

# MUR 23

UPPSALA REPORTS JULY 2003

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

New doctors at *the* UMC

Training in Uppsala, Riyadh and Kiev

News from Sweden, China, Moldova

Viewpoint translated

Information Component explained



# DIRECTOR'S MESSAGE



From time to time *the* UMC is criticised for its opinions and conclusions. We always take such views seriously, in case they do draw attention to something we could have done better or differently.

I think, however, it's in the nature of our work to be raising questions and challenges which are not always comfortable: are there grounds for worries about the safety of this drug? Will this new procedure or organisation really contribute to enhancing patient safety? Is the wheel being reinvented when there's already a great body of knowledge and experience? Are resources and opportunities being wasted?

Beyond our own survival, we have no agenda but the promotion of pharmacovigilance throughout the world. Given that we have absolutely no funding beyond what income we generate ourselves, we might be expected to take a more emollient line on some issues. But that is not what the World Health Assembly wanted when the collaborating centre was established in the 1960s: the mandate was for vigilance in all aspects of patient safety. When there's cause for concern, which we may sometimes see from the worldwide perspective, it's our duty to voice it. Inevitably, sometimes, some parties feel their interests are threatened by what we say.

We're interested in the truth, as far as it can be revealed, and in the best solutions. It's not our business to avoid debate or disagreement, but we do want to operate on the basis of collaboration, shared values and a shared passion for making things better. Nobody wants a watchdog that has had its brain and its critical edge removed.

On a lighter note, I'm very pleased to record that two of the team have recently won their PhDs on the basis of their scientific work at *the* UMC: Andrew Bate with his neural network research which has resulted in the pioneering BCPNN data-mining tool; Marie Lindquist on the basis of her twenty-four years in pharmacovigilance and her analysis of the present and future science in the field (hers was awarded 'cum laude' which is an exceptional achievement). Congratulations to them both!

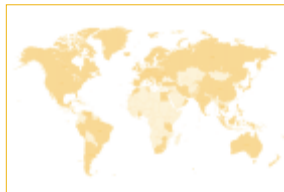
Please keep in touch with us and let us know how we can better serve your needs in the field and keep the debate and the momentum of progress going.

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

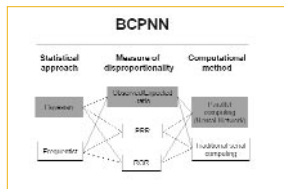
Ralph Edwards

Director  
*the* Uppsala Monitoring Centre

6  
Introducing the 71st member of the WHO Programme for International Drug Monitoring, plus news from Sweden and China



10  
What you need to know about the Information Component – a review of the current position



12  
Congratulations to Dr Marie Lindquist and Dr Andrew Bate



14  
Report on the 2003 two-week Uppsala pharmacovigilance training course



2 Director's message

3 Contents

4 Annual Meeting in Delhi

5 New Gulf initiatives

## NEWS FROM AROUND THE WORLD

6 Moldova and China

7 Sweden

8 UK; Vladimir Lepakhin retires from WHO

9 Zambia and Ukraine

10 IC explained

12 PhDs for UMC staff

14 Jubilee training course

16 New Publications from *the* UMC

17 News from Stora Torget

18 UMC Products & Services

19 Forthcoming Conferences

20 *the* Uppsala Team

## New DG at WHO

Dr Jong-Wook Lee was nominated by the World Health Organization's Executive Board for the post of Director-General of the agency and elected to the post on 21 May 2003 by the Member States of WHO. The Director-General is WHO's chief technical and administrative officer.

Born on 12 April 1945, in Seoul, Republic of Korea, Dr Lee received a Medical degree from Seoul National University and a Master of Public Health degree from the University of Hawaii. Dr Lee will take office and start his five-year term as Director-General of WHO on 21 July 2003.

Of particular interest to all of us working in drug safety, following his confirmation in the post Dr Lee committed that "as Director-General, I will substantially strengthen the audit function at WHO. Yet I understand accountability not just in terms of finances, but also in terms of the effectiveness of our contributions to health outcomes. More broadly, all of the work of countries needs more reliable and timely health data. Accordingly, improving global health surveillance and data management will be a key WHO objective in the coming five years."



### 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)  
sales & marketing enquiries: [sales@who-umc.org](mailto:sales@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 or sales

Internet: <http://www.who-umc.org>

Uppsala Reports © *the* Uppsala Monitoring Centre 2003



## For more details:

For information on the Annual Meeting in Delhi, please contact Sten Olsson ([sten.olsson@who-umc.org](mailto:sten.olsson@who-umc.org));

For the Mumbai conference, please contact the Conference Secretariat at the Department of Clinical Pharmacology, Multistoried Building, 1st floor, Seth GS Medical College & KEM Hospital, Parel, Mumbai, 400 012, India.

tel: +91-22-24174420  
fax: +91-22-24143435  
e-mail: [dcpkem@vsnl.com](mailto:dcpkem@vsnl.com)

Information may also be obtained via [www.kem.edu](http://www.kem.edu) (see Department of Clinical Pharmacology).

## Global pharmacovigilance and focus on India

This year WHO is inviting all countries participating in the WHO International Drug Monitoring Programme to India which hosts the 26th Annual Meeting in New Delhi, from 8th to 10th December. The venue of the meeting is the Grand Hyatt Hotel, Nelson Mandela Marg.

### Reporting on the agenda

This year's theme is '**Improved Reporting**'. Under-reporting is one of the inherent problems of spontaneous adverse reaction monitoring. To most of us under-reporting probably means that only a small fraction of all undesirable effects happening to patients while they are undergoing treatment with medicines actually gets reported to a pharmacovigilance centre. Under-reporting is not uniform however and can have a qualitative dimension, in that reported reactions in many ways are not representative of what is actually happening in the population. We know for example that Type B reactions are being reported more frequently than is warranted by their frequency in relation to reactions of Type A. There is a massive under-reporting of patient details like treatment dates, dose and underlying disease; information that we need to properly analyse case information.

The National Centres meeting this year will devote both plenary lectures and working group sessions to interventions that have been used or may be used to improve reporting, both in terms of quantity and quality. We would like to address how the impact of such interventions may be measured and documented in order to develop best practices.

Plenary sessions will also be devoted to:

- The ICH process and developments in pharmacovigilance
- Pharmacovigilance in public health programmes
- Public health and chemical risks.

### Current developments

Since the Indian Central Drugs Standard Control Organization (CDSCO) is in the process of introducing an ambitious new network for adverse reaction reporting, time will also be devoted to discussing recent Indian initiatives.

Finally, as at all the annual WHO meetings, presentations and discussion of current drug problems will have a prominent place on the agenda of the New Delhi meeting.

The local host of the meeting is Professor S K Gupta, Department of Pharmacology, All Indian Institute for Medical Sciences, New Delhi.

### Pre-meetings in Mumbai

Prior to the WHO Annual Meeting, the Drugs Controller General of India and the Department of Clinical Pharmacology, Seth GS Medical College and KEM Hospital are organizing pharmacovigilance meetings in Mumbai (Bombay) from 4th to 6th December, 2003. On 4th December there will be a workshop on 'Pharmacovigilance: from identification to reporting'. The programme is targeted towards new entrants in the area of pharmacovigilance and will consist of didactic lectures, case discussions and 'hands-on' training.

This will be followed on 5th to 6th December by an international meeting with the theme 'Pharmacovigilance - promoting drug safety through collaboration'.

Highlights of the scientific programme are:

- Pathways for pharmacovigilance in developing nations - A vision for the future
- Pharmacovigilance in public health programmes (non-allopathic systems of medicine, vaccines, public health)
- Medico-legal issues including the role of ethical committees and medical insurance
- Pharmacovigilance and the pharmaceutical industry
- Pharmacovigilance and pharmacoeconomics
- Integrating pharmacovigilance in medical education
- Pharmacovigilance and pharmacoepidemiology

Abstracts for both oral and poster presentations are invited. Closing date for submission is 1 September, 2003. Abstracts may be submitted via e-mail [dcpkem@vsnl.com](mailto:dcpkem@vsnl.com)

## New Gulf initiatives

The Co-operation Council for the Arab States of the Gulf (GCC) was established in 1981. It is a forum for co-operation between seven countries - Bahrain, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirates and Yemen. GCC also co-ordinates many activities in the health sector, the latest on pharmacovigilance.

### Course for regulators

The Executive Board of the Health Ministers' Council of GCC took the initiative to organize a pharmacovigilance symposium in Riyadh, Saudi Arabia, on 26th and 27th April, 2003. Representatives of the drug regulatory authorities from all GCC countries attended the meeting, at which the Director General of the Executive Board, Dr Tawfik Khoja took a very active part. The head of the registration department of the GCC Health Ministers Council, Dr M Al-Haidari chaired the meeting to which Professor Nicholas Moore (Bordeaux, France), Sten Olsson, (*the UMC*) and Dr F Wagniar (Les Laboratoires Servier, France) were invited as foreign speakers.



*A pharmacy shop in Riyadh*

Several of the participating countries presented their current position and future plans for establishment of pharmacovigilance systems. Discussions focussed on ways of teaching practising health professionals and students about the importance of drug safety monitoring, and the crucial role they can play in society to contribute to safer drug therapy.

### Recommendations

The meeting also adopted a set of core recommendations for the attention of GCC Health Ministers:

1. Each Ministry of Health in GCC countries should identify an appropriate unit for collection of case reports of adverse drug reactions and other drug related problems.

The unit should be formally appointed as a National Pharmacovigilance Centre. It should have close ties with the drug regulatory agency.

2. A National Centre should be provided with appropriate resources in terms of trained staff, equipment and a running budget in order to fulfil its functions as recommended by prevailing WHO guidelines.
3. Educational campaigns should be initiated in member counties, mobilising practising health professionals in identifying, reporting and preventing drug related health problems. Academic institutions should be engaged in teaching students about the importance of pharmacovigilance.
4. As soon as National Pharmacovigilance Centres are established, Ministries of Health should apply for their countries to obtain membership in the WHO International Drug Monitoring Programme. Co-ordination and collaboration should also be maintained on the GCC level.
5. Governments of GCC countries should ensure that the legal situation is such that the identity of the suppliers of adverse drug reaction reports and the names of the patients may be kept confidential.

Representatives from Bahrain, United Arab Emirates, Oman and Saudi Arabia have recently attended *the UMC* two-week pharmacovigilance training course (see pages 14-15). This should also have provided these countries with the technical competence needed for setting up and running pharmacovigilance systems.



*The main speakers are received by Dr M Al Haidari*



*Gulf Co-operation Council offices, Riyadh*

## Information

Dr Lucia Tsurcan is Head of the Moldovan National Centre in Chisinau.

Contact details:

Dr Lucia Tsurcan  
Head

National Centre for Adverse  
Reaction Monitoring  
of the Republic of Moldova  
National Institute of Pharmacy  
Str. Korolenko 2/1  
CHISINAU 2028  
Moldova

Tel: +373-2-73 70 02, 73 87 86

Fax: +373-2-73 70 45

E-mail: [pharmacovigilance@front.ru](mailto:pharmacovigilance@front.ru)



## Introducing Moldova

### 71st Member of WHO Programme for International Drug Monitoring

The Republic of Moldova is one of the new ex-Soviet states, located in south east Europe. Official independence of Moldova was declared on 27th August 1991. Before 1991 there was no proper drug legislation in Moldova, and drug surveillance, safety control and monitoring were very poorly developed.

### Beginnings

First steps were undertaken by creating a legislation base, particularly a law on pharmaceuticals. The National Institute of Pharmacy (NIP) was established in 1996. The main objectives of the Institute are administration of all aspects related to official drug authorization in Moldova, drug safety and quality control, including pharmacovigilance. Within the NIP, a **Clinical Drug Trial Pharmacovigilance Department** (CDTPD) was created. The head of the CDTPD is Dr Lucia Tsurcan, and there are three pharmacists and three physicians in the Department.

CDTPD activities include:

- Control of drugs authorized by local legislation
- Detection and monitoring of ADR cases
- Clinical drug trial management of domestic and imported drugs
- Expertise of drug specifications.

### Preparing for Programme membership

CDTPD activity in pharmacovigilance began in 1999 following an order of the Ministry of Health, which regulates the national pharmacovigilance network and obliges physicians and pharmacists to report ADR cases to CDTPD. The national network includes pharmacovigilance units within every medical institution in Moldova. Around the same time the reporting form for drug ADRs was approved, and the first reports were collected in 2000. During the following years, the number of spontaneous ADR reports has increased and Moldova was accepted as an associate member of WHO Programme. In 2003, Moldova fulfilled WHO requirements and became the 71st Member of WHO Programme for International Drug Monitoring.

CDTPD analyses the reports from pharmacovigilance units and informs the Drug Commission (NIP) – a structure responsible of drug efficacy and safety control – about ADR cases. The relations between CDTPD and pharmacovigilance units are based on mutual information exchange. The CDTPD team promotes the concept of rational drug use and pharmacovigilance in medical institutions of Moldova, and among customers by the organization

of thematic seminars and meetings with physicians, pharmacists and students of the State University of Medicine and Pharmacy. Another activity of CDTPD is the publication of a professional bulletin of pharmacovigilance.

### Future projects

CDTPD also deals with clinical evaluation of domestic and imported drugs, starting with the establishment of ICH Guideline for Good Clinical Practice according to the Ministry of Health Order (NR. N10 from 14.01.02). Detection of ADR cases for clinical evaluation is an important problem to resolve in the future. Our next projects will be focused on collaboration with producers and distributors of drugs, aiming to collect information about ADRs.

## More strides in China

Li Shaoli, Director, National Center for ADR Monitoring, China has sent this valuable update on the solid foundations for pharmacovigilance which her Centre has laid over the past year.

### ADR reporting system set up in China

By the end of 2002, 32 regional centres (including one army centre) have been set up in China, each province having its own ADR Monitoring Centre, and 50% of them having branch centres. Among the regional centres, 13 provinces have issued regional ADR monitoring regulation and 18 provinces have a regional ADR advisory committee.

### Doubling of ADR case reports

The Chinese National Centre received 17,000 ADR case reports during 2002 – 2.2 times that of last year (7,718). Among these there were 4,105 ADR case reports in electronic format from 18 regional centres.

### Larger national ADR database

With the use of National Pharmacovigilance Information Net, we are transferring case reports to computer format, electronic reports are encouraged, and, at the same time, typists have been taken on to enter the paper-form data into the national database. To the end of 2002, the National Centre has received 34,137 case reports, of which 11,500 cases are electronic.

## Wider and faster dissemination of information

Our main information channels are National ADR Information Bulletin and Chinese Adverse Drug Reactions Newsletter. National centres are trying to make the channel wider and faster, with the frequency of the Newsletter going from 4 to 6 times a year. The National ADR Information Bulletin was published three times, describing problems related to 19 different kinds of drugs.

## ADR Monitoring Training

By the end of 2002, 35 training courses had been completed on a national or regional basis, and more than 3,000 participants were involved in this training.

## Medical Devices Monitoring

A National Medical Devices Adverse Event Monitoring System was put into practice in December 2002. Authorized by the State Drug Administration, the National Centre for ADR Monitoring is in charge of this work. We are performing intensive monitoring on four kinds of medical devices: orthokeratology lens, stent, hydrophilic polyacrylamide and cardiac valve prosthesis.

# Focus on reporting suspected ADRs in Sweden

National and regional centres in Sweden have in recent years taken several initiatives to tackle the problem of under-reporting of suspected ADRs. As a first initiative, the national centre sent a questionnaire to 300 randomly selected physicians to study factors that prevent physicians from reporting suspected ADRs, and also to solicit ideas as to how to increase the reporting rate. The most common reason for not reporting was found to be a lack of time and forgetfulness. Suggested improvements included making the reporting easier (e.g., access to an electronic report form), increased resources, and improving the centre's response to the reporter. In addition to the questionnaire, one of the regional centres performed a study to investigate whether nurses, with advanced training in pharmacology and about ADRs could improve the reporting rate. The result of this study indicated that trained nurses can play an important role in detecting and reporting suspected ADRs. Based on these results, the following actions are being introduced in Sweden:

- There is now increased collaboration between the regional centres, with meetings on a regular basis to discuss methods and processes in reporting.
- A pilot study has been started to see if there is a need for a common procedure for handling ADRs reported by the drug information centres (where health professionals can turn with questions concerning drugs) and to find out how the case reports/answers to questions are communicated to the health care personnel.
- A letter will be sent to health care personnel who administer vaccines, in order to motivate them to report suspected ADRs. There are also plans to follow up patients more routinely after vaccination in the future, where questions regarding adverse reactions will be included.
- Two of the regional centres will initiate a pilot study in which nurses from six different clinical departments at three hospitals are trained to report ADRs. The reporting rate before and after the study and also between the wards will then be compared.
- An electronic ADR report form is soon to be tested in one region of Sweden.
- The national centre has started a co-operation with representatives from different drugs committees.
- An investigation is planned to see how training in ADR reporting can be extended in the standard education for physicians and nurses. Some local initiatives have already been taken in which the students (as part of their clinical pharmacology course work) were assigned to search for evidence of suspected ADRs in the hospital.

## Staff from the Swedish MPA



*Individual pictures of staff from the Swedish MPA.*

*Ylva Ekbohm, Karin Hedenmalm, Ingemar Persson.*

*The last picture is Martin Bäckström (author of the study of reporting by nurses) from the Regional Centre in the north of Sweden.*

*Huddinge University Hospital staff working with pharmacovigilance.*

*From left : Professor Ulf Bergman, Elin Kimland (Information Pharmacist), Ingela Jersenius (Research Nurse).*



## Adverse patient incidents

Although systems for reporting and analysing adverse effects of medicinal products have been in place for over 30 years, there has been little work done in gathering and using reports of medical error. The National Health Service in the United Kingdom is now embarking on an ambitious project to address incidents of medical error.

Andrew Bate of *the UMC* and Roland Orre of Neurologic (which works closely with *the UMC* on its data-mining projects) recently assisted a pilot data audit for The **National Patient Safety Agency (NPSA)** in the UK. The NPSA undertook this study of 'adverse patient incidents' partly to see if electronic reporting of such incidents would work across all the different sections of the UK's National Health Service and also to see if analysis of reports sent in would help to identify issues suitable for work leading to improvements in patient safety. *the UMC's* experience and expertise in data-mining was a key part of this audit, the results of which have been used to inform the setting-up of a UK National Reporting and Learning System for adverse patient incidents.

The National Patient Safety Agency (NPSA) is also hoping to strengthen its work directly with the WHO in a collaboration to improve patient safety in the UK and internationally. The two organisations are to sign an agreement which will set the framework for delivery of a joint programme of work on patient safety.

## Re-organisation in the UK

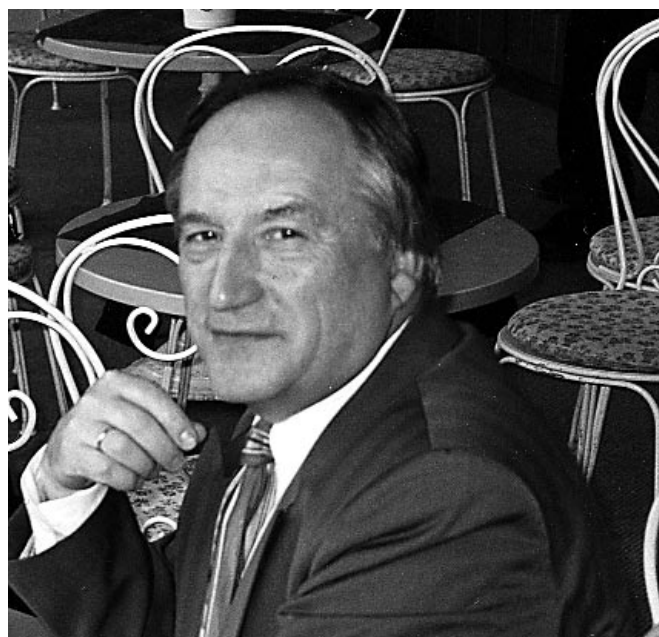
The Medicines Control Agency (MCA) in the United Kingdom merged with the Medical Devices Agency (MDA) on 1 April 2003 to form the **Medicines and Healthcare Products Regulatory Agency (MHRA)**. The MHRA is now the Executive Agency of the UK Department of Health protecting and promoting public health and patient safety 'by ensuring that medicines, healthcare products and medical equipment meet appropriate standards of safety, quality, performance and effectiveness, and are used safely'.

The central enquiry point is:  
Telephone 020-7273 0000 (weekdays 09.00 –17.00)  
Telephone 020-7210 3000 (other times)  
Fax 020-7273 0353  
E-mail: [info@mhra.gsi.gov.uk](mailto:info@mhra.gsi.gov.uk)

Address:  
Information Centre,  
10-2, Market Towers,  
1 Nine Elms Lane,  
London  
SW8 5NQ  
UK

## Vladimir Lepakhin leaves WHO, Geneva

Professor Vladimir Lepakhin retired from the WHO Department of Essential Drugs and Medicines Policy in April this year. He joined the organization some 6 years ago as assistant and special adviser to WHO's Director General. The last few years he spent much effort in supporting the development of pharmacovigilance, particularly in the newly independent states emanating from the former Soviet



Union.

Professor Lepakhin has a long career in clinical pharmacology. Before he joined WHO he was head of the Department of General and Clinical Pharmacology, Russian University of People's Friendship and he also served as Deputy Minister of Health, USSR. He has been active in many professional committees and professional associations and remains active in ISoP, the International Society for Pharmacovigilance.



# Update on Roll Back malaria

Oscar Simooya, Zambia, has been appointed by the WHO Malaria Control Programme to support and document progress in pharmacovigilance in the countries which participated in the pharmacovigilance training programme in Lusaka (see UR22).

Professor Simooya will be acting as a resource person for the project, supporting pharmacovigilance in countries which are introducing artemisinin-based combination therapies (ACTs), and working with the University of Cape Town Foundation. It is also expected that some form of intensive event monitoring is needed in addition to spontaneous reporting only, in order to gather reliable safety data over a short period of time for programmatic use.

The main aims of the on-going project are:

- to document process, requirements and results of setting up pharmacovigilance in Zambia for monitoring adverse events associated with anti-malarial drugs
- to develop standard operating procedures for the implementation of pharmacovigilance of anti-malarial drugs in Zambia
- to define strategies to respond to the pharmacovigilance needs of public health programmes, as complementary to spontaneous reporting
- to elaborate a strategic plan for pharmacovigilance in public health programmes for African countries.

## New Associate Member

Zambia has submitted an official application to join the WHO Programme and is consequently to be regarded as an associate member country. This is the first direct consequence of the training activity in Lusaka in March – April (see UR22).

# High-profile training in Kiev

A seminar 'Drug safety problems in post-marketing surveillance' was organized by the State Pharmacological Centre, Ministry of Health of Ukraine from 29th-31st May, 2003. Representatives of regional pharmacological departments all over Ukraine, pharmacists from the Inspection of the State Inspection of Drug Quality Control, domestic and foreign manufacturers, guests from Russia, Byelorussia, Moldova all took part in educational activities at a picturesque Kiev recreation area. The main goal of this seminar was to promote better understanding between industry and regulatory authorities, and documentation was published as a pharmacovigilance book with a translation of European Union guidelines, and a number of orders of Ministry of Health related to drug safety regulation.

**Professor Vladimir Maltsev**, Head of the Department of Co-ordination and Control in Drug Clinical Trials delivered a speech on the principles, demands and importance of drug safety. He explained in detail the history of the Ukrainian pharmacovigilance system, its legislative and administrative basis and stressed that mandatory reporting of adverse drug reactions to regulatory authorities is a common obligation for marketing authorization holders as well as for physicians in Ukraine.

**Dr Ronald Meyboom** – consultant from *the* Uppsala Monitoring Centre, gave a presentation 'Pharmacovigilance in Transition' which covered definitions, aims and methods of pharmacovigilance and signal detection. He also gave training in ADR

detecting, creating ADR case reports with causality assessment and possible prevention. **Sergey Sur**, WHO expert and Deputy Head of the State Inspection of Drug Quality Control, spoke about the prevalence of counterfeit and substandard generic drugs - a great problem in Ukraine. **Professor Olexy Victorov** demonstrated the importance of clinical pharmacology as drug-related issues, the necessity of providing information on drug safety to healthcare professionals and consumers, and monitoring the impact of activities on the safety of pharmacotherapy.

**Dr Marina Sharayeva**, Head of the Pharmacovigilance Department, explained that a system of post-marketing surveillance, including requirements for pharmaceutical companies in relation to continuous benefit/risk assessment and periodic safety update reporting, needs adequate information resources. She gave examples of the importance of maintaining contacts with international organizations.

The seminar also discussed education and postgraduate training on rational use of drugs, shared opinions of organizing meetings in hospitals, and gaining knowledge of ADR reporting through medical journals, other professional publications and communications activities, and preparing and distribution of educational materials to students, healthcare professionals, pharmacists and the public.

*Dr Ronald Meyboom speaking in Kiev*



# THE INFORMATION COMPONENT

## Information

This article is intended to explain and clarify how the UMC interprets and uses the Information Component, and particularly to set out what it can and cannot do in the detection of signals.

A full list of further reading is provided, which should be referred to for a fuller explanation of the method.

## IC explained

At the Uppsala Monitoring Centre we use a quantitative method for data-mining the WHO database as part of our signal detection strategy. The method used is called Bayesian Confidence Propagation Neural Network (BCPNN) (Figure 1).

It has become evident that there are doubts and misunderstandings on how to interpret the **Information Component (IC)**, calculated by the BCPNN and used by the UMC in the signal detection process as a quantitative filter for clinical review. We have described the method in different fora (see below for details), but feel that it would be useful to bring together some important points:

- The IC value expresses a **statistical dependency** between a drug and an adverse drug reaction (ADR) calculated on the **frequency of reporting**.
- The IC value does **not give evidence of causality** between a drug and an ADR.
- In order to get an indication as to **causality**, i.e. a clinical causal relation between a drug and an ADR, it is necessary to **study the individual case reports** in the WHO ADR database. These reports are summaries of the original case reports held at the National Centres.
- The IC value calculation is a **tool** that can guide us to **create hypotheses of associations** between drugs and adverse reactions, among the nearly 3,000,000 case reports in the WHO ADR database.

- The IC minus two standard deviations (**IC-2std**) is the lower 95% confidence limit. When that value newly becomes greater than zero for a particular combination, it is highlighted for clinical review. The standard deviation for each IC provides a measure of the robustness of the value. (Figure 2)

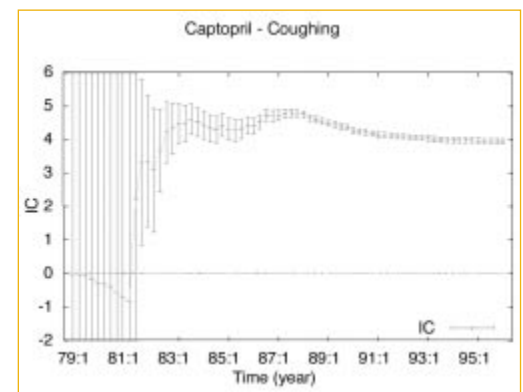


Figure 2

The change in IC between 1979 and 1996 for the association captopril - coughing. The IC is plotted at quarterly intervals with 95% confidence limits shown

- A **positive IC does not necessarily mean** that a drug-ADR combination **should be signalled** and, equally, a negative IC does not necessarily mean that it is not a signal. Signals may be created on the basis of qualitative merits of the case reports, not only because we have more cases than expected.
- A **positive IC** value for a drug-ADR combination means that this specific combination has been **reported** more frequently than expected, compared with the background of all cases reported to the WHO database. The higher the value of the IC, the more the combination stands out from the background.
- A **negative IC** value means that it has been **reported** less frequently than expected.
- As **new data** is added (new case reports entered into the WHO database), the IC value and its confidence limit changes. If an IC value increases over time and the confidence interval narrows, this strengthens the likelihood of a positive **quantitative** association between the drug and the ADR.

## BCPNN

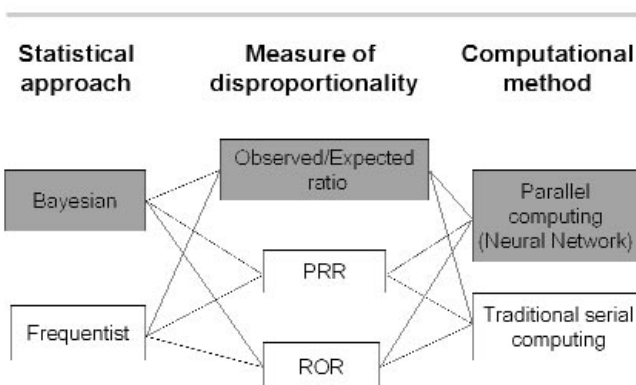


Figure 1

In data-mining different combinations of statistical approach, measurement of disproportionality and computational method may be used. BCPNN is built on the highlighted combination.

## Studies published related to IC

These points are based on published research and studies. The following are the main publications:

*An overview of the quantitative method used to highlight dependencies.*

Bate A, Lindquist M, Edwards IR, Orre R. A data-mining approach for signal detection and analysis. *Drug Saf* 2002; 25(6): 393-7.

*An explanation of the method that we are using for analysing the WHO database - with medical focus.*

Bate A, Lindquist M, Edwards IR, Olsson S, Orre R, Lansner A, DeFreitas RM. A Bayesian neural network method for adverse drug reaction signal generation. *Eur J Clin Pharmacol* 1998; 54: 315-321.

*A more theoretical focus on the explanation of the method.*

Orre R, Lansner A, Bate A, Lindquist M. Bayesian Neural Networks with confidence estimations applied to data-mining. *Computational Statistics and Data Analysis* 2000; 34(4): 473-493.

*An evaluation of the effectiveness of the signal detection method used in highlighting signals.*

Lindquist M, Ståhl M, Bate A, Edwards IR, Meyboom RHB. A retrospective evaluation of a data-mining approach to aid finding new adverse drug reaction signals in the WHO international database. *Drug Safety* 2000; 23(6): 533-542.

*How the BCPNN technique is implemented within the overall signalling strategy for the WHO database.*

Lindquist M, Edwards IR, Bate A, Fucik H, Nunes A-M, Ståhl M. From association to alert - A revised approach to international signal analysis. *Pharmacoepidemiology and Drug Safety* 1999; 8: S15-S25.

*Example of signal analysed using the BCPNN method.*

Coulter DM, Bate A, Meyboom RHB, Lindquist M, Edwards IR. Antipsychotics drugs and heart muscle disorder in international pharmacovigilance: a data-mining study. *BMJ* 2001; 322: 1207-1209.

*Some more details of the method used by the UMC.*

Bate A, Orre R, Lindquist M, Edwards IR. Explanation of data-mining methods. *BMJ* website 2001; <http://www.bmj.com/cgi/content/full/322/7296/1207/DC1.html>

*Comparison of the IC as used by the UMC to other measures currently used for highlighting unexpected associations in spontaneously reported data.*

van Puijenbroek EM, Bate A, Leufkens HGM, Lindquist M, Orre R, Egberts ACG. A comparison of measures of

disproportionality for signal detection in spontaneous reporting systems for Adverse Drug Reactions. *Pharmacoepidemiology and Drug Safety* 2002; Volume 11(1) pp 3-10.

*How signal detection approaches might be used to consider alternative therapies when considering drug specific side effects.*

Bate A, Lindquist M, Orre R, Edwards IR, Meyboom RHB. Data-mining analyses of pharmacovigilance signals in relation to relevant comparison drugs. *European Journal of Clinical Pharmacology. In Press.*

*How to interpret a negative IC value.*

Hepatic injury and pancreatitis during treatment with serotonin reuptake inhibitors: data from the World Health Organization (WHO) database of adverse drug reactions. Spigset O, Hagg S, Bate A. *Int Clin Psychopharmacol* 2003 May; 18(3): 157-61.

*Why the UMC does not routinely stratify in the BCPNN analysis.*

The authors' reply in *Drug Safety* 2003; 26(5): 364-366.

## Most recent research

*Theses published on these issues by UMC staff:*

Bate, A. (2003). The Use of a Bayesian Confidence Propagation Neural Network in Pharmacovigilance. Department of Pharmacology and Clinical Neuroscience. Umeå, Umeå University: Thesis dissertation.

Lindquist, M. (2003). 'Seeing and observing in International Pharmacovigilance - Achievements and Prospects in Worldwide Drug Safety'. University of Nijmegen: Thesis dissertation.



If you have any questions about IC, please do contact us at the UMC: [info@who-umc.org](mailto:info@who-umc.org)

## Uppsala WHO Centre staff receive doctorates

### Hard work pays off

Andrew Bate and Marie Lindquist from *the UMC* have received their doctorates after years of research and study.

#### Dr Andrew Bate

Andrew Bate, Programme Leader, Signal Research Methodology gained an MA in chemistry at Oxford University, England and has worked at the Uppsala Monitoring Centre for 6 years. He has been awarded a PhD in clinical pharmacology by Umeå University (Department of Pharmacology and Clinical Neuroscience) for his thesis on 'The Use of a Bayesian Confidence Propagation Neural Network in Pharmacovigilance'.

#### Dr Marie Lindquist

Marie Lindquist, Head of Data Management and Research and General Manager, gained her MSc (Pharmacy) at Uppsala University and has worked at the Uppsala Monitoring Centre for 24 years. She has been awarded a PhD (cum laude) in medicine by Katholieke Universiteit Nijmegen for her thesis on 'Seeing and Observing in International Pharmacovigilance – Achievements and Prospects in Worldwide Drug Safety'.

#### Strengthening of research base at UMC

Director of *the UMC*, Ralph Edwards commented "We are all delighted with their achievements and congratulate both Andrew and Marie for their contributions to the WHO Programme and to the science which underpins drug safety."



*Professor Stephen Evans challenges Andrew Bate during his defence in Umeå*

### At the interface

We asked Andrew why he chose the subject he researched: "I think the interface between medicine, computing and statistics/maths is a fascinating one. There is a lack of good collaboration and empathy between them, and this makes working in such an area challenging but also potentially fruitful. To work with an interesting data-mining project like this with great collaborators both at *the UMC* and Neurologic, on a project that has such a clear potential benefit for society has been a privilege and an honour."

The major difficulties in the preparation of his thesis were the necessary length of the text keeping a clear structure and maintaining consistency (eg of terminology), and of course to decide what issues to exclude.

Andrew felt that, apart from the subject he studied, he also learnt "the need for stress management, the different challenges of writing a long article rather than a 'normal' publication". As for further ambitions, "the thesis in many ways has raised more questions than answers, and I look forward to continuing research in the field of data mining, and specifically extending the method and testing it on other data sets".



*Marie and Andy celebrate*

## Benefit-Harm detective

Marie Lindquist shares some post-PhD thoughts:

"Since I was a young girl and read Sherlock Holmes stories I have seen myself as a detective. Events around me became detective stories – I observed what was going on, gathered more information, accounting for missing or unclear pieces of the puzzle, and drew conclusions based on the knowledge I had, and my intuition.

In 1979, when I'd finished my university pharmacy education, I was lucky to find a post with the WHO Collaborating Centre for International Drug Monitoring. From the start of my career in pharmacovigilance I could use the skills and interests I had developed over the years, along with professional training as a pharmacist. Now I would become a real detective, – albeit vigilant in the field of medicine and not crime.

After gaining the PhD I want to focus on making targeted analyses of drug safety issues with the aim of identifying risk situations, and, particularly, patients or groups at risk. I also want to explore using the BCPNN to make more fine-tuned evaluations of drugs and drug groups. Is it possible to predict the adverse reaction profile of a new drug based on early reports, or its chemistry? When does a reporting pattern become stable? Can new information on interactions be found using existing knowledge of drug effects on CYP enzymes? ... just some of the questions I hope to address.

Working in pharmacovigilance means that one focuses mainly on negative aspects of drug treatment. People talk about benefit-harm assessment, but few have tried to develop this as a scientific approach. In my thesis I put forward ideas about how to put our knowledge of adverse effects into a benefit-harm context.

The final step towards completing the pharmacovigilance cycle is communication. An interest in languages and human interaction has been part of my 'detective' personality since first reading Sherlock Holmes. One area I'd like to learn more about is the art and science of good communication, and how to make it work in practice.

So far most of what I have done has only indirectly benefited patients. I would like this to change by applying technical systems and scientific technical skills and experience to areas more directly involving patients and doctors. In doing this, I need to develop new communication methods and channels."



Marie Lindquist with her doctorate from the University of Nijmegen.

## Bate nailed

At the final submission of his thesis, Andrew took part in the old Swedish custom of **spikning** (means 'nailing' in Swedish). This is where a hopeful doctoral candidate nails his thesis to the wall in the university department where he has studied, to indicate that his work is ready for assessment and in the public domain. Here he is at the Department of Pharmacology and Clinical Neuroscience in Umeå.

From top to bottom - Andy fixing the nail in his thesis, nailing it to the wall and looking rather relieved when it is all over.



## Group photograph below

### Back row from left:

*John Pemba, Tanzania,  
Marina Sharayeva, Ukraine,  
Fatima Al Hadh Rami, United Arab  
Emirates,  
Sten Olsson, UMC,  
Shanthi Pal, WHO,  
Brijesh Regal, India,  
Hisham Al Awami, Bahrein,  
Arunas Vaitkevicius, Lithuania,  
Selassie Hayibor, Ghana,  
Peter Rozmán, Hungary,  
Marianne Furnes, Norway,  
Branislava Gagic, Serbia,  
Fanak Fahimi, Iran,  
Ronald Meyboom, UMC,  
Kuniko Sata, Japan,  
Asma A'tiyah Haji Abdul Hamid,  
Brunei-Darussalam*

### Front row from left:

*Inguna Adovica, Latvia,  
Nida'a Bawaresh, Jordan,  
Ijeoma Nnani, Nigeria,  
Ximena Gonzales, Chile,  
Jana Mlada, Czech Republic,  
Madia Al-Maskari, Oman,  
Shyamli Munbodh, South Africa,  
Renuka Munchi, India,  
Wafa'a Al-Khateeb, Jordan*

## Jubilee training course

There is a great demand for pharmacovigilance training around the world, but very few academic institutions offer teaching in the subject. The London School of Hygiene and Tropical Medicine runs a course in pharmacoepidemiology and pharmacovigilance, and the University of Hertfordshire in the UK, has flexible courses at certificate, diploma or Masters level in pharmacovigilance. If there are other academic courses in pharmacovigilance elsewhere in the world leading to a formal qualification, we would be happy to know about them.



*A session in progress*

### UMC course background

Since pharmacovigilance demands skills in a broad range of areas rarely covered by a single university department, the Uppsala Monitoring Centre began its own training programme in Uppsala ten years ago. The specific aim was to assist national pharmacovigilance centres in training new staff and to help countries without a pharmacovigilance system to acquire the technical competence for setting up and running a centre for collection and analysis of spontaneous adverse reaction reports. We decided early on that we would admit around 25 students to each course, which would run for two weeks. Course announcements are distributed widely to all WHO member countries and each course has attracted at least two applicants for each place. Selection of course participants is made on a number of criteria:

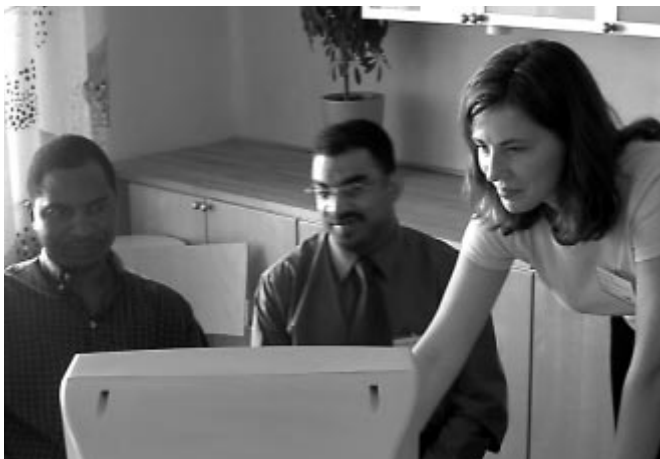
- personal professional competence
- need for pharmacovigilance competence in the country
- achieving a good geographical spread of participants
- achieving a mixed background in the group (authority/hospital/company/pharmacist/gender balance/physician etc)
- ability of students to obtain financial support.



*International course members with main tutors in Uppsala*



*Helena Fucik lecturing on requirements for submitting case reports to the WHO Programme*



*Erica Walette teaching John Pemba and Hisham Al Awami*

Unfortunately many early applicants have to withdraw their applications because of failure to obtain funding for the travel to Sweden, subsistence for the two weeks and the course fee. *the UMC*, unfortunately, has no means of supporting course participants financially.

With experience gained since 1993 the course syllabus has reached a certain stability. Theoretical lectures are mixed with group work, practical sessions and discussions. Each participant is requested to bring a poster or to make a brief oral presentation to the group about drug safety work in his/her country, department or company. Interactions between course participants play an important role in the course – breaks and social activities are consciously planned to facilitate networking.

### **2003 course**

The 8th UMC international pharmacovigilance training course took place in Uppsala from 12th to 23rd May. Participants came from Asia (10), Africa (4), Europe (10), Latin America (1) and WHO-HQ (1). The demand from Latin America is now less since the Spanish Ministry of Health has carried out three training courses there the last few years and the national centre in Chile one.

### **Distinguished faculty**

The major part of the teaching on the courses is done by UMC staff members and consultants. Lecturers are often stimulated by the dynamic atmosphere created in the groups and come back and teach on the next course. This year we were pleased to again have Dr Qun-Ying Yue (impact of genetic and inter-ethnic differences), Bruce Hugman (communications and design of forms), Dr Ronald Meyboom (causality assessment etc), Dr Jeremy Labadie (vaccines monitoring), Dr Wolfgang Schumann (industry perspective) joining our course faculty. We were equally pleased to welcome Dr Shanthi Pal (WHO and public health perspectives), Dr Alex Dodoo (dealing with media), Kerstin Jansson (Periodic Safety Update Reports) and Professor Hubert Leufkens (pharmacoepidemiology) as new teachers and facilitators. Professor Leufkens is worth a special mention since he managed to make the group enthusiastically involved in discussions on epidemiological methods and published studies, after 10 days of heavy studies.

The recurring pharmacovigilance training courses in Uppsala are important also for *the UMC*. We learn a lot about prevailing drug related problems in various parts of the world. Course participants have taught us that drug safety is not only about Type A and Type B adverse reactions. It is also about quality problems, irrational prescribing, irrational use, counterfeiting, adulterations of traditional medicines, resistance, dependence, etc. For *the UMC*, course participants bring to us the world we are living in. Only if *the UMC* and the WHO Programme can be helpful and useful in identifying and dealing with the drug related problems of today is there a justification for our existence. This year we got much reassurance that this is the case.

*Professor Hubert Leufkens grabs the attention of the group*



## New publications from *the UMC*

Bate A, Lindquist M, Orre R, Edwards IR (2003).

Violation of homogeneity: a methodological issue in the area of data-mining tools. The authors reply. *Drug Safety* 26(5); 364-366.

The article 'The WHO Drug Dictionary: an update' was reprinted in *Data Basics*, journal of the SCDM (Society for Clinical Data Management), Spring 2003

WHO Drug Dictionary: new structure – new focus. *WHO Drug Information* Vol 17, No 1, 2003

## Point de Vue – Punto de Vista

*the UMC* has just published a French and a Spanish translation of *Viewpoint*. These editions are part of *the UMC*'s drive to try to disseminate information on drug safety to as wide an international audience as we are able.

Although slightly abridged, each of the new translated versions contains essential information on drug safety, benefit and risk and other big issues in health care.

To receive a copy please apply to; [info@who-umc.org](mailto:info@who-umc.org) or the fax and postal details on page 3 or the back page.

If you wish to receive a bulk supply for a meeting or association let us know and we will try to assist.

A text-only pdf version of *Viewpoint* in English is also now available to download from *the UMC* website (under 'Publications'). This should be quicker to download and print than the full version, which of course is still available by post.

## Calling at *the UMC*

### Visitor from Japan

Dr Kaoru Morikawa, Director, Division of Safety Information on Drug, Food and Chemicals at the National Institute of Health Sciences, Ministry of Health, Labour and Welfare, Japan recently visited *the UMC*

### Serbian delegation

A delegation from Serbia visited Stora Torget from the 6th to 8th of May to find out more about how *the UMC* operates and how the various UMC products and services may best be utilized. This was a follow-up of a training activity in Belgrade in February 2003 (see UR22).

The group consisted of Ljiljana Vuckovic, Milena Miljkovic, Ljiljana Stojanovic, Branka Stojanovic and Ljiljana Petic. They also spent a day at the pharmacovigilance section of the Swedish Medical Products Agency.

### Chinese commission visit

Another delegation came to *the UMC* offices on 22nd April as part of a European tour. 16 officers from China's State Population and Family Planning Commission spent time telling us about their adverse reaction reporting programme on different contraceptive drugs. This is in parallel with the National Pharmacovigilance programme, and we were very impressed by the large number of patients that are included in their safety studies. The delegation was lead by Dr Fu Wei.





## UMC Presentations

### Data-mining in San Antonio

During the session on 'Clinical safety and pharmacovigilance' at the 39th Annual Meeting of the Drug Information Association in San Antonio, USA, Monica Pettersson spoke on '**Data Mining – it really works!**'. The session also included the UK General Practice Research Database and a presentation from the USA Food and Drug Administration.

Monica's talk covered

- Difficulties with detecting patterns in data
- WHO approach to unsupervised pattern recognition
- An introduction to complex pattern recognition
- Testing on synthetic data
- Implementation on WHO ADR database.

With the aid of diagrams, she also described how a true syndrome would be reported, with an ever-increasing overlap of symptoms as the number of cases increases, bearing in mind that all symptoms in a syndrome are almost never reported in any single case report.

She outlined how data-mining the WHO database allows patterns to be recognised; it can detect patterns from incompletely reported case reports and can handle noise ('other' reactions) as well as being computationally fast and capable of handling huge numbers of combinations and cases.

As there is no gold standard for ADR syndrome detection, in order to evaluate the method, performance tests have been carried out on artificial data. The results so far are promising, emphasizing the method's accuracy, speed and tractability. She also described research carried out on ADR reports, mentioning haloperidol and neuroleptic malignant syndrome.

In summary, the BCPNN tool (in routine use in the initial highlighting of associations for clinical review since 1998) will enhance signal detection procedures in the WHO ADR database. BCPNN has been, is, and will be used as a tool for further analyses of potential signals and detection of complex dependencies in the data. She finally mentioned the use of BCPNN on another database, the NPSA – National Patient Safety Agency in the UK.

### Documentation grading at EACPT

Anne Kiuru from *the UMC* has recently presented a paper on documentation grading to the 2003 conference of the European Association of Clinical Pharmacology and Therapeutics in Istanbul.

Her talk '**Documentation grading – a signalling and quality assurance tool for international adverse reaction data**' reviewed criteria for the type of information needed for well-founded signals from the WHO ADR database. The ADR case reports are categorized based on the amount of information in the reports. She described how the field 'documentation grading' was added to the WHO database to facilitate the signalling process following a study on agranulocytosis signals in 1990.

Documentation grading is also used for statistical purposes, and to identify problems related to missing data in the reports received.

In outlining the newly implemented database system (Vigibase) at *the UMC*, she explained how it allows the capture of more detailed information on each case report. As a result, the criteria for the documentation grading have been revised and will continue to be a useful tool for improving the quality of reports in Vigibase.

# UMC PRODUCTS & SERVICES

## Have you moved ?

Please help us! We'd like to keep our mailing lists in top condition, so do let us know if you haven't received post you are expecting from us, if there are mistakes on our labels, or if you have changed your position or address. Thank you!

Please e-mail [sales@who-umc.org](mailto:sales@who-umc.org)

## Updates – 4th Quarter 2002

The latest versions of the WHO Drug Dictionary (WHO-DD) and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 1st quarter of 2003 are now available and were sent to subscribers during June 2003. The WHO-DD pack contains the updated version of WHO-DD. If you have not yet received the update, please do contact Inger Forsell ([inger.forsell@who-umc.org](mailto:inger.forsell@who-umc.org)) who will be delighted to assist.

## Need help?

If you have any queries about the new format of the WHO-DD, or need further information about your current subscription or how to upgrade it, do call *the UMC*.

You can e-mail:

[drugdictionary@who-umc.org](mailto:drugdictionary@who-umc.org)

for comments about the DD, corrections, additions

or

[inger.forsell@who-umc.org](mailto:inger.forsell@who-umc.org) -

for queries about your subscription.

If you are a subscriber to either WHO-DD or WHO-ART and do not receive your updates, please contact Inger Forsell. Data files for the 2nd quarter of 2003 should be available during September 2003.

## Forthcoming exhibitions

UMC staff are planning to attend the following conferences in 2003:

- ISPE – Philadelphia, August 21-24
- Society of Clinical Data Management – Colorado Springs, September 21-24

We look forward to talking to many of you at these events; if you would like to arrange a meeting with us during one of them, do please contact Mats Persson via e-mail [mats.persson@who-umc.org](mailto:mats.persson@who-umc.org) or call us on +46 18 65 60 60



*Constable Scanlon in the safe hands of Erica Walette and Ralph Edwards*

## The Death of Constable Scanlon

The students of the 2002 pharmacovigilance training course in Canberra presented *the UMC* with a reproduction of a painting by Sidney Nolan hanging in the Australian National Gallery in Canberra. Through the kind assistance of the staff of the Therapeutics Goods Administration this reproduction has now safely reached its destination at *the UMC* office. The painting called 'Death of Constable Scanlon' is part of Sidney Nolan's Ned Kelly series and was completed in 1946.

# COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
21-24 August 2003	19th ISPE Conference and 1st International Conference on Therapeutic Risk Management	Philadelphia, USA	International Society of Pharmacoeconomics Tel: +1 301-718-6500 Fax: +1 301-656-0989 ispe@paimgmt.com
3-4 September 2003	'Reading between the lines' - a course on critical appraisal	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
15-16 September 2003	Medical Aspects of Drug Safety and Pharmacovigilance	London, UK	Management Forum Fax: +44 (0)1483 536 424 E-mail: registrations@management-forum.co.uk
18-19 September 2003	Adverse Event Reporting and Pharmacovigilance	London, UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
29 September - 1 October 2003	Pharmacovigilance in the EU in 2003	Paris, France	Drug Information Association Fax: +41 61 225 51 52 www.diahome.org
9-11 October 2003	ISoP Annual Meeting preceded by courses on 'How to write a paper for peer reviewed journals' and 'Compliance in pharmacovigilance'	Marrakech, Morocco	International Society of Pharmacovigilance Fax: +212 37 77 71 79 www.isop2003.org
15-16 October 2003	Signal Generation - Risk Management Initiatives in Pharmacovigilance	London, UK	IBC Life Sciences Training Academy www.ibr-lifesci.com/courses/
22-23 October 2003	Pharmacoeconomics	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
27-28 October, 2003	Medical Approach in Diagnosis and Management of ADRs	Paris, France	Drug Information Association Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org www.diahome.org
30-31 October 2003	Prepare to meet MedDRA challenges	London, UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
6 - 7 November 2003	Case Narrative Writing	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
17 - 18 November 2003	3rd Annual Workshop in Japan for Global Pharmacovigilance	Tokyo, Japan	DIA Tel +1 (215)442-6100
20-21 November 2003	9th Annual Training Course in Pharmacovigilance	Ottawa, Canada	Kusuri Inc www.kusuricanada.ca
26 November 2003	Data Safety Monitoring Boards	London, UK	Jan Phillips, Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
3-4 December 2003	Signal Generation - Risk Management Initiatives in Pharmacovigilance	Munich, Germany	IBC Life Sciences Training Academy www.ibr-lifesci.com/courses/
4-6 December 2003	Pharmacovigilance workshop and conference	Mumbai, India	Conference Secretariat Tel: +91 22 2417 4420 Fax: +91 22 2414 3435 E-mail: dcpkem@vsnl.com www.kem.edu
9-10 December 2003	Prepare to meet MedDRA challenges	London, UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
11-12 December 2003	Adverse Event Reporting and Pharmacovigilance	London, UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
28-30 January 2004	Medical Aspects of ADRs	Southampton, UK	Jan Phillips, Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org



Andrew Bate  
Manager, Research Methodology

Cecilia Biriell  
Head of Internal Affairs

Geoffrey Bowring  
External Affairs Co-ordinator

Ralph Edwards  
Professor in Medicine, Director

Jenny Ericsson  
Data Management

Sally Eriksson  
Team Support

Mohamed Farah  
Programme Leader, Traditional Medicines

Anna-Karin Flygare  
Medical Terminologies

Inger Forsell  
Sales & Customer Relations Executive

William Frempong  
Data Management

Helena Fucik  
Manager, Data Processing

Anne Kiuru  
Signal Detection & Analysis

Anneli Lennartsson  
Team Support, Internal Affairs

Marjatta Leván  
Manager, Finance and Administration

Stefan Lewenfalk  
IT Systems Developer

Anna Lindquist  
Team Support, Web Editor

Marie Lindquist  
Head of Data Management & Research, General Manager

Annica Lundström  
Data Management

Jessica Nilsson  
Data Management

Malin Nord  
Programme Leader, Database Products

Sten Olsson  
Head of External Affairs

Bo Östling  
IT Systems Developer

Mats Persson  
Head of Marketing & Sales, Business Development Manager

Monica Petterson  
Manager, Signal Detection & Analysis

Sven Purbe  
Data Management & Quality Assurance Co-ordinator

Helena Sjöström  
Data Management

Malin Ståhl  
Programme Leader, Signal Detection

Kristina Star  
Signal Detection & Analysis

Daniel von Sydow  
Project Co-ordinator

Erica Walette  
Programme Leader, Database Services

Magnus Wallberg  
Programme Leader, Systems Development

## Baby boom at *the* UMC

Three UMC staff have become parents over the last six months. Malin Ståhl gave birth to Alva and Helena Sjöström had Maja last December, and Magnus Wallberg became a father to Sigrid in May.

Our congratulations to all of them!



*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) [sales@who-umc.org](mailto:sales@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)) in place of info or sales

Internet: <http://www.who-umc.org>

## *the* Uppsala Team

