WMUR 48

UPPSALA REPORTS January 2010

For everyone concerned with the issues of pharmacovigilance

WHO Programme Annual Meeting

Haemovigilance

VigiSearch survey

Vaccines news

New Canadian database

DIRECTOR'S MESSAGE

Marie Lindquist
Director
the Uppsala Monitoring Centre

I do not envy anyone who has had to face the media and the public through the turbulent trials of H1N1 communication. While I am not sure that officials and professionals have handled the issues as well as they should have done, I cannot for a moment claim that I would have done any better; the urgency and uncertainties involved pose a huge communication challenge.

In the Swedish media, WHO recently came in for severe criticism about its handling of H1N1 issues, particularly regarding secrecy about those advising the Director General, the raising of pandemic threat levels, the alleged undue influence of vaccine-industry interests in advisory groups, and the top-down, non-consultative process of decision-making. Such concerns risk serious damage to the credibility of the organisation and require robust clarification and justification, which the DG quickly provided. It's a matter of sadness to see WHO under such attack, but is not surprising given the heated climate of controversy surrounding the development of the pandemic and the initiation of influenza vaccinations of unprecedented scale.

There are risks of this kind of criticism for all specialist and centralised organisations, not least for us at UMC. It is all too easy to be driven by one's sense of mission and to become absorbed in the internal processes and external communications that serve it – without paying sufficient attention to the real wishes (maybe requirements) of those we are here to serve.

We have a very clear set of values at UMC. They include loyalty to the mission of WHO; commitment to patient safety as our prime goal; and the pursuit of scientific excellence. You can find the statement in full at www.who-umc.org in the 'About the UMC' section.

We are also committed to listening to partners' views and to favour openness and transparency. These words slip so easily off the tongue and are uttered in every professional forum – yet they are tough to achieve and so very rarely fulfilled. I can only promise that we are doing our very best to live up to these ideals.

Getting out and about

At the UMC we aim to get out and meet people in their own environment; talking, listening, explaining, seeking opinion and criticism, asking for guidance and advice. But time in the office is also needed to bring into being useful services and products.

Together with country representatives and UMC and WHO colleagues I attended the WHO Programme annual meeting in Morocco (see p4-5) and I believe we achieved a great measure of engagement and understanding of each other. African countries showed great initiative in forming the African Society of Pharmacovigilance at the meeting! Recently I had the chance of meeting the Drug Controller General (India) and senior colleagues in a face-to-face encounter: a very effective way to come to know and understand each other and set the foundations for future collaboration.

We are trying hard, as always, to get out and about and engage with people, and our colleagues at WHO HQ are equally active in travelling to different parts of the world. But there is never enough time to travel as much as we would like – and at the same time do enough at home.

I need to focus on the continued development of the UMC as a dynamic and efficient organisation and to steadily increase resources for pharmacovigilance work both inside and outside the UMC. One of my major challenges is to make sure that we are as effective as possible in supporting member countries, WHO and public health programmes. To do this, we must extend our capacity for outreach into the regions and countries where our expertise and resources are most needed. My approach to realise a stronger presence in the field is to engage individuals with ambassadorial and scientific skills who have the ability and interest in representing the UMC in their regions, as a complement to our internal experts. I have already taken a significant step towards achieving this vision by creating a Secretariat for Global Outreach in the UMC, which is directly linked to a satellite office in Accra, Ghana (which will be referred to as UMC-A), headed by Alex Dodoo, well known to many of our readers. If this approach is as successful as I hope, and when resources permit, more people can be recruited to cover more regions and a broad range of expertise.

We must all try to find ways of spreading the word and the skills to others, so that patient safety becomes a truly shared responsibility!

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the UPPSALA MONITORING CENTRE

The Uppsala Monitoring Centre (*the* UMC) is the field-name of the WHO Collaborating Centre for International Drug Monitoring, responsible for the management of the WHO Programme for International Drug Monitoring.

An independent centre of scientific excellence, *the* UMC offers products and services, derived from the WHO database of Adverse Drug Reactions (ADRs) reported from member countries of the WHO Programme.

With an independent and global perspective on drug safety, *the* UMC provides resources for regulatory agencies, health professionals, researchers and the pharmaceutical industry.

The UMC's important worldwide work is financed solely by the organisation itself, without support from WHO, the Swedish Government, member countries of the WHO Programme or any grant-making body.

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National Centres in Morocco

Sten Olsson

Morocco was the perfect venue for the 2009 WHO Programme meeting; its national pharmacovigilance centre has been one of the most active and dynamic centres in the global drug safety programme since it joined 17 years ago. So over 100 representatives from 50 countries met in the Moroccan capital, Rabat from 2 to 5 November for the 32nd Annual Meeting of Representatives of the National Centres participating in the WHO Programme for International Drug Monitoring.

This year the meeting was prefaced by more opportunities than ever for delegates to meet and learn together. On the Sunday, the Centre Anti Poison et de Pharmacovigilance du Maroc welcomed study sessions on MedDRA and Strategies for Identifying and Preventing Medication errors, along with the usual Introductory seminar for new countries to the Programme.

Kees van Grootheest leads a working group in Rabat

The Annual Meeting itself began at the old Hotel de la Tour Hassan on the Monday by receiving reports from the Uppsala Monitoring Centre* (with the annual summary on trends in reporting to VigiBase), and presentations on Cohort Event Monitoring for anti-malarials in Nigeria and Tanzania, after which a technical lecture on Data management in Cohort Event Monitoring was given. Other plenaries on succeeding days covered:

- Proposed WHO Guidelines on similar biotherapeutic products (SBPs)
- Pharmacovigilance of medicines for neglected diseases
- Special training needs to promote patient reporting (follow-up from 2008)
- Pharmacovigilance in the Affordable Medicines for Malaria (AMfM) initiative
- Safety monitoring of vaccines used against the A/H1N1flu pandemic
- Risk Management Plans - is harmonization possible/desirable?
- Pharmacovigilance of medicines in HIV/AIDS
- Performance indicators in pharmacovigilance

In a discussion led by Australia and China, the meeting looked at Development plans for pharmacovigilance centres; the impressive number of ADR reports collected in China was a particular point of comment. Inevitably the session on the current flu pandemic, led by Switzerland, gave rise to much discussion and sharing of problems among the delegates.

The working groups this year ranged widely, as ever, the titles being:

- Patient safety, including medication errors
- Reporting and database needs and practicalities
- Interaction between pharmacovigilance centres and academia
- Use of pregnancy and other registers in pharmacovigilance
- Role of generic manufacturers in pharmacovigilance: old and new issues
- Mobilizing resources for pharmacovigilance
- Pharmacovigilance for medicines in neglected diseases
- Vaccines

There were fewer 'Problems of current interest' this year, although as ever they represented a cross-section of concerns at national level, of international interest:

- SSRIs and violence (Netherlands)
- MMR Vaccine (Croatia)
- A web-form for monitoring of vaccination against A/H1N1 influenza (Netherlands)
- Fatal hepatic failure following sevoflurane anaesthesia (Serbia)
- Eltroxin formulation change (Denmark)
- Safety concerns on adulterated excipients in manufacture of pharmaceutical products (Nigeria)
- Stevens - Johnson syndrome and toxic epidermal necrolysis: epidemiological characteristic of Thai database, 1999-2008 (Thailand)
- LATIN case-control studies on: Incidence and risk factors of aplastic anaemia and agranulocytosis in Latin America (CEATOX, Brazil)

Rachida Soulaymani-Bencheikh, Mary Couper and Marie Lindquist

'Murilo Freitas Dias, Jerry Labadie, Priya Bahri, Alex Dodoo, all participants in the 2001 UMC training course, all working still in pharmacovigilance, together in Rabat, in the gardens leading off the conference hall

Posters

Delegates brought along a broad range of posters, covering different aspects of national safety reporting programmes in Namibia, Madagascar, Canada, Sudan, and Cote d'Ivoire, as well as one from Croatia on 'Knowledge about reporting system of ADRs and reasons for their underreporting', and a selection of recent posters from the UMC.

Other meetings

Outside the formal programme other related activities of high importance took place:

- The VigiFlow users met as a group for the second time after a successful session in Uppsala in 2008.
- African delegates met and decided to form an African Society of Pharmacovigilance. The host of the meeting, Professor Rachida Soulaymani-Bencheikh, was elected interim president.
- Delegates from Arabic speaking countries met to discuss the appropriate Arabic language expressions for certain words and concepts frequently used in pharmacovigilance.

The meeting also agreed on the content of a statement to be released as a common appeal from the assembled national representatives.

Social activity is essential in meetings where the delegates rarely see each other face-to-face in the group – the Moroccan hosts provided ample opportunity, not only with a tour of important sites in Rabat (ending up in the Medina), but also with a splendid dinner with Moroccan music and dancing in a private mansion in Sale.

At the close, the meeting President, Rachida Soulaymani-Bencheikh thanked the team from her Centre for their contributions. There were also thanks to Mary Couper, at her last National Centres meeting before her retirement, and Marie Lindquist who had recently assumed the directorship of the UMC.

Jonathan Martey of the Ghanaian Foods and Drugs Board gave a witty and eye-opening presentation on Accra and Ghana, where the WHO Programme will assemble at the end of October 2010 for the 33rd Annual Meeting (with pre-meetings), to be followed by the first sub-Saharan African meeting of the International Society of Pharmacovigilance (ISoP).

* the UMC's Annual Report for 2008-2009 is downloadable as a pdf from www.who-umc.org > Publications

A new society for Africa

After sessions had finished for the day at the WHO Programme meeting in Rabat on 3rd November 2009, representatives from 16 nations across Africa met to discuss a pharmacovigilance society for professionals working around the continent. The result was the founding of an African Society of Pharmacovigilance, which is intended to be a chapter of the International Society of Pharmacovigilance. Interim Officers selected by consensus during the meeting were Rachida Soulaymani-Bencheikh (President), Ambrose O Isah (Vice-President), Raja Benkirane (Secretary-General) and Jayesh Pandit (Treasurer). Priscilla Nyambayo was elected as Vice-Secretary/Vice Treasurer. Executive committee members nominated and elected by consensus were Esperanca Sevene, Edinam Agbenu, Witshire Johnson and Ryadh Daghfous.

Further information about ASoP may be obtained by contacting:
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African delegates in Rabat photographed after the inaugural meeting of the African Society of Pharmacovigilance

Prof Ralph Edwards, Dr Mary Couper and Mr Sten Olsson were elected Benefactor Members and Patrons of ASoP.

Montenegro

Maja Stankovic

Montenegro is a country located in south-eastern Europe, with an estimated population of 650,000. Until it became independent on May 21, 2006, Montenegro was part of the former Yugoslavia.

(Left to right) Maja Stankovic (Head of Pharmacovigilance department, Agency for medicinal products and medicinal devices of Montenegro), Dr Majda Sahman (Deputy Director), Zeljka Besovic (Head of Marketing Authorisation department)

During the 1990s, the National Centre for adverse drug reactions monitoring of Serbia and Montenegro was the central administration for collection and evaluation of adverse reactions sent in by health care professionals and the pharmaceutical industry. The Centre was also responsible for decision-making on regulatory measures to be taken and the other activities important for patient well-being. However, health care professionals in Montenegro did not participate particularly actively in pharmacovigilance activities, until an Agency for Medicinal Products and Medical Devices of Montenegro was established at the beginning of 2008.

According to the law on medicinal products, the department for pharmacovigilance is responsible for the safe use of medicinal products available on the Montenegrin market and the following activities:

- Collecting adverse reactions and scientific evaluation (severity, expectedness, causality assessment)
- Entering data from ICSRs into the WHO Database (Vigibase) through VigiFlow
- Generation of potential signals
- Comparison of medicines safety profiles within the same therapeutic class
- Undertaking regulatory action for safety reasons related to medicinal products, for protection of public health
- Communication to health care professionals ('Dear Doctor' letters) and to the public when it is necessary
- Regular updates of the Agency web pages with new safety information.

For better functioning of the pharmacovigilance system in Montenegro, at the Agency's request all health care institutions have appointed a co-ordinator for pharmacovigilance, responsible for promoting pharmacovigilance activities in their institutions. The importance of education is recognized, and the fundamental principles of pharmacovigilance and awareness of key issues related to safe use of medicines are communicated.

At the end of October 2009 Montenegro officially became the 96th full member of the WHO Programme for International Drug Monitoring. We are strongly devoted to developing pharmacovigilance and foster collaboration with our stakeholders. The Agency for Medicinal Products and Medical Devices and the Institute for Public Health strongly collaborate in monitoring Adverse Events Following Immunisation. By combining regulatory and epidemiological knowledge we hope that we will successfully confront the very challenging safety monitoring of swine-flu pandemic vaccine.

Jamaica

WHO in Geneva has received an application from Dr Sheila Campbell Forrester, Chief Medical Officer for Jamaica to join the WHO Programme for International Drug Monitoring. While the initial batch of ICSRs are processed for entry in the WHO database, Jamaica, which set up its national system in 2006, becomes an Associate of the Programme. An ADR reporting form, revised in 2009, has been distributed as part of the 'PharmWatch' programme.

Russian Federation

In November notification was received from the Director of the Federal Service for Surveillance in the Sphere of Public Health and Social Development (Roszdravnadzov) in the Russian Federation requesting intensified co-operation with the UMC. Dr Mariam Khubieva is the centre head.

Over the last two years Roszdravnadzov has set-up a national system for collection of data, with online submission of alerts from health practitioners, regional centres and the pharmaceutical industry. Roszdravnadzov is also co-ordinating a network of 52 regional centres, based on WHO recommendations.

Farewell Mary

Sten Olsson

As mentioned in our report from the WHO meeting in Rabat, Mary Couper has retired as Medical Officer in Quality Assurance & Safety for Medicines (QSM), in the WHO Department of Essential Medicines and Pharmaceutical Policies. She was well-known around the pharmacovigilance world in her role as first contact at WHO Headquarters for the pharmacovigilance programme.

Over the years Mary was closely involved in many projects touching on pharmacovigilance. Her career included work with the WHO Essential Drug List, the WHO Model Formulary, WHO GCP (Good Clinical Practice) Guidelines, E2E, ICDRA (International Conference of Drug Regulatory Authorities), Drug Utilization, MedDRA and pharmacovigilance. Her contributions were greatly appreciated by the many individuals and groups with whom she had contact.

Approachable and friendly, in recent years she has been particularly involved in training for developing countries, assisting emerging national drug safety systems in Africa, and planning of the Annual Meeting of the WHO Programme. She has also been a regular presence at the UMC Board and the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP).

We wish Mary all happiness in her retirement.

Spain

Francisco de Abajo of the Spanish Medicines Agency – Agencia Espagnola de Medicamentos y Productos Sanitarios – has recently been appointed as a Professor at the University of Alcalá. He has been replaced by Dr Dolores Montero who becomes the head of the Division of Pharmacoepidemiology and Pharmacovigilance. In addition, we learn that the suffix of e-mail addresses from AEMPS will change to @aemps.es

Finland

The national centre in Finland (formerly National Agency for Medicines - Lääkelaitos) has now become the Finnish Medicines Agency Lääkealan turvallisuus- ja kehittämiskeskus, and has a new website: www.fimea.fi

Introducing pharmacovigilance of HIV medicines

Magnus Wallberg

In November 2009 a group of enthusiastic pharmacovigilantes met for a six-day Training Course for Introducing Pharmacovigilance of HIV Medicines, at a hotel just outside Dar es Salaam in Tanzania. The very international group – from Côte d'Ivoire, Ghana, Kenya, Nigeria, Tanzania, Uganda, Ukraine and Zambia – were not all from traditional pharmacovigilance backgrounds; many also came from HIV/AIDS programmes.

The facilitators were also international: Drs Micheline Diepart and Shanthi Pal from WHO/HQ Geneva, Dr Thomas Lapnet-Moustapha from WHO-AFRO, Dr Richard Banda of HIV Drug Resistance WHO/IST/ESA, Drs David Coulter and Geraldine Hill from New Zealand, Magnus Wallberg from the UMC and Dr Paula Munderi of WHO/HQ Uganda. So the scene was set for dynamic and successful training!

Monday laid the foundations for the rest of the week, then on Tuesday the course really got going with intense training on pharmacovigilance tools (or 'the Vigis') led by Magnus Wallberg. Included was a thorough walk-through of VigiBase, WHO-ART, WHO Drug Dictionary and VigiSearch. After lunch there was a session on toxicities linked to ARTs, facilitated by Paula Munderi, and a causality assessment session by David Coulter. The evening barbeque got the group to get to know each other at the poolside bar; pharmacovigilance was not talked about much, but most of the other problems in the world were discussed and solved.

Wednesday started with a long practical session on VigiFlow and its search capabilities, with more toxicities after lunch, plus working exercises on ARV-ADR case management. Thursday was dedicated to Cohort Event Monitoring (CEM), starting with general principles from Geraldine Hill and after a presentation on CEM related to ARVs by David Coulter. To hear about practical experiences, two CEM programmes on malaria were presented by Tanzanian and Nigerian representatives. Thursday concluded with a presentation of CemFlow and hands-on exercises on using the CemFlow tool. Friday was devoted to CEM data analysis and signal identification, a presentation on how to establish a pharmacovigilance programme for HIV medicines and more group work, where participants had to create or refine existing country plans for pharmacovigilance.

Those plans were presented on Saturday morning; after that the training was wrapped up and at the closing ceremony all participants received a diploma and CD with the training material. All participants took an active part with many interesting discussions, and the activities and knowledge sharing in the hands-on sessions and exercises was very good.

Improving reporting in Europe

Helena Wilmar and Cecilia Biriell report

For some time there have been problems with the timely submission of ICSRs[1] from countries within the European Union (EU) to the WHO global ICSR database, VigiBase. EU countries are required to submit their ICSRs to the European Medicines Agency (EMA) and the EudraVigilance database, but also to supply the ICSRs to the WHO database[2]. However, since the EudraVigilance became fully operational, consistent and regular submission from certain European countries has fallen off. The UMC has been working for some time to try to remedy this situation with both technical and operational avenues being explored. As part of this on-going attempt to obtain reports from countries where they have recently been lacking in VigiBase, it was decided to contact each national centre within the EudraVigilance area to ascertain what reporting issues existed.[3]

Survey

In September 2009 a survey was launched to the 28 WHO Programme member countries within EEA (European Economic Area). Out of the 28, 26 responses were received and the material gave UMC valuable knowledge, and specific problems about the ICSRs procedure were identified. Since there is no streamlined way of sending ICSRs to the EMA and UMC at the same time, many WHO Programme member countries experience technical difficulties when having to send separate ICSRs batches to both organizations. It was also apparent that where countries sent their reports to both EudraVigilance and WHO, submissions to the former were often made on a weekly basis, while those to the WHO database were far less frequent. For several countries the technical solution used today makes ICSR submission time-consuming, and sometimes results in duplication of work.

Working with countries for solutions

The UMC has started the work of facilitating the reporting from EEA member states to VigiBase and will contact countries individually where we see that procedures can be simplified. One identified problem was that the UMC interpretation of E2b definition of case identifiers (Ids) differed from the EMA interpretation. Adjustments to the VigiBase import process have now been made to harmonize the UMC and the EMA case Id handling. This means that countries submitting ICSRs to EMA no longer have to change case Ids before submitting to VigiBase. The Reporting Team have also updated their knowledge about the EudraVigilance system. In December three UMC staff members took a three-day course at EMA in London to learn about 'Web Trader', the web-based component for entering of ICSRs into the EudraVigilance database.[4]

The result from the survey was presented at the WHO Meeting of National Centres in Rabat in early November. Anyone interested in receiving a printed copy of the overall results may contact Helena Wilmar at: Vigibase@who-umc.org.

Notes

1. ICSR: Individual case safety report
2. Section 6.2 of VOLUME 9A (The Rules Governing Medicinal Products in the European Union), September 2008.
3. The EudraVigilance system covers all EU countries, plus Norway and Iceland (European Economic Area members).
4. The UMC has no access to EudraVigilance.

Important European Agency changes

The President of the European Commission, José Manuel Barroso, recently announced that the new 'Health and Consumer Policy' portfolio for the European Union will include responsibility for pharmaceutical products and medical devices. The change will move the European Medicines Agency from the Directorate of Enterprise and Industry (ENTR) to the Directorate of Health and Consumers (SANCO).

Consumer organizations and advocacy groups have been urging such a move, which will place responsibility for the European Medicines Agency, and pharmaceutical and medical devices policies generally, with a Health and Consumer Policy Commissioner, who will have an overall view of public health policy and patient and medicines safety throughout the European Union.

It has also been announced that the European Medicines Agency has decided to drop the EMEA acronym in its communications, and create an updated logo. However, they will simply be calling themselves either by their full name or 'The Agency'.

A new 'ema.europa.eu' address has also been introduced for its website and e-mails as of 8 December 2009. From that date, the address of the public website is www.ema.europa.eu and e-mail addresses will take the form name.surname@ema.europa.eu. A further, major initiative is underway to improve communications, and as part of this the European Medicines Agency is to completely redesign its public website for early 2010.

VigiSearch and VigiMine usage in National Centres

Maria Tengstrand, on behalf of the Signal Detection team

VigiSearch and VigiMine have been developed to access and query VigiBase, the global database of nearly 5 million individual case safety reports. Both systems are accessed together over the Internet with a single log in. The WHO Drug Dictionary and MedDRA/WHO-ART terminologies are incorporated in the systems.

VigiSearch and VigiMine

During 2008 the Uppsala Monitoring Centre made some major changes to the features of VigiSearch and VigiMine (see p10-11, UR44). VigiSearch is a search tool that allows access to overviews and individual case reports in VigiBase. VigiMine provides access to IC values and other statistical data for all drug-event combinations reported to the database. In VigiSearch, a simple query is constructed using drug and reaction terms. In an advanced query, further criteria can be added, such as reporting country, age, sex, and outcome, among others. In VigiMine the result can also be filtered on numerical values, such as the IC and the number of reporting countries. The result can also be stratified (for example, by age, sex, and reporting country), and a 'time scan' is also available, showing how the number of reports and the IC value have varied over time.

In order to improve the work of providing all National Centres with relevant information and useful tools, the UMC sent out a request for feedback to all VigiSearch/VigiMine users in June 2009. Those who replied received a link to an online questionnaire.

Survey results

The survey was completed by 23 people, from 19 countries around the world. The participants' experience in the field of pharmacovigilance ranged from one to 25 years.

VigiSearch

From the survey, it appears that most users retrieve data through VigiSearch several times per month, both by standard drug-ADR searches and with the addition of criteria from 'Advanced view'. Searches are performed almost as often in WHO-ART as they are in MedDRA. For MedDRA the level of terminology most often used is Preferred Term, and in WHO-ART searches are often made on either Preferred Term or System Organ Class. Regarding drugs, information is most often retrieved on Preferred Base level, although the ATC-structure is also commonly used. The available output formats: overviews, report listing and the individual reports are all used. 82% of the respondents said that the results from VigiSearch were always or often useful.

Examples of how VigiSearch is used:

- Addition of international data to national data
- Looking at safety profiles for drugs that are new on the national market, but which have been used globally over some time
- A basis for signal detection and/or strengthening of a potential signal

VigiMine

Although not used as often as VigiSearch, VigiMine users are pleased with its features: out of 23 respondents, 19 were using VigiMine, and of these, 9 used it more than once per month. All the functions of VigiMine were used, i.e. filters, stratification and report details. Many use the data to compare to statistics from their own database, as an aid in national signal detection. 75% of the respondents said that the results from VigiMine were always or often useful. Both VigiSearch and VigiMine have User guides available on the web-site, which were well rated.

Examples of how VigiMine is used:

- Inclusion in potential signal investigations
- Comparing domestic potential signals to international data

The questionnaire also contained queries on how the VigiSearch/VigiMine services could be improved. UMC is very grateful for all the input that was provided by the users and will use comments made to develop the services. If you want to contribute to the improvement of VigiSearch and VigiMine, please send your ideas to: signals@who-umc.org

Denmark – corrections

Since our report (UR47 p5) 'Reporting in Denmark', Danish agency colleagues have advised us of clarifications.

The 15-day reporting requirement applies to suspected serious ADRs – and the inclusion of civil registration number is strongly recommended, but not mandatory.

The Danish medicines agency decided in January 2009 that correspondence about ADR reports between doctors and companies should be undertaken via the Agency. Previously pharmaceutical companies could contact a doctor directly with queries about ICSRs; this is now undertaken by the Agency (except where the doctor reported directly to the company in the first place).

Swiss haemovigilance system

Measures and recommendations to enhance transfusion safety

Markus Jutzi, MD, Morven Rüesch, med. pract. and Pia Caduff, MD

Introduction

In Switzerland 13 regional Red Cross Blood Transfusion Services guarantee the blood supply for a population of about 7.5 million. Blood donations are collected exclusively from voluntary, non-remunerated blood donors. Approximately 300,000 units of red cells, 75,000 units of plasma and 25,000 therapeutic units of platelets are transfused annually. Since the enactment of the Federal Law on Therapeutic Products (which also covers blood and blood components) in 2002, reporting of Adverse Transfusion Events (ATEs) is mandatory in Switzerland.

The blood establishments must possess an operating authorisation for the collection, manufacture and distribution of blood and components, issued by the national regulatory authority (Swissmedic) and are obliged to designate a person responsible for haemovigilance.

All donations have to be tested for the presence of Anti-HIV-1 + 2 antibodies, Hepatitis B surface antigen, Anti-HCV antibodies, antibodies against treponema pallidum, ALAT as well as HIV and HCV-Virus using a nucleic acid amplification technique. Components for allogenic transfusion must be leucodepleted, and plasma for transfusion has to be either virusinactivated or requires for release an additional set of negative test results of the donor after at least four months.

The law further requires that institutions where blood components are transfused implement a quality assurance system for their application and also designate a haemovigilance officer. Adverse events are reported directly to Swissmedic by the Haemovigilance officers in hospitals and blood establishments. The system is non-punitive and confidential.

Material and Methods

The Haemovigilance officers report suspected adverse events by a standard notification form. Separate forms are available for reporting Transfusion Reactions (TR) and Incorrect Blood Components Transfused (IBCT)/Near Miss events (NM, error that has been detected before the transfusion was initiated).

In Switzerland, all transfusion-related adverse events and reactions, irrespective of their grade of severity, are eligible for reporting. The reporting criteria as stated under the Law on Therapeutic Products define as mandatory for reporting serious and/or unexpected events, clusters of events, quality defects and supply bottlenecks. The reports are reviewed by the Haemovigilance team at Swissmedic and evaluated regarding classification, imputability and severity of the event.

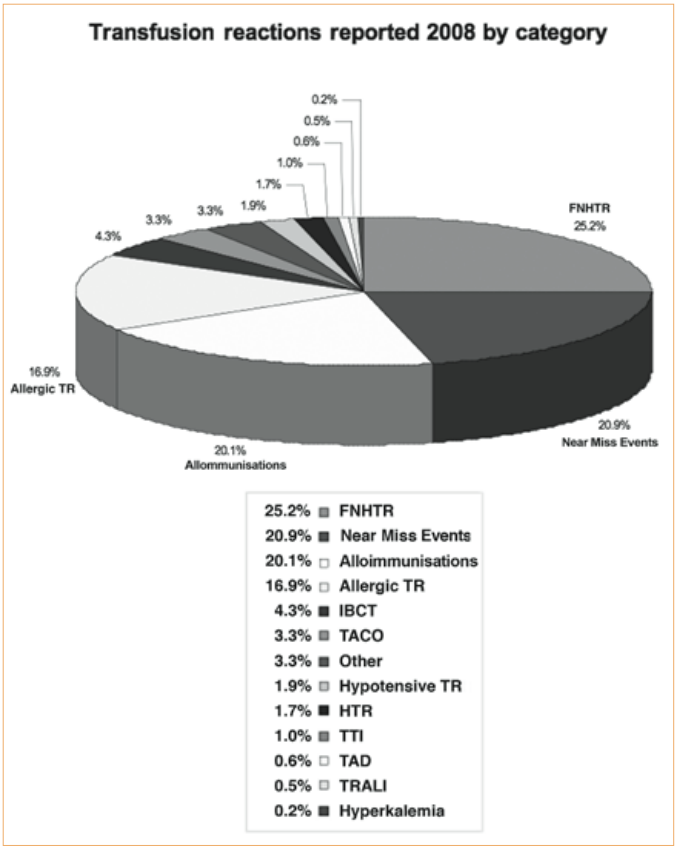
IBCTs and NMs are subject to an error analysis using methods for error and risk analysis comparable to those described in the 'London Protocol' with regard to determining the site of primary error in the transfusion process and deriving corrective measures.

These data allow us to quantify the current risks of transfusion in order to inform patients adequately. Furthermore, we can identify areas of possible improvement in the transfusion process.

Results

Approximately 400,000 transfusions are administered annually. The number of reports has increased steadily from 271 in 2002 to 1084 in 2008, reflecting the continuous development of Haemovigilance in the 200 hospitals transfusing blood. Nevertheless we estimate a current under-reporting of around 50%. Of the 1084 reports received in 2008, 851 described 881 events of TRs and/or IBCTs and 233 described NMs. The distribution of categories of reported events remained stable between 2002 and 2008, with Febrile Non-Hemolytic Transfusion Reactions (FNHTR) (25.2%), near miss events (20.9%), alloimmunisations (20.1%) and allergic transfusion reactions (16.9%) accounting for more than 80% of the reports in 2008, the majority of which was classified as non severe transfusion reactions.

Figure 1



Of the events reported in 2008, 52 (6%) were severe or fatal, with imputability certain or probable in 33 cases. The two fatal events reported in 2008 were one Transfusion Associated Circulatory Overload (TACO) and one Transfusion Related Acute Lung Injury

(TRALI). This corresponds to a risk for a severe or fatal ATE of approximately 1:12,000 transfusions.

Figure 2. Current Risks for ATEs in Switzerland by category

Category	Risk (One event per number of transfusions)
FNHTR	1 : 3,000
Allergic TR	1 : 2,500
Alloimmunisations	1 : 2,000
IBCT	1 : 9,000
HTR	1 : 25,000
Hypotensive TR	1 : 37,000
Bacterial Infection due to Transfusion	1 : 200,000 (1:12,000 for platelet concentrates)
TACO	1 : 20,000
TRALI	1 : 200,000
TAD	1 : 80,000
Near Miss	1 : 2,000

The errors leading to the 48 IBCTs reported in 2008 can be assigned to the following types of event:

Prescribing an incorrect component (2), ordering the blood product (16), misidentification of the pretransfusion sample (2), testing of the pretransfusion sample (5), delivery of the component (9), intermediate storage of a product to be transfused not respecting all necessary conditions (2) and administration of the blood component (12). There was a total of 233 Near Miss events reported comprising deviations at the following steps: Identifying pretransfusion samples 65%, ordering blood 7%, releasing the blood 5%, interim storage (i.e. on wards) 15%, application 2%.

Further measures and recommendations

- Based on Swiss Haemovigilance data concerning TRALI and encouraging preliminary reports on effects of comparable measures in other countries, the production of quarantined fresh frozen plasma is restricted to donations from men or from women who have never been pregnant (to their knowledge) or who test negative for antibodies against HLA class I and II, as of January 1st 2007. The analysis of further vigilance data will determine the efficacy of this preventive measure.
- Additional testing of all donations for Hepatitis B Virus using a nucleic acid amplification technique has been introduced on September 1st 2009 to further minimise the risk of HBV transmission.
- In order to reduce transfusion transmitted bacterial infection, a feasibility study was initiated in December 2009 to determine how and when pathogen reduction methods may be introduced countrywide in the routine production of platelet concentrates. Currently we consider 24 months as a realistic timeline for the implementation of this measure to enhance transfusion safety in Switzerland.
- Hospital transfusion guidelines should address detecting patients at risk for TACO and adjusting the transfusion rate. Close surveillance of patients under transfusion allows early intervention.
- Further haemovigilance issues are the current under-reporting, patient identification, alloimmunisations and the systematic collection and analysis of donor complications.

Abbreviations:

ALAT	Alanine Amino Transferase
ATE	Adverse Transfusion Events
ERA	Error and Risk Analysis
FNHTR	Febrile Non-Hemolytic Transfusion Reaction
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HTR	Hemolytic Transfusion Reaction
IBCT	Incorrect Blood Component Transfused
NM	Near Miss Event
TACO	Transfusion Associated Circulatory Overload
TAD	Transfusion Associated Dyspnoea
TR	Transfusion Reaction
TRALI	Transfusion Related Acute Lung Injury
TTI	Transfusion Transmitted Infection

A more detailed description of the reported events 2008 is available in the Haemovigilance Annual report 2008 at the following link:
http://www.swissmedic.chmarktueberwachung/00159/00160/00437/index.html?lang=en

Behind the Canadian database

New Developments for the Canada Vigilance Adverse Reaction Monitoring Program and Database

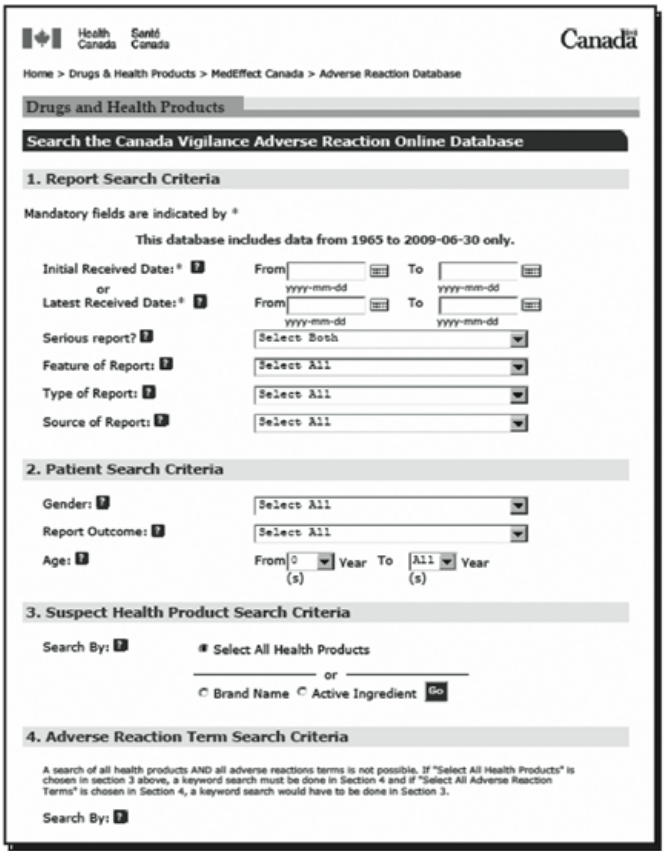
Heather Sutcliffe

In November 2009 Health Canada launched a new version of the Canada Vigilance Adverse Reaction Online Database (http://www.hc-sc.gc.ca/dhp-mps/medeff/databasdon/index-eng.php). The Online Database provides the public with searchable web access to information about adverse reactions reported to Health Canada. It contains a data subset extracted from the Departmental adverse reaction database of information about suspected Canadian adverse reactions to health products, such as prescription and non-prescription drugs, natural health products, biologics and radiopharmaceuticals.

Online database enhanced

The new version of the Canada Vigilance Adverse Reaction Online Database includes the following enhancements:

- The search criteria page layout has been simplified
- The ability to search brand name(s) or active ingredient name(s) of a health product has been added
- The ability to search by reported adverse reaction term(s) or group(s) of adverse reactions terms has been included
- Additional help and background information have been provided to the user
- The ability to print/save/export search results in Adobe pdf format or MS Excel format has been provided.



Canada Vigilance Adverse Reaction Online Database

Implementation of new database

The revised Online Database follows the implementation of a new Departmental Canada Vigilance Adverse Reaction Database in March 2008. This new database represents a significant step forward in technology from Health Canada's previous database. The first phase of the implementation involved deploying the fully ICH compliant system with electronic workflow management for post-market adverse reactions. As a result of the implementation of the MedDRA medical terminology for data management and retrieval, including Standardized MedDRA Queries (SMQs), the program now has a signal detection business transformation and data-mining project underway. The Canada Vigilance Database will also eventually manage adverse reactions from clinical trials. Thus the database will track adverse reactions over the entire lifecycle of a product from clinical trials through to its experience in widespread use once it is approved. The second phase of implementation will utilize the system's capacity to handle electronic filing of adverse reaction reports pre-coded in MedDRA from market authorization holders (MAH), who are mandated to report adverse reactions to products they market in Canada.

Canada Vigilance promotional Poster

The Canada Vigilance Program relies on MedEffect™ Canada, which provides a simple and efficient means for health professionals and consumers to report an adverse reaction to the Canada Vigilance Program. It also serves as a centralized point to access the latest health product safety information such as advisories, warnings and recalls.

Promoting reporting

MedEffect™ Canada launched a social marketing campaign in early 2009 encouraging Canadian health professionals and consumers to use MedEffect™ Canada to report suspected adverse reactions from health products and access the latest safety information. As part of the marketing campaign, brochures were displayed in pharmacies, guidelines for reporting were distributed to both health professionals and consumers and advertisements were included in newspapers and medical journals across the country all in an effort to promote the importance of reporting adverse reactions.

Guides for all

Not only does the program plan to release an adverse reaction reporting form and guidelines specifically designed for consumers in 2010, the following Guidance Documents were released in 2009:

WHO's Global Network for Post-marketing Surveillance of Pre-qualified Vaccines

Adwoa Bentsi-Enchill (WHO) and Jerry Labadie (UMC)

The Global Network

In UR46 we reported on a WHO project to establish a Global Network for Post-marketing Surveillance of Pre-qualified Vaccines (Global PMS Network) with the UMC and other pharmacovigilance experts as partners. The primary goal of the Global PMS Network is to ensure a standardized approach to monitoring and assessing the safety of pre-qualified vaccines supplied through UN agencies primarily to developing countries. The Network is managed by the WHO Department of Immunization, Vaccines and Biologicals (IVB), and comprises 11 countries across the six WHO Regions: Albania, Brazil, India (Maharashtra State), Iran, Kazakhstan, Mexico, Senegal, Sri Lanka, Tunisia, Uganda, Vietnam. Representatives of the network met in Rabat, Morocco from 6 to 8 November 2009 (following the 32nd Annual Meeting of the WHO Programme for International Drug Monitoring) to evaluate progress and plan for the next cycle of implementation, with actual reporting planned to commence in 2010.

WHO vaccine pre-qualification

Vaccine pre-qualification by WHO (http://www.who.int/immunization _standards/vaccine_quality/vq_index/en/index.html) is based on quality and safety (and effectiveness) standards clearly demonstrated through pre-licensure animal studies and human clinical trials (and supported, where available, by post-licensure data obtained during use in a limited number of countries). In most cases, post-licensure safety data are limited at the time of pre-qualification. This network will therefore support the WHO vaccine pre-qualification programme by providing safety data during the post-licensure phase when the vaccine is marketed for wide use in the general population.

Reporting via VigiFlow

VigiFlow™ will be the standard means for reporting by the majority of network countries. In preparation for regular reporting of AEFIs by network countries, in-country training on VigiFlow has been provided to 10 of the 11 network countries to date. In addition, the network has defined a core set of vaccine safety data to be included in reports. To meet the network needs for reporting by countries of these core data, there is on-going work by the UMC to modify VigiFlow with the addition of fields relevant for vaccine-associated adverse events. The requirements of the Network have also fed into the development of a vaccine dictionary to enhance the existing WHO Drug Dictionary. Further information about the network and its activities are available through the WHO website (http://www.who.int/immunization_safety/activities/en/).

Members of the Global Network on the roof of their conference venue, with the Tour Hassan in the background.

Broader benefits

Through the Global PMS Network, enhanced reporting of vaccine safety data to the UMC is expected in coming years. In turn this will assist on-going efforts (supported by WHO's Global Advisory Committee on Vaccine Safety) to use the resources and experience of UMC for data-mining and signal detection to improve global vaccine safety monitoring. In future issues of Uppsala Reports, we will update on activities of the Global PMS Network, including the resources developed to support the network which will benefit other non-network countries. A more extensive description of the work on the vaccine dictionary will be published in the next Uppsala Reports.

Continued from page 12

- Guidance Document for Industry—Reporting Adverse Reactions to Marketed Health Products (http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2009-guidance-directrice_reporting-notification/index-eng.php) which provides Market Authorization Holders with assistance on how to comply with the Canadian regulations with respect to reporting adverse reactions to marketed health products.
- Guidelines for Reporting Suspected Adverse Reactions to Antiviral Drugs During an Influenza Pandemic (http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2009-ar-ei_anti_guide-ldir/index-eng.php) which provides health professionals and consumers information on reporting adverse reactions to antiviral drugs.
- Adverse Reaction Reporting and Health Product Safety Information: Guide for Health Professionals (http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-prof/index-eng.php)
- A Patient Guide for Reporting Side Effects from Health Products (http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_fs-if/2009-ar-ei-guide-patient/index-eng.php)

Health Canada has embarked on a Product Vigilance Transformation Initiative to deliver a comprehensive, co-ordinated approach to federally regulated health product vigilance. This involves the development and implementation of an over-arching product vigilance framework integrating various product vigilance tools such as adverse reaction monitoring, product safety update reports, development safety update reports and risk management plans. The Canada Vigilance Program is an important component of this initiative.

ISoP sparkles in Reims

Geoffrey Bowring

Trying to cover the full range of current issues in pharmacovigilance over just three days is the annual challenge which the International Society of Pharmacovigilance sets itself. As a prelude to its 9th annual meeting from 6-9 October, an enticing range of pre-conference training courses were offered, with varying degrees of uptake, on 'Basic concepts and application in pharmacovigilance', 'Keeping the lights green - your risk management roadmap', 'Qualified person for pharmacovigilance', and 'Communications challenges in patient safety: Partnerships, PILs and preventing patient harm in cyber space'.

Peter Arlett, Head of Sector Pharmacovigilance and Risk Management, European Medicines Agency, gives the keynote opening address in Reims.

The main meeting with over 300 delegates began with the over-arching theme of the year: risk management; then looking at global problems (India, Spain, Latin America, Africa) and a talk 'From legislation to implementation: The challenge of taking regulation into day-to-day practice' from Robin Ferner (Birmingham, UK). 'Risk Communication' managed to cover most angles: developments and challenges for regulatory authorities in the EU, Patient reporting and co-operation with patient associations, evidence-based medicine and effective communication and dealing with the media.

Signal detection and verification

A series of lectures examined new data sources and methods for signal detection: ENCePP and PROTECT, 'Pharmacoepidemiology, drug safety and drug abuse evaluation in France' (which introduced a new word, addictovigilance), the FDA's Sentinel Initiative, and, as an example of the UMC's work, research on a temporal association between prescriptions of anti-psychotic drugs and pneumonia in electronic health records. 'Pharmacovigilance and clinical trials' and 'Improving the efficiency of pharmacovigilance' gave delegates plenty to think about.

Initiatives from Europe and beyond

By Thursday the conference was onto 'Regulatory initiatives with a global impact', which included reports on risk management initiatives in HIV medicines, and risk minimisation with biological medicines. 'Prediction and prevention of ADRs' included lectures by researchers into this burgeoning field. The ISoP Swiss chapter organized a satellite symposium on several high-level topics with particular emphasis on the role of health care practitioners.

Hot topics

Pharmacovigilance for vaccines was highlighted, with presentations from WHO, UMC, GlaxoSmithKline Biologicals, along with views from Ghana and India on progress in resource-poor countries. 'Haematological reactions by vaccines' was based on current experiences in Italy. After 'Undesirable psychiatric and behavioural effects of medications' and 'Counterfeit Medicines', there was a session on 'Hot topics'. Rheumatoid arthritis, the safety profile of biologicals using post-marketing safety data, continuity of pharmacovigilance systems during transfer of marketing authorizations and company mergers and buy-outs were followed by a survey on HIV-negative patients with Non-Hodgkin's lymphoma receiving rituximab and cardiovascular risk of sulfonylureas on newly diagnosed type II diabetes mellitus patients.

Friday brought a fascinating session on 'Ethical considerations in pharmacovigilance', introduced by Ralph Edwards, with two important lectures, on 'Pharmacovigilance and patients: symbolic logics and ethical aspects' by Sylvie Fainzang, France, and 'Could happiness ever be tyrannical? Reflections on Mental Health' by Lubomira Radoilska, UK. Finally, the 2009 Bengt-Erik Wiholm Lecture was given by Bernard Bégaud of the Université Victor Segalen, Bordeaux, on 'Drug regulation: a decision under uncertainty. A tribute to Bengt-Erik Wiholm'.

The UMC had seven posters among the 200 exhibited at the meeting. The winner of the Poster Prize was 'Preventability of ADRs leading to hospital admissions assessment of inter rater variability' by Schmiedl et al (Germany).

While an evening reception for delegates took place at the grand Hôtel de Ville in Reims, the gala dinner was held – where else? – in the cave of the well-known Pommery estate.

Patient safety in the Balkans

Sten Olsson

A major pharmacovigilance symposium took place in the city of Vršac, northern Serbia, on 19-20 November 2009. The title was 'Patient Safety – Common Goal of Pharmaceutical Industry, Regulatory Authorities and Healthcare Institutions'. It was organized by the Serbian regulatory authority, ALIMS, together with national health professional organizations, under the patronage of the Serbian Ministry of Health.

The organizers had engaged many national and international experts to cover a wide range of subjects from causality assessment of ICSRs

Milena Miljkovic speaking at the Vršac symposium

to pharmacovigilance planning, pharmacoepidemiology, global pharmacovigilance and benefit/harm assessment. The WHO Programme was represented by Mary Couper, WHO-Geneva and Ronald Meyboom, Sten Olsson and Ulf Bergman (board member) from the UMC.

There were about 170 health professionals of varied backgrounds in the audience. Participating were regulatory authority staff from Bosnia & Herzegovina, Macedonia, Montenegro, Russia and Turkey, and presentations were made by speakers from agencies in France, Ireland and the United Kingdom. Many prominent representatives of the Serbian Ministry of Health, healthcare insurance system, clinical specialities and the pharmaceutical industry were present. The event received considerable attention in national media including radio, television and daily newspapers. Since Serbia was on the verge of initiating its immunization programme against the pandemic A/H1N1 influenza many questions raised at the

(left to right) Anita Rakic Ignjatovic, Ivan Kovacevic and Marija Petronijevic of ALIMS

symposium and by the media concerned the safety of pandemic influenza vaccines and experiences already gained in other countries. The Serbian pharmacovigilance system has shown a very positive development since UMC was engaged in running a basic pharmacovigilance training course in Belgrade in 2003. The national centre has now a staff of around ten highly qualified and dedicated professionals. A successful twinning programme with the French regulatory agency, Afssaps, has contributed to a high level of competence and confidence, making the Centre prepared to take on the challenge of joining the European Union pharmacovigilance collaboration once the political processes are completed.

Coping with uncertainty

Ola Caster

I attended the Fourth IIASA Workshop on Coping with Uncertainty, which was held in beautiful Laxenburg outside of Vienna, Austria, between 14th and 16th December. IIASA (the International Institute for Applied Systems Analysis) is a research institute that focuses on issues of global character, such as global warming. It is a renowned organisation that has hosted four Nobel laureates, and its premises are of equally high standard: an old Habsburger castle.

The focus of the workshop was theory and practice aimed at supporting robust decision making in areas where major uncertainties are present. This is clearly relevant in pharmacovigilance, where signals of new adverse drug reactions are inherently uncertain, and need to be evaluated in the context of the drug's positive effects. I was fortunate to be selected to present recent joint UMC-Stockholm University work on methodological developments within the area of decision analysis, which will hopefully be useful in pharmacovigilance in the future.

UMC team at work in India

Bruce Hugman

Late November saw a varied and busy week in India for UMC Director Marie Lindquist, Medical Advisor Ralph Edwards, and Communications Consultant Bruce Hugman.

First was participation in the ninth annual meeting of the Society of Pharmacovigilance India (SOPI), held at the Rajendra Institute in the north-western city of Sirsa in the state of Haryana. Several hundred participants came from all over the country, joining the large crowd of local staff and students.

Programme topics

The UMC team delivered lectures and workshops and assisted in judging of the more than two hundred posters. Topics on the agenda included pharmacovigilance in oncology; psychotropic ADRs in geriatric patients; safety and quality of traditional drugs; pharmacovigilance of antiretrovirals, and much more. Marie Lindquist delivered the key-note speech on the current state of global pharmacovigilance and future challenges; Bruce Hugman gave the John Autian oration on the frequently great gap between the tough realities of front-line practice and official decision-making in pharmacovigilance and patient safety; and Ralph Edwards spoke about the pharmacovigilance of herbal medicines.

In the city

Back to Delhi, and meetings at the Swedish Embassy and the office of the Drug Controller General of India. The latter was an opportunity for two new office holders to get to know each other and to discuss

Marie Lindquist waits to take part in the lamp-lighting ceremony at the beginning of the meeting. In the picture are also Professor K C Singhal; Dr Sandeep Agarwal; and the Chairman of the Rajendra Institute, Dr Rajendra Singh Sra.

how India's great potential for contribution to global pharmacovigilance could be fulfilled. Then on to two days of teaching at the International Institute of Health Management Research in Dwarka. Here, the theme was Risk Management, and the thirty or so students from three pharmacovigilance and medical science courses had sessions on theory and practice in signal detection and strengthening, data management, risk management planning and risk communication. The enthusiasm of the students and their existing familiarity with pharmacovigilance were notable.

Indian hospitality

Bringing the SOPI meeting to the relatively remote city of Sirsa was something of a triumph for the local hosts, and they celebrated their achievement by rolling out red carpets in every possible direction for their guests. There was an evening of spectacular local music and dance, including an orchestra of young players interpreting western music on an unusual selection of instruments, strongly led by percussion. The kindness of Rajendra students and staff was remarkable.

The UMC trio were able to renew friendships with many Indian colleagues and to forge new relationships in the field of pharmacovigilance. There is optimism that Indian pharmacovigilance will soon take its rightful place on the world stage, after many years of hesitant beginnings: the UMC team certainly met more than enough enthusiasts for the science to promise great things.

Vaccine safety meetings

Sten Olsson

Jerry Labadie, the UMC's Vaccine Safety Specialist, was an invited speaker at the 5th Pan-Hellenic Congress on Management, Economics and Health Policy (Athens, 2-5 December 2009). His presentation 'The safety of pandemic vaccines' was part of a well-attended session on 'Pandemic vaccines against the pandemic virus A(H1N1)' on December 4. This session was organized by Georgia Terzi-Vaslamatzi, head of the Greek National Centre and featured H Giamarellou, Professor of Internal Medicine setting out 'The Greek strategy against the pandemic virus A(H1N1)' and L Klironomos on 'Pharmacovigilance for pandemic vaccines in Greece'.

Shortly after this, Jerry attended Eurovaccine 2009, the first European conference on vaccination and immunization, organised by the European Centre for Disease Prevention and Control (ECDC) in Stockholm, Sweden, on 11 December. Topics addressed during the one-day conference included implementation of the Pandemic A(H1N1) vaccination and strategies for measles elimination in Europe. The conference was webcast live, thus allowing for a broad international audience to follow the presentations and participate in the discussions. The video stream of Eurovaccine 2009, as well as the posters presented during the conference's virtual poster session, will be available on demand for a period of 6 months after the conference at the Eurovaccine website http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/Eurovaccine/Pages/default.aspx.

DIA in New York

Niklas Norén

The 2nd Drug Information Association Conference on Signal Detection and Data Mining was held in New York City from November 16th to 18th 2009. It hosted an international panel of speakers and gathered more than a hundred participants from academia, industry, and government agencies.

The theme of the conference was international perspectives on individual case safety reports (ICSRs) and other healthcare data sets. The section on ICSRs covered the state-of-the-art of both computerised pattern discovery methods and manual clinical review. It also included various perspectives on best practice in day-to-day pharmacovigilance. The section on other healthcare data sets was highly topical and combined methodological presentations, such as an overview of the self-controlled case series methodology, with presentations of the two main US initiatives in the area: the FDA's Sentinel Initiative and the Observational Medical Outcomes Partnership (OMOP) study.

The UMC made a range of contributions to the meeting. Niklas Norén served on the programme committee, co-taught the pre-conference tutorial, and gave a presentation summarising the UMC's work on data mining electronic patient records over the past five years. Ralph Edwards concluded the two-day conference with a presentation entitled CIOMS VIII and the future, with a visionary outlook towards improved patient safety in the future.

Thalidomide victims meet

Sten Olsson

The 3rd world conference of thalidomide victims was organized in São Paulo, Brazil, from 27–29 October 2009, by the Brazilian and Swedish Thalidomide Societies. Over 140 participants had come from many parts of the world to discuss experiences and ways to address common problems.* The conference was supported by a grant from the Swedish governmental aid agency Sida and a representative of the Swedish embassy in Brazil welcomed all delegates. The presidents of the Brazilian and Swedish thalidomide societies, Claudia Marques Maximino and Björn Håkansson were happy to be able to greet the participants coming from afar to this unique conference. They alluded to the fact that 50 years have passed since the thalidomide syndrome was first identified and still there were affected individuals in the audience as young as 25 and even 3 years. They both saw this as a sad and unacceptable failure of society safeguards and invited the establishment of a global action plan to achieve the vision of the thalidomide societies: no more thalidomide babies!

Compensation and support

Brazilian politicians and representatives of social authorities gave an outline of the development of compensation schemes and support systems for thalidomide victims in the country and gave a lot of credit for the development to the struggle of Claudia Marques Maximino and her organization. Country representatives from Canada, Germany, Italy, Norway, Sweden and United Kingdom presented the situation facing thalidomide syndrome sufferers in each of their countries.

Clinical indications

Professor Kerstin Strömland, paediatric neurologist from Queen Silvia Children's Hospital in Göteborg, Sweden, who has investigated all the 110 thalidomide syndrome patients in Sweden, gave a thorough overview of the clinical manifestations of the syndrome. Some effects are less known, for instance the inability of some individuals to shed tears when sad; instead tears may be shed while eating. A show of hands indicated that this is not an uncommon problem. Brazilian geneticist Lavinia Schüler Faccini presented the circumstances around the birth of three recent babies with thalidomide syndrome in Brazil. The study has been published in the scientific literature. One presentation demonstrated how thalidomide distribution and use follows the epidemiology of leprosy in Brazil. Sten Olsson from the Uppsala Monitoring Centre gave a presentation with the title: 50 years after thalidomide – are medicines now safe? He also later gave a presentation about the WHO Programme for International Drug Monitoring.

Appropriate healthcare

The difficulty for thalidomide syndrome patients to receive competent and appropriate healthcare was raised by Geoff Adams-Spink. Healthcare professionals have little knowledge about how to treat patients with an anatomy deviating from the norm. Thalidomide victims using unorthodox means of transporting themselves may end up with worn-out joints needing replacement. There is very little knowledge in healthcare systems about how to deal with such situations. Mr Adams-Spink promoted a database for collection of thalidomide syndrome related health problems and how to manage

Björn Håkansson, Kerstin Strömland and Geoff Adams-Spink on the platform at the São Paulo conference

and treat them so that such information is shared and not lost. It was also noted that virtually all the scientists who originally investigated the thalidomide syndrome and its effects after it was first discovered are now retired. There is a general lack of competence in healthcare systems around the world to provide thalidomide syndrome patients with appropriate medical support. This development is a major issue for thalidomide associations to highlight and try to counteract.

If you are interested in a video recording from the conference it is viewable on the internet here:
http://www.talidomida.org.br/video.asp

* *The first conference was held in Nijmegen, Netherlands in 1992, the second in Båstad, Sweden in 1994.*

Building a system in Cambodia

Bruce Hugman reports from Phnom Penh

A high profile workshop, chaired by the Secretary of State for Health, H.E. Pharmacist Chou Yim Sim, was held in Phnom Penh in early December 2009. Its overall purpose was to provide a boost to the infant pharmacovigilance system in Cambodia and to appoint a technical Advisory Committee. It was the last event in a long programme supported by USP (DQI)* funded by USAID, prior to new funding coming on stream from AMFm† in 2010.

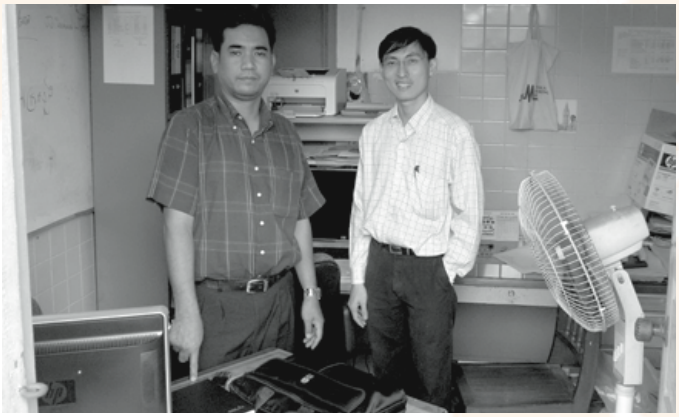
Barriers to reporting

Along with senior officers from the Department of Drugs and Food (DDF), about forty professionals from hospitals and academic institutions spent the day reviewing how awareness of pharmacovigilance and patient safety issues could be raised in Cambodia and how ADR reporting could be launched and promoted. The question of the reluctance of busy professionals to fill in complex forms was raised, and the possibility of SMS notification of the wish to report was strongly recommended. While this would transfer the burden of follow-up work to pharmacovigilance centre staff, it was felt that the requirement for such minimal effort by reporters might encourage more to participate.

VIPs at the workshop: Dr Chantha Chak, Infectious Disease Team Leader, USAID, Cambodia; Prof. Tea Kim Chhay, Director, DDF; H.E. Pharmacist Chou Yim Sim, Secretary of State for Health; Dr Chroeng Sokhan, Vice Director, DDF

Workshop topics

Bruce Hugman provided an overview of the importance of pharmacovigilance in helping prevent injury, death and the squandering of resources in healthcare systems. Progress and problems since the Pharmacovigilance Centre was established in June 2008 were reviewed by Mr Bunso Sok, from the core pharmacovigilance team, and, as is so often the case, resources, support and organisational dynamism were issues to be addressed. Membership of the Advisory Committee, with a prime responsibility for evaluation of signals, was agreed.



The core pharmacovigilance team in their tiny office: Mr Mam Dattara and Mr Bunso Sok, hoping for a few more square metres in the new DDF building

Ways forward

The workshop developed a strong conceptualisation of the importance of pharmacovigilance for the health and welfare of the people of Cambodia and a determination to get things moving and stimulate ADR reporting. The DDF's imminent move from its old and run-down offices to a brand new building adds a further dimension of hope that that things will soon change for the better.

The AMFm programme, which is being supported locally by the Clinton Foundation, has a significant pharmacovigilance component which will provide further opportunity for the development of the national system.

*USP (DQI) – United States Pharmacopeia, Drug Quality and Information Program

†AMFm – Affordable Medicines Facility (malaria), Global Fund

Pharmacovigilance in a tuberculosis programme

G Parthasarathi, Professor, JSS Medical College Hospital, Mysore

The Revised National Tuberculosis Control Programme (RNTCP) of India is probably the largest public healthcare programme in the world. The programme treats 1.5 million tuberculosis (TB) patients per annum in 684 Tuberculosis Units (TUs) with over half a million trained staff. The World Bank funded project is expected to spend US$ 256 million in phase II between 2006 and 2011. However, safety profiles of anti-TB medications in the Indian population are lacking. The increasing access to anti-TB treatment (ATT) is not accompanied by processes to monitor medication safety, so there is an urgent need to develop the monitoring system, as a moral obligation of the RNTCP.

Project background

The Clinical Pharmacy Department of JSS College of Pharmacy and JSS Medical College Hospital, JSS University, Mysore initiated the SMART (**S**afety **M**onitoring of **A**nti-tubercula**r** **T**herapy) pilot project in September 2009 with the objective to develop ten RNTCP centres within the Mysore TU as sentinel sites for monitoring of adverse drug reactions (ADRs) to ATT. The project also aims to characterize the incidence and risk factors of ADRs in our local population.

Tuberculosis control logistics

RNTCP centres attached to a primary health centre, staffed with a medical officer, pharmacist and TB health visitor, were identified in consultation with the District TB Medical Officer. Workshops on 'Safety Monitoring of Anti-TB Therapy', sponsored by the Mysore Physicians Medical Research Trust, were organized for sentinel site personnel. Ten medical officers, eight pharmacists, ten TB health visitors, six nurses and ten other staff of RNTCP centres were trained in ADR detection, reporting and patient counselling. A SMART trigger tool was developed and implemented to assist the personnel in detecting ADRs to ATT. Health visitors participating saw that such projects help develop their skills and improve their contribution to the success of RNTCP.

Trainers and participants in the SMART workshop in Mysore

Results

Pre and post workshop assessments of non-medical staff of RNTCP centres revealed a 25% increase in the understanding of pharmacovigilance and ADRs to ATT, and 68% of the participants detected the ADR to ATT in dummy TB patients using the trigger tool. ADR reporting forms and patient information leaflets regarding ADRs to ATT were made available at all selected sites. During the two months of project implementation, among 191 patients in the initial/continuation phase of ATT, 140 ADRs were reported from 80 patients (prevalence 41.9%).

Pharmacovigilance and public health

SMART is the first project in India to attempt to integrate pharmacovigilance in a public healthcare programme. The project is expected to build capacity and impart skills in the existing workforce in the area of safety monitoring of ATT. This approach will help in safety monitoring of ATT, create awareness about pharmacovigilance, and develop a database of ADRs to ATT in the local population with no extra investment on human resources. Professor G Parthasarathi, principal project investigator plans to expand the SMART project to include more RNTCP centres in a phased manner. Such projects will pave the path for capacity building to monitor medication safety within other public healthcare programmes in India.

Studying the impact of pharmacovigilance

Viviana Bologna, of the Argentinean National Centre ANMAT has recently presented her doctoral thesis at the Universidad de Buenos Aires. Her subject was the 'Health impact of the implementation and development of the National System of Pharmacovigilance of Argentina'. The impact of pharmacovigilance is a recurring theme among professionals working in the field.

The purpose of Dr Bologna's thesis was to investigate the effects of interventions of the national system of pharmacovigilance (NSP) of Argentina on the safety of medicines. Working from the normative aspect of drug safety in Argentina, the national pharmacovigilance system itself, the results of NSP interventions and the views of health professionals, the objective was to describe and analyze the implementation and development of the NSP in Argentina as a contribution to the safety of drugs.

The specific objectives were developed from the concepts of quality of structure, process and results using as reference the quality criteria proposed by Ronald Meyboom (Meyboom RHB. Good Practice in the Postmarketing Surveillance of Medicines. *Pharm World Sci* 1997; 19(4):186-190.).

The study looked at the implementation and development of the NSP, its actions from 1993 to 2005, and from this developed a process indicator to analyze the relationship between rules generated by the drug safety NSP (process) and safety regulations issued by ANMAT. The results and impact of NSP interventions on population health were analyzed along with the attitudes and skills of health professionals as stakeholders in pharmacovigilance systems, and interviews with experts in pharmacovigilance.

The conclusions in the thesis are a valuable contribution to understanding of how pharmacovigilance works, with discussion of the contribution of NSP to the safety of drugs, the effect of regional centres, examples of the incidence of neutropenia and agranulocytosis for clozapine and malformations of thalidomide following special monitoring programmes, and growth of reporting per million inhabitants from 1993 (the year the NSP began) to 2009. The results of a survey of 646 physicians and pharmacists as well as interviews with seven pharmacovigilance experts are also presented. Each of the sections in the thesis provides evidence of a progressive change in drug safety in Argentina.

Božidar Vrhovac

We learn with great sadness of the death on 4 December 2009 of Božidar Vrhovac, Professor Emeritus, University of Zagreb, Croatia. At the UMC 'Darko' is fondly remembered as a friendly and witty person, with a great dedication for clinical pharmacology, patient safety and international collaboration. He was deeply respected by colleagues around the world, and he called the preferred international language as 'slowly spoken broken English'. Igor Francetic and Michael Orme have written this appreciation of Darko, as a doctor and as a man.

Darko Vrhovac was born in 1936 in Zagreb (where he lived all his life) into a highly intellectual family; his father Vuk was the founder of endocrinology in Croatia and a major influence throughout his professional career.

During his medical studies in Zagreb Darko undertook an exchange programme to hospitals in Munich and Zurich – a unique opportunity for exposure to high-quality medicine. Graduating in 1961, from 1963 to 1965 he worked in the emergency department in Zagreb, where, puzzled by the fact that colleagues used so many different medicines for the same diseases, he first realised the importance of rational drug therapy. From 1965 he worked in the Department of Medicine at the University Hospital Centre in Zagreb, spending the rest of his career there.

In 1971 he became assistant professor in clinical pharmacology (the first in any Yugoslav medical school) and head of the intensive care unit, and started to promote and fight for rational drug therapy. As vice-director of the Drug Center, an important unit of the Hospital Association of Croatia, he used his position to spread the ideas and principles of rational drug therapy, first in Croatia, then throughout Yugoslavia. After a scholarship in London in 1972 under Professor Desmond Laurence, he became the undisputed authority in rational drug therapy in Yugoslavia and started activities which resulted in founding a postgraduate course in clinical pharmacology. From 1972 he represented Yugoslavia in several bodies of the WHO, and was especially proud of being a lecturer at meetings organized by WHO on the role of clinical pharmacology in drug evaluation and control.

In 1973 Professor Vrhovac organized, and became head of the first clinical pharmacology unit in the country and co-founded the Section for Pharmacotherapy of the Croatian Medical Association (later Society for Clinical Pharmacology and Therapeutics), and was its first President until 1997. He wrote the first clinical pharmacology PhD thesis in the region in 1976 and became Associate Professor (in 1980 Professor) at the Medical School of Zagreb. In 1974 Yugoslavia became the 18th country to join the WHO monitoring programme, and for over 30 years the operational base of the National Centre was his Clinical Pharmacology department.

Early on Professor Vrhovac saw the importance of the written word for spreading the principles of clinical pharmacology, and started editing bulletins, journals, textbooks, and wrote 600 papers related to the rational use of drugs. He was soon highly respected among colleagues in Croatia and surrounding countries for his publishing and organization skills. He edited the first edition of the Textbook of Internal Medicine and three subsequent editions, the last in 2008.

He edited the Hospital Drug Bulletin in Zagreb, was chief editor (1981-2007) of Pharmaca (national drugs journal), editor of the first book on Clinical Trials (1984) and organized translation of 'Clinical Pharmacology' (Laurence and Bennett) with commentaries on local drug prescribing practices. In 1980 he co-edited the first National Drug Formulary and was chief editor for four editions, most up to 2007.

Darko became internationally recognized: co-author of Meyler's 'Side Effects of Drugs' (1984, 1988, 1995 and 2000), co-editor of 'Clinical Pharmacology' (McGraw Hill, 2000), an author in the IUPHAR Compendium of Basic Principles for Pharmacological Research in Humans (2000), and on the editorial board of several international clinical pharmacology journals.

He was a member of the WHO Collaborative Centre for Adverse Drug Reactions Advisory Group, Uppsala from 1983–1986, and one of the founders of the Vienna School for Clinical Research, lecturing there for many years. An active member of many international societies, in 2004 he received honorary membership of the Royal College of Physicians of London. When the European Association for Clinical Pharmacology and Therapeutics (EACPT) was founded in 1993 he was elected to the Executive, where for eight years his experience and sound common sense were of immense help, meetings often enlightened by his humorous asides.

Beyond all the achievements, Darko was was above all a warm-hearted person who liked meeting people, always ready to help regardless of status, position or profession. He had a great sense of humour and it was hard to tell whether he preferred listening to or telling jokes.

Always hard-working, he often gave the impression of being in a hurry. On one occasion he told me that because of his diabetes he knew that he did not have time to lose. His dealing with diabetes was impressive; while others would consider it a handicap, with his strict control of the disease he used it as motivation – a positive example both for physicians and patients. He enjoyed life in many ways, playing tennis, which he did on the day he passed away, and never missing an opportunity to have a dance.

Evident from working with Professor Vrhovac for 30 years was his enormous energy, enthusiasm and passion for medicine, and particularly clinical pharmacology. He never slowed down; he either did not know how to, or did not want to. Full of plans and with a belief that there are still many things to be done, he died quietly at home. Many European clinical pharmacologists experienced the hospitality that he and his wife Yvonne offered to visitors; I felt that he enjoyed more being a host than being a guest.

We will miss Darko: the loss is enormous for European clinical pharmacology and greater still for Croatian clinical pharmacology. The best we can do is to continue from where he stopped and try to finish at least some of the projects he had in mind. Professor Vrhovac is mourned by his wife Yvonne, Professor at the University of Zagreb, his son Radovan, Associate Professor of Medicine, his family and very many friends and colleagues.

New staff

Ola Strandberg

Ola, born in Umeå on the northern Baltic coast of Sweden, moved to Uppsala when a teenager. Apart from a few years spent in Manchester, UK and in Irvine, California he has lived here ever since.

"My position as Vendor Liaison Officer entails working with the companies that develop software for our end customers, to ensure that in turn, they enable the best possible use of the WHO Drug Dictionary and other UMC products by pharma companies, CROs, etc. I will work with these software companies so that our Drug Dictionary customers make full use of the UMC data and harness its potential in their own day-to-day work. I have a technical background, so in addition to bringing these skills to the marketing team, I also look forward to working closely with my UMC software colleagues."

As Chief Technology Officer at Pharmasoft, Ola was part of the team that originally developed VigiBase and other UMC technical solutions. Since then, he has worked with software for medicinal product approval maintenance and adverse event reporting. Most recently, he was Director of Software Development at Biotage in Uppsala and looks forward a lot to returning to his field of core competence.

"I have three children living at home, but at ages where I actually have time for hobbies. I swim, bike and run as often as I can, and my not-so-secret talent is that I build guitars. I have a small business called *Strandberg Guitarworks,* developing and selling guitar hardware. This is part of a bigger concept for a complete ergonomic guitar that I launched at the 2009 Uppsala International Guitar Festival."

Visitors

The last quarter of 2009 saw several new visitors to the UMC office.

In late October Tomás Moraleda from the MedDRA maintenance organisation visited to discuss the MedDRA workshop in Rabat, and also to learn about the UMC's use of terminologies.

Vera Semenova Tyan Shanskaya, Professor of Computer Science at St Petersburg Marine Technical University came to the UMC in October. She was in Sweden for two weeks visiting various institutions prior to setting up a module including data-mining in her university in Russia.

Vera Semenova and Ola Caster

In early November Dr Marcus Schmitt-Egenolf, Deputy Head of Dermatology and Venereology, Department of Public Health and Clinical Medicine, Umeå University, gave a talk at the UMC about a long-term database his department has developed to monitor safety and effectiveness of different systemic psoriasis treatments. Dr Schmitt-Egenolf's special interest is to compare side-effects of new biological systemic medicines with conventional systemic medicines.

Dr Alexander Vlasov, from the new Russian centre (see p6) spent a day at the UMC learning about technical issues of the WHO Programme from various UMC staff.

Helena Wilmar and Alexander Vlasov

In December the UMC Board came for their last meeting before a new cycle starts; a full report will come in the next Uppsala Reports.

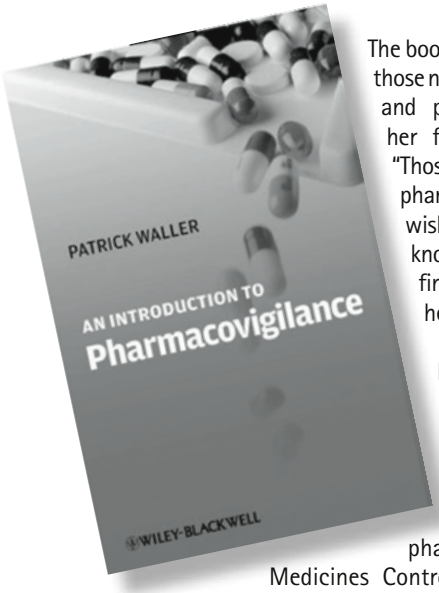
An introduction to pharmacovigilance

by Patrick Waller

We are delighted to see a new introductory guide to pharmacovigilance. It contains examples illustrating drug safety issues, and covers not only the processes involved, but also regulatory aspects, and ethical and societal considerations. Its chapters cover:

1 What is pharmacovigilance and how has it developed?
2 Basic concepts
3 Types and sources of data
4 The process of pharmacovigilance
5 Regulatory aspects of pharmacovigilance
6 International collaboration
7 Ethical and societal considerations
8 Future Directions
9 Learning more about pharmacovigilance

Appendices on books, journals, websites, courses and international societies.



The book is ideal for beginners and for those new to drug safety departments and pharmaceutical medicine. In her foreword June Raine writes "Those embarking on a career in pharmacovigilance or simply wishing to gain a sound working knowledge of the discipline will find what they need to know here in one place".

Patrick Waller holds honorary appointments at the London School of Hygiene and Tropical Medicine and the University of Dundee, having worked in pharmacovigilance for the Medicines Control Agency in London from 1990-2002. In his preface he comments "My purpose is to aid rapid understanding of the environment and key principles of pharmacovigilance at the industry/regulator interface" and underlines his aim to "enable newcomers to see where they fit into a bigger picture... and appreciate that they are working in an interesting and important field that is likely to develop much in the near future".

Papers

From the UMC

G Niklas Norén, Johan Hopstadius, Andrew Bate, Kristina Star, I Ralph Edwards
Temporal pattern discovery in longitudinal electronic patient records
Data Min Knowl Disc, DOI 10.1007/s10618-009-0152-3.

This paper presents a framework for open-ended pattern discovery in large patient records repositories, with a graphical statistical approach to summarising and visualising the temporal association between the prescription of a drug and occurrence of a medical event. The usefulness of the proposed pattern discovery methodology is demonstrated by a set of examples from a collection of over 2 million patient records in the UK. The identified patterns include temporal relationships between drug prescriptions and medical events suggestive of persistent and transient risks of adverse events, possible beneficial effects of drugs, periodic co-occurrence, and systematic tendencies of patients to switch from one medication to another.

Consumer reporting in Malaysia

Subish Palaian, Mohammed Alshakka, Mohamed Izham.
Commentary - Developing a consumer reporting program in Malaysia: a novel initiative to improve pharmacovigilance.
Pharm World Sci DOI 10.1007/s11096-009-9342-8.

A short article but including the Adverse Drug Reaction Reporting Form used by consumers in the project.

Changes at PDS

After 18 years as Founding Editor of Pharmacoepidemiology and Drug Safety (PDS), Professor Ron Mann has stepped down as Editor-in-Chief. Professor Mann was involved from the very first issue of PDS in January 1992 and has seen the journal blossom into an important monthly journal. Although he remains as Editor for UK and Rest of the World for a further year, Professor Brian Strom, Director of the Center for Clinical Epidemiology and Biostatistics, Philadelphia has become the new Editor-in-Chief.

Spanish booklet

Ser miembro del Programa Internacional de Farmaco-vigilancia de la OMS

A year after the UMC produced a booklet for national centres setting out the workings of the WHO Programme for International Drug Monitoring, it has been translated into Spanish. Thanks, as ever, to Mariano Madurga for his work on translating UMC documents for use in Spanish-speaking countries, we are now able to provide material in Spanish on advantages of membership – things that countries receive automatically from the UMC (access to VigiBase, Signal, terminologies and software, guidelines and resources, and access to the international network). The booklet also sets out what is expected from national centres, including reporting format compatibility and quality, frequent submission of ICSRs, and involvement in Vigimed and the National Centres Annual Meeting.

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
8-12 February 2010	Excellence in Pharmacovigilance: Clinical Trials and Post Marketing	Paris, France	DIA Europe Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
24 February 2010	Pharmacovigilance aspects of licensing agreements	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 www.management-forum.co.uk E-mail: registrations@management-forum.co.uk
3-4 March 2010	Interpretation of Laboratory Results in Pharmacovigilance	Fareham, UK	DSRU Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org ; www.dsru.org/
15-16 March 2010	Pharmacovigilance: Systems for Drug Development & Post-Marketing Surveillance	London, UK	Smi www.smi-online.co.uk/goto/ pharmacovigilance.asp?emref=U69ES191145915&t
22-24 March 2010	Advanced Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 www.management-forum.co.uk E-mail: registrations@management-forum.co.uk
24-25 March 2010	P2T 2010 - including 31emes journées de pharmacovigilance	Bordeaux, France	Société Française de Pharmacologie et de Thérapeutique http://www.congres-p2t.fr/index.php/ index.php/congres-reunions
24-25 March 2010	Back to Basics in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org ; www.dsru.org/
10-12 April 2010	ISPE Mid-Year Meeting	Raleigh, North Carolina, USA	ISPE www.pharmacoepi.org/meetings/ E-mail: ISPE@paimgmt.com
21-22 April 2010	4th European Forum for Qualified Person for Pharmacovigilance (QPPV)	London, UK	DIA Europe Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
26 April 2010	Introduction to Signal Detection and Data Mining in Pharmacovigilance in Europe	Paris, France	DIA Europe Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
5 May 2010	Introduction to Signal Detection and Data Mining	Horsham, PA, USA	DIA Phone: +1-215-442-6158 E-mail: Ellen.Diegel@diahome.org
27-28 May 2010	Basic pharmacovigilance course	Belgrade, Serbia	International Society of Pharmacovigilance www.isoponline.org
2-4 June 2010	Practical Guide for Pharmacovigilance: Clinical Trials and Post Marketing	Prague, Czech Republic	DIA Europe Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
19-22 August 2010	International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ICPE)	Brighton, UK	International Society for Pharmacoepidemiology (ISPE) www.pharmacoepi.org/meetings/ E-mail: ISPE@paimgmt.com
20-22 September 2010	Drug Safety Surveillance and Epidemiology	Horsham, PA, USA	DIA Phone: +1-215-442-6158 E-mail: Ellen.Diegel@diahome.org
29-31 October 2010	5th Asian Conference on Pharmacoepidemiology	Tokyo, Japan	International Society for Pharmacoepidemiology (ISPE) www.pharmacoepi.org/meetings/ E-mail: ISPE@paimgmt.com

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