

# MUR53



**6 million reports | Latest UMC research**

**UMC products news | Mauritius, Indonesia, Cuba, Jordan**



Marie Lindquist  
Director  
the Uppsala Monitoring  
Centre

*I am writing this on March the 8<sup>th</sup>, International Women's Day, marked in many countries as a day to "celebrate the economic, political and social achievements of women past, present and future". Why is it then that, opening the morning paper, I read about women working for the local council in well-off Uppsala, Sweden, not being able to support themselves on their income – not only are their jobs looking after children and the elderly relatively low paid, but one third of the female council employees are only offered part-time positions instead of full-time jobs.*

*Moving to the next page, I find an article about the continued high global maternal mortality rates. Although there has been substantial improvement over the last 20 years, a Lancet report in 2010 showed that there are still over 300,000 women dying per year during pregnancy, childbirth or up to 42 days after giving birth<sup>1</sup>. A vast majority of these women live in poor countries, some of which have a maternal mortality rate of more than 1,500 per 100,000 live births (the figure for Sweden is 5), and where widespread endemic disease is an added burden.*

*These figures are staggering, and it would be easy to sink into despondency. A better choice, I'm sure, is to resist feelings of helplessness about the state of the world, and all its problems, and instead put our energy into making concrete contributions and bringing positive change to areas that are within our reach. Widening the scope of pharmacovigilance beyond scrutiny of adverse reactions caused by the intrinsic characteristics of drug substances is in my view a real achievement – indeed of economic, political and social importance. Women have played an important role in this development, but I prefer to think of it as the result of efforts made by good people, women and men, rather than turning it into a gender issue. Pursuing patient safety and health requires determination, collaboration and the ability to resist the negative effects of insufficient resources and other obstacles.*

*Talking about resistance, antimicrobial resistance is an area which I believe must be included in the scope of our activities. Two of the most reported reactions in VigiBase are 'medicine ineffective' and*

*'therapeutic response decreased' (which together account for more than 200,000 reports, with only eight other reactions more commonly reported). Until now, we at the UMC have not thoroughly analysed the underlying reasons for these reports, although we know from previous work on drug-drug interactions that the result of an interaction is often reported as a lack of effect. Could it be that these terms also are indicators of other therapeutic failure, as a result of counterfeit or sub-standard drugs, or because of resistance? This area of research is now being addressed as part of the Monitoring Medicines project; preliminary findings are very encouraging and show that we can identify reports of suspected antimicrobial resistance using clustering techniques.*

*The recent trend of introducing an International or National Day of Something on almost each day of the year trivialises what could otherwise be a good way of putting an important issue in the spotlight. Many of these days are just a commercial trick to market goods, e.g. the Swedish 'Cinnamon Bun Day' (although I must admit that I fell for it, and that it gave me pleasure to see my grandson, four years old, happily chomping a huge bun to celebrate that day, whenever it was). But let us focus on the important Days, like the World Health Day on April 7, when WHO this year highlight a policy package to combat the spread of antimicrobial resistance. I think this a good time to put antimicrobial resistance high on our agenda<sup>2</sup>, and to request that those who fund pharmacovigilance give us the resources we need to make our contribution to fight this growing, and very serious, problem.*

A handwritten signature in black ink, reading "Marie Lindquist".

1. Hogan MC, Foreman KJ, Naghavi M, et al. Maternal mortality for 181 countries, 1980–2008: a systematic analysis of progress towards Millennium Development Goal 5. *Lancet*, 2010 May 8; 375(9726):1609–23
2. See page 20 for UMC's involvement in one initiative to combat this problem.



## FEATURES

**4-5**

Our twice-yearly report on the WHO global database of individual case safety reports (ICSRs)

**6**

A look forward to the 2011 WHO Annual Meeting in Croatia

**7**

ARV safety monitoring in Africa

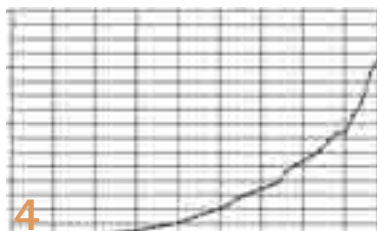
**12-13**

What does the UMC do? An introduction to the Product Management team

**14-15**

Recent Research at the UMC

**4**



**Over 6 million case reports now available in the WHO database**

The status of the global database of ICSRs

**8**



**Training around the world in the last few months**

Indonesia, Cuba, India, Jordan

## REGULARS

**2**

Director's Message

**8-11; 16-18**

News from Around the World – Indonesia, Cuba, Netherlands, USA, India...

**19-21**

News from Bredgränd – visitors and new staff

**22**

Publications – three new books about drug safety

**23**

Forthcoming courses and conferences

**12**



**The Product Management team**

Anders, Magnus, Monica and Ulrika present their work on VigiFlow, VigiSearch and VigiMine

**New books for the library**

Our suggestions include an important history of pharmacovigilance and a collection of medicines articles for the layperson

**18**



# VigiBase hits 6 million

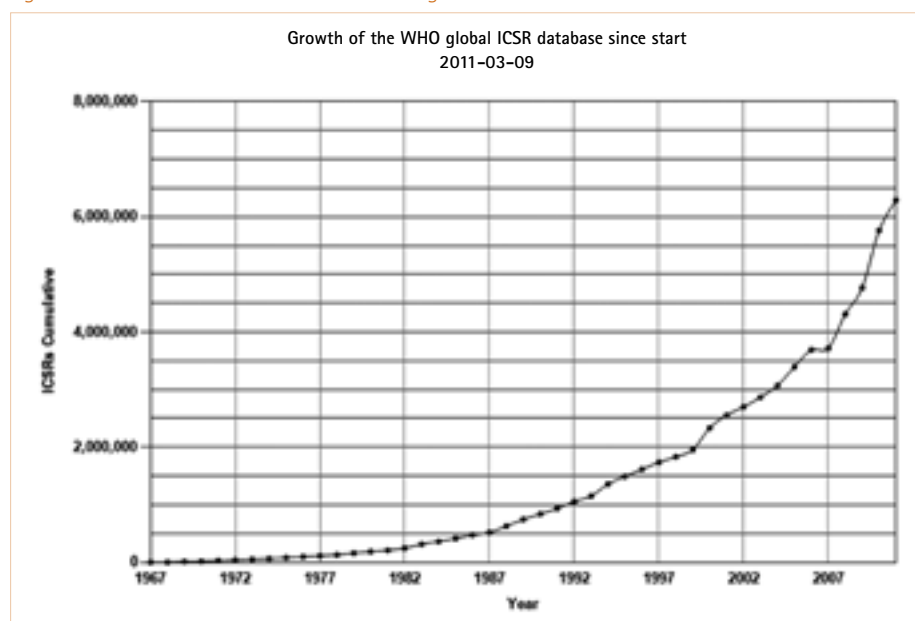
*Hanna Pedersen, Reporting, Analysis & Country Support*

Statistics on reporting to the WHO global ICSR database (VigiBase™) are presented twice a year in Uppsala Reports and on the UMC website.

of six million reports in VigiBase was reached in early 2011. During the course of 2010 the UMC received over 1,000,000 reports from member countries; this is the largest yearly increase so far. As reported in UR51 in

change are given on page 13 of this edition of Uppsala Reports). As of 9 March 2011, the total number of active ICSRs in VigiBase was 6,291,784 (see Figure 1).

Figure 1. Cumulative number of active ICSRs in VigiBase



## Cumulative Reporting

Thanks to the continuous submission of 'individual case safety reports' - ICSRs - from members of the WHO Programme for International Drug Monitoring, the milestone

October 2010, one reason for this rapid increase of ICSRs is the backlog of vaccine reports submitted to us by the US FDA. Another reason for the increase is a change in the validation of the ICSRs, which allows more ICSRs to be searchable (details of this

## Reporting rates and country distribution

Figure 2 shows the top 20 countries in terms of their reporting rates per million inhabitants per year, during the last five years. New Zealand is still at the top, but Singapore has climbed the list from 5<sup>th</sup> place in October 2010 when the last statistics were presented (see UR51), and now has the second highest reporting rate.

As shown in Figure 3, the proportion of ICSRs in VigiBase from different countries stays mainly the same as before, with USA accounting for nearly half of the database.

## Reporting format

As of March 2011, the number of member countries in the WHO Programme was 104, out of which 71 were reporting in the recommended ICH-E2B format, and of these 39 were using VigiFlow™ as their ICSR management system.

## Submission frequency

WHO Programme member countries are encouraged to submit ICSRs to the UMC on a regular basis, preferably once a month, but

Figure 2. Reporting rates (per million inhabitants and year) to the UMC

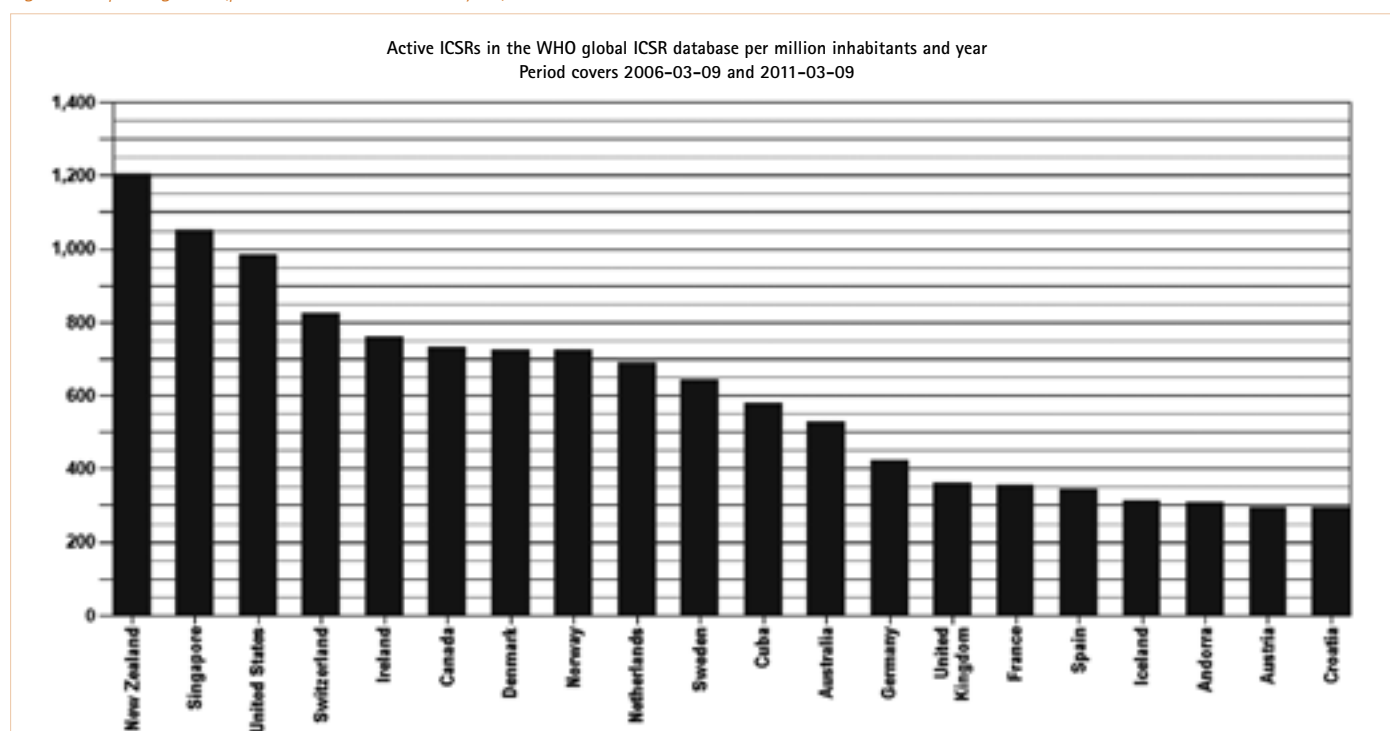
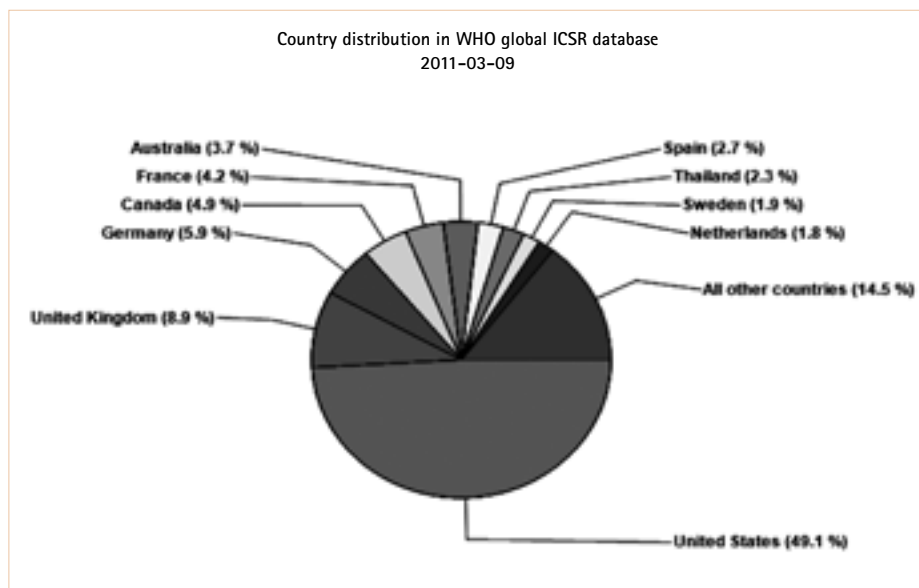




Figure 3. Country distribution of ICSRs in VigiBase as of March 2011



at least every quarter. This is important in order to keep VigiBase as complete and as useful as possible for all member countries. During the last 12 months, approximately 55% of the member countries fulfilled the minimum criteria of submitting ICSRs at least every quarter.

As shown in Figure 4, approximately 57% of the countries have sent reports during the last three months. However, 23 of the 104 countries in the Programme (22.1%) have not submitted any ICSRs to the UMC over the last 12 months, which sadly is an increase since October 2010 when the last statistics were presented (see UR51).

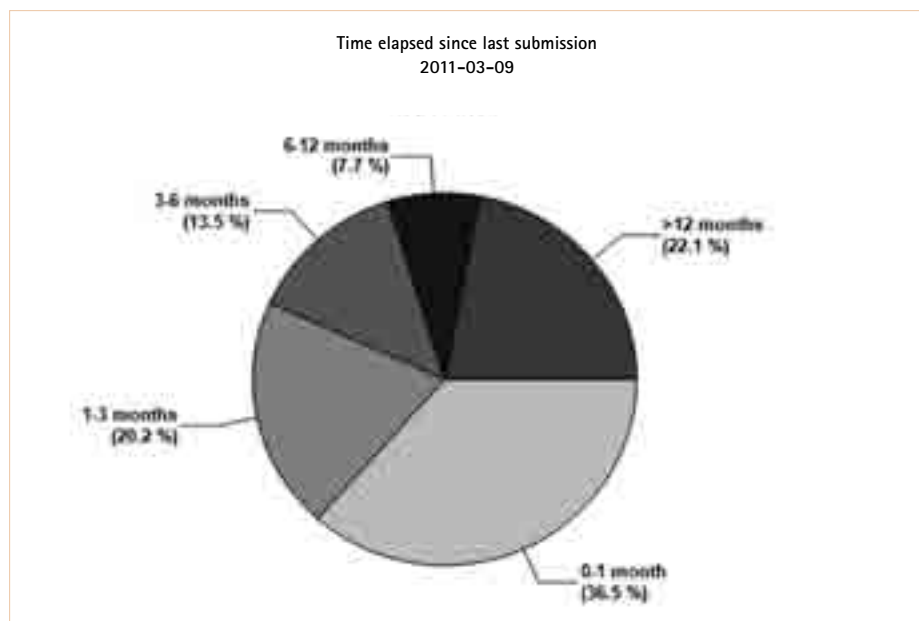
### Quality focus

A particular focus for the UMC during 2011 is to give feedback to member countries on

their report quality. This will mainly be done through the 'documentation grading', a system which measures the amount and quality of information provided on ICSRs as they appear in VigiBase. Two parameters have been defined: completeness and relevance. Report completeness is a quantitative measure determining to what extent an ICSR is completed. Relevance is a qualitative measure, still under development by the UMC.

To help evaluate the report completeness measure, a pilot version has been sent out to a few member countries and the UMC is now making adjustments based on their comments. In due course, the results of the report completeness measure will be communicated to all member countries on a regular basis.

Figure 4. Time elapsed since last submission (proportion of countries as percentage) as of March 2011



### Continued attention to the EEA

The focus on countries within the EEA (European Economic Area) that started last year will continue throughout 2011. The UMC is in the process of contacting some countries and offering site visits. The purpose of these visits is to establish a closer collaboration with the national centres. The UMC wishes to get a better understanding of the pharmacovigilance work performed in the countries, specific routines around ICSR reporting and also what kind of support the countries need from the UMC in order to comply with the reporting requirements.

### Pandemic influenza

The fifth and final UMC update on pandemic influenza vaccine safety monitoring (pdf report) was made available from the UMC website in March.

### Albania and Maldives

On behalf of the National Centre of Drugs Control in Albania, in January Dr Besnik Jakaj applied for associate membership for Albania in the WHO Programme for International Drug Monitoring. Following training and professional activities since mid-2009 a number of case reports of suspected ADRs have been received. Ms Fjoralda Prengaj is the officer in charge of pharmacovigilance activities.

Dr Jorge Mario Luna, WHO Representative for the Republic of Maldives, issued a request in March to WHO Geneva for the Maldives, to become an Associate member of the WHO Programme. Dr Ibrahim Yasir Ahmed, Director General of Health Services, Ministry of Health and Family, the Maldives has arranged for four staff from the Medicines and Therapeutic Goods Division (MTG) of the Maldives Food and Drug Authority (MFDA) to attend external training courses, and preliminary reporting activities have commenced.

# Dobrodošli u Dubrovnik!

Geoffrey Bowring

This was the message at the close of the 2010 National Centres Meeting in Ghana, when Viola Macolić-Šarinić, head of the Croatian pharmacovigilance programme and her colleague Darko Krnić presented – in their national dress – the venue of the 34<sup>th</sup> Annual Meeting of Representatives of the National Centres participating in the WHO Programme for International Drug Monitoring.

## Meeting invitation

Official invitations to heads of national pharmacovigilance agencies are currently being sent out, inviting countries in the WHO Programme to join together in the ancient medieval city of Dubrovnik, from 30 October – 2 November 2011 (pre-meeting tutorials and other courses on 30 October, main meeting from 31 October).

Dubrovnik is one of the most attractive and important visitor destinations on the Adriatic, although the capital of Croatia is Zagreb, in the centre of the country.

## Croatia in the Programme

The Croatians are rightly proud both of their sporting heroes and of their pharmacovigilance history; the former Yugoslavia joined the WHO Programme in 1978 with its base at the University Hospital in Zagreb. In 1992 the Republic of Croatia joined the WHO Programme for International Drug Monitoring anew. In offering to host the 2011 meeting, the Croatian Agency for

Medicinal Products and Medical Devices will in fact be bringing the Programme back to the site of the 8<sup>th</sup> Annual Meeting deliberations in 1985.

## Heritage

The old city of Dubrovnik, a UNESCO World Heritage Site, is justly renowned for its beautiful historic marble buildings set between lush mountains and the limpid sea. Although the ground plan of the Dalmatian Gothic and Renaissance architecture remains, much of it was renewed within the baroque style after a major earthquake in 1667. For several hundred years Dubrovnik was an independent and powerful maritime city-state (whose name 'Ragusa' was corrupted into the poetic English word for a merchant ship, 'argosy' – used by Shakespeare in his plays). Perhaps more of interest is one of the oldest pharmacies in Europe, dating from 1317, within the city's Franciscan monastery.

## Venue

The conference venue chosen for this year's meeting sessions is the 270-room Dubrovnik Palace Hotel, which has all the facilities expected of a 5\* hotel, and is located overlooking the Adriatic, outside, but within walking distance of the old town. The temperature in late October should still be around the upper teens centigrade: enough to enjoy an evening stroll along the Placa, the main street of the old city.

The draft agenda and more information regarding the meeting will be sent to national centres and placed on the Collaboration Portal shortly. Information on travel and accommodation will also be provided in due course by the UMC at the Vigimed section of the Collaboration Portal.

**So, "Dobrodošli u Dubrovnik!" – Welcome to Dubrovnik in 2011!**



# Monitoring the safety of ARVs

Sten Olsson

In 2009 WHO published 'A practical handbook on the pharmacovigilance of antiretroviral medicines' which advocates Cohort Event Monitoring (CEM) as the method of choice for safety follow-up of newly introduced antiretrovirals (ARVs), with spontaneous reporting to be available for routine monitoring. Although CEM programmes can provide reliable information, e.g. risk profiles and incidence rates, they also require considerable investment in terms of funding and human resources. A joint effort by the Department for HIV/AIDS and Quality & Safety of Medicines, WHO is currently testing best practices for the safety surveillance of ARVs in low- and middle-income countries. Efforts are now being made to field test several approaches and compare their performance in different settings; UMC is a technical partner in the implementation of the monitoring methods. The activities of the WHO initiative integrates well with the Monitoring Medicines project (see p. 16) which will add to the capacity building and training in best pharmacovigilance practice.



*Alex Nkayamba, Chris Duncombe, Henry Irunde and Alambo Mssusa at the Tanzania Food and Drugs Authority discussing the CEM implementation plan*

## Eldoret partnership

In March 2011 Chris Duncombe from the WHO Department of HIV/AIDS and I visited Kenya and Tanzania to assess the conditions on site for implementation of two different approaches to ARV safety monitoring. In Kenya Jayesh Pandit, head of pharmacovigilance at the Pharmacy and Poisons Board (PPB) joined us in the city of Eldoret in western Kenya where we visited AMPATH (Academic Model Providing Access to Healthcare) which is a partnership between Moi University School of Medicine, Moi Teaching and Referral Hospital and a consortium of US medical schools led by Indiana University.

## Recording reactions

AMPATH treats over 125,000 HIV-positive patients at 53 sites in and around Eldoret. We were provided with an overview of the AMPATH approach to HIV care which is very comprehensive and includes treatment of HIV-related TB, cancers and chronic diseases, departments of paediatrics and gynaecology and provides support to adequate food supply too. The general HIV testing of the population as a whole has been successful which is of major importance for HIV prevention. Electronic patient records are being kept but have so far not included details regarding toxic effects of ARVs.

Discussions were held with the AMPATH research team lead by Dr Paula Braitstein and Dr Sonak Pastakia regarding the feasibility of modifying the patient record system and using the Kenyan National ADR reporting form for recording of serious reactions related to ARV treatment. The challenge is to find a model of recording that does not over-burden the busy clinicians but allows sufficient information to be recorded for meaningful safety follow-up. Several models of data collection will be tested, including patient interviews. In addition to pharmacovigilance of ARVs there will be components of safety monitoring of TB and oncology medicines as well. The commitment and enthusiasm of the AMPATH team is promising for the successful outcome of the project, which is firmly integrated with the national pharmacovigilance system in Kenya.

## Agency meeting

Before leaving Kenya Chris and I also had a meeting with the management team of the drug control authority, The Pharmacy and Poisons Board (PPB), in Nairobi. We reported on the positive impressions of the Eldoret visit and discussed how PPB resources could be strengthened to cope with the demands of the expanding pharmacovigilance programme. We also discussed some details of the Monitoring Medicines project training that is planned to take place in Kenya in June 2011.

## Clinics in Dar-es-Salaam

The following day our journey continued to Dar-es-Salaam in Tanzania. A visit was paid to the Tanzania Commission for AIDS where current treatment policies, the medicine supply situation and the need for safety follow-up were discussed. This visit was followed by one to the WHO country office. Discussions were held with the acting WHO



*Sonak Pastakia, Chris Duncombe and Sten Olsson with the pharmaceutical officer and the clinical officer of the Mosoriot health centre outside Eldoret, Kenya*

Representative. A visit to two HIV/AIDS clinics in Dar-es-Salaam followed. Both have been selected to take part in the CEM programme planned to start in May-June, 2011. The implementation plan for the CEM programme was then discussed in detail with the responsible team at Tanzania Food and Drug Administration (TFDA), headed by Henry Irunde. Scientific, logistic and financial issues were covered. Once agreement was reached, a meeting was held with the TFDA Director General Hiiti Sillo.

## Positive impressions

Chris and I returned to Europe from our East-African trip with very positive impressions of the conditions presented at the planned monitoring sites. We are excited about the imminent implementation of the safety surveillance studies and we hope to gain unique data both on the relative merits of the chosen methods and approaches and about the safety profiles of the medicines being used in these low-income settings.



## Training in basic pharmacovigilance – Indonesia

*Siti Asfijah Abdollah and John McEwen*

Following closely on the participation of three representatives of the National Agency for Drug and Food Control, Republic of Indonesia (BADAN POM) in the training course for ASEAN countries in Singapore (see Uppsala Reports July 2010; page 9), the Agency hosted training in basic pharmacovigilance, held over four days (November 22–25) in Jakarta. The course was coordinated by an Organising Committee from the Sub Directorate of Surveillance and Risk Analysis of Therapeutic Products and Household Healthcare Product (Pharmacovigilance Unit Team). The course was opened by Mrs. Lucky S. Slamet, Deputy Director of the Agency for Therapeutic Products, Narcotics, Psychotropics and Addictive Substances Control, who presented details of planned initiatives for invigorating pharmacovigilance in Indonesia. These include promoting the role of clinical pharmacists in hospitals and introducing regulations about the reporting of adverse drug reactions by pharmaceutical companies.



*John McEwen, Mrs Lucky Slamet and Dr Roland Hutapea at the Opening Ceremony.*

### Presenters

On each of the first three days, training included a presentation by a local expert from the Department of Medicine, University of Jakarta. The experts and their topics were Dr. Nafrialdi, Drug-induced allergic and hypersensitivity reactions; Dr. Dante Saksono, Recognizing common adverse events of anti-diabetic drugs and their management; Prof. Dra. Arini Setyawati, Drug Interactions. John McEwen (Australia) gave a series of presentations, ranging from The Need for Pharmacovigilance to The Role of the Pharmaceutical Industry in Pharmacovigilance. The course included two practical exercises – identifying Risk Minimisation Activities able to be utilised in Indonesia and

making Causality Assessments of sixteen Individual Case Safety Reports.



*Participants hard at work in the causality assessment exercise*

### Broad participation

There were 45 participants – 16 staff of the Agency; 12 doctors and pharmacists from hospitals and academia and 17 staff of pharmaceutical companies (both multinational and local Indonesian). The participants came from a number of cities in Java and in Western Sumatra. A concluding speech was made by Drs. Roland Hutapea, Director for Distribution Control of Therapeutic Products and Household Healthcare Products who, with John McEwen, presented a Certificate to each attendee.

## 10<sup>th</sup> anniversary of Cuban unit

*Mariano Madurga*

From 13<sup>th</sup> to 16<sup>th</sup> December 2010 the 4<sup>th</sup> International Congress of Pharmacology and Therapeutic and 9<sup>th</sup> National Congress of the Cuban Society of Pharmacology were held in

that beautiful city, Havana, named the 'Caribbean Pearl' (<http://www.pharmacologyhavana.com>).

Under the umbrella of 'Pharmacology Havana, 2010', over 400 participants attended more than 170 sessions, workshops and symposia, with 25 plenary lectures. The organizer was the Cuban Society of Pharmacology, under the direction of its current President, Dr René Delgado.

On 12<sup>th</sup> December a pre-congress course was led by Professor Dr Gianni Tognoni (Institute for Pharmacological Research 'Mario Negri', Milan, Italy) on 'Strategies and methodologies to integrate pharmacovigilance and the outcome research: from primary healthcare to practical hospital'.

Over the four days the meetings ranged through pharmacogenetics, medication errors, pharmacoepidemiology, natural products, toxicology, vaccines, pharmacotherapy in cancer, childhood, pharmaco-economy, etc. One event in particular of note was the 5<sup>th</sup> International Workshop on Pharmacovigilance in the 10<sup>th</sup> Anniversary of Pharmacovigilance Cuban Coordinating Unit. In 2000 a coordination unit of the Cuban Pharmacovigilance System evolved into the Centro para el Desarrollo de la Farmacoepidemiología (CDF - Pharmacoe-epidemiology Development Centre) under the direction of Dr Julián Pérez Peña. At present, the Cuban pharmacovigilance system is the most efficient of the Latin-American systems. It is involved in interesting activities in several areas, within and outside of Cuba, under current coordinator Dr Gisela Jiménez. I wish another ten-year period could permit such activity to expand throughout all Latin-American countries.



*During Cuban Congress*



## A pharmaco-epiphanic visit to Utrecht

*Ola Caster*

Following an accidental visit to Amsterdam central station, I arrived in the marvellous medieval Dutch city of Utrecht just in time for Epiphany. However, my goal was not the grand dome with its free-standing tower, but the building right next to it, the so-called Faculty Club. This heart of Utrecht University was the venue for this year's 'Utrecht WHO Winter Meeting', a two-day mini conference jointly arranged by the Utrecht WHO Collaborating Centre for Pharmacoepidemiology and Pharmaceutical Policy Analysis, and the Department of Essential Medicines and Pharmaceutical Policies at WHO.



*The Faculty Club in Utrecht*

The overall theme of the meeting was pharmaceutical policy analysis, with the first day devoted to invited keynote speakers, and the second to presentations of submitted abstracts. The combination of a small and diverse group of participants, and well moderated sessions, allowed for open and stimulating discussions. The focus on broader issues such as what regulators' mandates really are and how they should be managed, rather than details of specific studies, was particularly enjoyable.

On the second day, I had the pleasure of orally presenting my abstract, which described some ongoing UMC research of relevance to the meeting. My presentation 'Decision-analytical benefit-risk assessment allowing for qualitatively related clinical outcomes' was well received and stimulated some discussion.

Whether the many similarities with Uppsala – the old university, the dome, the canal that looked like a small river, and the cyclists – made me feel at home, I do not know. However, I do know that I left Utrecht with a positive feeling, since both the meeting as such and the city were a pleasant experience.

## UMC Temporal Pattern Discovery on Trial

*Niklas Norén*

The Observational Medical Outcomes Partnership (OMOP) held its second annual symposium in Washington DC on January 11, 2011. OMOP is a public-private partnership funded by the Foundation for the National Institutes of Health in the United States. It aims to evaluate analytical approaches and data sources for safety surveillance in longitudinal observational medical data<sup>1</sup>.

As expected, results so far indicate that none of the automated analytical approaches for safety signal identification reliably highlights all true positives while excluding all true negatives. However, performance should reasonably be compared with what is achieved in routine screening of individual case safety reports rather than with customized epidemiological confirmatory studies. That said, perhaps the most striking result is the sensitivity of the findings to choices within each method such as control groups, risk periods, and eligibility criteria. This highlights important variability that may be hidden in single confirmatory studies using a pre-specified single design.

The Uppsala Monitoring Centre participates as a methods collaborator, having implemented its temporal pattern discovery methodology<sup>2</sup> for use and evaluation within OMOP. At the 2011 symposium OMOP's principal investigators summarized a major comparative study across data sets and methods. The evaluation is based on a set of nine drug-outcome pairs considered to represent true causal relationships (e.g. ACE inhibitors and angioedema) and 44 drug-outcome pairs used as negative controls (e.g. ACE inhibitors and aplastic anaemia). There was considerable variation in performance between methods and data sets, but no method or data set globally outperformed the others. Reassuringly, temporal pattern discovery as used by the UMC was one of the top performing methods in this limited study and was reliable across all data sets in which it was evaluated. Still, the OMOP study re-emphasizes the great room for improvement and the importance of effective triages in exploratory analysis of longitudinal observational data<sup>3</sup>. UMC will continue its efforts in this area, both within the OMOP study as it continues into 2011 and within the PROTECT sub-project on Signal detection in Electronic Health Records.

More information can be found at:

OMOP: <http://omop.fnih.org/>

OMOP 2011 Symposium:

<http://omop.fnih.org/OMOP2011Symposium>

PROTECT <http://www.imi-protect.eu/>

References:

- 1 Stang PE, Ryan PB, Racoosin JA, Overhage MJ, Hartzema AG, Reich C, Welebob E, Scarnecchia T, Woodcock J. Advancing the Science for Active Surveillance: Rationale and Design for the Observational Medical Outcomes Partnership. *Annals of Internal Medicine*, 2010. 153:600-606.
- 2 Norén GN, Hopstadius J, Bate A, Star K, Edwards IR. Temporal pattern discovery in longitudinal electronic patient records. *Data Mining and Knowledge Discovery*, 2010. 20(3):361-387.
- 3 Norén GN, Edwards IR. Opportunities and challenges of adverse drug reaction surveillance in electronic patient records. *Pharmacovigilance Review*, 2010. 4(1):17-20.

## Broad span of training in Delhi

*Ulrika Rydberg*

As part of WHO's continuing training strategy to help establish – at least – the minimum standards for pharmacovigilance as identified by WHO and the Global Fund, a course was held in Delhi from 21–25 February facilitated by many experts in the field. The facilitators included Shanthi Pal (WHO HQ), Ian Boyd (Australia), Anders Viklund and Ulrika Rydberg (Uppsala Monitoring Centre) and other staff from WHO (HQ and South-East Asia Regional Office, SEARO). The workshop also allowed some of the facilitators to participate in concurrent meetings with the Indian pharmacovigilance centre and with a pharmacovigilance training school in New Delhi.



*Participants in discussion in Delhi*

## Link with lymphatic filariasis

The increasingly broad nature of pharmacovigilance was acknowledged in the topics covered on the course, and included

discussion of medicine safety issues associated with the lymphatic filariasis public health programme. The training focused particularly on technical aspects, such as data management, causality assessment, product quality issues, communication, risk management, protocol for pharmacovigilance in neglected tropical diseases, and rational use of medicines.



*Shanthi Pal and Ian Boyd arrive with other participants at the WHO office in Delhi*

## Six countries take part

The participants from Cambodia, India, Lao PDR, Maldives, Nepal and Viet Nam represented the lymphatic filariasis programme and / or the pharmacovigilance programme in their countries. On the first day the participants presented the pharmacovigilance systems in their own countries. The take home message from this was the need of a two-pronged approach: from above with planning and government support and from below to get the actual reporters to understand the need for pharmacovigilance. Social activities at the course included a reception at SEARO and a much appreciated bus tour of New Delhi. On the last day of the course, participants presented draft plans of priority activities for the next 10 months to improve pharmacovigilance in their settings, with key deliverables, timelines and expected outcomes.

## Practical and useful

Overall, the majority of the participants thought the training course was excellent and found it very useful for continuing pharmacovigilance activities in their countries. The integration of pharmacovigilance in public health programmes was naturally of special interest to the participants. They also found VigiFlow, VigiSearch and VigiBase information and training of interest and suggested more time to be spent on these.

Two parallel meetings were conducted at the Indian national centre. One with more in-depth VigiFlow training was facilitated by Ulrika

Rydberg and Anders Viklund (see their travel report on page 17). The other was attended by Shanthi Pal and Valerio Reggi and looked at issues related to cohort event monitoring in malaria, developing geriatric pharmacovigilance, and methods for the monitoring of 'nano' medicines delivery systems.

## Mauritius – a vision and a mission

*Alex Dodoo*

Mauritius, a small but very prosperous country in the Indian Ocean may for some look like just an exotic holiday resort or a destination for lovers looking for a dream wedding event. Both do happen, but Mauritius, with its 1.3 million inhabitants, completely free public health service and fully supportive Minister of Health and government is sure to be an iconic place for global pharmacovigilance.

## Background

Even though Mauritius is part of Africa, it is one of the few countries in the continent which has completely eradicated malaria. The main causes of morbidity and mortality are

annually are used rationally and patients do not suffer unnecessarily. Another reason for the keenness to have a pharmacovigilance system is the increasing choice of Mauritius as a possible location for clinical trials, leading to the promulgation of a Clinical Trials Bill, which is passing through the National Assembly.

## Pharmacovigilance consultancy

Upon request from the Government of Mauritius, the World Health Organisation provided technical support for a 9-day consultancy on the establishment of pharmacovigilance in Mauritius. As consultant, I was representing the WHO Collaborating Centre for PV in Accra and of the Global Outreach Secretariat of the UMC. With a very diverse population (Indians, Africans, Chinese, Caucasians) and a public health service that is free to every citizen, there are bound to be drug-related problems which need to be understood. In addition, Mauritius has one of the most modern private hospitals in the world – the Apollo Bramwell Hospital which, with its seamless care electronic patient management system, offers the opportunity to undertake pharmacovigilance and pharmaco-epidemiological studies of this unique country and population.



*The Honourable Minister of Health and Quality of Life of Mauritius, Mrs S Hanoomanjee delivering her address at the Opening of the Pharmacovigilance Workshop*

diabetes and diabetes and cardiovascular complications. With a high GDP and a life expectancy of more than 70 years for both men and women, it may come as a surprise that Mauritius has no national pharmacovigilance system. This is not for want of trying; for several times in the past decade, attempts have been made to get a national pharmacovigilance system going without much success. However, the government is keen on having a pharmacovigilance system to ensure that the millions spent on medicines

## Workshops

During the consultancy, there were two one-day workshops on pharmacovigilance attended by over 110 physicians, pharmacists, nurses and technologists from both the public and private sector.

At the formal Opening Ceremony of the workshops, the Honourable Minister of Health and Quality of Life of Mauritius, Mrs S Hanoomanjee pledged the government's

commitment towards pharmacovigilance and patient safety in the country. She called for co-operation and collaboration between all sectors in Mauritius to ensure that the country has the best pharmacovigilance system anywhere in the world. She also called for an immediate development of the national pharmacovigilance framework and promised to provide the necessary support to ensure that Mauritius becomes a full member of the WHO Programme for International Drug Monitoring in the next few months.

### Commitment from all

Mrs Sheesha Jankee, Acting Director Pharmaceutical Services is the contact point for the activities in pharmacovigilance and is ably supported by Mrs Sarita Boolell of the same department. The WHO Liaison Officer for Mauritius Dr Munbodh, through whose office funding was secured, promised to assist the Ministry of Health and Quality of Life to set up a sustainable system. He entreated the Ministry to seek the support of the WHO office technically, and where feasible financially as well.

There was enthusiastic support from all stakeholders – academia, the public and private health sectors, the health professional associations, the media – towards pharmacovigilance in Mauritius, and with such good signs, the future definitely looks bright. Not just for pharmacovigilance in Mauritius but for pharmacovigilance in the Indian Ocean Arc and in the world at large. The WHO Programme is set for exciting times in the months ahead!

## UMC landing in Jordan

*Sten Olsson*

The Drug Information Association (DIA) invited the UMC to give a global and regional perspective on pharmacovigilance at the 9<sup>th</sup> Middle East Regulatory Affairs Conference in Amman, Jordan, held on 1–2 February, 2011. The pharmacovigilance session had two speakers. Before me, Dr Ghazi Saeed, Director of Pharmacovigilance Department, Saudi Food and Drug Authority, gave a comprehensive account of the considerable progress made after the formal launch of Saudi Vigilance two years ago. After my presentation there was a panel discussion in which Ms Nidaa Bawaresh from the Jordan national pharmacovigilance centre took part. The DIA conference had several other sessions with patient safety interest, e.g. on substandard and counterfeit medicines, and on so-called biosimilars. WHO was represented in these sessions by Dr Lembit Rägo.

After the conference I had the pleasure of spending half a day with Nidaa Bawaresh and Ms Rania Haddadin at the Jordan Food and Drug Administration. I was first given a description of the general features of the Jordan pharmacovigilance system. We then discussed many issues of topical and common interest, e.g.



*Jordan centre, from left Nidaa Bawaresh, Laila Jarrar and Rania Haddadin*

- Communications between the Jordan centre and the WHO Programme and how UMC could better serve the specific needs of the country.
- The need for regional collaboration in pharmacovigilance and training material and guidelines in Arabic. It was noted that Jordan has been collaborating in a project on harmonizing pharmacovigilance terminology in Arabic, initiated by the Moroccan centre.
- Terms of reference for the newly established Drug Safety Advisory Committee. I learnt with satisfaction that the committee was created because of the new WHO minimum requirements for national pharmacovigilance systems. I suggested that they might consider inviting a representative of the public onto the committee.
- Best practice in post marketing surveillance of biosimilars. I suggested that Risk Management Plans include a requirement for a Cohort Event Monitoring programme, using methodologies proposed by WHO.
- The recent interest of Public Health Programmes and Global Health Initiatives such as Global Fund to support development of systems for pharmacovigilance. The pharmacovigilance centre would approach the national tuberculosis programme for discussions.

My hosts gave a short outline of their action plan for development of pharmacovigilance which includes the establishment of regional centres and nomination of pharmacovigilance contact persons in private hospitals. I also had an opportunity to meet with the Director of JFDA, Dr Laila Jarrar where I requested at least one representative of the Jordan centre be sent to the 2011 annual meeting of the WHO Programme in Dubrovnik. She promised to consider the proposal seriously.

## UMC at Ghana FDB

*Sara-Lisa Fors*

On March 21<sup>st</sup> Helena Wilmar and I had the great pleasure to visit the Safety Monitoring Department at the Food & Drugs Board (FDB) in Accra, Ghana.

Ghana has been a member of the WHO Programme since 2001 and as they are also using VigiFlow since 2004, this was a big opportunity to follow-up on their experiences. After a brief presentation about the UMC and the WHO Programme, an interactive VigiFlow session was held to update the team on old and new functions in the system. In addition, specific questions were discussed and valuable suggestions on how to improve the output from VigiFlow were presented. Since the centre did not use VigiSearch actively, we also gave a basic demonstration of the search tool.



*(from left) Helena Wilmar, Abena Asamoah-Amoakohene, Mimi Delese Darko, George Sabblah, Yvonne Adu-Boahene, Adela Gwira, Sara-Lisa Fors*

Overall we had a very productive and educational day at the centre and we would like to thank the Head of the centre Dr Mimi Delese Darko and her team for their generous hospitality.



# Pharmacovigilance Product Management

*Ulrika Rydberg and Monica Plöen*

In Uppsala Reports 51, the Report Analysis & Country Support (RACS) section of the Pharmacovigilance Services department was introduced. Now it is time to introduce the Product Management section of the same department.

## Purpose of product management

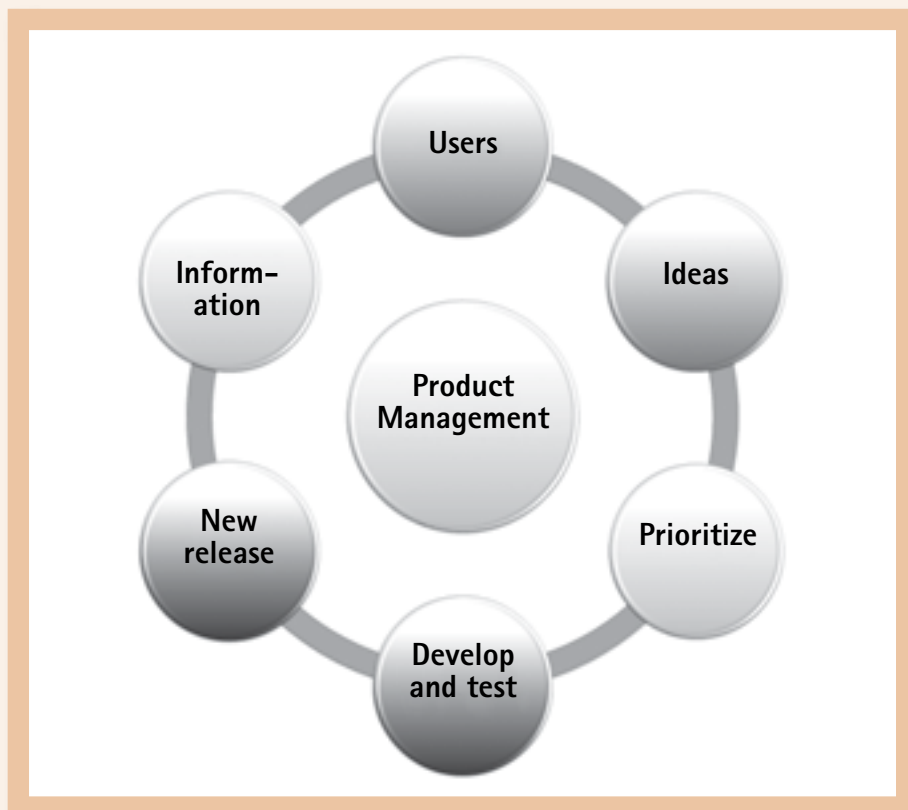
The primary function of our section is to be the main hub for the collection and implementation of user requirements and user information regarding the pharmacovigilance systems provided by the UMC; VigiFlow™, VigiSearch™/VigiMine™, PaniFlow™ and CemFlow™. Product management is an important part of a product's life-cycle, and the need for a dedicated section taking care of these tasks within the Pharmacovigilance Services department is the reason for creating this Product Management section.

## How we fulfil our purpose

The activities we perform to achieve our purpose can be described as a cycle that starts and ends with the users of our products (see picture). To begin the cycle, we ask for and collect suggested improvements and ideas from the users (both externally and internally). These ideas can be about an existing system or a new system that does not as yet exist. The next step is to sort and prioritize all requests in collaboration with other sections at the UMC. PDQ (Product, Development and Quality department) will have a view on what is possible due to technical and time constraints; RACS (and the external users) on what is most important for them. All collected information needs to be considered and very tough decisions need to be taken when two very good ideas compete for the same limited development time.

## The Product Management section consists of:

- Monica Plöen – section manager and product manager for VigiFlow, VigiSearch/VigiMine, CemFlow and PaniFlow
- Magnus Wallberg – head, systems development strategies (works half his time for Product Management section and the rest for PDQ)
- Ulrika Rydberg – product specialist, VigiFlow
- Anders Viklund – product specialist, VigiSearch/VigiMine



*The continuous cycle of improvement and information-sharing described in the text.*

During the development period, we represent the users' wishes towards the development team. This demands a good understanding of what the users want done and sometimes continuous discussions with the users during this phase. All development should be tested to check that the intent of the suggested improvements has been fulfilled in the new version.

Before, or at the release of a new version of a product, all users need to be informed about the changes. This is done by making release notes available and updating user guides. It can also be followed-up by articles in Uppsala Reports (see opposite page) for information about the latest changes in VigiSearch/VigiMine). Other information material may also need to be updated.

Informing users about our products also includes writing and updating information and educational materials. These can be white papers, PowerPoint slides, e-Learning courses and so on. We also take part in courses as teachers and help with support if users have problems using our products. In addition, we are involved in the licence agreements that need to be signed to get access to most of our products.



*Ulrika, Anders, Monica, Magnus – the*



## Selected topics in more depth

Some of our tasks deserve a deeper presentation than the overview given above.

### User groups

One of the most important events for us during the year is when we can meet several users face-to-face at the user group meetings. These meetings are a valuable forum for gathering feedback and recording user experiences. So far, user groups exist for VigiFlow and VigiSearch/VigiMine. User group meetings are usually held in conjunction with the annual national centres' meeting for the WHO Programme since this is a great opportunity for many countries and users to be represented together at the same time. The next occasion to attend will be in Croatia later this year, so make sure to put this event in your diary if you want to talk to other users and meet us from the UMC and influence the development of our products!

At the user group meeting in Uppsala 2008, we promised to set up virtual user groups where users can discuss their needs with us at the UMC and with each other over the Internet. At last, we now have the UMC Collaboration Portal, which hosts not only the new Vigimed (see page 16 of UR52), but also a new VigiFlow user group site. Invitations to join this site are being sent out as this article goes to press, however, if you

want to be part of this web-based group and have not received an invitation do not hesitate to contact us.

### Training

We are involved in training activities on all levels regarding our products, both internally and externally. Examples of where we participate are; at the biannual Uppsala pharmacovigilance course, courses at the Uppsala University and other events where UMC is invited to participate. A recent instance can be found in the travel report by Anders and Ulrika on page 17. Another example is when UMC staff present CemFlow training jointly with WHO-HQ. We also help our colleagues in keeping training material they use regarding our products up-to-date and correct.

An important training initiative which we are involved in is the VigiFlow e-Learning course; this is in collaboration with the UMC Training Officer, Anna Hegerius. To offer courses such as this over the web is an important – and 'environmentally friendly' – alternative, and allows users to learn on a practical level without needing a teacher on site. For the future we hope to be able to develop more use of this kind of technique.

## In the pipeline

Currently we are working on a new version of VigiSearch/VigiMine. Input from users was collected at the national centres' meeting in Accra (November 2010), and during country visits since then. Over the coming year a test panel will be convened where we will seek more input from users to refine the new search tool while the development is progressing.

If you would like to take part please let us know.

A new version of CemFlow is under development. The biggest change will be using Microsoft Silverlight to allow for off-line data entry. CemFlow is also being adapted to capture information about HIV/AIDS treatment (see page 22 in UR52).

Still at an early planning stage is the new version of VigiFlow, expected to be released late in 2011.

If you would like to get in touch with us you can contact us via [vigiflow@who-umc.org](mailto:vigiflow@who-umc.org) or [info@who-umc.org](mailto:info@who-umc.org).

# Making searching better!

Monica Plöen

## Two key improvements

A major change in the February 2011 release of VigiSearch has been to make more data available during searches; an additional 400,000 ICSRs (individual case safety reports) are now available for searches in VigiSearch and VigiMine. The other improvement has been that, for the import process of ICSRs from the National Centres into VigiBase, many validation steps have been performed, to check the consistency of data being entered.

### Date consistency

The validation of ICSRs submitted to VigiBase has included steps to check date consistency. For example, the 'date of onset of reaction' cannot logically come before the 'start date of drug administration'. This dubious pair of data may now be accepted in the validation step, because we feel that these ICSRs might still have important information, and it is left to the person undertaking an analysis to interpret the information.

To be noted also is that some countries, if they are not aware of the actual date, are using an algorithm when coding the dates on their ICSRs, for example:

20090801 – 1<sup>st</sup> of a month can mean sometime during the month

20090101 – 1<sup>st</sup> of January can mean sometime during the year but both can of course also be real dates as well.

## Drug reported as 'interacting'

If an ICSR has a drug reported as interacting, the rule that has been applied hitherto was that there needed to be at least two drugs reported as involved in the interaction. From now on ICSRs are searchable if they have only one drug reported as interacting.

These examples, which caused a number of ICSRs not to be searchable before will now make an additional 400,000 ICSRs available for searches in VigiSearch and VigiMine.

All National Centres have access to VigiSearch/VigiMine as part of their membership of the WHO Programme for International Drug Monitoring, and all can access the over 6 million ICSRs as a tool in their work. If any still do have not access and would like to get it, please contact [vigibase@who-umc.org](mailto:vigibase@who-umc.org).



# Research on adverse drug interactions

Johanna Strandell

The Uppsala Monitoring Centre has a long-standing interest in developing better methods for drug interaction surveillance and has recently published two papers on this topic. The first article sets out our initial efforts to develop a system for systematic drug interaction surveillance in individual case safety reports (ICSRs). This paper covers a broad basis of data including clinical data and the disproportionality measure,  $\Omega$  (Omega), to highlight adverse drug interactions, i.e. a problematic drug combination resulting in adverse drug reactions (ADRs).<sup>[1]</sup> The second article is an explorative study identifying drug combinations most frequently co-reported as interacting in VigiBase and categorising them according to the drug interaction mechanisms.<sup>[2]</sup> The articles are summarised below.

Collections of ICSRs are underutilized for the systematic surveillance of adverse drug interactions, even though drug interactions are responsible for a large proportion of ADRs.<sup>[3-5]</sup>

Historically, the most precise way to indicate a suspected drug interaction (a problematic drug combination) on a report has been to assign two drugs as interacting. However, only 0.5% of all reports in the WHO Global ICSR database, VigiBase, include such information. When the E2B format and MedDRA terminology were introduced additional possibilities to explicitly describe a suspected interaction on a report were established: in the case narrative, or as an ADR term referring to a drug interaction. Even so, such information is rarely listed; from 1990-2009 only 0.7% of all reports in VigiBase exhibit one of the following patterns: two drugs listed as interacting, or an interaction noted in the case narrative, or as an ADR term referring to a drug interaction.

In the process of early discovery of signals in collections of ADR reports there are three main approaches: case-by-case analysis, identifying clinically strong cases which generate further investigations, systematic screening using measures of disproportionality

and specific criteria, or filters, for instance screening all cases resulting in death. However, these approaches may be combined. For drug interaction safety signals, a large proportion of published material has so far been generated from regular case-by-case analysis by national or regional centres worldwide.<sup>[6-8]</sup> However, in VigiBase, containing more than 6 million reports, such an approach is not alone effective. In terms of systematic screening for potential drug interactions, the published literature has so far primarily focused on the development of disproportionality measures. In VigiBase, a measure referred to as  $\Omega$  (Omega) is used.<sup>[9]</sup> This measure highlights when co-reporting of two drugs and one ADR is greater than expected related to the background in the dataset (see box below for more detail). The literature is still limited regarding selection strategies to detect drug combinations of particular interest in terms of potential drug interactions.

## Reporting patterns indicative of adverse drug interactions – a systematic evaluation in VigiBase

Strandell J, Caster O, Bate A, Norén GN, Edwards IR. *Drug Safety* 2011; 34(3):253-266

This study is our first effort to develop a comprehensive system for automatic screening of potential drug interactions reported on ICSRs in VigiBase. We were interested in this analysis to systematically study reporting patterns in VigiBase which characterise adverse drug interactions before they become known in the literature. We considered both clinical information and the disproportionality measure,  $\Omega$ .

In previously published drug interaction signals, certain reported information has strengthened the likelihood that a suspected drug interaction might have caused the adverse reaction in individual cases. Such information is:

- metabolism via the same cytochrome P450 (CYP) enzyme,
- two drugs explicitly reported as interacting,
- suspicion of interactions as noted by the reporter in a case narrative,
- through an ADR term referring to a drug interaction,

- a resolution of the ADR upon withdrawal of either of the two drugs, and
- plausible time relatedness of drug therapy.

In addition to these, ADR terms of altered therapeutic effect have also been proposed as potentially indicative of drug interactions.

In this analysis, the clinical information mentioned above and the lower limit of  $\Omega$ 's credibility interval ( $\Omega_{0.25}$ ) (these parameters are referred to as indicators) were systematically studied in a reference set of adverse drug interactions and drug pairs not known to interact. The reference set was constructed from information in Stockley's *Drug Interactions Alerts*. We studied the differences in reporting patterns for adverse drug interactions before they were generally established and ADRs to drug pairs that are not known to interact in VigiBase. The analyses were carried out with and without concomitant medicines.

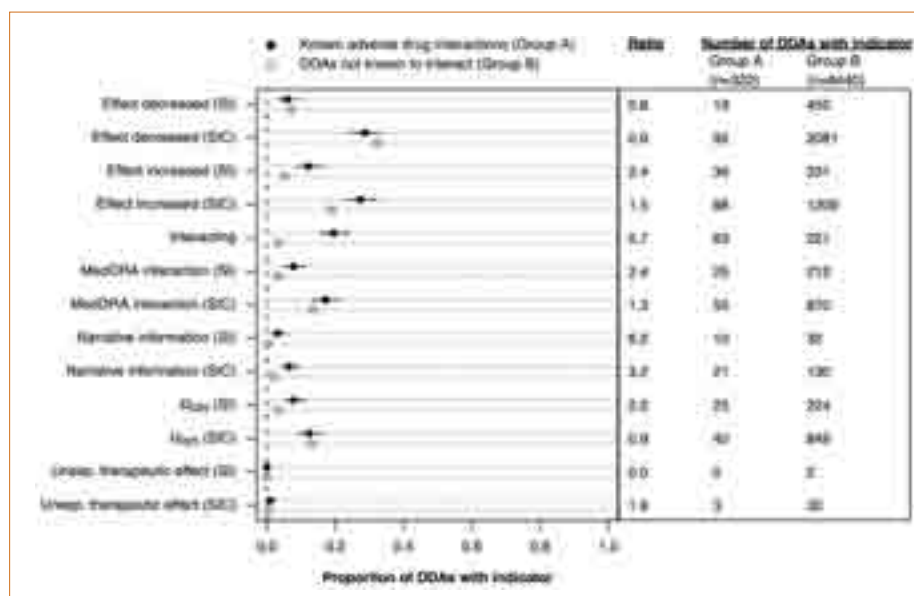
There were five reporting patterns that were highlighted as particularly strong indicators

of adverse drug interactions before they become known:

- suspicion of interaction as noted by the reporter in a case narrative,
- in the assignment of the two drugs as interacting,
- suspicion of interaction as noted through an ADR term,
- the co-reporting of effect increased;
- and finally an excess total number of reports on the ADR together with the two drugs as measured by  $\Omega$ .

We found that the inclusion of concomitant medicines led to a larger number of true adverse drug interactions being highlighted, but at a substantial decrease in specificity of most indicators.

From this study we can conclude that ADR reports carry valuable information indicative of what becomes recognised as an adverse drug interaction in the future. Our results demonstrate that reported suspicions of adverse drug interactions and  $\Omega_{0.25}$  each



provide unique information to highlight adverse drug interactions before they become known in the literature.

Figure shows the proportions (with 95% confidence intervals) of DDAs (drug-drug-ADR)

occurring with indicators that may independently drive suspicion of an adverse drug interaction, as they provide clinical information to suggest that a suspected drug interaction has occurred among DDAs constructed from known adverse drug

interactions and from drug pairs not known to interact, respectively. The ratio between the groups, and the numbers behind the proportions, are given in the text.

SI = using reports where the drugs are reported as suspected or interacting

SIC = using reports where the drugs are reported as suspected, interacting or concomitant

$\Omega$  (Omega) is a shrinkage observed-to-expected ratio for the number of reports of the ADR with the two drugs together.  $\Omega_{0.95}$  is the lower limit of a 95% credibility interval for  $\Omega$ .

When  $\Omega_{0.95}$  exceeds zero the DDA is reported reliably more often than expected if the attributable risks of the ADR from each drug would be additive.<sup>[9]</sup>

## Pharmacodynamic and pharmacokinetic drug interactions reported to Vigibase, the WHO Global Individual Case Safety Report Database

Strandell J, Wahlin S. *Eur J Clin Pharmacol*. Online first 21 Jan 2011

In this study we investigated drug combinations most frequently co-reported as interacting in Vigibase, and categorised them according to the drug interaction mechanism.

In total, 3766 case reports of drug interactions from 47 countries were identified. Of 123 different drug combinations 113 were described in the literature to interact. Of these 46 (41%) had a pharmacodynamic mechanism, 28 (25%) had a pharmacokinetic mechanism, 18 (16%) exhibited a combination of both types, and 21 (19%) had an unidentified mechanism. The pharmacodynamic drug interactions primarily concerned pharmacological additive effects whereas enzyme inhibition was the most frequent pharmacokinetic interaction. Of the interactions acknowledged to a specific enzyme, cytochrome P450 (CYP) 3A4 and 2C9 were particularly frequent, accounting for 42% and 24%, respectively.

The reviewed combinations primarily concerned well established drugs, i.e. drugs that have been marketed for more than 10 years. Among pharmacodynamic interactions antithrombotic agents were most frequent, which was reflected by the overall ADR pattern reported for these in Vigibase. Pharmacokinetic interactions involved a range of drugs and reported ADRs. However, alterations in therapeutic effect were common for these interactions. The ADRs reported for verified interactions were well associated with the expected effect of the drug causing the ADR.

From this study we can conclude that the scope of drug interactions reported on globally collected ADR reports is broad and concerns interactions with both pharmacokinetic and pharmacodynamic mechanisms. Finally, reports of suspected adverse drug interactions often concern serious threats to patients' safety, particularly related to use of high-risk drugs such as warfarin and heparin.

## References

1. Strandell J, Caster O, Bate A, Norén N, Edwards IR. Reporting Patterns Indicative of Adverse Drug Interactions: A Systematic Evaluation in Vigibase. *Drug Safety*. 2011 Mar 1; 34(3):253-66.
2. Strandell J, Wahlin S. Pharmacodynamic and pharmacokinetic drug interactions reported to Vigibase, the WHO global individual case safety report database. *European Journal of Clinical Pharmacology*. 2011 Jan 21.
3. Davies EC, Green CF, Taylor S, Williamson PR, Mottram DR, Pirmohamed M. Adverse drug reactions in hospital in-patients: a prospective analysis of 3695 patient-episodes. *PLoS One*. 2009; 4 (2):e4439.
4. Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, et al. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ*. 2004 Jul 3; 329(7456):15-9.
5. Leone R, Magro L, Moretti U, Cutroneo P, Moschini M, Motola D, et al. Identifying adverse drug reactions associated with drug-drug interactions: data mining of a spontaneous reporting database in Italy. *Drug Safety*. 2010 Aug 1; 33(8):667-75.
6. Ohlsson S, Holm L, Myrberg O, Sundström A, Yue QY. Noscipine may increase the effect of warfarin. *British Journal of Clinical Pharmacology*. 2008 Feb; 65(2):277-8.
7. Yue QY, Strandell J, Myrberg O. Concomitant Use of Glucosamine Potentiates the Effect of Warfarin. *Drug Safety*. 2006; 29(10):911-1010.
8. Netherlands Pharmacovigilance Centre, Lareb. Signal [serial on the Internet]. July 2009; Accessed from: <http://www.lareb.nl/kennis/zoeksignalen.asp?lg=EN>.
9. Norén GN, Sundberg R, Bate A, Edwards IR. A statistical methodology for drug-drug interaction surveillance. *Statistics in Medicine*. 2008 Jul 20; 27(16):3057-70.

# Medication Errors training in Rabat

Ennita Nilsson

Twenty representatives from ten national pharmacovigilance centres received training on medication errors at the Morocco pharmacovigilance centre (CMPV) in Rabat this March. The training was organized under the Monitoring Medicines project funded by the European Commission (FP-7), aimed at identifying preventable safety problems associated with medicines.

The countries attending were Morocco, Kenya, Iran, New Zealand, Thailand, Spain, Switzerland,

Nigeria, Brazil and Tunisia. Two project partners, David Cousins from National Patient Safety Agency and Rachida Soulaymani and her team CMPV organised and facilitated the training. David U President and CEO of the Institute for Safe Medication Practices Canada was the invited facilitator.

The focus was on identifying, analysing, and preventing medication errors, aiming to encourage national pharmacovigilance

centres to expand their activities and to learn more from existing data through:

- Hands-on practicalities, in order to improve reporting of medication errors and most importantly to learn about various prevention methods from best practice.
- Increase the capacity of national pharmacovigilance centres to analyse reports of medication errors
- Increase the capacity of national centres to identify preventable medication errors and take action to change the behaviour of health care providers in order to minimize their recurrence.

Following this work a summary scientific paper on preventable medication errors will be developed and submitted to an appropriate journal of patient safety. National pharmacovigilance centres will analyse reports of medication errors and further awareness-raising will take place. This will stimulate co-operation between national pharmacovigilance centres, the World Alliance for Patient Safety and stakeholders identified during the training.



*The international group which undertook medical errors training in Rabat*

## ICDRA backs pharmacovigilance

Shanthi Pal

A 14<sup>th</sup> International Conference of Drug Regulatory Authorities (ICDRA) was held in Singapore from 30 November to 3 December, with 364 participants from over 90 countries. The meeting, marking 30 years of this forum of national, regional and international medicines regulation, was hosted by the Health Sciences Authority of Singapore in collaboration with WHO.

### Pharmacovigilance

Pharmacovigilance was on the delegates' agenda. The focus was on interest in the field from global health initiatives, particularly those supporting public health programmes. The view was expressed that introducing the basic principles of pharmacovigilance in resource-limited settings via such programmes was a key step. The pharmacovigilance workshop underlined the importance of pharmacovigilance in medicines regulation; it also highlighted the importance of pharmacovigilance in informing policies in priority disease programmes.

The session was moderated by Cheng Leng Chan (Singapore) and Luisa Helena Valdivieso (Venezuela), with presentations:

- Minimal capacity for vaccine vigilance (Murilo Freitas Dias, Brazil)
- Working with public health programmes: addressing minimum requirements for pharmacovigilance (Helen Byomire, Uganda)
- Recent developments in monitoring of adverse drug reactions in China (Min Yan, China)
- Pharmacovigilance in the national HIV/AIDS treatment programme (Olena Matveyeva, Ukraine).

### Recommendations

This workshop urged WHO to:

- make pharmacovigilance a key topic of the next ICDRA
- reinforce recommendations that the pharmacovigilance system be nested within the healthcare system to address multiple growing safety needs
- develop robust strategies for sharing safety information

- target training on risk communication and crisis handling and develop platforms for sharing good pharmacovigilance cases
- integrate the minimum core requirements for vaccine monitoring through the WHO Programme for International Drug Monitoring.

and that WHO Member States should:

- integrate pharmacovigilance into proposals to the Global Fund to fight AIDS, Tuberculosis and Malaria, and other donors
- implement at least minimum core requirements for pharmacovigilance as integral components of drug regulation and paramount in safeguarding public health
- ensure good collaboration between pharmacovigilance centres and public health programmes.

A full meeting report appears in *WHO Drug Information* Vol. 25, No. 1, 2010.



## UMC in India

*Anders Viklund and Ulrika Rydberg*

As newly appointed Product Specialists for VigiSearch/VigiMine and VigiFlow, respectively, we (Anders Viklund and Ulrika Rydberg) set out to travel to New Delhi. This would be the first time to Asia for both of us, although Ulrika should have gone to New Delhi in November of 2010; that trip had to be replaced with videoconferencing. For these reasons, this trip generated some extra excitement and when our plane failed to start on schedule, even nervousness. However, everything worked out and we landed at the Indira Gandhi International Airport as planned.



*YK Gupta, head of the Indian pharmacovigilance system, speaking during the intensive VigiFlow training at the Pharmacovigilance Programme of India National Coordinating Centre*

The first goal was to teach at the Inter-regional Pharmacovigilance Training Course in New Delhi (see page 9–10). We participated on the first two days of this five-day course and were very impressed by the plans and accomplishments of the participating countries. On the second day, most of the morning was used for giving the participants a solid base for understanding the ICSR management system VigiFlow. On the afternoon it was time for them to learn how to search the WHO Global ICSR database VigiBase by using the VigiSearch/VigiMine tools and something about the statistical basis of the IC values. The course participants kept us alert with many intelligent questions and promptly found the tricky parts of the training assignments given them.

On the third day, we went to the All India Institute of Medical Sciences (AIIMS) to meet with the newly established Indian pharmacovigilance centre – the Pharmacovigilance Programme of India National Coordinating Centre (PvPI NCC). (See page 10 in UR52 for more information about this initiative to re-establish pharmacovigilance in India!) At the PvPI NCC, we provided more in-depth training in using VigiFlow for management of ICSRs on a national level and

discussed their impressive progress since the start in November. In total they have entered more than 6,000 ICSRs into VigiFlow, thereby entering more than half of the 11,000 reports collected so far. It was very exiting to meet these people and talk to them about their experience in using VigiFlow as a national database and ICSR management system.

During this short trip we have met current and potential new users of the systems we see mostly from the inside in our daily work at the office. We also had the privilege to listen and learn from those with greater knowledge and/or different perspectives on pharmacovigilance. Together, this has made for a rich soil for new ideas and thoughts and inspired

us with new enthusiasm for our continued work with our respective systems and reminded us of the goal of our daily work and for pharmacovigilance – the safe use of medicines.

## 8<sup>th</sup> ACSoMP

*Sten Olsson*

The WHO Advisory Committee on Safety of Medicinal Products (ACSoMP) held its 8th annual meeting in Geneva from 31 March – 1 April 2011. Lembit Rätgo, Coordinator of the Quality and Safety of Medicines unit at WHO opened the meeting and welcomed two new members of the Committee, Dr Yen Min, P.R China, and Claudia Vaca, Colombia.

The meeting, co-chaired by Ken Hartigan-Go and Gunilla Sjölin-Forsberg, made some recommendations for WHO and UMC to consider, regarding:

- The need for further follow-up studies to verify or refute the current signal from African countries regarding extrapyramidal disorders associated with the combination of artesunate and amodiaquine in malaria treatment

- Widening access to data in VigiBase and rewording the Caveat document accompanying such data when released to third parties
- Establishing an editorial committee and involving ACSoMP in the quality assurance and maintenance of the pharmacovigilance toolkit
- The importance of reporting unexpected lack of effectiveness of medicines to VigiBase, also for the identification of possible antimicrobial resistance particularly with the availability of new analytical tools developed by the UMC
- Methods to assure quality of pharmacovigilance training offered particularly with the background of the demand anticipated from low- and middle-income countries applying for funds for pharmacovigilance development from Global Fund
- Integration of efforts and databases between the WHO Drug Monitoring Programme and vaccine AEFI monitoring by immunization programmes currently considered by WHO in the so-called Blueprint project
- A strategy for improving outreach and country support through establishment of centres of excellence and WHO Collaborating Centres.



*Dr Yen Min and Claudia Vaca, new members of ACSoMP*

The Committee also received updates on activities and projects previously presented to it including:

- Activities at CIOMS and collaboration with WHO
- Pharmacovigilance activities in the WHO HIV/AIDS and TB Programmes
- The Monitoring Medicines project
- A strategy for the WHO pharmacovigilance programme
- Development of pharmacovigilance indicators

Further details of the recommendations of the ACSoMP meeting will be given in the *WHO Pharmaceuticals Newsletter*.

## The Global Vaccine Safety Blueprint Project

*Jerry Labadie*

According to WHO assessments, sixty percent of the world's population live in countries with non-functional vaccine safety systems (WHO unpublished data). Most of those countries are among the least developed economically. Vaccines that were introduced in these countries used to have well-established safety profiles because they were first introduced in countries with effective vaccine safety systems.

Increasingly vaccines are introduced in countries with non-functional vaccine safety systems that have not been previously used in parts of world with effective vaccine safety systems. With support from the Bill and

Melinda Gates Foundation, WHO launched the Global Vaccine Safety Blueprint Project in 2010. This initiative aims to develop a concerted global approach to improve vaccine safety assessment and response systems.

In the first stage, the current performance of vaccine pharmacovigilance systems in low- and middle-income countries and of existing inter-country and global support mechanisms will be analyzed. Following this, a 'blueprint' for a global, regional and country level vaccine safety assessment and response system will be developed. In this blueprint, indicators of the minimal capacity needed to ensure vaccine safety will be defined. In

addition a strategic plan for enhancing global vaccine safety activities will be proposed. But the focus will be on bringing national vaccine safety capacity in the world's poorest countries up to the minimal capacity level. To achieve this, a coordinated effort of the major stakeholders in vaccine safety around the world will be needed. As a global stakeholder in vaccine safety monitoring UMC has contributed to several surveys. Other surveys in the analysis of current performance were aimed at regulators and vaccine manufacturers.

## Global Collaborative Network for Vaccine Safety Studies

*Jerry Labadie*

A meeting to explore the creation of a global collaborative network for vaccine safety studies took place on 28-30 March in Annecy, France. The theme was that vaccine safety issues must be addressed rigorously and in a timely fashion, otherwise a loss of confidence and decreases in vaccine acceptance occur.

In several high-income countries and regions, databases containing patient-based longitudinal data are being compared with spontaneous reporting to test possible

strengthening of vaccine safety signals. One such example is the VAESCO consortium of several European countries that currently investigates the association between narcolepsy and vaccinations.

In situations where high-quality computerized databases are absent or resources are limited alternative strategies for analysis are needed. Some of the objectives of this meeting were: to bring investigators together from low- to high-income countries, to share information and

experiences, to explore and identify ways forward to a global collaborative vaccine safety network.

## UMC staff meets colleagues in Accra

*Helena 'Ama' Wilmar*

In March 2011, the pharmacists Sara-Lisa Fors and Helena Wilmar (UMC *Country support team, PV Services Department*) visited the UMC-Africa (UMC-A) in Accra, Ghana. The UMC team later on grew to four staff when joined by system developers Magnus Wallberg and Martin Strömberg (with the purpose of training in Cohort Event Monitoring/ CemFlow).

On the first day we discussed strengthening the collaboration and streamlining our joint work with current/potential African members of the WHO Programme. This was the first meeting of its kind together with the core staff. The newly launched UMC Collaboration Portal will certainly be a key in the future communication between the two teams, with

easy access to shared documents, to upload shared presentations for training needs, to share calendar bookings etc.

Day two covered VigiFlow, with updates from the latest release (December 2010) and specific training for UMC-A staff. Both basic (report entry) and more advanced training ('Search & statistics' and other ICSR management features) were given. During the afternoon Magnus Wallberg and Martin Strömberg covered some specific technical areas.

Days three and four focused on CEM training, CemFlow demonstration and 'hands-on', as well as analysis and access to the collected data. Not only UMC-A staff participated, but



*UMC staff from Uppsala and Accra*

also staff from the Food & Drugs Board (FDB) and two statisticians from INDEPTH Effectiveness and Safety Studies of Anti-malarial Drugs in Africa (INESS).

# Can we prevent bleeding from anticoagulants?

*I Ralph Edwards*

Warfarin is a major cause of death and permanent disability from bleeding and stroke, globally. We know it is one of the most difficult drugs to use because of its narrow therapeutic window, long half-life, and multiple interactions with other drugs and food. Another problem is that the dose needed in a particular patient changes slowly over time. Some patients need life-long anticoagulation. Measuring the INR (International Normalised Ratio for prothrombin time, as a measure of the anticoagulant effect) is an essential aid for keeping the dose of warfarin within the therapeutic range.

I have treated many patients with anticoagulation, but it was not until my daughter needed long term anticoagulation that I realized just how difficult it can be to stabilize active, young patients on a dose of warfarin. In the end I bought my daughter a hand-held CoaguChek INR measurer which gives an instant INR value, and which she found helpful and reassuring. But not everyone wants to buy such things, or wants to prick their own finger to use them. Even if one can get an INR result, how does one use it?

In the UK, where my daughter lives, most primary care practices not only have an INR measurement machine, they also have software to predict on the dose of warfarin that should be used. The most common software is INRstar (<http://www.inrstar.co.uk/>).

Because I know the Marketing Director of INRstar from meeting him at the British Computer Society, I have found that INRstar will shortly be available for use via the web, thus making it much more easily available.

This brings me to the point (at last!). There are very few medicines that stay on the market that can be monitored to reduce risk outside specialist facilities – but here is a chance for very many more patients to be monitored globally and for the difficult dose predictions with warfarin to be aided by easily available software.

I have a clear declared interest in writing this (but no financial interest), but I hope that it will help readers to look for ways of reducing serious risks from warfarin, and to promote affordable monitoring where it will be most useful in their countries.

## Footnote

Even though the results of self-testing for INR are not all convincing in showing direct benefit, and studies show that not all patients should do this, for my daughter she felt that managing her own therapy meant independence to enjoy an active life.

## A couple of recent references

Shah SG, Robinson I. Patients' perspectives on self-testing of oral anticoagulation therapy: Content analysis of patients' internet blogs. *BMC Health Serv Res.* 2011 Feb 3; 11:25.

Bussey HI. Transforming oral anticoagulation by combining international normalized ratio (INR) self testing and online automated management. *J Thromb Thrombolysis.* 2011 Apr; 31(3):265–74.

# Counterfeits on TV

Marie Lindquist, Director of the UMC, was interviewed for the main news magazine on Swedish TV4 channel on 3<sup>rd</sup> April 2011. The feature looked at the on-going problems caused by counterfeiting of medicines in Sweden. Marie's comments were also picked up and reported further in other newspapers.

The issue affects all countries in the WHO Programme, and it is very much part of the UMC's agenda to provide tools and methods that can help contribute to tackling this problem.

A web version of part of the feature is available:

<http://www.nyhetskanalen.se/tv?videoid=1.2081542>

(Photo courtesy TV4)



## Antimicrobial resistance – new focus

*Sten Olsson*

WHO has declared antimicrobial resistance the theme of the World Health Day, 7 April, 2011. The issue is emerging as a major threat to human and animal health in all parts of the world. Many organizations are involved in the identification, analysis and prevention of antimicrobial resistance. One of them is Action on Antibiotic Resistance, ReAct ([www.reactgroup.org](http://www.reactgroup.org)) which has its global coordinating office in Uppsala.



*Andreas Heddini and Niyada Kiatying-Angsulee*

The international secretariat of ReAct, represented by Andreas Heddini, executive director, Otto Cars, chairman of the international secretariat and Cecilia Stålsby-Lundborg, scientific adviser, visited the UMC in January, 2011. An open discussion was held regarding the overlapping interests of our two global networks working to support rational use of antimicrobials and better patient safety. We agreed that antimicrobial resistance is covered by the WHO definition of pharmacovigilance and that VigiBase contains a great number of reports describing symptoms of unexpected lack of efficacy which, among other possible underlying factors, could indicate cases of antimicrobial resistance. UMC has developed, as part of the Monitoring Medicines project, a data mining algorithm to identify reports of possible substandard or counterfeit medicines among reported cases of unexpected lack of efficacy. It was agreed that UMC would run a pilot project modifying this algorithm in an attempt also to identify suspected antimicrobial resistance from the ICSRs in VigiBase.

On 28 March Andreas Heddini came back to the UMC in the company of Dr Niyada Kiatying-Angsulee from Chulalongkorn University, Thailand. The preliminary results of the pilot were among many issues discussed. The results showed that the data mining algorithm had been able to identify a long list of clusters suspected of indicating antimicrobial resistance to specific products in a limited number of countries. The suspicions need to be confirmed on a national level, which has yet to happen.

We noted with satisfaction that the Danish Medicines Agency recently sent an urgent request to all health care practitioners to specifically report incidents of suspected antibiotic resistance to the pharmacovigilance centre. Another positive recent development is that the subject is on the agenda for the WHO Advisory Committee on the Safety of Medicinal Products (ACSoMP) at its meeting 31 March – 1 April (see page 17).

## David Healy – the challenge of antidepressants

*I Ralph Edwards*

David Healy, Professor of Psychiatry, University of Cardiff in Bangor, Wales, is well known for his work and writings on the use of antidepressant drugs and their adverse effects, particularly suicide. From this background, Professor Healy came to the UMC to talk and discuss around two broader issues:

- Causality in a few cases, when epidemiological studies show no effect, or even show that the expected effect should be opposite
- That patient reports should have a greater place in drug safety considerations.

In both of these matters, which are of considerable challenge and importance, Prof Healy and I agree!

The use of SSRI antidepressants has been a matter of considerable debate. It seems clear to many that treating depression should reduce completed suicide and probably suicide attempts, but from early suggestions that the SSRIs increased the risk of suicide there has been a controversy. Some have said that perhaps SSRIs stimulate the depressed brain to relieve the anergic side of depression whilst leaving the patient feeling hopeless, therefore more able to get going

and kill themselves! Prof Healy has a different view, in part based on the fact that normal volunteers and those taking SSRIs but who don't have depression sometimes report suicidal ideation. These people form a minority group, but their feelings are real and are reproducible on rechallenge in some cases. This group is so small as to be overshadowed in any epidemiological study. Having controls will not help sort this out: only the consistency and clarity of patients' reported experience can show that a causal relationship is more likely than not, together with other information such as a plausible mechanism and possibly shared risk factors.

This brings us to the second reason for Prof Healy's visit, which was to talk about how to improve patient reporting. For a very long time we have been concerned by under-reporting of adverse drug reactions, but this was in times when in most countries we were trying to get health professionals interested in sending anything in to pharmacovigilance centres. Now we definitely need to move towards quality reports that tell us much more about the patients' adverse experiences, which will help us towards being more certain about a

causal relationship in a case or small group of cases, as well as allowing us to get a better grasp of how an adverse effect affects a patient's life, including both its quality, personal economics and family and society. We should also try to establish where systematic mistakes occur which may lead to medication errors and adverse outcomes.

The EU-funded FP7 project, which WHO/UMC are coordinating, has a part which is looking at patient reporting, both in background and needs, as well as with the practical endpoint of having a web-based software to aid patient reporting to national centres and to WHO. Prof Healy's interests were very much complementary and we are looking forward to the kind of synergies that should come from EU-funded projects in order that they should grow into active and sustainable public health improvements.



## Five from Pfizer

*Anna Hegerius*

A grey afternoon in mid-January, five representatives from Pfizer visited UMC. The delegation consisted of the Country Safety Leads for the Nordic countries (Denmark, Finland, Iceland, Norway and Sweden), as well as a Medical Advisor. This Nordic safety group meets regularly to discuss current safety issues and this time the meeting in Uppsala was combined with a closer look at UMC. During presentations about UMC activities, WHO Drug Dictionary and Signal detection, many questions were asked which led to interesting discussions. The delegation left the office with a better understanding of UMC and our position in the pharmacovigilance network, and the meeting was fruitful for all.



*From left to right: Tina Perborn (Sweden), Marianne Svith Hansen (Denmark/ Iceland), Ewa Ahnemark (Sweden), Tor Seim (Norway) and Timo Ovaska (Finland).*

## Kew collaboration

The UMC and the Royal Botanic Garden, Kew are exploring ways to collaborate and with this in mind Bob Allkin visited us in February this year. Bob came to Uppsala to meet Marie Lindquist and other people involved in the development of the Herbal Dictionary, looking at different technical questions.



*Bob Allkin and Elki*

## UMC welcomes...

**Hanna Pedersen**

Hanna originally comes from Sveg, in Härjedalen province in the centre of Sweden, but moved to Uppsala in 2004 to obtain her Bachelor of Science in Pharmacy degree. From 2008 Hanna worked at the Swedish Medical Products Agency for two years.

She joined the UMC in April 2010 as a consultant within the Reporting, Analysis & Country Support section, a position which has now become permanent. The job involves supporting member countries in their reporting to the WHO database (VigiBase). Hanna is currently the assigned contact person for countries within the South East Asian and Pacific Region.

"I learnt about the UMC and its activities through a course at Uppsala University. I saw a flyer about the course 'Adverse Drug Reactions and Pharmacovigilance', and I remember thinking "what is pharmacovigilance?". I decided there and then to take the course and find out! I really enjoy working at the UMC, I like the atmosphere and that I get to interact with people from all over the world!"

When not working, Hanna likes to spend time with friends and family, and visit flea markets and auctions in the hope of finding some bargains. In the winter she enjoys ice skating and alpine skiing.

**Klas Östlund**

Klas, from Östersund, also in central Sweden came to Uppsala to study in the mid 80s. "When I started my studies in Engineering Physics here in Uppsala there was one field of work I was convinced not to make a career in – and that was computers and software! After finishing my degree that was of course where I ended up. The last 15-16 years I have been an IT consultant and mainly worked with systems for telecom, government and pharmaceutical products."

"I started working at the UMC as a consultant in the spring of 2010. I felt at home from the first day, so when I was offered a permanent post I naturally took it up. The professional team spirit at the UMC is wonderful to be a part of, working with people who are highly skilled in their respective areas, doing things of benefit to people all around the world."

Currently Klas works mainly with software development in the Drug Dictionary Hosted Services project. He has responsibility to make some of the visions the UMC has for its



services come true. He also has an interest in working more with requirements to secure solutions which the customers and users really need.

"I have a fascination for how things are made; from toothbrushes to super tankers, and especially to follow the automated process from raw material to a complicated product. At the UMC I see similar processes taking place where raw material of varying quality is turned into really sophisticated and useful stuff."

"Outside work I would like to spend my spare time with good food, friends and interesting discussions, preferably in our summer house in Roslagen, but most of the time I seem to a) manage the local computer network at home, b) drive 12-year old players covered in mud to and from football matches, or c) decide whether or not to take our cocker spaniel Dobby to the veterinarian after he has eaten something odd."

## The Dawn of Drug Safety

By Myles Stephens

Hardback: 448 pages

ISBN: 9780956087485

Price: around £25 plus postage (see website below)

In this original and comprehensive book Dr Stephens asks many fascinating questions about the early history of pharmacovigilance. The author says "This is not a history book, but rather a scientific account of the evidence concerning the adverse effects of herbs and drugs prior to and including the Thalidomide disaster."

He nonetheless examines many topics:

- Why were so many of the reactions to mercury discovered in the 16<sup>th</sup> century?
- The factors causing sudden death during chloroform anaesthesia
- What stopped UK drug regulation from almost coming into being 50 years before thalidomide
- Would thalidomide phocomelia have occurred if they had listened to Hippocrates?
- A herb which allowed the Greeks to capture a city...



The book is in four parts:

- a chronological account of the discovery, reporting and management of the adverse reactions to medicines in the context of important contemporary medical events, from the beginning of time until the thalidomide disaster.
- an analysis of six marker drugs representing typical medicines covering a period of over 3,000 years: hellebore, henbane, mercury, opium, aspirin and streptomycin.
- an analysis of the fifty drugs that had been on the market prior to 1960 and which have been either withdrawn or restricted because of one or more adverse reactions.
- a discussion, and lessons from this experience.

Myles Stephens was a general practitioner in a semi-rural part of England for several years before working in drug safety within pharmaceutical industry; his 'The Detection of New Adverse Drug Reactions' has reached five editions.

The book may either be ordered via the website [www.dawndrugsafety.com](http://www.dawndrugsafety.com) (payment via PayPal) or from MDB Stephens 49 King's Court, Bishop's Stortford, Hertfordshire. CM23 2AB, UK, e-mail: [stephmdb@onetel.com](mailto:stephmdb@onetel.com)

## Health Secrets – a layman's guide to health issues

By Alex Dodoo



Dr Alex Dodoo will need little introduction to most Uppsala Reports readers. A pharmacist and clinical pharmacologist trained in Ghana, UK and Canada, he is the Director for the Centre for Tropical Clinical Pharmacology and Therapeutics at the University of Ghana Medical School, as well as the Director of the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, and heads up UMC-Africa.

Equally he has considerable experience in dealing directly with patients 'over the counter' and an ability to understand their real concerns about health problems and what to do to deal with them. Furthermore, he is a keen 'patients' rights' advocate, and has travelled widely as both active conference participant and a member of several international groups dedicated to improving drug safety across the continents. He is also a vivid commentator and prolific writer, both in lay and scientific newspapers and journals, and appears regularly on radio and TV in Ghana on issues ranging from medicines and pharmacy to social issues and politics.

The book contains 50 health issues previously published as weekly articles in Ghana's

'Spectator' from 2005-2007 which cover the widest range of health and medicines questions. Although not specifically about drug safety, pharmacovigilance nonetheless has its rightful and prominent place in this book. Each article starts with an individual story, anecdote or 'fait divers' recounted in a no-nonsense manner. To get a flavour of the subject matter covered, articles include: shyness, bed-wetting, snoring, athlete's foot, among many other everyday personal health issues. The articles are sub-divided into

- ◆ Medications
- ◆ Ailments
- ◆ Drug interactions
- ◆ Medicines and gender
- ◆ Health professionals
- ◆ Lifestyle and health promotions

Not only a common-sense and easy-to-read guide for the layman, but a wonderful example of lively – and sound – communication of medicines use.

ISBN: 978-9988-1-4370-1

Available from Creative Trends, Osu Forico Mall, Mission Street near Blue Gate, PO Box AN15606, Accra-North, Ghana  
Tel +233 (0)302 785255, Fax +233 (0)302 785270

## The Risks of Prescription Drugs

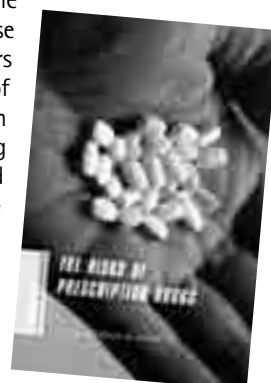
Edited by Donald W. Light

– 184 pages

\$15.00 / \$45.00 – paper / cloth

ISBN: 978-0-231-14693-7 / ISBN: 978-0-231-14692-0

This book tackles questions about the pharmaceutical industry and the 'privatization of risk'. It examines the extent to which the FDA protects the public from serious side effects and disasters, and the private sector and markets have been given a greater role in this area, while reducing public oversight. The authors consider whether the current rules of regulation undermine the health of patients and the effect of the expansion of disease categories. Chapters include the risks of statins for high cholesterol, SSRI drug use in depression and anxiety, and hormone replacement therapy for menopause. The final chapter sets out changes to help make drugs safer and more effective.



DATES	TITLE	PLACE	ORGANISER/CONTACT
2-13 May 2011	UMC Pharmacovigilance training course	Uppsala, Sweden	UMC <a href="http://www.who-umc.org">www.who-umc.org</a>
9-10 May 2011	Introduction to Signal Detection and Data Mining in Pharmacovigilance	Amsterdam, Netherlands	DIA Europe Tel.: +41 61 225 51 51 Fax: +41 61 225 51 52 Email: <a href="mailto:diaeuropa@diaeuropa.org">diaeuropa@diaeuropa.org</a>
10-11 May 2011	How to Prepare for Pharmacovigilance Audits and Inspections	Amsterdam, Netherlands	DIA Europe (see above)
16-18 May 2011	Practical Guide for Pharmacovigilance: Clinical Trials and Post Marketing	Nice, France	DIA Europe (see above)
17 May 2011	Pharmacovigilance for support staff	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 <a href="http://www.management-forum.co.uk">www.management-forum.co.uk</a> E-mail: <a href="mailto:registrations@management-forum.co.uk">registrations@management-forum.co.uk</a>
18-19 May 2011	Staying current in the regulatory environment for pharmacovigilance	London, UK	DSRU Tel: +44 (0)23 8040 8621 <a href="http://www.dsru.org/">www.dsru.org/</a> E-mail: <a href="mailto:jan.phillips@dsru.org">jan.phillips@dsru.org</a>
19-20 May 2011	Benefit/Risk Management	Prague, Czech Republic	DIA Europe (see above)
26-27 May 2011	ISoP training courses: Reporting, Causality Assessment, Risk factors & Mechanisms of ADR; Risk Management and Regulatory inspections	Minsk, Belarus	International Society of Pharmacovigilance <a href="http://www.isoonline.org/training.html">www.isoonline.org/training.html</a>
8-9 June 2011	6 <sup>th</sup> Biennial Conference on Signal Detection (pre-conference workshop on 7 June)	London, UK	DSRU (see above)
14-16 June 2011	Pharmacovigilance – Basic Training Course for those working on safety monitoring in the EU, USA and Japan	London, UK	Management Forum Ltd (see above)
20-22 June 2011	Medical Aspects of Adverse Drug Reactions	Southampton, UK	DSRU (see above)
22-23 June 2011	Periodic Safety Update Reports	Southampton, UK	DSRU (see above)
28 - 29 June 2011	Pharmacovigilance India 2011	Mumbai, India	IQPC Worldwide IQPC <a href="http://www.iqpc.com.sg/redSearch.aspx?keyword=Pharmacovigilance">http://www.iqpc.com.sg/redSearch.aspx?keyword=Pharmacovigilance</a>
5-6 July 2011	Pharmacovigilance China 2011	Beijing, China	IQPC Worldwide IQPC <a href="http://www.iqpc.com.sg/redSearch.aspx?keyword=Pharmacovigilance">http://www.iqpc.com.sg/redSearch.aspx?keyword=Pharmacovigilance</a>
6-7 July 2011	Introduction to Pharmacoepidemiology	Southampton, UK	DSRU (see above)
14-17 August 2011	27 <sup>th</sup> International Conference on Pharmacoepidemiology and Therapeutic Risk Management	Chicago, USA	ISPE <a href="http://www.pharmacoepi.org/meetings/">www.pharmacoepi.org/meetings/</a> E-mail: <a href="mailto:ISPE@paimgmt.com">ISPE@paimgmt.com</a>
19-20 September 2011	Medical Approach in Diagnosis and Management of ADRs	Paris, France	DIA Europe (see above)
3-7 October 2011	Excellence in Pharmacovigilance: Clinical trials and post-marketing	Zagreb, Croatia	DIA Europe (see above)
26-28 October 2010	11 <sup>th</sup> ISoP Annual Meeting (also training courses)	Istanbul, Turkey	International Society of Pharmacovigilance <a href="http://www.isop2011.org">www.isop2011.org</a>



The Uppsala Monitoring Centre (UMC) is a not-for-profit foundation and an independent centre of scientific excellence in the area of pharmacovigilance and patient safety. We provide essential research, reference, data resources and know-how for national pharmacovigilance centres, regulatory agencies, health professionals, researchers and the pharmaceutical industry round the world.

Many of our services and products have been developed as a result of our responsibility – as a World Health Organization Collaborating Centre – for managing the WHO pharmacovigilance network of over 100 countries and the WHO global individual case safety report database, VigiBase™. A core function is the screening and analysis of data with the aim of detecting potential issues of public health importance in relation to the use and safety of medicines. Other services include technical and scientific support to WHO and its member countries, and provision of tools, such as VigiSearch™ and VigiFlow™, for data entry, management, retrieval and analysis.

Our main commercially available products are the family of international WHO Drug Dictionaries, used by most major pharmaceutical companies and CROs.

## Communications information

### Visiting address

Uppsala Monitoring Centre  
Bredgränd 7  
SE-753 20 Uppsala  
Sweden

### Mail Address

Box 1051  
SE-751 40 Uppsala  
Sweden

**Telephone: +46 18 65 60 60**

**Fax: +46 18 65 60 88**

### 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. [sten.olsson](mailto:sten.olsson@who-umc.org)) in place of info

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

A full list of UMC staff may be found on the [About the UMC](#) page on our website.

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

Uppsala Reports © the Uppsala Monitoring Centre 2011

Editors: Sten Olsson and Geoffrey Bowring

Uppsala Reports ISSN 1651-9779



## 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 above.

## Prefer to get the digital version?

If you would like to receive the pdf version of *Uppsala Reports* every quarter, please let us know your details and the e-mail to which we should send it. Current and past issues of *Uppsala Reports* may also be downloaded from the UMC website.