006, 29(4): 341-370.

## A progress report on the Erice Declaration on Communicating Drug Safety?

### *Bruce Hugman surveys the contemporary scene*

There is not much doubt that Michael Balint<sup>1</sup> was one of the authentic pioneers in the modern field of medical communication, especially when it concerned what was going on between a doctor and a patient. His book, *The doctor, his patient and the illness*,<sup>2</sup> published in 1957, set the scene for what we now take for granted: the shift from medicine as a mechanistic activity, concerned largely with the functioning (and malfunctioning) of the body, to a focus on the patient as a multi-dimensional, whole person, with opinions, feelings and rights.

That perspective, however, does have a long history: Hippocrates<sup>3</sup> and Huang Ti<sup>4</sup> (and all Chinese traditional practitioners since) have held views about whole-person medicine, though it is only in the last fifty years or so that it and its associated communication skills have come to prominence in western medicine.

In the 1970s and 80s there was substantial interest in the whole area, and many acute questions were being asked.<sup>5,6,7</sup> The 1991 Toronto Consensus Statement on doctor-patient communication provided further impetus for development. The account of it by Stewart et al.<sup>8</sup> was extensively cited during the following decade. An internet search will generate tens of thousands of communications references for recent years.

The path to Erice began with the Verona Initiative in 1996<sup>9</sup>, when the urgency and complexity of drug safety communications were first extensively explored.

What, then, is special about the Erice Declaration (1997)<sup>10</sup> and its vision to influence thinking and practice in the area of drug safety communication?

For the first time, the entire scope of drug safety communications, embracing manufacturers, governments and regulators, lawyers, healthcare professionals, academics and researchers, journalists and patients – from 34 countries, which were all represented at the



*The participants in the international conference at Erice, 1997*

meeting which gave birth to the document – came together and related to a single set of ethical and professional standards. The critical ideals were those of openness, transparency and independence. The objective of drug safety communication was to 'serve the health of the public' giving rise to 'profound implications' that 'depend on the integrity and collective responsibility of all parties.'



*Lareb's website*

Like many statements of ideals, much of the content of the Erice Declaration seems obvious when you read it, but its radical demands reach into every corner of practice. For example: 'The inherent uncertainty of the risks and benefits of drugs need to be acknowledged and explained'; 'Facts should be distinguished from speculation and hypothesis...' Communication was to be judged not only by content but also by method and effectiveness. These are ideals with profound practical implications.

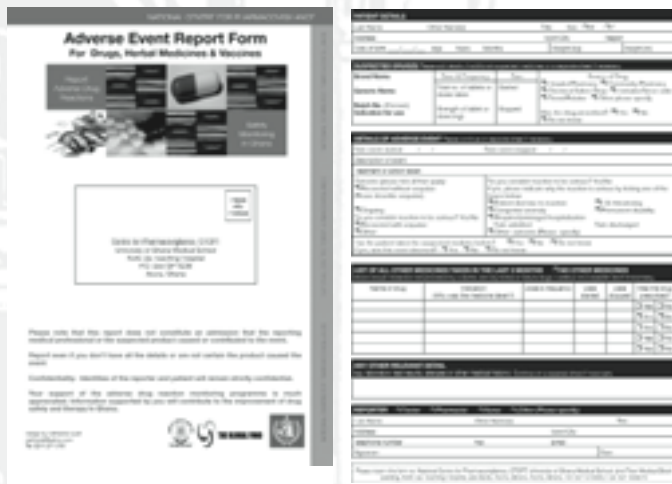
The Erice Declaration has been widely cited in the literature, and translated into a number of languages, but it would require a very large project to assess its actual impact on practice. What we can observe, as no more than an association in the past decade, is the growing priority and attention given to communications (and particularly the patient's perspective) in conferences and in regulatory and professional discourse, and an increasing clamour for improvement.

The Declaration calls for 'independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated, and made accessible to all' through systems with 'non-partisan' funding. Few governments have had the courage to take such steps. The recent controversy in Ghana dramatically illustrates how such conflicts can damage science.<sup>11</sup> In recent years, patient information leaflets (PILs) have been accepted as an important element in any sound medicines information strategy: increasingly they are the rule rather than the exception. Their provision and quality are good indicators of the seriousness with which regulators and manufacturers regard

patients' needs for useful information, yet it seems to be an activity which has become routinised and been influenced little by accumulating knowledge over the years: patients are still left with less than adequate information about many aspects of their medicines, or feel that they are being neglected.<sup>12,13,14</sup>

Regulatory scares and crises can reasonably be attributed partly to failures of communication: would the Vioxx fiasco have occurred if the risks had been well communicated and managed, if warnings had been heeded, if there had been a better understanding of the inevitability of some risk as the trade-off for great benefit? Would medicine and drug manufacture have suffered the damage brought about by the third generation oral contraceptive scare<sup>15</sup> or SSRIs have had such a rough ride<sup>16</sup> or litigation have been so popular<sup>17</sup> if regulators and manufacturers had followed Erice's priorities of openness and transparency in all their communications from the very beginning?

We know that the impact of 'Dear Healthcare Professional' letters is unreliable;<sup>18,19</sup> that, in general, ADR reporting schemes have a very low uptake;<sup>20</sup> and that regulators keep the media (those great communicators) at arm's length and are frequently criticised by those who appear to have no axe to grind except concern for truth.<sup>21</sup> We know that the incidence of serious ADRs is alarmingly high and that irrational prescribing and medical error are not uncommon – all, attributable in part, to insufficiently creative, persistent and effective communication with those who have it in their hands to prevent injury and save lives.



Ghana's reporting form

The vision of the Erice Declaration was of a world in which effective drug safety communication and patient safety would be given the highest priority, without reservation. This would demand immense research and investment by governments, regulators and manufacturers, in collaboration with patients and the organisations that represent them. It would mean taking medical and drug safety communication into a new era of energy and creativity, where design was understood to be as important as content; where patients and the multiplicity of their needs were the driving force; and where the peculiar concerns of regulators, lawyers and bureaucrats took a back seat when they had anything but patients as their primary concern.

Progress has been made – in the accumulation of recorded knowledge and wisdom, and in some excellent information delivery systems;<sup>22,23</sup> in energetic consumer-driven information;<sup>24</sup> in the design and presentation of information and materials;<sup>25</sup> in the development of exceptional website resources<sup>26</sup>; in the imaginative use of modern media<sup>27</sup>; and in collaboration with patients and the groups which represent them<sup>28</sup> – but we are still a long way from the time when regulators and manufacturers observe, and are trusted to be observing the Erice standards; when benefit, risk and uncertainty are really understood; when every patient has the targeted information they ought to have and feel they need at the moment they need it; and health professionals have the critical, up-to-the-moment information they need for safe and effective therapy, and communicate it well.

### Notes and references:

1. Born Budapest, 1896; died London 1970.
2. Balint M. The doctor, his patient and the illness. London: Pitman Medical, 1957.
3. 460-377BC, reputedly the 'father of modern medicine'.
4. "The Yellow Emperor" to whom the earliest Chinese medical classic, Huang-ti Nei Ching, is attributed.
5. Mechanic D. Social psychological factors affecting the presentation of bodily complaints. *N Engl J Med*, 1972, 286:1132-1139.
6. Korsch BM, Gozzi E, Francis V. Gaps in doctor-patient communication, 1: doctor-patient interaction and patient satisfaction. *Pediatrics*, 1968, 42:855-871.
7. Cassell EJ. The Theory of Doctor-Patient Communication. Cambridge, Mass: MIT Press; 1985. Talking With Patients; vol 1.
8. Simpson M, Buckman R, Stewart M, Maguire P, Lipkin M, Novack D, Till J. Doctor-patient communication: the Toronto consensus statement. *BMJ*, 1991, 303(6814):1385-7.
9. McNamee D. Speaking about Pharmacovigilance. *Lancet*, 1996, 348:908.
10. The Erice Declaration is available from the UMC, and can be downloaded from the Practical Pharmacovigilance page of the UMC website ([www.who-umc.org](http://www.who-umc.org)); it also appeared in: Hugman B. The Erice Declaration. *Drug Safety*, 2006, 29(1) 91-93.
11. Yeboah K. Front page lead: Daily Graphic (Ghana), Thurs 8 May 2006. The controversy concerned the regulatory authority's wish to wrest control of national pharmacovigilance from its independent, established hospital and academic home.
12. Svarstad BL, Mount JK, Tabak ER. Expert and consumer evaluation of patient medication leaflets provided in US pharmacies. *J Am Pharm Assoc*, 2005, Jul-Aug;45(4):443-51.
13. Gal I, Prigat A. Why organizations continue to create patient information leaflets with readability and usability problems: an exploratory study. *Health Educ Res*, 2005 Aug;20(4):485-93. Epub 2004 Dec 21.
14. The annual *Revue Prescrire* awards for best and worst practice in drug packaging and information are good indicators of aspects of what can be achieved and what needs to be done. [<http://www.prescrire.org/signature/evenements/index.php>]
15. G Benagiano and FM Primiero. Social consequences. Safety of modern oral contraception: the options for women: lessons to be learned. *Human Reproduction Update*, 1999, Vol.5, No.6 pp.633-638.
16. Boseley S. Drug safety body accused of cover-up. *Guardian Weekly*, March 18-24 2004.
17. See [www.acsh.org/factsfears/newsID.768/news](http://www.acsh.org/factsfears/newsID.768/news), on Lipitor, Tysbari and Garsadil (14.06.06)
18. Smalley W, Shatib D, Wysowski DW, et al. Contraindicated use of cisapride: impact of food and drug administration regulatory action. *JAMA*, 2000, 284 (23): 3036-9.
19. Graham DJ, Drinkard CR, Shatin D, et al. Liver enzyme monitoring in patients treated with troglitazone. *JAMA*, 2001, 286 (7): 831-3.
20. Nita Y, Plumridge RJ, Batty KT. Adverse drug reaction reporting in Australian hospitals. *Int Jnl of Pharmacy Practice*, 2004, Volume 12, Number 3, pp. 155-161(7).
21. Miller HI. To America's Health: A Proposal to Reform the Food and Drug Administration. Stanford, Hoover Press, 2000; and The American Council on Science and Health (<http://www.acsh.org>).
22. The US FDA's Medwatch (<http://www.fda.gov/medwatch>).
23. For example, Patient FASS, produced by the Swedish Pharmaceutical Manufacturers' Association.
24. For example, Public Citizen's Worst Pills, Best Pills website and email alerts ([www.WorstPills.org](http://www.WorstPills.org)); NAM ([www.aidsmap.com](http://www.aidsmap.com)).
25. WHO Pharmaceuticals Newsletter ([www.who.int/medicines/publications/en](http://www.who.int/medicines/publications/en)); Viewpoint from the UMC; and ADR reporting forms from Ireland ([www.imbie.ie](http://www.imbie.ie)), Australia ([www.tga.gov.au](http://www.tga.gov.au)) and Ghana.
26. For example, the Netherlands ([www.lareb.nl](http://www.lareb.nl))
27. For example, training videos and TV and radio spots in the Philippines and Ghana.
28. Exemplified in the World Alliance for Patient Safety ([www.who.int/patientsafety/en](http://www.who.int/patientsafety/en))

## The Combinations database table

by Anne Kiuru

The National Centres (NCs) of Pharmacovigilance contribute to the WHO Programme for International Drug Monitoring by submitting national spontaneous reports of suspected adverse drug reactions (ADRs) to the WHO ADR Database, Vigibase, which contains over 3.7 million case reports from close to 80 countries. Information exchange between *the* UMC and the NCs is one of the most important functions of the WHO Programme and *the* UMC has a number of channels for sharing information from Vigibase, including the *Combinations database* and the SIGNAL document.

The recent questionnaire to the NCs showed that the SIGNAL document\* is clearly recognized as a forum for signals of possible drug safety problems, where the hypotheses described are of varying levels of suspicion and are in need of further investigations or monitoring. The questionnaire however revealed that many people do not understand what the Combinations database is and how to use it.

### Combinations database table

The Combinations database is one way of informing the NCs of what has recently been reported to Vigibase. Each quarter approximately 60,000 new reports are entered into Vigibase, and in order to get an overview of recent international reporting trends, a line listing of all drug-ADR combinations reported over the last quarter is produced by *the* UMC Signal team and sent to NCs. The Combinations database table includes the Information Component (IC) value, i.e. the measure of the quantitative strength of relationship, for each drug-ADR combination. Information on the BCPNN methodology and how to interpret the IC values has previously been presented in detail.<sup>1-3</sup>

#### Practical information

- The Combinations database table is distributed on a CD together with search instructions and a basic search tool.
- The search tool was developed by *the* UMC for searching the data, and/or for those National Centres without their own software.
- The table (Access database format) is either imported into the search tool, or opened as it is.

#### Content information

The Combinations database contains information on those combinations of drugs, reported as suspected or interacting, and ADRs that have been entered into Vigibase during the last quarter.

**Figure 1** opposite explains in detail the information included for each drug-ADR combination in the Combinations database.

**Figure 2** on page 15 is an excerpt (not all available fields are displayed) from the latest Combinations database (on drug names beginning with "SE" and ADRs within the System Organ Class 0800 "Metabolic and nutritional disorders").

<b>Field name</b>	Explanation and Comments
<b>Drug name</b>	WHO Preferred Drug name
<b>ADR name</b>	WHO Preferred Adverse Drug Reaction term
<b>Drecno</b>	The WHO Drug Record Number
<b>Arecno</b>	The WHO Adverse Drug Reaction Record Number
<b>Ingred</b>	Indicates if the drug is a Single ingredient drug (S) or a Multiple ingredient drug (M) or the drug is mapped as an ATC code (blank).
<b>Critical term</b>	If the adverse reaction term is on the WHO critical terms list it is marked (Y) otherwise the field is blank. Reports including critical terms warrant special attention, because of their possible association with serious disease states and may lead to more decisive action than reports on other terms.
<b>Dependence indicator</b>	This field flags ADR terms that are indicators of possible drug dependence. Dependence indicators are marked (Y); for all other terms this field is blank.
<b>ATC code</b>	Anatomical Therapeutic Chemical classification of the drug. Some drugs are assigned more than one ATC code. For drugs with more than one ATC code, all information on the combination will be repeated for every different ATC code for the drug.
<b>SOC code</b>	This field indicates which System Organ Class (SOC) the ADR term belongs to. An ADR term may belong to more than one SOC but only the main SOC (SOC1) is given in this field.
<b>SOC name</b>	Short name of the System Organ Class the ADR term belongs to.
<b>IC</b>	Current value of the Information Component (IC). This is the measure of the quantitative strength of relationship for the specific drug-ADR combination. A positive IC value indicates that the combination is reported to the database more often than statistically expected from the generality of the database, whilst negative IC values indicate combinations occurring less frequently than statistically expected
<b>old IC</b>	This is the previous quarter's value of the IC for the drug-ADR combination.
<b>IC025</b>	The value of the lower 95% confidence limit for the IC.
<b>old IC025</b>	This is the previous quarter's value of the IC025 for the drug-ADR combination.
<b>Ndrug total</b>	Total number of reports with the drug reported with any ADR in the Vigibase
<b>Ndrug quarter</b>	Number of reports with the drug reported with any ADR during the quarter
<b>Nadr total</b>	Total number of reports with the ADR reported with any drug in the Vigibase
<b>Nadr quarter</b>	Number of reports with the ADR reported with any drug during the quarter
<b>Ncomb total</b>	Total number of reports with the drug-ADR combination reported in Vigibase
<b>Ncomb quarter</b>	Number of reports with the drug-ADR combination reported during the quarter
<b>1st Year drug</b>	Year when drug was first entered into the WHO Drug Dictionary. Note, for all drugs entered before 1986 the year given is 1985.
<b>Association</b>	An association is a combination selected from the database on a quantitative basis: combinations that on addition of the new quarter's data change from a negative IC025 value to a positive (that is when "Old IC025"<0 and "IC025">0) will pass the statistical threshold for evaluation. This field flags (Y) new associations, i.e. combinations that became associations during the last quarter; for all other combinations this field is blank.
<b>Countries</b>	The number of countries that have contributed reports on the drug-ADR combination to Vigibase.
<b>Doc grade 1</b> <b>Doc grade 2</b> <b>Doc grade 3</b>	The documentation grading is a tool that has been in use in the WHO ADR database since 1990 showing the completeness of information on case reports. In connection with the transfer to our new database, Vigibase, in 2002 the criteria for the documentation grading were revised. This new system of algorithms is under development, in order to give room for both quantitative and qualitative information for the case reports in our quarterly productions of the Combinations database, and therefore the fields are currently blank.
<b>Fatal outcome</b>	The number of reports with the combination in Vigibase that had fatal outcome, i.e. outcome reported as "Died - due to adverse reaction", "Died - drug may be contributory" or "Died - unrelated to drug".
<b>Litref</b>	Literature references. If the combination is found in <i>the</i> UMC literature database (based on selections from <i>Reactions Weekly</i> , Adis Press) the field is marked with Y. If the combination has been presented in the SIGNAL document the field is marked S. If a combination has been assessed by <i>the</i> UMC the combination is indicated with an A. For combinations described both in <i>Reactions Weekly</i> and presented in the SIGNAL document or assessed, the field will be only marked Y (not S or A).

Figure 1

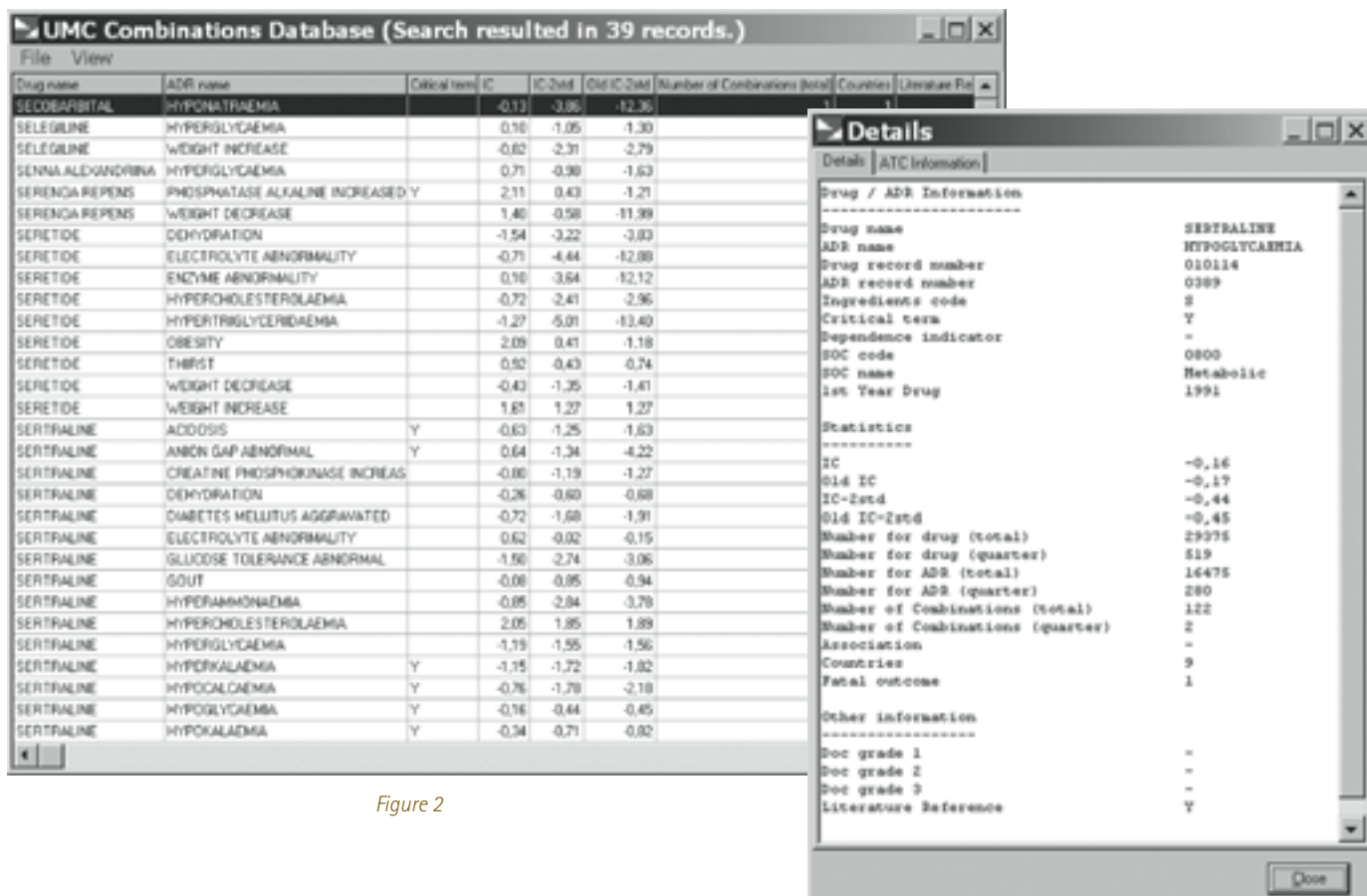


Figure 2

## How to use the data

The Combinations database can be used for many purposes. Although some NCs never use it, other NCs do so weekly. By searching the Combinations database they can easily find the latest news on global reporting that might prompt further analysis or monitoring.

The NCs that actively use the Combinations database use it as a tool to find the latest additions in Vigibase. By browsing the data, trends of IC-values are studied (by looking at the difference between the 'old IC' and the current one), as a part of their signal detection process.

The latest increase in reporting can be investigated and by focusing on the combinations highlighted as 'Associations', the combinations that recently reached a positive IC025 value are identified (previously IC-2std was used to express the lower confidence limit). The case reports for the combinations of interest can then be extracted via Vigisearch for closer clinical review.

The data can be sorted or filtered on number of reporting countries or 'Critical terms'. Searches can be performed on ATC level to find the latest updates on specific side effects of drugs with a particular ATC code, or on SOC level for the ADRs reported during the last quarter. You will also find all newly-reported fatal cases and information on literature references available in the UMC literature database (collected from *Reactions Weekly*). Some NCs use the Combinations database as a reference source, or as support for their own assessments, or external queries, of possible drug safety problems.

## Improving the output

The Combinations database only covers those combinations that have new cases reported to the UMC during the last quarter. Since the Combinations database does not thereby list IC information for all combinations in Vigibase, a so-called Total Combinations database has been requested by some NCs. The Total Combinations database includes information for all drug-ADR combinations ever reported and is currently only available in-house at the UMC, but the possibilities of distribution of this database are currently under investigation. In the mean time, information on IC-values of any combination not available in the latest Combinations database can be requested from the UMC at [info@who-umc.org](mailto:info@who-umc.org).

## References

1. Uppsala Reports 23, July 2003.
2. Viewpoint 2. the Uppsala Monitoring Centre, Uppsala, 2005.
3. Bate A et al. A data mining approach for signal detection and analysis. *Drug Safety*, 2002. 25(6): p. 393-7.

\* (distribution currently restricted to NCs, regulatory authority staff and their advisers participating in the WHO Programme)

## London School of Hygiene and Tropical Medicine

### *Short course on Pharmacoepidemiology and Pharmacovigilance*

*Ann Arscott writes*

Another pharmacovigilance anniversary is being celebrated this year, with the London School of Hygiene and Tropical Medicine's part-time post-graduate certificate course reaching its 10th year. The course provides a formal introduction to pharmacoepidemiology and pharmacovigilance for workers in public health, pharmaceutical companies, and regulatory authorities seeking to extend and reinforce their existing skills. The intake has gone up from 16 students ten years ago to 24 now; entry requirements are a first degree in medicine, pharmacology, or life sciences, with some experience in pharmacovigilance. Most students work in the UK, Europe or the USA, but in recent years students from Ghana, Nigeria and Uganda have successfully completed the course. The 2006 group included a scientist from Poland's regulatory authority and one from Israel, who wished to obtain a formal qualification in pharmacovigilance, and two students from the USA.

The course extends over 3 teaching blocks totalling 11 days, spread over 5 months, followed by a written examination. Lectures on the historical perspective of pharmacovigilance, statistics, epidemiology, study design, critical appraisal, research databases, health economics and regulatory procedures complement workshops; together these equip students with the analytical skills necessary to write their projects. The course content has developed since its inception to reflect the latest thinking in drug use and surveillance, the increasing emphasis on health economics, and changes in national and international regulatory procedures. Workshops which give students the opportunity to formulate and present a response to a drug safety alert are particularly popular.



*Some of the students at the LSHTM course in 2006*

A 3,000 word project is written on a topic defined by the School (materials are provided) – essentially a critical appraisal of topical papers. Students write a review taking the standpoint of prescribing physician, patient, regulatory authority or pharmaceutical company. Although this appears daunting, it is ultimately enjoyable, achieving its purpose of making students look at papers in a critical and analytical manner. Project topics have included anorectic drugs and valvular disease, seligiline for Parkinsonism, safety of albumin in treatment of

critically-ill patients, the MMR and autism controversy, and the HRT and osteoporosis debate. All students are allocated an experienced academic adviser who provides constructive criticism after reading the outline project summary that students are required to submit halfway through the course. There are now 'practice MCQ' (multiple-choice) papers in Blocks 2 and 3, which identify areas which need clarification, so that these may be addressed in follow-up sessions.



*Nicholas Dunn looks on as students concentrate on their work*

The Course Organiser is Professor Stephen Evans, and approximately one third of lectures are delivered by him and other LSHTM colleagues. Students are fortunate to be taught by a number of distinguished external lecturers from industry, academia, regulatory authorities and pharmacovigilance units. Past students of the course, one of whom is Andrew Bate from *the UMC*, have joined the team of lecturers.

The London School of Hygiene & Tropical Medicine is internationally recognized as a centre of excellence in public health, and tropical medicine, and is part of the University of London. Students who pass the exam and project receive a certificate from LSHTM, thus making this one of the few university certificated short courses available to workers in pharmacovigilance. About 98% of students pass, with around 10% achieving a distinction, and students' evaluations of the course are consistently high.

A particularly important aspect is the opportunity it gives students from different backgrounds and countries to compare experiences and to co-operate together in workshops. Students completing the course are often keen to pursue further study at LSHTM which offers short courses on medical statistics, and masters' degrees in epidemiology, statistics and public health, all of which are pertinent to workers in pharmacovigilance.

The first student has already enrolled for the 2007 course, details of dates will be published on the school website shortly – [www.lshtm.ac.uk/shortcourses](http://www.lshtm.ac.uk/shortcourses), or e-mail [Stephen.Evans@lshtm.ac.uk](mailto:Stephen.Evans@lshtm.ac.uk) or [Ann.Arscott@lshtm.ac.uk](mailto:Ann.Arscott@lshtm.ac.uk).



# Pharmacovigilance – what to look for in continuing education

*A personal view from Andrew Bate*

In judging the potential of different educational opportunities, we should look at the range of essential components: curriculum, content, teaching style, faculty. The particular strength of the London School of Hygiene and Tropical Medicine course, which probably makes it unique, (I am not aware of any comparable course certainly in Europe) is that it aims to, and succeeds, in covering in reasonable detail the principles of pharmacoepidemiology and pharmacovigilance. The LSHTM faculty are very experienced in the field but are also good teachers. I think the way the course is set up with teaching but also an opportunity to test understanding as one undertakes a short project is ideal. I also like the idea of three intense one week blocks of teaching with long breaks in between, that allow an opportunity to consolidate learning, and to manage work, so as to be able to focus on learning during those three weeks. As an accredited course – with formal 'sit-down' exams at the end – it made sure one focussed on actually learning something!

Young professionals in drug safety need to reflect when seeking training. They need to know what they don't know, as much as what they do know, and where to find out more about such gaps in their knowledge. They need to get a good grasp of the different aspects of pharmacovigilance, and why the aims of the diverse players differ.

With open courses such as this, catering for a wide geographical and cultural intake, all the participants were very aware of how pharmacovigilance challenges contrast between countries. Sometimes in Europe and US the subject is treated in a very narrow-minded way.

The importance attached to gaining formal accreditation varies around the world, from those for whom it is essential (or desirable to their employers) to those outside that education framework who cannot 'claim' the educational credits. Whatever the background however, accreditation is a 'seal of approval' that emphasises the quality of a course, and the fact that each participant has had to demonstrate a certain level of understanding of pharmacovigilance. So accreditation helps the credibility of the training with everyone, and participation on a formal academic course always looks good on the CV!

From my own experience, and looking back at what I gained both in the short and long-term, I was experienced with spontaneous reporting and so enjoyed learning more about other integral parts of pharmacovigilance – such as the types of pharmacoepidemiological study designs. A practical session where we discussed a recent drug scare gave me a great insight into the challenges of addressing such issues; with a lack of time and data it is an extremely demanding task! I met lots of interesting people from different backgrounds. In the long-term this has given me the confidence to know that I understand the principles of pharmacovigilance and pharmacoepidemiology and given me a network of contacts (both contemporary students and course lecturers) that I always enjoy catching up with at conferences in the field.

*Andrew Bate took the LSHTM course in 2001.*

*See also: Dunn N, Thorogood M. Short Course in Pharmacoepidemiology and Pharmacovigilance at the London School of Hygiene and Tropical Medicine. Drug Safety, 2002, 25(14): 1045-1046.*

## UMC management meet for planning

*the UMC has two occasions each year where staff meet outside the offices for planning. A meeting on the first days of May took place at Gimo Herrgard, a country house by a lake 40kms from Uppsala.*

Among the various topics discussed were issues arising from the questionnaire sent to National Centre at the beginning of the year and how individual departments will respond to problems raised by countries. The senior staff are extremely grateful for all the useful comments and criticisms that have been contributed from 53 members of the WHO Programme and 4 Associates.



*The UMC management team at their planning meeting*

## Zambian launch

On Friday the 16th June 2006, at the Hotel Intercontinental in Lusaka, the Zambian National Pharmacovigilance Unit (NPVU) was officially launched by the Acting Minister of Health, Lt General Ronnie Shikapwasha. The launch was attended by several people including health ministry officials, diplomats, members of the press and several local and international health experts.

The NPVU, which will be the hub of all PV activities in Zambia, is a unit of the Pharmaceutical Regulatory Authority, the country's national regulator. The unit has already swung into action and prior to the

launch a series of training workshops was held for health workers to acquaint them with drug safety monitoring. Oscar Simooya writes "All the country's major institutions were involved and we should now expect a more active Zambia PV system. For me personally this was a very happy moment as I have waited for more than five years to see this dream come true. I will continue to coordinate the activities of the NPVU and send more reports in due course."

Contact:

Dr Oscar O Simooya, Copperbelt University Health Services, P.O. Box 21692, KITWE, Zambia E-mail: [cbumed@zamnet.zm](mailto:cbumed@zamnet.zm)

## News from the Philippines

In May, Kenneth Hartigan-Go was appointed Chair of a new committee created within the Philippines College of Physicians, called 'Pharmacovigilance and drug safety'. This is good news because a professional specialty society is now seriously incorporating pharmacovigilance into their work, and also comes at a point when the College is working on a strategy to develop the 'complete physician' and promoting culture change.

Kenneth Hartigan-Go comments "This comes at an opportune time, when I can advocate better ethical behaviour of doctors towards dealings with drug industry marketing and promotion. The work on pharmacovigilance will entail education, training standards for residents or house officers, reporting systems, and liaising with the eleven chapters of the College around the country."

This is important progress for pharmacovigilance in the Philippines and may lead to a coordinated effort giving healthcare professionals a coherent message towards patient safety.

On another front, following the ISO-P Annual Meeting held in Manila in October 2005, Dr Hartigan-Go was approached by the Philippines Hospital Association to give monthly talks on pharmacovigilance and medication errors in promotion of patient safety in different places around the country. A team approach, with Philippines Society of Experimental and Clinical Pharmacology board members undertaking the lectures, is used to spread the workload.



*Ken Hartigan-Go teaching in one of the workshops*

## ANVISA visit to Spain

On 17 -19 April 2006, a delegation from the Brazilian "Agencia Nacional de Vigilância Sanitária" (ANVISA) visited the Unit of Pharmacoepidemiology and Pharmacovigilance of the Spanish Medicines and Healthcare Products Agency (AGEMED).



*Hortensia Segrelles (left), Mariano Madurga, Carmen Ibañez, Miguel Angel Maciá (AGEMED), Murilo Freitas, Dirceu Raposo, and Antonio C Becerra (right)*

The ANVISA delegation consisted of Dr Dirceu Raposo de Mello, President-Director, Dr Antonio Carlos Becerra, Manager of Human Medicines Unit, Dr Murilo Freitas, Head of the Pharmacovigilance Unit, and Ms Marta Fonseca, Head of International Relations.

The aim of the visit was to exchange experiences in pharmacovigilance, to explain the structure and functions of the Spanish Pharmacovigilance System and the Pharmacovigilance Unit. Recent experience with sentinel community pharmacies in the Madrid region was especially interesting for the delegation. Over two days (17, 18 April) the Spanish Pharmacovigilance team explained several aspects: spontaneous reporting scheme with 17 regional centres, the Spanish database (FEDRA), data-mining process for signal generation on the new database, risk assessment, management and communication. All the Pharmacovigilance Unit staff including Dr Carmen Ibañez, the responsible of Madrid Regional Centre, ensured a pleasant stay and productive visit. On the last day, ANVISA personnel met with the head of the AGEMED International Unit, Ms Hortensia Segrelles and several professionals of the Spanish Ministry of Health and Consumers Affairs.

## Andorra

Patient safety is an important issue not only for big countries but also for small ones. On 16 May we had the pleasure of welcoming at *the UMC* two representatives of one of WHO's smallest countries, Andorra. Andorra, situated between France and Spain in the Pyrenean mountains, has close to 70,000 inhabitants. Ms Cristina Vilanova and Ms Gemma Cummelles Bassols, representing the Ministry of Health, spent a day with us discussing how systems can be developed to improve monitoring of medication-related problems in the country. Andorra also wants to be a partner in the international exchange of information about drug-related safety issues. The authorities wish to ensure that Andorra does not become an easy entry point for unsafe medicines or medicines not accepted in the surrounding EU countries. During the discussions it was concluded that Andorra, without major efforts or investments, would be able to join the WHO Pharmacovigilance Programme.

## Madagascar

Professor Philippe Rasoanaivo of the Madagascar Institute of Applied Research played an important role in putting *the UMC* in touch with the Medicines Agency of Madagascar about a year ago. This contact later led to Madagascar becoming an Associate Member of the WHO Pharmacovigilance Programme. Professor Rasoanaivo is involved in a research collaboration with the Department of Pharmacology, University of Uppsala and in May this year he combined his visit to his pharmacology colleagues with a visit at *the UMC*. At the visit the further development of the pharmacovigilance system in his home country was discussed and how the WHO Programme can support in this development.



*Philippe Rasoanaivo with Mohamed Farah at the UMC*

## Korea

A delegation from the Republic of Korea visited *the UMC* at the end of June, consisting of four pharmacists; Assistant Professor Oh, Jung Mi from College of Pharmacy, Seoul National University, accompanied by her graduate student Lee, Young Joo, Professor Shin, Hyun Taek from College of Pharmacy, Sookmyung University and Dr Shin, Joon Su, Deputy Director of the Korean Food & Drug Administration (KFDA).



*Lee, Young Joo, Asst Prof Oh, Jung Mi, Professor Shin, Hyun Taek, Dr Shin, Joon Su in Uppsala*

The aim of the visit was to learn more about *the UMC*, ADR reporting, Vigibase Online, WHO-ART, Vigisearch and signal detection. Korea became a full member of the Programme in 1992 but due to reorganization, has not submitted any ADR reports since 1998. Dr Shin, Joon Su is determined to start reporting again in the end of this year.

## ISO and medicines

### Marie Lindquist reports

For many years, the ISO (International Organization for Standardization) has had a Technical Committee (TC) dealing with Health informatics. The mandate of this technical committee, TC215, is to develop standards in the field of information for health, and Health Information and Communications Technology (ICT) to achieve compatibility and interoperability between independent systems. Also in the scope is to ensure compatibility of data for comparative statistical purposes (e.g. classifications), and to reduce duplication of effort and redundancies.

More recently, the TC215 Working Group 6 (WG6), Pharmacy and Medication Business, was set up. The scope of this working group includes:

- reviewing the need for health informatics standards in the area of e-pharmacy and applications relating to medicines
- reviewing existing relevant TC 215 standards activity and match it against perceived needs
- encouraging the creation of any necessary new standards within the existing groups of TC215, and to ensure their suitability and their interoperability in e-pharmacy and/or medicines applications
- where necessary and appropriate, encouraging the creation of the necessary standards by bodies other than TC215 and to seek to adopt such created (or existing) standards as ISO standards if practicable and appropriate.



Secretary, Joy Reardon, convenor, Ray Rogers (both now retired from their posts), and the new convenor of WG6, Ian Shepherd, UK

The list of work items of the TC215 WG6 covers several topics of interest for those working in pharmacovigilance. Jeju in South Korea was the setting in April 2006 for a meeting of this group to review and discuss the current work items:

- Business requirements for an international coding system for medicinal products
- Functional characteristics of prescriber support systems
- Electronic reporting of adverse drug reactions
- Specification of a terminology model for representation of medicinal products

- Specification of a pharmacy patient record
- Business requirements for electronic transfer of prescription event data and e-prescribing.

These work items are in different stages of development: the group resolved that the Business requirements for an international coding system for medicinal products will proceed to next draft, in liaison with ISO TC215 WG3, WHO and FDA; the Electronic reporting of adverse drug reactions will proceed to next draft, in liaison with WHO and FDA, and in the context of adopting ICH E2B with additions as the ISO standard.

### Presentations from WHO and UMC

Mary Couper (WHO QSM) and Marie Lindquist (UMC) were invited as WHO representatives to the meeting in South Korea. Mary Couper gave a presentation of WHO, in general, and of its work in medicines safety. I gave an overview of the work of the UMC, and what we do in the harmonisation area: terminologies and classifications and our links to WHO HQ and ICH. At the end of the meeting I was asked to give a more detailed technical presentation of the WHO Drug Dictionary. Using the example of products from South Korea, I showed the structure and contents of the Drug Dictionary, and explained the hierarchical structure and the use of codes and corresponding text values for the data elements included.

Our presentations were well received, and we look forward to an intensified collaboration between WHO and ISO in the area of pharmacovigilance and eHealth.

### The extent of ADRs

Mary Couper and colleagues from Quality Assurance and Safety: Medicines, Medicines Policy and Standards at WHO have had an important letter published in the *BMJ* in which they argue for greater attention to ADRs globally.

Couper MR, Pal S N, Rågo L, Sawyer J. Letter: WHO perspective on preventing avoidable harm from medicines. *BMJ*, 2006;332:1393-1394 (10 June). This was in response to a news item about UK research on hospital admissions for ADRs (Hitchen L. Adverse drug reactions result in 250 000 UK admissions a year. *BMJ*, 2006;332:1109).

### Also recently published:

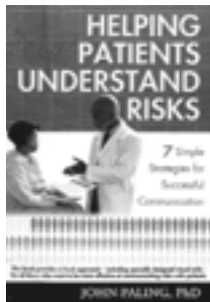
Olsson S. Drug safety surveillance – a concern for everyone. *Essential Drugs Monitor*, WHO, 2005, 34, p24-25. (An overview of the WHO Programme in 2005).

# Book reviews

## Helping patients understand risks

John Paling

The Risk Communication Institute 2006, \$29.95 plus postage, pp 208 ISBN 0 9642236 7 8 [www.riskcomm.com](http://www.riskcomm.com)



John Paling has succeeded in making a complex topic both entertaining and accessible in this excellent, thoughtful and thought-provoking book. As well as very well-written descriptive and analytical material, there are cartoons, quotations, useful charts and diagrams – and, above all, a great deal of information and good sense in an area which is occasionally somewhat obscure.

The author describes the purpose of the book in his foreword:

...a toolbox of strategies – including specially designed decision aids – for all those who want to be more effective at communicating risks with patients (p. xiii)

He especially advises those who have been communicating risk for many years (probably without training) to keep an open mind and decide if the book does not bring a fresh perspective, particularly to the issue of the deeply different perspectives of physicians and patients in understanding risk in medicine.

He elegantly covers the topics of ambiguous descriptive terms ('low', 'moderate') when not attached to standard, mutually-understood figures of incidence, the horrors of misused relative risk statistics, and the dangers of poor framing (lack of balance in presenting positive and negative odds).

There are several very useful sample risk perspective scales – for everyday risks, for bone marrow donors among others – based on the author's own development work for his Paling Perspective Scale, designed to make sense of risk statistics for patients. There are also samples of 'palettes' of 100 and 1000 icons of people, used for demonstrating visually percentage and incidence figures, and guidance on how to use these and other visual aids.

The book is also a model of good communications practice in itself with several levels of entry, and guidance for readers with different priorities.

Any professional for whom risk communication is a critical element of clinical practice, commerce or study – in healthcare, manufacturing or academia – should enjoy this novel, effective and engaging approach to the subject.

*Reviewed by Bruce Hugman*

## Reporting Adverse Drug Reactions: A guide for healthcare professionals

The British Medical Association (BMA) is a scientific and professional body for medical practitioners in the UK. This guide acts as a signposting resource for healthcare professionals on the effective reporting of adverse drug reactions (ADRs). It aims to reinforce the importance of pharmacovigilance and the reporting of ADRs in particular.

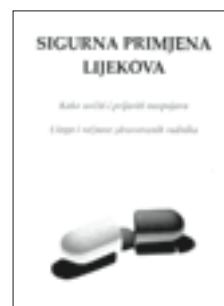


While acknowledging the good record of ADR reporting in the UK, Professor Sir Charles George in his Foreward notes "it is vital that healthcare professionals remain vigilant, are aware of the need to report and keep track of any changes to the systems in place".

Although mainly of use to health professionals in the UK, sections such as 'Why is the rate of spontaneous reporting so low?' and some of the appendices will be of interest to a much wider audience. In Adobe pdf format, the report is downloadable from the BMA: [www.bma.org.uk/ap.nsf/content/home](http://www.bma.org.uk/ap.nsf/content/home).

## Croatian handbook

The new Croatian National Centre has just produced a handbook for health care professionals. The starting point was the WHO booklet 'Safety of Medicines - A guide to detecting and reporting ADRs' (2002) but the text carefully adapted for the situation in Croatia. It is available from:



Croatian Agency for Medicinal Products and Medical Devices  
Ksaverska Cesta 4  
H 10000  
ZAGREB  
Croatia  
Tel +385 146 93 830

## Training on the web

In response to user requests, UMC Product & Services has developed a web-based course, 'Introduction to the WHO Drug Dictionaries'. Participants will be introduced to basic coding concepts necessary when using WHO Drug Dictionaries as well as how coding will effect data retrieval. On completion of the course each participant should have an understanding of the content and structure of the dictionaries, and - after passing a 'final exam' - the students receives a certificate.

### Course Length

The course will take, on average, 8 hours to complete, although users will learn at different speeds, and explore resources and examples at different lengths. The course is accessible for three months after a user name and password is provided.

### Learning Objectives

Upon completion the student should have a basic understanding of the codes used in the dictionaries and the structure and the different formats of the dictionaries to:

- understand how to interpret the elements of a verbatim (name, name specifier, pharmaceutical form etc), and where in the dictionary the corresponding information can be found
- understand differences between the C format and the B format
- facilitate the investigation of omission lists
- understand how to code with highest possible precision (form, strength if available)
- understand how the WHO Drug Dictionaries can be used for analysis.

The student should also get basic knowledge of the Anatomical Therapeutic Chemical (ATC) Classification, to:

- understand how and why drugs are assigned ATC codes
- understand how to best use ATC in the coding process
- understand how to use the ATC classification when analyzing clinical data and identify protocol violations.

The course also enables students to:

- understand what types of medicinal products are included in the dictionaries and therefore which verbatims are likely/unlikely to find a match in the dictionaries
- understand the need for coding herbal remedies and benefits of WHO Herbal Dictionary.

### Course outline

**Introduction** - A short background to the WHO Drug Dictionaries

**Content** - What medicinal products are to be found in the dictionaries. Benefits with the WHO DD Enhanced.

**Codes and IDs** - How codes are used; how to interpret information from the Drug Code.

**Structure and Format** - How the dictionaries are structured; why there are two formats and the differences between them.

**Main Tables** - An overview over the most important tables.

**C-format** - The differences between the C format and the B format.

**ATC classification** - What is an ATC code? How and why is the ATC classification integrated in the dictionaries?

**Coding co-medication** - The general principle of coding verbatims found in CRFs and ADR reports.

**Analysis** - What goes into a database decides what is possible to extract from it.

**WHO Herbal Dictionary** - Why a Herbal Dictionary is needed. The St John's Wort interaction incident, and the need to code herbal co-medication.

### Testing

Every chapter ends with a 'Test your knowledge' section. The exercises can be repeated and are followed by comments to clarify the examples.

### Ordering the course

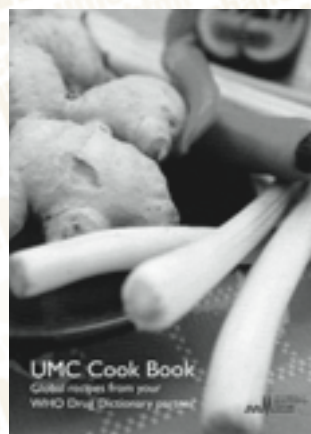
The web-course will be available on *the* UMC Products & Services website from 1 July 2006, and was launched at the DIA's 42nd annual meeting on 18-22 June 2006 in Philadelphia, USA.

More information via the web shop ([www.unc-products.com/training](http://www.unc-products.com/training)). If you have questions about the course or training in general, please contact [training@unc-products.com](mailto:training@unc-products.com)



## *the* UMC cookbook!

Filled with recipes from around the world collated from National Centres, *the* UMC cookbook contains delicacies such as Singapore chilli crab or Lemon rice from India. There's also information about herbs from featured countries: such as raudene from Latvia or cloves from the Netherlands, and their different properties.



You can collect a free copy of the cookbook from *the* UMC Products & Services exhibition stand at conferences.

# COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
28 July 2006	Advanced GCP (Pharmacovigilance) Course	Singapore	National University of Singapore Tel: +65 6516 3023 Fax: +65 6778 5743 E-mail: kamaliah@nus.edu.sg
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
25-26 August 2006	Symposium on Pharmacovigilance & Patient Safety (part of FIP congress)	Salvador Bahia, Brazil	Conselho Federal de Farmácia Tel.: +55 61 2106 6535 Fax: +55 61 3349 5509 E-mail: presidencia@cff.org.br
6-7 September 2006	Critical Appraisal of Medical and Scientific Papers	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
13-14 September 2006	Signal Detection & Risk Management	Brussels, Belgium	IIR Tel: +44 (0)20 7915 5055 E-mail: registration@iir-conferences.com
21-22 September 2006	Drug Safety & Pharmacovigilance	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
28-29 September 2006	1st European Conference on Risk Management Planning and Pharmacovigilance Safety Specifications	London, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
11-13 October 2006	International Society of Pharmacovigilance (ISoP) Annual Scientific Meeting. Pre-conference training courses.	Liège, Belgium	International Society of Pharmacovigilance E-mail: info@isop2006.org www.isop2006.org
18-21 October 2006	The Role of Communication in Patient Safety and Pharmacotherapy Effectiveness	Vienna, Austria	European Society of Clinical Pharmacy Tel: +32-2-743 1542 Fax: +32-2-743 1550 E-mail: info@escpweb.org www.escpweb.org
1-2 November 2006	Introduction to Pharmacoepidemiology	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
2-3 November 2006	Safe Studies throughout the life cycle – a cradle to grave approach	Paris, France	DIA Fax : +1 215 442 6199 www.diahome.org
9-10 November 2006	Pharmacovigilance – A Blueprint for Risk Management – 12th Annual Training Course in Pharmacovigilance	Ottawa, Canada	KUSURI Canada Corp. PO Box 8304, Stn. 'T', Ottawa, Ontario, Canada Tel/fax : +1 (613) 523-5993
15-16 November 2006	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
4-5 December 2006	1st Annual Cardiac Safety Conference	Berlin, Germany	DIA E-mail: tatjana.topalovic@diaeurope.org
22-23 March 2007	Safety of immunotherapy development and patient care	Budapest, Hungary	International Society of Pharmacovigilance Tel/Fax: +44 (0)20 8286 1888 www.isoonline.org
11-13 April 2007	28ème journées de pharmacovigilance	Toulouse, France	Secrétariat de la Société Française de Pharmacologie et de Thérapeutique Tel: +33 2 35 14 86 04 Fax : +33 2 35 14 86 09 E-mail : secretariat@pharmacol-fr.org
14-26 May 2007	Pharmacovigilance – The Study of Adverse Drug Reactions and Related Problems	Uppsala, Sweden	the Uppsala Monitoring Centre Tel: +46 18 65 60 60 E-mail: info@who-umc.org www.who-umc.org



## 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

Maja Östling PA and Team Support

Linda Wallin Team Support

### Science and Technology

#### Safety Reporting Support & Service, and Systems Development

Magnus Wallberg, MSc Eng Phys Manager

Anna Celén, MSc Pharm Data Management

Bill Dagéus Senior Systems Developer

Stefan Lewenfolk Systems Developer

Annica Lundström, BSc Pharm Data Management

Jessica Nilsson, BSc Pharm Programme Leader, Data Management (on maternity leave)

Helena Sjöström, Pharmacist, Data Management

Bo Östling Senior Systems Developer

#### External Affairs

Sten Olsson, MSc Pharm Manager, Head of External Affairs

Geoffrey Bowring, BA External Affairs Co-ordinator

William Frempong, BSc Pharm Signal Detection & Analysis

Mohamed Farah, Pharm D Senior Specialist, Traditional Medicines

#### Research & Development

Andrew Bate, MA (Oxon), PhD Manager

Jonathan Edwards Programme Leader, Data Mining Development

Johan Hopstadius Research Engineer

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

Jenny Bate, BSc Pharm Programme Leader, Traditional Medicines

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, Pharmacist Programme Leader, Drug Dictionary Services (on maternity leave)

##### 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

## How was your address?

### Mistakes?

If there is a mistake in our database, or you have changed your address, please let us know. Either return the envelope label with corrections marked on it, by post or fax, or e-mail your correct address to us. We will then be able to correct our address lists. Many Thanks!

### Want a personal copy?

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

### Prefer to get the electronic version?

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



the Uppsala Monitoring Centre  
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](mailto:info@who-umc.org)

(sales & marketing enquiries) [info@umc-products.com](mailto:info@umc-products.com)

(Drug Dictionary enquires) [drugdictionary@umc-products.com](mailto:drugdictionary@umc-products.com)

Internet: [www.who-umc.org](http://www.who-umc.org)

Uppsala Reports ISSN 1651-9779

