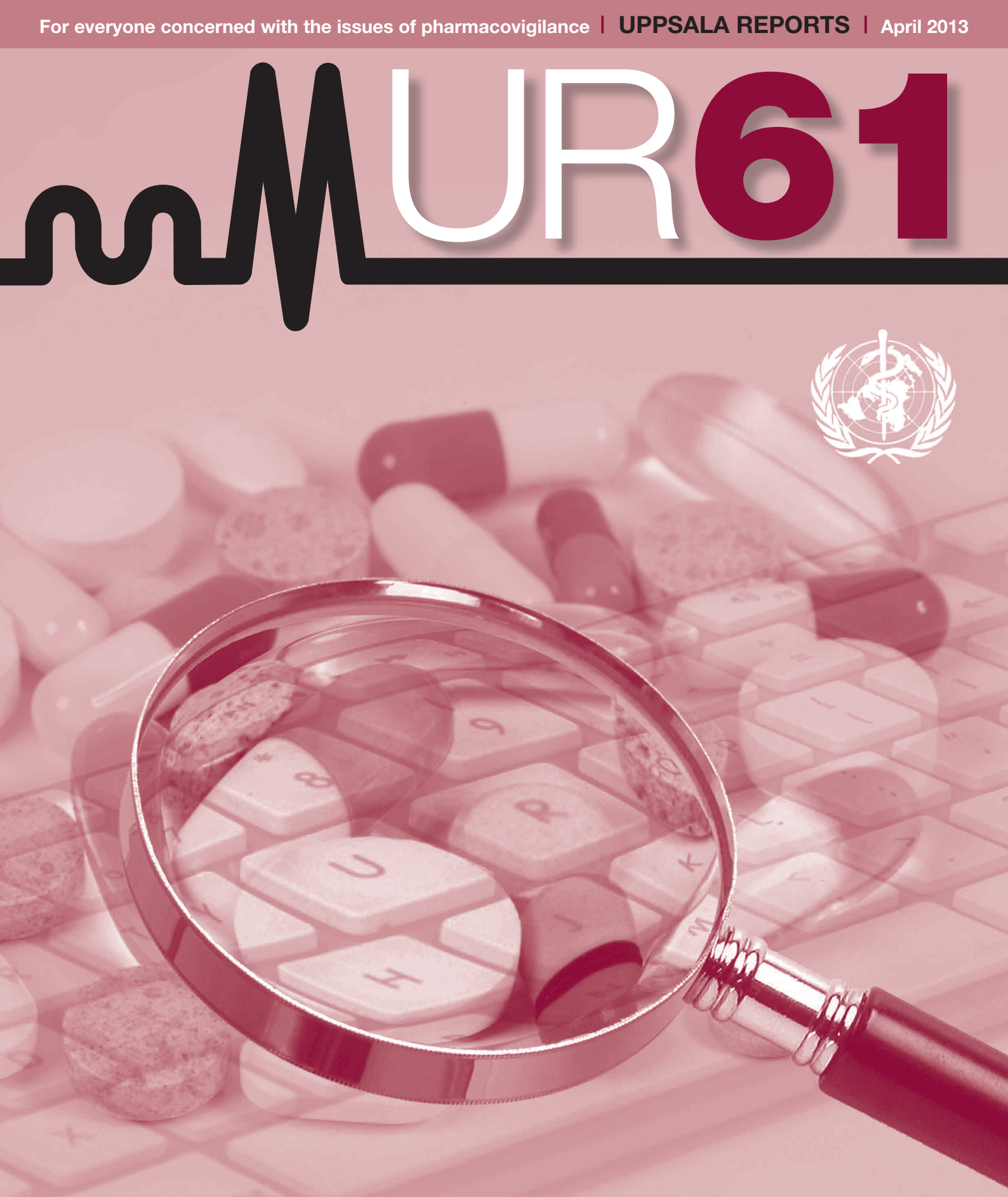
For everyone concerned with the issues of pharmacovigilance | UPPSALA REPORTS | April 2013

MUR61



8 million reports | Focus on CEM | Rubber dangers

History of a national policy | Side Effects?

Marie Lindquist
Director
Uppsala Monitoring Centre

My aunt B rang me a couple of months ago. She wanted to talk to me about a problem which was important to her. "I don't want to talk to my doctor" she said, "because she does not understand." It was about her medication. Some years ago she had been prescribed a statin, having previously been only on a beta-blocker for her blood pressure – which had been well controlled for a long time.

Having taken the statin for a while, she started feeling bad. "It is so difficult to explain," she said, "but I felt so rotten I didn't want to go out or do anything." There were physical symptoms, too, but what really bothered her was the way her state of mind was affected. "I couldn't stand it, and I stopped taking the drug without telling my doctor. I soon felt normal again, and what a relief it was. The problem now is that my new doctor insists that I should take a statin since my cholesterol is a bit higher than it should be. I can't stand the thought of what might happen to me if I do. I will be 89 in a few months, and I am at peace with the knowledge that my life can end anytime soon. My life is still meaningful to me, but only if I can enjoy my normal simple pleasures, like going out for a stroll, or sit in the garden listening to the birds. I'd rather die tomorrow than live another day feeling like I did last time I tried that drug".

When I asked what she wanted me to do, it was clear that she had already made her mind up; taking the drug would cause her more harm than she was prepared to accept. She just wanted to have some reassurance that she wasn't crazy, thinking the way she did.

I told her that, in my view, her thinking was perfectly sound. She knew why the statin had been prescribed, and what the expected benefits were. She had made her own risk assessment and made a choice that was right for her, and she was prepared to take the consequences of her actions. I also said that I was prepared to take the risk, by not having protested vigorously, of being accused of colluding in a decision which might shorten her life expectancy. We both laughed at the absurdity of the whole situation.

Now don't get me wrong. I am full of respect for practising physicians, and would not normally advise anyone to ignore their doctor's ordinations. But there are always exceptions, and I happen to believe that this is a case in point. My aunt's story is an important reminder that patients may not always agree with their doctor on what is best for them. There is no magic 'one-size-fits-all' formula for benefit and harm assessment!

The story is also an illustration of the importance of case histories for a more complete understanding of adverse reactions. How would one interpret an ICSR with 'feeling rotten' as the only clue to what happened`? In my aunt's case, 'dechallenge positive' would not tell us much, either, of the intensity of relief and the feeling of having got one's life back. There is clearly a danger in reducing what would be a meaningful and important message to coded bits of information that won't give us the full picture, and which may lead to the wrong conclusions.

Having said this, should we reject a report just because it lacks sufficient detail for a thorough assessment? I don't think so. However, for any regulatory pharmacovigilance system to be taken seriously, it should have functions in place to encourage health professionals and patients to provide the best information possible. To achieve this, trust is vital. Without trust (and empathy!) between health professionals and patients, problems in medicines use may not be reported in the first place. Secondly, those who report need to feel confident that the data they provide will be kept secure and used in a responsible way.

Data protection must be taken seriously, but not to the point where it overwhelms the protection of patients from harm. Judging from the multitude of patient groups and forums available on the internet, where detailed (but anonymised) individual data is freely discussed and exchanged, the impression is that many, many patients positively want their stories told; and that they are not worried about the information being publicly available.

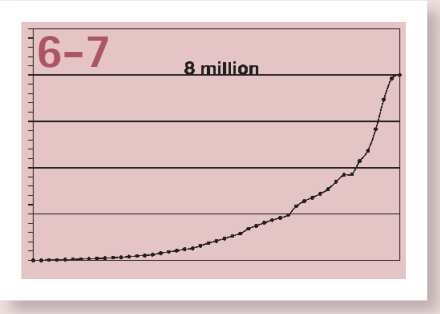
Is there any evidence that patients have been improperly or criminally identified from ICSRs in the last 50 years of pharmacovigilance? If not, who are we protecting, and why?

P.S. When I talked to B today she said that she had had a good day, going for a walk, and tending her geraniums. She is happy for me to tell you her story.

FEATURES

REGULARS

the UPPSALA MONITORING CENTRE

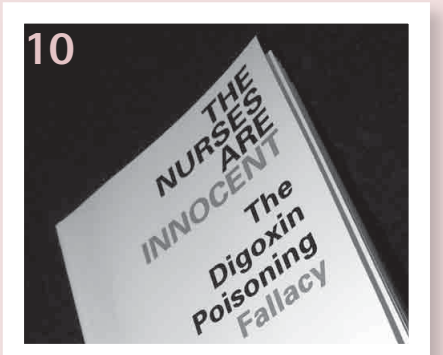


Database reporting news

The WHO global ICSR database passes the 8 million mark.

Government approved pharmacovigilance

How Nigeria achieved a national legal pharmacovigilance framework.



The digoxin poisoning fallacy

One doctor's crusade to reveal the truth about a deadly risk.

The power of CEM

Cohort event monitoring been implemented in Europe and Africa.

All Programme paths lead to Rome

Geoffrey Bowring

National centres in the WHO Medicines Safety Programme meet each year to discuss matters of mutual interest and help guide the future direction of the Programme. For 2013 Italy will be the destination. Fernanda Ferrazin and her team at the Italian Medicines Agency (AIFA, L'Agenzia Italiana del farmaco) are the hosts in Rome for the WHO Programme representatives at the 36th annual meeting of the Programme.

Central venue

The conference will take place from 26th-28th September (with pre-meetings on the 25th) at the Centro Congressi Roma Eventi, in the centre of the city, close to the famous Fontana di Trevi. The venue will be within walking distance from the suggested hotels.

A welcome reception at the 7th century San Lorenzo de' Speziali in Miranda will give representatives a chance to renew old acquaintances and make new friends before the real work begins; there will be another social event during the meeting.

Then on to ISoP

The annual meeting will take place a few days before the annual scientific meeting of ISoP in Pisa on the 1st-4th October, and a joint half-day meeting is planned.

The setting for this year's annual WHO Programme meeting

Return to Italy

Global pharmacovigilance has met once before in Italy: in 1982 the WHO Programme met in Ancona on the Adriatic coast, when there were only 22 countries in the Programme. 2013 should prove to be a rather larger gathering.

Getting ready

We hope that as many national centres as possible are planning their attendance. Official invitations and an agenda questionnaire have just been sent to all national centre heads in the WHO Programme.

WHO Programme news

Papua New Guinea

An application has been received by Dr Lembit Rägo at WHO from the Department of Health in Papua New Guinea, which has established a National Drug Information and Pharmacovigilance Unit. They have applied and been accepted as a new Associate member of the WHO Programme.

The appointed national centre Head is Mrs Shirley Gaiyer-Kore; we look forward to further progress for Papua New Guinea and their full participation in the Programme.

Tanzania

There have been several changes recently at the Tanzania Food and Drugs Authority.

Among them, Henry Irunde has been appointed as the Assistant Director of Pharmaceutical Services within the Ministry of Health and Social Welfare, and Chief Pharmacist. Dr N. B Chukilizo is now the Manager of the Clinical Trials and Pharmacovigilance Department. Prior to this recent appointment, Dr Chukilizo was the Manager of the Medicines Registration Department.

Republic of Korea

Following a governmental reorganization act in the Republic of Korea, the Korea Food and Drug Administration, KFDA, has become the Ministry of Food and Drug Safety (MFDS). Previous contacts remain the same.

The MFDS has elevated agency status with restructuring and expansion following the consolidation of the food management system. There are six Regional Food and Drug Administrations.

Pharmacovigilance at WHA

Just like last year, there will be a pharmacovigilance side event organized for delegates of the 66th World Health Assembly. The event will take place from 18.00 – 19.30 on 21 May 2013, in Salle XII of the Palais de Nations, Geneva. The precise programme of the event is not finalized as Uppsala Reports goes to print.

Time to celebrate access to clinical trials information

I Ralph Edwards

We must all congratulate GlaxoSmithKline (GSK) that they will publicly release all their protocols, clinical trials and other trial papers and results.[1] This release of information will be made after a product is marketed or when development is discontinued. It is a major step forward but needs monitoring, and implementation by all other pharmaceutical companies. The devil will be in the detail – will all the studies be released with enough information to allow critical review?

According to another news source, 26 drug companies – including eight of the ten biggest global players – have been fined a total of more than $11bn (£7bn) in the last three years after having been found to have acted dishonestly.[2]

Clinical trials for registration of products are usually funded by the drug industry and negative studies are apparently often withheld. This distorts the overall impression of the efficacy of a product.

GSK said in a statement it would sign up to the alltrials.net campaign which is seeking the registration of all clinical trials, the reporting of all summary results and for full Clinical Study Results – the detailed findings – to be made public.

Openness supporters

Drs Ben Goldacre, author of Bad Pharma, Fiona Godlee, editor of the British Medical Journal, Sir Iain Chalmers, of the Cochrane Library, and others, have been strong campaigners for more openness by industry through www.alltrials.net/, where one can find the statement from GSK and other useful information on this vital topic. There is also reference to a significant paper on the site by Professor Peter Gøtzsche of the Nordic Cochrane Centre who wrote on 'Deficiencies in proposed new EU regulation of clinical trials'.[3]

Allowing new developments

If you go to the alltrials site you will see that there are many individuals and organisations that have signed up to the campaign and you may feel that you wish also to do so. Personally it seems to me that we do need full information to achieve the ultimate goal of pharmacovigilance. In my view that goal is to be able to do meaningful, accurate effectiveness-risk assessments on all marketed medicines. On the other hand we must not go so far as to damage the pharmaceutical companies' competitiveness to give us new and useful products. We must allow some 'commercial confidentiality' to remain for this to happen, but not to the extent that the public and individuals are deprived of important information they need for decisions on their health and treatments. This great dilemma demands much more thought and wisdom than supporting the current campaign, but it is probably a reasonable step to support it now and it will pressure other pharmaceutical companies to follow suit, and to keep a 'level playing field' with other companies.

Do share your thoughts on this issue, and particularly whether the UMC should sign up for the campaign.

References

1. GlaxoSmithKline to publish clinical trial data (2013) The Guardian. Found at URL: http://www.guardian.co.uk/business/2013/feb/05/glaxo-smith-kline-publish-clinical-trial-data. Accessed 26 March 2013.
2. GSK to publish clinical trial data for drugs (2013) The Independent. Found at URL: http://www.independent.co.uk/life-style/health-and-families/health-news/gsk-to-publish-clinical-trial-data-for-drugs-8482289.html. Accessed 9 April 2013.
3. Gøtzsche, PC. Deficiencies in proposed new EU regulation of clinical trials. BMJ 2012;345:e8522.

Vaccines on the table

Sten Olsson

UMC interactions with WHO headquarters are coordinated by Shanthi Pal, manager of the WHO Medicines Safety Programme at the Quality and Safety: Medicines unit (QSM). Shanthi's coordination has lead to UMC working with many of the WHO public health or disease specific programmes. In 2008 an agreement was signed regarding UMC technical support to The Global Network for Post-marketing Surveillance of Newly Pre-qualified Vaccines (PMS Network).

Network standards

The primary objective of the PMS Network, in which 12 countries participate, is to ensure a standardized approach to monitoring and assessing serious, rare or unexpected AEFI (Adverse Events Following Immunization) with newly pre-qualified vaccines. The specific agreement ended in October 2012. With this background UMC considered it timely to invite representatives of the management team of the PMS Network from the WHO Quality, Safety and Standards (QSS) to Uppsala for a discussion about lessons learnt and opportunities for future collaboration.

Discussions in Uppsala

Christine Maure and Madhava Balakrishnan from QSS and Shanthi Pal from QSM spent 16-17 January in Uppsala discussing management and analysis of AEFI data with various UMC technical specialists. Depending on the issues at hand, UMC was represented by Sten Olsson, Pia Caduff, Magnus Wallberg, Monica Plöen, Gunilla Osmund, Johanna Eriksson and Madeleine Krieg.

AEFI and E2B

Christine and Madhava gave their perspectives of the experiences of national immunization programmes of using VigiFlow and other means for submitting AEFI data to the UMC. In particular, the difficulties of persuading immunization programme representatives to accept the international standard format for ICSR data submission (ICH-E2B) was discussed. Madhava presented requirements for the next generation of data catchment software that would be needed to support AEFI monitoring by immunization programmes. UMC demonstrated tools already available to support ADR reporting, including the facility for direct patient reporting and also its tools for data analysis. UMC also presented its process for software design, building on direct user input throughout the process, to ensure user satisfaction with the end result. The desirability and feasibility of creating and maintaining a specific Vaccine Dictionary was explored at the meeting.

One database for all

It was agreed that the recent WHO reorganization (see UR60), bringing QSM and QSS into the same WHO department, could support a closer collaboration between pharmacovigilance and immunization programmes on the WHO level. The vision of collecting ICSRs for all pharmaceutical products, including vaccines, into one global database was also accepted by all.

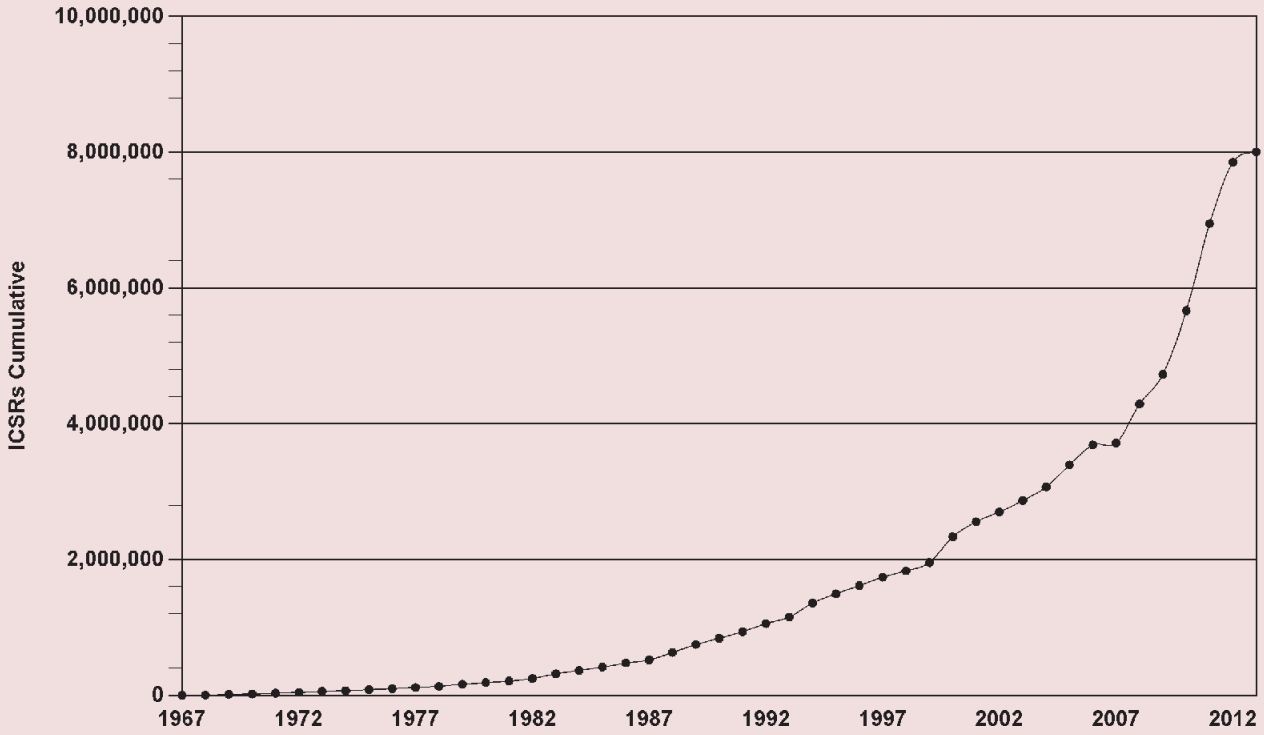
See also final item on page 20, Publications.

VigiBase – 8 million ICSRs

Cecilia Biriell

Figure 1

Growth of the WHO global ICSR database since start
2013-03-22



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

8 million ICSRs

VigiBase is still steadily growing, and the 8 million ICSRs mark was reached at the end of March, when the total number of case reports in the database hit 8,039,178 (Figure 1). Since the last report in UR (September 2012 statistics), the database has increased by over 500,000 case reports. The annual increase is now around 900,000.

The top 10 reporting countries are still the same as the last few years, with the US now accounting for exactly 50% of the database (Figure 2). Can any of the other countries make it to the top 10?

MAH case reports from Japan

In January, a large batch of more than 26,000 ICSRs from Market Authorization Holders (MAHs) was received at the UMC from the National Centre in Japan, PMDA. This is the first time that PMDA has been able to extract and send MAH reports in addition to the regular case reports from medical institutions. Continuous efforts to find the technical solutions have made this step possible, and will increase the value and usefulness of VigiBase to all members of the WHO Programme.

Submission frequency

As usual when showing statistics from VigiBase we emphasize the importance of regular submission of ICSRs from member countries. The number of countries now submitting ICSRs at least every quarter, which is the minimum criterion for submission, is 68, or 62%, which is a slight decrease from the last statistics report in September 2012. A total of 27 of the current 111 Programme member countries have not submitted any ICSRs during the last 6 months. As always we encourage member countries to submit case reports regularly, and to contact UMC if there are any particular reasons why case reports can't be submitted. UMC is always willing to help if we can be of any technical assistance.

Figure 2

Country distribution in the WHO global ICSR database
2013-03-22

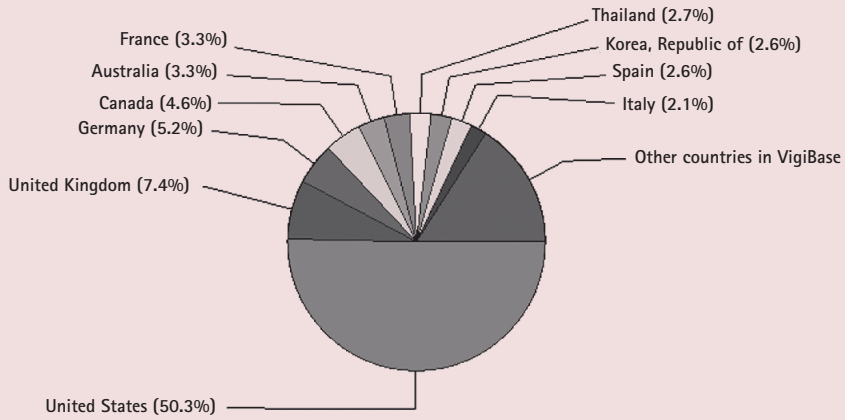
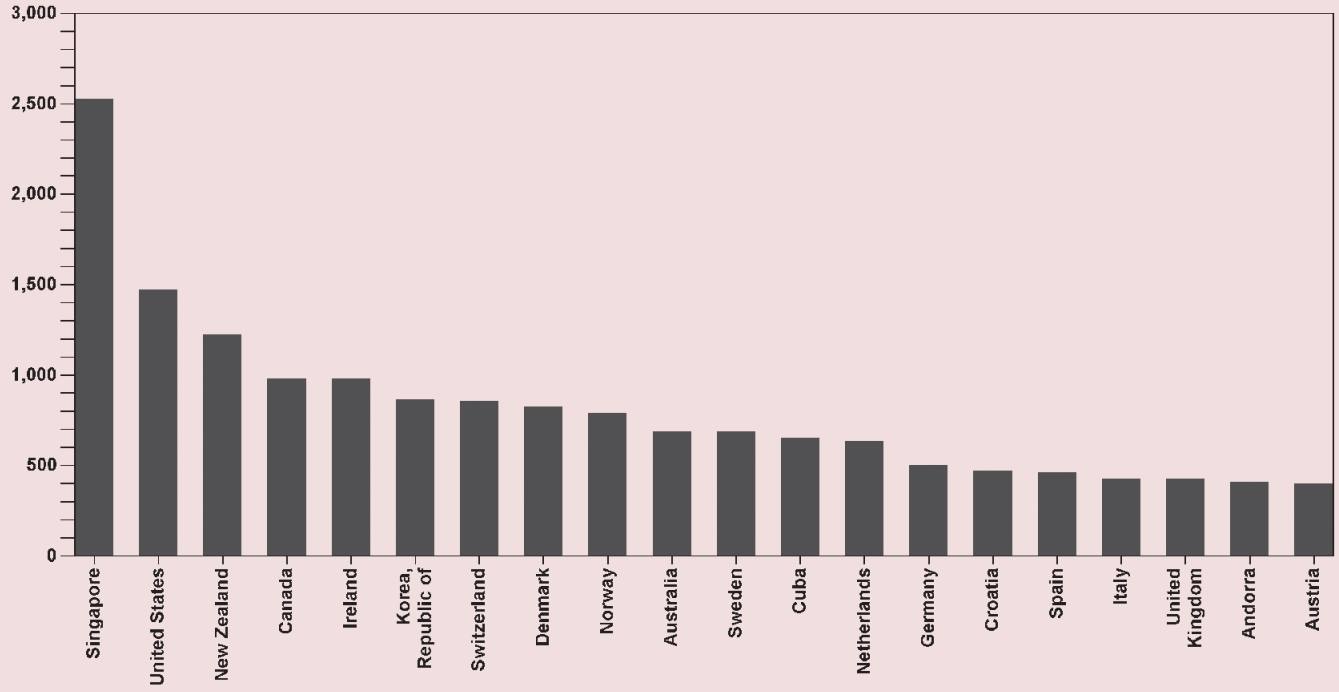


Figure 3

Active ICSRs in the WHO global database per million inhabitants and year
Period covers 2008-03-22 to 2013-03-22



Reporting rates by population

Singapore is still leading in number of case reports per million inhabitants and year, as shown in Figure 3, and has even increased from around 2,200 to 2,500. The statistics cover the last five years. The rest of the top 20 countries are also the same as last time, with some countries changing places in the league.

It is obvious that it is difficult for many countries just starting pharmacovigilance and with big rural areas to compete with a country like Singapore with long experience in pharmacovigilance, advanced health care systems and a dense population in a small area. Countries should maybe compare with countries in their own region. For example the highest rate in Africa is around 110 case reports per million inhabitants per year, and in Latin America it is just over 200.

Fact sheet about submission of ICSRs to VigiBase

Sometimes member countries contact the Pharmacovigilance Consulting department to ask details on what ICSRs should be forwarded to UMC and have questions about the submission of case report. To be able to give an answer to all these questions in a consistent and comprehensive way a fact sheet about the submission of ICSRs has been developed. The fact sheet has been sent to all member and associate countries in the Programme.

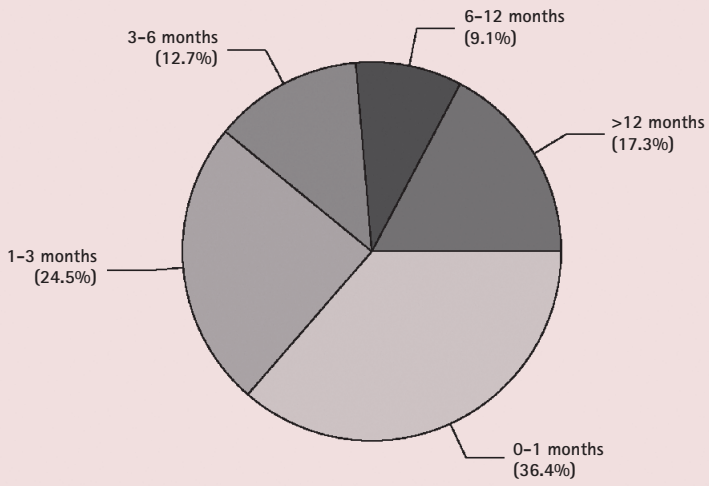
The fact sheet emphasizes that all adverse events occurring in a post-marketing situation should be submitted to UMC, including ICSRs on medication errors, counterfeit/substandard drugs and on therapeutic failure.

During the last year UMC has emphasized the need for quality case reports through the Documentation grading procedure. Some countries have come back to UMC and asked if only fully documented ICSRs should be submitted. In the fact sheet it is pointed out that while quality of information is important, all national case reports fulfilling the minimum criteria; case report ID, reporter, patient, suspect drug and reaction/event should be submitted to UMC.

We believe that this information is useful also to others interested in the work in the WHO Programme and the character of ICSRs in VigiBase, and the information is published at the UMC website; www.who-umc.org, (Public services – Pharmacovigilance – The WHO Programme – VigiBase).

Figure 4

Time elapsed since last submission
2013-03-22



Nigeria adopts national policy

Adeline Osakwe

Nigeria joined the WHO international collaboration on monitoring of adverse drug reactions and other medicine-related problems in 2004. Its national database as of February 2013 holds a total of 12,400 documented Individual Case Safety Reports, which, with a population of over 167 million is approximately 5% of what is expected.

Trail-blazing

As part of its strategic plan to institutionalize pharmacovigilance systems and practice in the country, Nigeria embarked on systematic development of a policy document that could give legal backing to the practice, and spur practitioners and the public to active participation in the system.

During the 35th meeting of National Centres in Brazil in 2012, the Nigerian National Pharmacovigilance Centre made a presentation on **Developing a National PV Policy: the Nigerian Experience**, where it was noted that Nigeria is probably the first country in the world so far to have a national government approved policy dedicated to pharmacovigilance.

Development and approval process

The process predates the launch of the Nigerian pharmacovigilance system in 2004 and input was developed and submitted to the Nigerian Authority for Developing Policies – Federal Ministry of Health (FMoH). The FMoH with support from NGOs and development partners organized a series of expert committee and stakeholder meetings from 2009 to 2010 to make technical input and review submitted drafts. The zero draft was generated after three rounds of committee meetings while the Expert Consultant Committee reviewed the zero draft to produce a 1st draft. The Final draft of the document was adopted in September 2010 and reverted to FMoH for government approval. The document has recently been approved by the Federal Executive Council, the highest decision-making body in the country, in October 2012, after ratification by the National Council on Health held in Abuja the previous month. The document was presented to the general public by the Honourable Minister of Health in Nigeria, Prof. Christian Onyebuchi Chukwu in the presence of all stakeholders, including legislators who pledged their support for promotion of a pharmacovigilance culture in the country.

Stakeholders posing with the Honourable Minister of Health Prof. Onyebuchi Chukwu (arrowed) at the launch of the Nigerian National Pharmacovigilance Policy document.

Goal and objectives

The aim of developing the National Pharmacovigilance Policy is to provide a strategic framework for the entrenchment of pharmacovigilance in the healthcare system in Nigeria and to ensure the overall safety in the use of medicines.

Objectives

The objectives of the National Pharmacovigilance Policy are:

a) To ensure effective and prompt reporting of ADRs and other medicine related problems in healthcare institutions (primary, secondary and tertiary), public health programmes, pharmaceutical industry and the private sector including not-for-profit and faith-based organisations.

b) To ensure the development and implementation of systems for pre- and post-marketing surveillance activities including the monitoring of safety and effectiveness of all medicinal products.

c) To promote the rational use of medicines by prescribers, dispensers and consumers.

d) To entrench sound pharmacovigilance principles and practice in the Nigerian healthcare system by promoting its understanding and training of health professionals on the subject.

Framework for implementation

The policy stipulates that pharmacovigilance being a new and important discipline should be integrated into the healthcare system to ensure the safe and rational use of medicines.

A holistic approach is being put in place in the National Pharmacovigilance Policy to cover the entire scope of pharmacovigilance products at all tiers of the healthcare system. To achieve the goal and objectives the various stakeholders in the healthcare system are in the process of being adequately engaged.

The FMoH is expected to publicise the Pharmacovigilance Policy document and further support the Nigerian Pharmacovigilance Centre in doing so to all stakeholders. According to the plan, all relevant stakeholders would be adequately informed and engaged by the end of the first year after launch.

Areas being addressed include:

- Pharmacovigilance structures
- Advocacy and creation of awareness
- Human resource development
- Educational and professional training
- Market authorization holders
- Herbal and other traditional remedies
- Integration of pharmacovigilance into public health programmes and other donor agencies
- Quality of medicines
- Research
- Funding
- Monitoring and evaluation

Conclusion

The document will serve as a tool for providing an enabling environment for effective planning, implementation, monitoring and evaluation of pharmacovigilance activities by all stakeholders. It provides a legal framework and road map for implementation. It will also provide standards for measuring activities and hold individuals responsible and accountable through enforcement of developed regulations.

A closer look at Oman

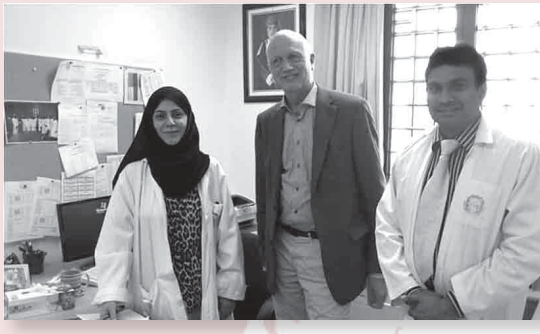
Sten Olsson

Last autumn I undertook an assignment to provide technical assistance to the Ministry of Health in Oman. My task was to assess the national pharmacovigilance system, provide recommendations for future developments and also to contribute to a series of pharmacovigilance workshops in the country.

The pharmacovigilance system in Oman was established in 1994, and the country joined the WHO Programme in 1995. However in recent years it has struggled to keep pace with developments on the international scene in the science and activities of pharmacovigilance. In part, this is a result of limited human and technical resources and a lack of participation in international networks by key staff. Responsibility and management of the different types of data used in pharmacovigilance is diluted throughout various directorates in the health ministry and greater co-ordination is needed to achieve a smoother running of the system.

Overall reporting rates of ICSRs from health professionals are actually fairly high by international standards, but achieved mainly through very dedicated work in one university hospital; most reports (80%) are submitted by pharmacists and involvement of the private health sector is low. Processes for data management are sub-optimal.

Although the current system has deficiencies in various respects, there is clear interest in improving, to the level of the WHO Minimum Requirements for a functional national pharmacovigilance system and beyond. I am also hopeful that a process will be initiated to again improve the quality of the information submitted in ICSRs and that resources will be allocated to analysis of data to inform policies. The formation of a pharmacovigilance advisory committee would be a positive step in that direction.



Ageela Taqi Lawati and Nibu Nair, clinical pharmacists at Sultan Qaboos University Hospital, the major ADR reporting source in Oman, with the author.

The pharmacovigilance workshops carried out in four different parts of the country provided me with very welcome opportunities to interact with active health professionals and listen to their concerns related to medicines and their safe use.

EU Regulatory workshop on medication errors

Anne Kiuru, Medical Products Agency, Sweden

Acknowledging medication errors (ME) as a major public health burden, the new EU pharmacovigilance legislation covers the reporting of suspected adverse reactions associated with MEs and liaison with national patient safety organisations. In order to facilitate implementation of these legal provisions to improve public health at EU level, a two day regulatory workshop was organised by the European Medicines Agency (EMA).

Stakeholder awareness

Over 150 representatives from organisations for patients and consumers, healthcare professionals, industry, public and regulatory bodies were brought together in order to raise awareness amongst all stakeholders involved in the reporting, evaluation and prevention of ME. Objectives of the workshop were to get a broader understanding of what constitutes a ME and highlight the need for a common terminology and a definition. Another aim was to share and create best practices for the prevention of ME. A better comprehension of how medication errors are managed in different countries will enable the EU regulatory network to improve cooperation at national and international level.

Issues of great diversity were addressed, e.g. how reporting of medication errors could be stimulated. Reporting systems with a 'no-blame' approach, anonymity and confidentiality were discussed. But "Merely collecting data contributes little to patient safety advancement"; it is therefore of utmost importance to increase knowledge, implement preventative measures and make sustainable changes.

Possible ways forward

Proactive medication error risk assessment during the development of a medicinal product and improvement of product design were identified as vital tools for the prevention of ME, both pre- and post-marketing. Evaluation of invented names, presentation (e.g. size, shape and colouring of the pharmaceutical form and packaging), instructions for use (e.g. regarding reconstitution, dose calculation) and labelling are vital. All medicinal product information must be presented in a legible and easily understood manner by all users. Another challenge faced is making sure that vulnerable populations (e.g. illiterate, visually-impaired, children and elderly) are safe-guarded. User-testing and engaging patients will be important tools to achieve success.

The final words of this workshop – and a good summary of its atmosphere – were "working together for public health".

For more details, please see http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/03/news_detail_001729.jsp&mid=WC0b01ac058004d5c1

Lethal, odd and 'new' in pharmacovigilance

I Ralph Edwards

'The Nurses are Innocent – The Digoxin Poisoning Fallacy' is an important book for anyone interested in broader challenges that face pharmacovigilance. It relates how a nurse became caught up in a major miscarriage of justice.*

The cause of her ordeal was the deaths of four children under her care who died apparently from digoxin overdose. Based on the interpretation of specimens taken by a pathologist in Canada's Toronto Hospital for Sick Children (HSC) autopsy rooms, a theory arose of intentional lethal overdosing with digoxin. Eventually it was found that 2-mercaptobenzothiole (MBT), an accelerant widely used in the rubber industry, could lead to false positive tests for digoxin. It seems that MBT can in some circumstances leach from rubber in medical equipment, with serious consequences and the risk of false conclusions.

MBT v Digoxin

This hypothesis was proposed during later research into the cause of two clusters of anaphylactic reactions/toxic effects encountered during injections of X-ray contrast media that implicated a toxic/allergenic contaminant. That contaminant was MBT but was read as digoxin by testing methods. In 1987, Health Canada's adverse drug reaction specialist Dr. Ed Napke suggested that the natural rubber/MBT leaching contamination might explain the 1980-81 HSC deaths. It may also indicate a possible problem with injections of any pharmaceuticals, intravenous fluids and blood transfusions in contact with natural rubber.

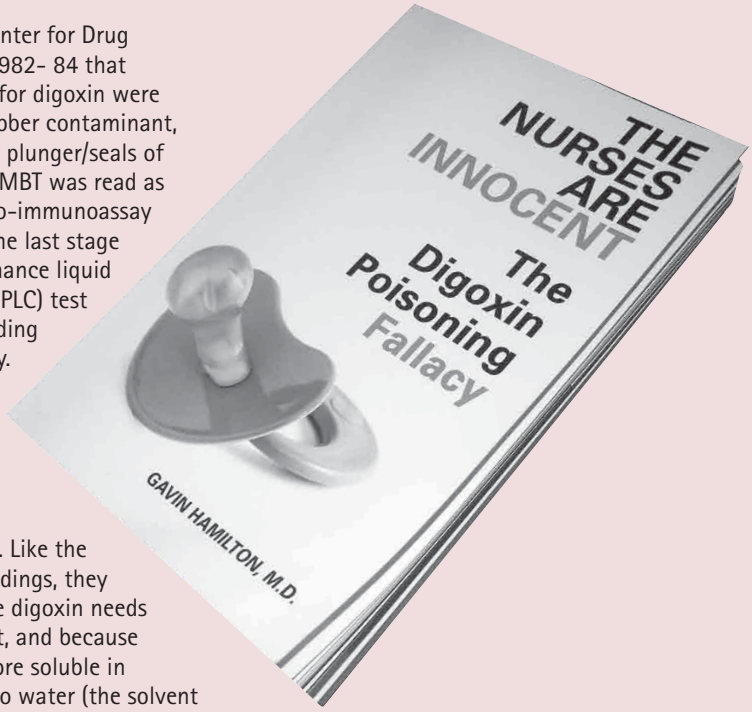
Book raises major issues

The following summary, made at the writer's request, is by the book's author and Dr. Napke, the pharmacovigilance expert involved in the investigation in Canada in the 1980s, of key issues raised by the book:

1) In 1969 MBT/H-MBT contamination of injections from natural rubber plunger seals of disposable syringes was identified in a pharmacology laboratory in Australia as the cause of the death of human cells in cultures (Guess and O'Leary, *J. of Pharm. Sc.*).

2) A 1983 cluster of allergic reactions (including anaphylactic shock) was linked to MBT leaching from natural rubber tips of disposable plastic syringes in clinical practice (Hamilton G, *Radiology*, 1984).

3) The US National Center for Drug Analysis found in 1982- 84 that falsely high assays for digoxin were due to a natural rubber contaminant, MBT, leaching from plunger/seals of unit dose syringes. MBT was read as digoxin by the radio-immunoassay (RIA) test used in the last stage of the high performance liquid chromatography (HPLC) test to get the final reading of the digoxin assay.



4) Reepmeyer and Juhl reported significant MBT contamination of drugs in 50% of disposable syringes. Like the 1969 Australian findings, they noted that, because digoxin needs alcohol as a solvent, and because MBT is 40 times more soluble in alcohol compared to water (the solvent used for most pharmaceuticals), MBT contamination of digoxin would be far greater than with most other drugs.

5) In 1983-85 scientists at Hammersmith Hospital, England found a spike of an unknown chemical in the serum electrophoresis patterns of 91 neonatal babies being followed for serum levels of theophylline. Only babies on this one drug, theophylline, were studied, but it seems possible that all patients receiving multiple injections might have similar exposure to natural rubber's MBT contamination and perhaps would have registered "potentially toxic" levels of MBT as found in this study (Meek J.H, Pettit B.R, *Lancet*, 1985.)

6) In 1987 a cluster of allergic reactions (including anaphylactic shock) from MBT leached from natural rubber sealing caps on pharmaceutical ampoules (Hamilton G, *CMAJ*, 1987). At that time similar natural rubber seals were used to seal most ampoules worldwide.

7) Health Canada's Dr. Ed Napke suggested in 1987 a possible link between the Toronto HSC baby deaths and MBT-contaminated injections, triggering the investigation described in this book.

8) In 1994 a report by Lasser described how injections of radiological contrast media for intravenous pyelographic (IVP) studies have always been associated with a significant incidence of anaphylactic reactions/toxic reactions, some fatal. After 1990, disposable syringes and the seals on IVP contrast ampoules were free from natural rubber and from its leachates, MBT and H-MBT (Lasser E.C, Lyon G.L, Berry C.C, *Radiology*, 1997). Lasser's report revealed that there was a marked reduction in severe reactions and deaths following IVP contrast injections in his 1992 study, during which period natural rubber was no longer used as ampoule seals or plunger tips of disposable plastic syringes.

9) FDA's Health and Human Services issued a "Final Rule" for labelling in 1998. This applied to medical devices, needing clear labelling indicating when natural rubber is present. The Final Rule identified syringe plungers, parenteral drug vial stoppers, and intravenous injection ports as components in the natural rubber/MBT exposure. This Final Rule proves that these MBT exposure sources still existed in the US market on September 30, 1998, when it came into effect. In the document. The author goes on to say, *"...the Center for Drug Evaluation and Research (CDER) and the Center for Biologics Evaluation and Research (CBER) of the FDA, which have jurisdiction over medication-device combination products such as pre-filled syringes, did not adopt the natural*

ADRs in children: off-label and unlicensed

Sten Olsson

A major benefit of working in a global network is that you meet with many interesting and knowledgeable people with perspectives other than your own. I had the pleasure of meeting David Woods from Dunedin, New Zealand, when attending a pharmaco-vigilance conference in Nizwa, Oman, in 2012 (see UR57). He is a consultant in pharmaceutical tech-nology to the University of Otago, New Zealand and the managing editor of the New Zealand drug formulary. He has a special interest in compounding and drug formulation factors leading to adverse reactions, particularly in children.

David Woods

Off-label use in children

When David was on a private mission to Norway he offered to come by the UMC office on his way back to New Zealand to discuss these risks. In his lecture to UMC staff he explained that off-label use, i.e. use outside the terms indicated in the product licence, with regard to dose, age-group etc., is very common in paediatrics and also unlicensed use, referring to compounding and modification of commercial formulations. This happens because of lack of appropriate commercial formulations for children and also lack of evidence-based dosing recommendations.

Documenting the problem

The limited scientific literature documenting adverse events related to off-label and unlicensed use indicates that the incidence is high but the real scale of the problem is unknown. The level of underreporting is higher than for adverse drug reactions in general. All compounding-related adverse events should in principle be preventable. The first step in reducing the risks is to encourage reporting as with other medication errors. By learning from reported cases we can improve practices. It is not acceptable that we give the "riskiest" medicines to the most vulnerable patients – our children.

Since David Woods is also deeply involved in the production of the New Zealand national formulary he also had discussion with several UMC staff members about the potential benefits of using features in WHO Drug Dictionary to support risk information to prescribers.

rubber latex labelling rule" and thus did not demand the removal from the market of injectable pharmaceuticals that are packaged in unit-dose syringes.

10) In 2008 a U.S. Government Centers for Disease Control document, "Latex in Vaccine Packaging," listed 28 vaccines with natural rubber seals in contact with the vaccine. ActHIB (SanofiPasteur) whooping cough vaccine, one of those listed, was the first foreign-made vaccine that was allowed to be sold and used in Japan. ActHIB vaccine was withdrawn from the Japanese market in March 2011 following a number of deaths in children being immunized with it. No specific information surfaced regarding the exact nature of the contamination; the deaths were attributed to "a contaminant" but it seems likely that the laboratory would have known the exact chemical structure of the contaminant.

Little-known, little-discussed

This summary illustrates a risk to patients using medication that is little-known or discussed, even after decades. Drs. Hamilton and Napke argue that it, "…. reveals the systemic failure of government health protection agencies to protect citizens from a known allergenic and toxic chemical, MBT, a worldwide contaminant of injections for 30 years, with medical journals aiding and abetting the process by refusing to publish informative articles on public health issues related to MBT contamination of injections". A cursory internet search for MBT as an accelerant in the rubber industry shows that it is still widely used: wherever we are, we should be alive to possibilities of unusual anaphylactic reactions/toxic effects!

* Hamilton, Gavin. *The Nurses are Innocent – The Digoxin Poisoning Fallacy.* Dundurn, Toronto, 2011. ISBN 978-1459700574

Experiences from CEM in Kenya

Hanna Lindroos

In February a survey team consisting of Magnus Wallberg and Hanna Lindroos from the UMC and Serge Xueref from WHO travelled to Kenya to follow up a study on the cohort event monitoring (CEM) of an anti-malarial medicine executed by the Pharmacy and Poisons Board in collaboration with the Division of Malaria Control in Kenya. The study is partly funded by the EU-financed FP7 project 'Monitoring Medicines'.

The study is being conducted at eight hospitals in malaria-endemic regions. We visited Port Reitz district hospital, Msambweni district hospital and Coast provincial general hospital, the participating hospitals located in and around the city of Mombasa in the Coast province. At all sites we had the opportunity to discuss the set-up of the study with the hospital staff involved and look at their facilities.

At the initiation of the study in June 2012, staff from participating hospitals were given an introduction to CEM and training on how to use the reporting forms. The target cohort for this study was 400 patients/site, i.e. just over 3,000 patients in total. After six months the cohort has reached approximately 2,200 patients.

Malaria is a big problem in Kenya: 30% of outpatient clinic visits and 15-19% of hospital admissions are due to the disease. Artemether Lumefantrine (AL), an artemisinin-based combination therapy is the first-line treatment of malaria in Kenya and is given to all patients with confirmed, uncomplicated malaria. AL is not a new medicine, being already in use in Kenya, but no comprehensive study has previously been performed in the country on the adverse events associated with it.

When a patient comes to any of the participating hospitals with symptoms of malaria, the disease is first confirmed by microscopic investigation of a blood sample. The patient is then asked to consent to participate in the CEM programme. When the nurse or physician has recorded the patient's details, treatment is initiated immediately. Patients are asked to come back to the hospital three and seven days later for a follow-up and are provided with funds to cover their travelling expenses. If patients fail to come for their follow-ups, the nurse or physician has in most cases performed the interviews by phone.

Challenges

During this study the CEM teams at the hospitals faced several unforeseen challenges. Some patients reside so far from the hospital that the funds provided for transportation were not sufficient, and they could not afford to return to the hospital for follow-up. Some of these patients did not have telephones and could not be reached for a follow-up interview over the phone either. Many of the patients are children brought in by an adult guardian who is not their parent. Getting consent from the parents before enrolling the patient in the study is often difficult as the parents are working full-time, sometimes far away.

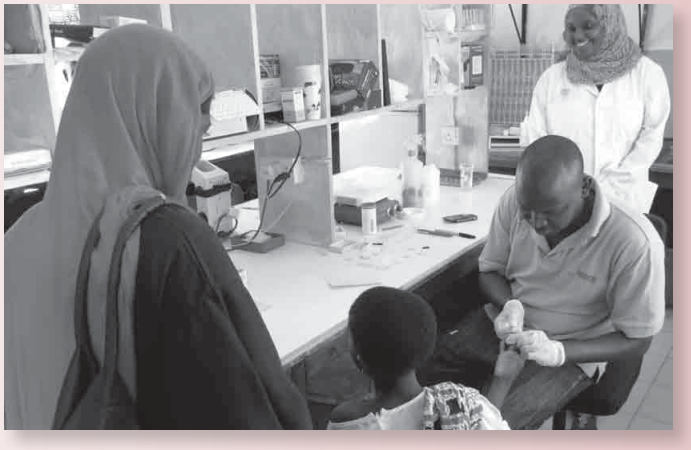
Strikes among health professionals interrupted the patient flow to hospitals. Two strikes involving nurses and one involving physicians occurred during the time of the study. Even though most hospitals had staff available, the patients turned to private health clinics with their ailments. Yet another strike, this time for the local buses, prevented patients from turning up at the hospitals. In total, more than two months were in some way affected by local strikes.

Ramadan, the Muslim month of fasting, coincided with the initiation of the CEM study. Even though people suffering from an illness are exempt from fasting, many Muslims with medical conditions insist on fasting during Ramadan anyway. This led to a much lower number of malaria patients than initially expected at the clinics during this time.

Outcome

In general the participating staff have been enthusiastic about the CEM programme. They have found it rewarding to be able to meet the patients after the prescribed regimen has been taken and to observe that AL is working well in cases of uncomplicated malaria. Taking the time to explain the consent form to the patients and to fill in the reports increased the patients' confidence in the hospital staff and understanding of their medication. By introducing the concept of CEM at the hospitals they also feel that the awareness of pharmacovigilance has increased among their colleagues. Pharmacy and Poisons Board intends to continue the CEM programme until the target of 3,000 patients has been reached.

Medicines



In the clinic

Serge at the micr

Monitor

Geraldine Hill

A Cohort Event Monitoring (
the safety of antiretroviral
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the Monitoring Medicines p
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In February, a survey team
(Programme Manager, Esse
WHO), Sten Olsson (Chief W
and Geraldine Hill (CEM spe
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including practical aspects
programme and how doctors
incorporated CEM into their

(from left): Alla Kuchko, Svetlana Setk
in the Soligorsk potassium mine (Na

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Pharmacovigilance in Public Health Programmes

Sten Olsson

WHO is recommending Cohort Event Monitoring (CEM) and Targeted Spontaneous Reporting (TSR) as preferred pharmacovigilance methods to complement regular spontaneous reporting in public health programmes (PHP).[1,2]

The Monitoring Medicines project supports capacity building and piloting of CEM and TSR in selected countries. We present below reports on progress made in a CEM pilot programme of HIV/AIDS patients in Belarus and one such programme of malaria patients in Kenya. These pilots are significant as proofs of the feasibility of CEM in these settings but also because of the consistent conclusion that such programmes bring pharmacovigilance centres and PHP closer together with a patient safety focus.

1. Pal SN, Duncombe C, Falzon D, Olsson S. WHO strategy for collecting safety data in public health programmes: complementing spontaneous reporting systems. *Drug Safety*, 2013; 36: 75-81.
2. A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis. WHO, 2012

ing Medicines in Belarus

(CEM) programme to monitor
medicines was launched on
Republic of Belarus as part of
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in Health Services (RCETH).

n consisting of Shanthi Pal
ntial Medicines Programme,
HO Programme Officer, UMC)
ecialist, UMC) visited Belarus
eriences with the monitoring,
s of implementing a CEM
s at the monitoring sites have
already busy schedules.

ina, Sten Olsson and Shanthi Pal down
tional Speleotherapy Clinic, Soligorsk)

CEM for ARVs in Belarus

On the first day of our visit, we met our hosts Dr. Svetlana Setkina, Dr. Iryna Chernysh and Dr. Alla Kuchko, all pharmacovigilance specialists at RCETH. They gave a detailed presentation about implementation of the CEM programme for ARVs. Preparations for the monitoring programme have included: preliminary sentinel site visits, meetings with the Ministry of Health to obtain official approval, piloting and printing of monitoring materials (data collection forms, enrolment cards and information posters), adaptation of the CemFlow data management tool, and a series of training workshops for sentinel site doctors. Data collection was piloted at two sites before being rolled out to all five monitoring sites. The ARV regimens being monitored are: ZDV+3TC+EFV (or NVP) and TDF+3TC+EFV (or NVP). The aim is to enrol approximately 850 patients over 12 months and, at the time of our visit, 68 patients had already been enrolled.

We visited three of the monitoring sites: Minsk Infectious Diseases Hospital, Zhlobin Central Regional Hospital (210 km south-east of Minsk) and Soligorsk Central Regional Hospital (140 km south of Minsk). At each site we met the HIV doctors who are collecting the CEM data. We also visited the Ministry of Health where we saw the Head of the Department of Primary Medical Care, Dr. Liudmila Zhilevich, who was very aware of the importance of monitoring the safety of medicines.

What did we learn?

- Detailed and effective planning has gone into the preparation of CEM for ARVs in Belarus.
- Having sign-off from the highest levels within the Ministry of Health greatly facilitated the implementation of CEM. We were encouraged that the Ministry was quickly able to identify the benefit of such a programme and that it took only two weeks to issue their approval.
- We were also very encouraged to learn that the doctors participating in the CEM programme were enthusiastic about the project and did not view the extra work required to complete the data collection forms as a burden but as an integral component to their patient follow-up.
- Patients were generally happy to participate in the monitoring and were reassured to know that such a programme is in place to ensure that their medicines are safe and effective.
- The doctors involved in data collection had a good understanding of the CEM method, particularly the need to record all new clinical events and not just suspected adverse drug reactions.

(back row, from left): Prof. Marina Dotsenko (HIV doctor, Minsk Infectious Diseases Hospital), Dr. Iryna Chernysh and Dr. Svetlana Setkina and in front Geraldine Hill, Shanthi Pal and Sten Olsson.

While we were there

During our visit, our hosts took us to see the Minsk Ballet performing Tchaikovsky's Swan Lake at the Opera House - an exceptional performance and an absolute joy to see. We were also treated to an experience of a lifetime by going 420 metres underground into the Soligorsk potassium mine! The section that we visited is no longer actively mined, but has been developed into a clinic for patients with non-infectious respiratory diseases (National Speleotherapy Clinic). Because the air in the mine has been filtered and mineralised as it passes through the long tunnels before reaching the clinic, it is purported to have a beneficial effect on the lungs. Being closer to the centre of the earth, it was also surprisingly warm down there!

Our hosts were extremely generous with their time and gave up their Saturday morning to take us on a walking tour of the centre of Minsk.

The growing capacity in Viet Nam

Nguyen Dang Hoa, Hoang Anh & C.K. Ogar

The National Drug Information – Adverse Drug Reaction Monitoring Centre (DI & ADR Centre) of Viet Nam was established in 2009 under the auspices of the Hanoi University of Pharmacy (HUP). HUP was appointed Sub Recipient to the Ministry of Health (MoH) for the Health System Strengthening (HSS) Project funded by the Global Fund to implement an intervention to strengthen the national pharmacovigilance system. One of the major objectives of the intervention is to strengthen the operations of the DI & ADR Centre and build capacity for its staff in pharmacovigilance.

Modifying existing structure

The DI & ADR Centre assumed management of the national pharmacovigilance programme from the Drug Administration of Vietnam. The Centre currently has 3 part-time senior pharmacists and 11 full-time staff (10 pharmacists and 1 IT expert). Prof Nguyen Dang Hoa, who is also Rector of the HUP, heads the Centre. He is assisted by Dr Nguyen Hoang Anh and Mrs Vo Thi Thu Thuy, both also lecturing at the HUP.

The Centre has been collecting and assessing the 10,570 ADR Reports received from healthcare providers in the country since 2009, bringing the total number of reports in the Centre's national ADR database from inception to 17,107. The new Centre has been working on increasing visibility and acceptance for pharmacovigilance as an indispensible component of healthcare by working closely with stakeholders to foster understanding of the crucial role of pharmacovigilance.

Pioneer staff of the national centre

Given the size (length) of the country, a Regional pharmacovigilance Centre (RC) was established at the Cho Ray Hospital in Ho Chi Minh City in 2011, with responsibility to coordinate ADR reporting in the south of the country. The RC has four staff (2 full- and 2 part-time), all employees of the hospital, and forwards all reports to the National Centre (NC) for central processing and assessment. In addition, it sends acknowledgement letters and provides feedback and assistance especially in serious cases where immediate intervention may be required. The Centre also works closely with an expert committee of 9 members who advise on safety related issues and, with an expanded team of 25 external experts, carry out causality assessment on reported serious ADRs.

Division of labour for greater impact

The Centre's activities have been divided into three work groups as outlined in Box 1.

Enhancing existing capacity

Involvement of external experts has helped build capacity and improve the functioning of the pharmacovigilance system. This has taken various forms, including training in pharmacovigilance for 114 health care professionals (academia, regulators, public health programmes and staff from sentinel hospitals) as provided by Bordeaux University, with plans to cascade this to other levels of healthcare delivery. Some staff spent 3-4 months in New Zealand to learn first-hand how a pharmacovigilance system operates; it is planned to repeat this experience for other staff in 2013. One person at the NC has obtained a Masters degree in Pharmaco-epidemiology and Pharmacovigilance from Bordeaux University. Day-to-day provision of operational and technical assistance has been provided by an external expert Mrs C.K. Ogar; periodic technical support through training and collaboration in active surveillance from organizations such as Management Sciences for Health (MSH), WHO, USP, etc has taken place. The Centre is winding down the Sentinel Site based Active Surveillance for Safety of Antiretroviral medicines and working with the Viet Nam Authority for HIV/AIDS Control (VAAC) and WHO to monitor nephrotoxicity with Tenofovir, and Central Nervous System disorders with Efavirenz among sero-discordant couples using Targeted Spontaneous Reporting.

The Centre is developing legal and professional documents such as pharmacovigilance guidelines, reporting forms, SOPs, and other tools necessary to standardize and coordinate pharmacovigilance activities among all stakeholders. In phase 2 of the Global Fund project focus will be on building management and communication capacity, vaccinovigilance, risk management and pharmacoepidemiology and implementation research.

Roles and responsibilities of work groups

Drug Information group

- Processing information and giving feedback to regional and local centres, organizations and bodies involved in drug manufacturing, distribution and use.
- Setting up and updating of database(s) (information on medicines, drug interactions, ADRs, etc).
- Participating in development of publications.
- Organizing and participating in research, projects, conferences, training abroad and in the country.
- Information exchange with drug information and pharmacovigilance networks.
- Supplying guidelines to health professionals, the public, organizations and individuals.

Publication group

- Publishing periodic journals and bulletins.
- Coordinating the development, publication and updating of drug information and communication resources.
- Receiving, examining and selecting papers for publication in the bulletin.
- Managing the Centre's website on drug information and pharmacovigilance (http://canhgiacduoc.org.vn).

Pharmacovigilance group

- Receiving and reviewing ADR reports from regional and local centres and other bodies working in drug manufacturing, sale, distribution and use.
- Providing feedback on reviewed ADR information, sharing new information on ADRs with stakeholders.
- Coordinating the creation and update of the Viet Nam ADR database.
- Development and publication of professional documents on drug information and pharmacovigilance.
- Supporting under- and post-graduate training and in-service training.
- Supplying guidelines on ADRs and pharmacovigilance.

Roll Back Malaria advocates pharmacovigilance

Serge Xueref

The Roll Back Malaria (RBM) Partnership is the global framework to implement coordinated action against malaria. According to its website (http://www.rbm.who.int/), *"it mobilizes for action and resources and forges consensus among partners. The Partnership is comprised of more than 500 partners, including malaria endemic countries, development partners such as WHO, the private sector, NGOs... RBM's overall strategy aims to reduce malaria morbidity and mortality by reaching universal coverage and strengthening health systems."*

RBM operates in working groups (WG). Interestingly, pharmacovigilance moved recently from the 'Procurement and Supply Management' WG to the 'Case Management' WG. This WG focuses on delivery of care and quality of service. Within this group, Alex Dodoo and Shanthi Pal co-chair the sub-WG on pharmacovigilance.

Priority setting for 2013

The 'Case Management' WG met for the 7th time on 5-7 March 2013 near Annecy, France. Around 50 representatives reviewed progress and identified priorities for 2013. This WG's slogan is to 'test, treat and track' malaria cases. In a global context of reduction in the incidence of malaria, but with a lot of challenges to achieve global malaria eradication, the 'Case Management' WG is asking pharmacovigilance systems to be more active.

A set of priorities are suggested to the pharmacovigilance community in malaria for 2013: in addition to being part of the routine malaria treatment (the '*track*'), the WG suggests that pharmacovigilance systems be active in the scale-up of specific Case Management activities, especially in severe malaria and in seasonal malaria chemoprophylaxis. Building local pharmacovigilance systems is key, as is the coordination between local initiatives and the national system.

Sharing with a national centre

It was stressed that ADR reports produced within a specific pharmacovigilance effort (e.g. a private company, university or research group) should be made available to the national pharmacovigilance centre. Then the national pharmacovigilance centre would process it as per international norms and standards, including reporting to the WHO ICSR database, VigiBase™.

Additional pharmacovigilance issues were considered, such as

- the need for a mapping of pharmacovigilance activities in malaria
- a review of the malaria PV Toolkit
- the need to enhance ADR information management (coordination and data-sharing among different initiatives
- the need to update the analysis of pharmacovigilance systems in malaria endemic countries
- translation of key pharmacovigilance documents into French/Spanish/Portuguese
- the opportunities of establishing a pharmacovigilance fellowship, and a roster of pharmacovigilance consultants.

More details on this meeting will be found on the RBM website: http://rbm.who.int/mechanisms/cmwg.html.

From plans to reality

The UMC training team

At the end of the UMC's annual pharmacovigilance course, participants are asked to draw up an action plan for things they want to achieve and focus on in their countries after the course. The range of accomplishments goes all the way from disseminating the new information amongst the personnel at their centre and starting drug safety committees, to influencing changes in legal frameworks or even one country joining the WHO Programme as a full member. Cape Verde became an official member in October 2012, and the national centre has been involved in both pharmacovigilance advocacy and proposing legislative changes.

Awareness and communication

Brazilian participants recognized the need for better information in pharmacovigilance to health care professionals and the general public and decided to restart two periodicals on the topic which had previously been withdrawn. Many countries organized workshops and presentations for health care professionals, which sometimes led to an increase in ICSRs from health care areas which until then had been inactive. In order to raise awareness amongst pharmacists one country sent an e-mail to all public sector pharmacists emphasizing the role that pharmacists can play in ADR reporting and prevention. A couple of countries worked closely with Marketing Authorisation Holders in order to promote the need for well-functioning post-marketing surveillance systems.

Obstacles and constraints

The main obstacles in several countries were staffing and political interest. Lack of funding for programmes remains a recurring problem. Many of the delegates mentioned that they have many administrative tasks on their desk and some felt that drug safety was down-prioritized compared to other health topics. In one country a new ADR form and a web-based reporting system were developed and launched but met with scepticism from some stakeholders who did not understand the necessity of these changes.

Many participants found the UMC course useful both in daily work and to gain a broader understanding of pharmacovigilance. Some participants would appreciate more hands-on sessions where as others would like more regulatory aspects to be included in the course.

An Asian perspective

Helena Wilmar

The ISoP-Asia 2013 Symposium held in Singapore in mid-March offered a well-structured and practical programme. Lectures from ISoP academics and presentations from UMC combined with opportunities for representatives from national pharmacovigilance centres to exchange ideas about the organization of pharmacovigilance in their respective countries, sharing achievements and issues not limited to one single country.

Out of 77 participants (from 22 countries), the majority were represented by the pharmaceutical industry (multinational as well as local pharma). The presentations by national centres came from Thailand, Singapore, Philippines, Indonesia, Vietnam, Malaysia, Republic of Korea, India, Cambodia, and Taiwan. Lao DR was represented with a poster.

Harmonization and quality

The first day was dedicated to the importance of harmonization of safety reporting requirements in the region with a key presentation from UMC (Data Management of Individual Case Safety Reports: Points to consider) on how to improve reporting and quality of ICSRs.

On both day one and day two representatives from national centres presented their experiences with current systems and their plans for the future. Day two also touched on how to involve patients in pharmacovigilance, as well as the recent EU legislation and its impact in Asia. The last day was all about risk minimization; methods, implementation and measures.

An absorbed audience in Singapore

A circular activity

Discussion panels that involved heads of centres from almost every ASEAN country reflected a desire to adopt ICH-E2B, but exposed a lack of political will in some countries to fulfil this activity. The introduction of the circle of pharmacovigilance and UMC's improved and user-friendly search/analysis tool VigiLyze* helped many countries understand the need to have structured data. Several one-to-one conversations reinforced the fact that reporting and analysis of data are key to effective pharmacovigilance. In addition, although the UMC and WHO do provide guidelines and basic tools, the actual activity of signal analysis and policy development is the responsibility of each country.

** full details will appear in the next Uppsala Reports in July*

Indian society at 12

Sandeep Agarwal (Secretary, SoPI)

The 12th annual conference of the Society of Pharmacovigilance India took place in NIMS University, Jaipur, with the theme 'Pharmacovigilance and Biomedical approaches in health and diseases'. More than 300 delegates from the disciplines of medicine, pharmacy and biomedical sciences presented data, discussed topics and identified research needs related to the issues of drug safety in clinical and basic research. Over 100 posters were presented by postgraduate research scholars and faculty members. Dr Nicholas Dunn of the University of Southampton, UK delivered the K.C. Singhal Oration based on his research on contraceptive safety.

Indian traditional medicines

A prominent topic of the conference was safety evaluation of drugs of the Indian system of medicine, with speakers from Gujarat Ayurved University, Jamnagar. The Society proposed the establishment of a unit of pharmacovigilance in every medical and health centre to reduce the risks of medicines. President of the Society, Prof. C. P. Thakur stressed the need for greater emphasis on pharmacovigilance in under- and post-graduate medical curricula and in pharmacy education. The Medical Council of India, which regulates the curriculum and examinations in Indian medical colleges has, on an earlier recommendation of SoPI, made the setting-up of a pharmacovigilance centre in each medical college mandatory.

The 13th annual SoPI conference will be held from 22-24 November 2013 at PS Medical College, Karamsad, Anand, Gujarat.

Meyler course in pharmacovigilance

Linda Härmark

Every year in February the Meyler course in pharmacovigilance is given. The course is named after Professor Leopold Meyler who was the first professor of clinical pharmacology in the Netherlands and the founder of the book *Meyler's Side Effects of Drugs*. It is a joint collaboration between the University of Groningen (professor of pharmacovigilance Kees van Grootheest) and the Netherlands Pharmacovigilance Centre Lareb.

Participants at the 2013 Meyler course

In early February 24 students from 16 countries gathered for a week in Groningen to learn more about pharmaco-vigilance. They had various backgrounds but most of them were active in a pharmaco-vigilance centre or at a university. During the week, lectures were given covering all aspects of pharmacovigilance such as causality assessment, methods used to gather data, patient reporting, signal detection and of course cases to illustrate the difficult decision processes in pharmacovigilance. The course was highly appreciated by all the students.

Below is an illustrative quote from one of the participants:

"The international nature of the course: good examples were provided from other countries. This enabled me to compare the Netherlands and other countries, but most importantly to re-evaluate my own activities and take a more critical look at my work back home. This strengthened my resolve to publish my work as a means of giving others the opportunity to also learn from it".

The course will be given again next year.

Amsterdam hosts Euro DIA

Monica Plöen and Anki Hagström

On 4-6 March, staff from UMC attended the DIA EuroMeeting in Amsterdam.

Many of the presentations related to the implementation of the new pharmaco-vigilance legislation in the EU. Questions were raised about guidance and practical implications and it is clear that there is a need for further clarification, especially from the European Medicines Agency.

From UMC, Anki Hagström, had the honour to moderate a session on Attributing Safety Reports to Medicinal Products, where Madeleine Krieg from the UMC presented 'ICSRs Monitoring in Global Pharmaco-vigilance, Communication in the Evolving Pharmacovigilance Community'. The talk examined how to perform effective pharmacovigilance on global data and the challenges of operating in a global regulatory landscape far beyond ICH.

In the session New opportunities for information technology in pharmacovigilance, UMC presented 'Online Patient Reporting of Adverse Events: A case study' by Monica Plöen, where experiences from developing and launching a patient reporting system as part of the Monitoring Medicines project were shared.

In the exhibition hall, UMC had a booth, where we met both new and old customers and friends.

Monica Plöen at Euro DIA

Side Effects on the Big Screen

Film review by Bruce Hugman

Most critics have been very enthusiastic about Steven Soderbergh's latest (maybe last) film, *Side Effects*, released worldwide in early 2013. It's a tense, engaging, surprising, misdirection thriller and deserves high praise for its script, acting, cinematography and music.

It doesn't have much to surprise the pharmacovigilance community in terms of its technical content, but it's a great story for everyone and there are some stunning insights and revelations for a general audience. Peter Bradshaw in the UK's *Guardian* described it as "...an acid satire on big pharma, the mental health profession and its terrifyingly powerful priestly caste of doctors".

The central themes are depression, anti-depressant medication and their potential weird and frightening side effects - which, in the case of this film, include not only direct pharmacological impact on patients, but also collateral ethical and professional damage rippling out from the trade in pills.

It's a misdirection thriller because the assumptions you make as a viewer are constantly being undermined and taken apart. Even after two viewings, this reviewer remained uncertain about just exactly what he had seen at many points: was this behaviour faked or real? Was the drug responsible or not? Rooney Mara, as Emily, the protagonist depressive, plays a brilliantly ambiguous role, part victim, part ruthless manipulator. Jude Law as her psychiatrist, Jonathan Banks, an empathetic but weak and vain professional, is all but destroyed by his wanton and self-confident prescribing and seduction by big consultancy fees for enrolling his patients in trials.

Everyone in Manhattan appears to have been depressed at one time or another and to have swallowed their way through a succession of SSRIs with more or less tolerable or awful side effects; everyone has their favourite and is only too pleased to recommend it to their friends. Medicines are shown as the instruments of power and wealth-generation in the hands of doctors and big pharma, casting their shadow on friendships, professional relationships and even the processes of the law.

These and many more themes are woven into the story, but it is essentially a clever, engrossing thriller in which the people and the outcomes are what drive the tension and the interest: a violent death, an attempted suicide, a doctor/patient conspiracy, the destruction of a professional reputation - these and many more are the ingredients of this rich narrative. You may leave the cinema wondering just exactly what the truth was, and you may have some very mixed emotions about how the plot unravels, but you'll have had a very good time in the company of some very good acting and directing.

Science silenced

another view, from Geoffrey Bowring

Cinema has, from time to time, encountered the subject of the safety of medicines and the personal dramas it enfolds, notably in Nicholas Ray's 1956 film *Bigger Than Life*, and more recently *The Constant Gardener*. *Side Effects* depicts the story of a consulting psychiatrist whose patient is apparently affected by the anti-depressant treatment he has prescribed for her.

If the critics' reaction has been generally positive, pharmacovigilantes tempted by the film's title may feel on watching it, somewhat short-changed.

The doctor at the centre of the film is compromised by his attitude to participation in a clinical trial and in his treatment approaches to a patient (the other principal character). The film does raise pharmacovigilance related issues, such as the manner and setting in which the psychiatrist is engaged in the trial, his conduct in monitoring the patient's clinical records and his responses as the reported side effects come to his attention.

However, any sketching in of the dilemmas involved in the practice of clinical pharmacovigilance is not allowed to get in the way of an intriguing but conventional thriller, albeit with a few unexpected twists. Ultimately the spectator is more affected by the struggles of a person unjustly accused, than by the harm to patients suffering side effects from medicines.

Unless there is a major crisis, the science of pharmacovigilance has few chances to bring itself to the attention of the general public. There is however enough drama and intrigue in the science to furnish a decent full-length feature film with a focus on what happens to real patients. Maybe one day cinema will attempt that.

Cross Reference Tool Japan

Malin Jakobsson

The UMC has recently released a product intended to assist in analysis of Japanese medicines data. Working with Ijoken, the maintenance organization of the Iyakuhinmei Data File (IDF), a Cross Reference Tool (CRT Japan) has been created to enable users to specify the WHO Drug Dictionaries Drug Code corresponding to a selected code in the IDF dictionary. This makes it easy to analyze IDF-coded data with the tools included in the WHO Drug Dictionaries.

The national dictionary of Japan for coding clinical and drug safety data is IDF, which is used by companies when reporting medicines safety data to the Pharmaceuticals and Medical Devices Agency, PMDA. In the rest of the world, the UMC's WHO Drug Dictionaries are the de facto standard for coding medicinal product information in clinical and safety data.

The IDF dictionary contains drug names and substances in Japanese characters and can be used for coding of medication in Japan both in clinical trials and pharmacovigilance. The IDF codes can be submitted in safety data to the PMDA and the WHO Drug Dictionaries can be used when the clinical or safety data is compared with data from outside Japan. The classifications in the WHO Drug Dictionaries can be used in the analysis of the data.

What is mapped, and how?

The mapping between IDF and WHO Drug Dictionaries is done manually, and for each IDF code the corresponding WHO Drug Dictionaries Drug Code is chosen. The IDF codes that are mapped are 3-, 7-, and 9-character codes. For the vast majority of the records the match of trade name and ingredient between IDF and WHO Drug Dictionaries is exact. For records where the match is not exact it is due to different conventions for data entry and naming conventions in the different dictionaries. The mapping has been made in a standardized and consistent way to ensure high data quality.

Cross references from UMC

UMC aims to provide cross references to other medical dictionaries that are mandated in a specific country or other dictionaries of medicinal products used by WHO Drug Dictionary users. In this way, the WHO Drug Dictionaries can be used for global databases and drug data can easily be received from and sent to regulatory authorities, local branches of global companies or to local Contract Research Organisations (CROs).
For questions about the Cross Reference Tool Japan, please contact our support team at drugdictionary@umc-products.com.

News for VigiFlow users

A minor update of VigiFlow will be released during the second quarter of 2013. The changes affect the receive date handling (for National Centres and Regional Centres) and the import of follow-up cases.

Any user wanting to know more can contact: vigiflow@who-umc.org

Cases Database

A new medical resource has just been launched, called Cases Database. This online tool presents thousands of peer-reviewed medical case reports, including content integrated from PubMed Central, BioMed Central, Springer and BMJ Group. By allowing comparison between reports, Cases Database is aiming to provide clinicians, researchers, regulators and patients a simple resource to explore content, and identify emerging trends.

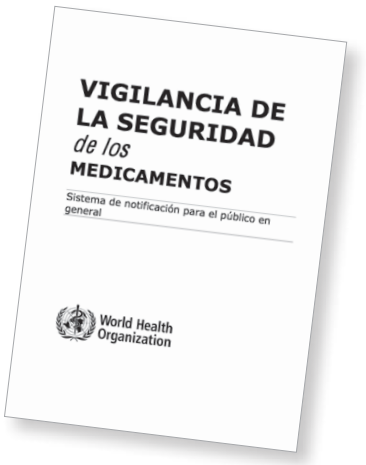
The website allows for searches in its database by patient condition, symptom, intervention, pathogen, patient demographics, and many other data fields. Results can be downloaded and exported and full text case reports are also accessible.

Details of costs and more information are at www.casesdatabase.com

Safety reporting for the general public

Safety monitoring of medicinal products: reporting system for the general public is an important guide freely downloadable in English, Spanish and Russian.

A handbook for consumer reporting of ADRs was discussed and requested at the thirty-first meeting of the National Pharmacovigilance Centres held in Uppsala, Sweden from 20–23 October 2008, and the development of this publication has been incorporated into the aims of the Seventh Framework Programme of the Research Directorate of the European Commission and its project Monitoring Medicines (http://www.monitoringmedicines.org/).



The 36-page document was published in English a year ago, but recently translations into Spanish and Russian have appeared, which should greatly increase its use and value. See: www.who.int/medicines/areas/quality_safety/safety_efficacy/qas_safetymonitoringmp/en/index.html

❖

Strategies for public health programmes

WHO Strategy for Collecting Safety Data in Public Health Programmes: Complementing Spontaneous Reporting Systems
Shanthi N. Pal, Chris Duncombe, Dennis Falzon, Sten Olsson
Drug Safety (2013) 36:75–81 (DOI 10.1007/s40264-012-0014-6)

This open access paper looks at reporting systems to complement the universally used spontaneous reporting system in which suspected adverse drug reactions (ADRs) are reported to a national coordinating centre by health professionals, manufacturers or patients. Easy to set-up and cheap to run, spontaneous reporting is regularly criticised for the poor quality of many reports and for under-reporting.

The need in public health programmes to quantify and characterize risks from medicines to individuals and communities, alongside the importance of maintaining public confidence in such programmes leads to the consideration of additional methods to monitor medicines.

The authors here explore two methods: cohort event monitoring and targeted spontaneous reporting, both being implemented by the WHO, in its public health programmes, to complement spontaneous reporting. The advantages and disadvantages of these methods and how each can be applied in clinical practice are discussed. They conclude that "routine safety monitoring [...] is best handled by a spontaneous reporting system. But if the aim is to better understand, with minimum resources, the occurrence of a specific ADR in a specific population, TSR is an appropriate choice. If the aim is to actively follow patients to characterize the safety profile of new medicines, then CEM is a relevant choice". They emphasise however that clear goals are essential in order to design the relevant data collection method.

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Reporting in Nepal

Attitudes among healthcare professionals to the reporting of adverse drug reactions in Nepal
Santosh KC, Pramote Tragulpiankit, Sarun Gorsanan and I R Edwards
BMC Pharmacology and Toxicology
2013, 14:16 doi:10.1186/2050-6511-14-16
www.biomedcentral.com/2050-6511/14/16

This open access article with authors from Nepal and Thailand describes the results from a survey circulated to 450 healthcare professionals working at four teaching hospitals in Nepal.

The aim was to investigate the attitudes towards – and find ways to improve – adverse drug reaction (ADR) reporting among healthcare professionals working in these regional centres. Three-quarters of the respondents replied that they had seen a patient who was experiencing an ADR, but only a fifth had reported it. Reasons for non-reporting included not having access to a reporting form and colleagues not reporting ADR cases. Some health professionals responded that the seriousness or rarity of the reaction, or that it was a new product or a new reaction to an existing product, were key factors in their decision of whether to report or not.

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Overview of the WHO Programme

An article presenting an overview of the WHO Programme and its relevance in developing countries was published by WHO towards the end of 2012:

WHO Programme for International Drug Monitoring – Strategy for promoting best pharmacovigilance practices in resource-limited settings. *WHO Drug Information*, Vol 26, No 4, 2012, p362-370.

Vaccines paper

A recent article describes the background to the Global Vaccine Safety Initiative (GVSI) and what it is expected to achieve. It is published in a special issue of the journal Vaccine devoted to the 'Decade of Vaccines'. Authors are vaccine safety coordinators at WHO headquarters and regions and members of the GVSI planning group.

Effective vaccine safety systems in all countries: A challenge for more equitable access to immunization.
Ananda Amarasinghe, Steve Black, Jan Bonhoeffer, Sandra M. Deotti Carvalho, Alexander Dodoo, Juhani Eskola, Heidi Larson, Sunheang Shin, Sten Olsson, Madhava Ram Balakrishnan, Ahmed Bellah, Philipp Lambach, Christine Maure, David Wood, Patrick Zuber, Bartholomew Akanmori, Pamela Bravo, María Pombo, Houda Langar, Dina Pfeifer, Stéphane Guichard, Sergey Diorditsa, Md. Shafiqul Hossain, Yoshikuni Sato.
Vaccine 31S (2013) B108– B114
http://dx.doi.org/10.1016/j.vaccine.2012.10.119

To address the issues around the rare, serious vaccine-associated adverse events, vaccine pharmacovigilance systems have been developed in many industrialized countries. The impetus of effective pharmacovigilance systems in low- and middle-income countries (LMIC) is increasing.

In 2011 WHO developed the Global Vaccine Safety Blueprint, a strategic plan based on an in-depth analysis of the vaccine safety landscape which reviewed existing systems, international vaccine safety activities and the resources required to operate them.
The Blueprint sets three main strategic goals to optimize the safety of vaccines through effective use of pharmacovigilance principles and methods:

- to ensure minimal vaccine safety capacity in all countries
- to provide enhanced capacity for specific circumstances
- and to establish a global support network to assist national authorities with capacity building and crisis management.

WHO Assistant-Director General

Sten Olsson

Before her two-day visit to Sweden on 6–7 March 2013, WHO Assistant Director-General Marie-Paule Kieny had requested to meet with representatives of the UMC. In negotiations with the Swedish Ministry of Social Affairs, hosting her visit, it became possible to welcome her at the UMC office in Uppsala for a two-hour discussion. Dr Kieny is heading the WHO cluster on Health Systems and Innovation. She was accompanied by Kees de Joncheere, Director, Department of Essential Medicines and Health Products, WHO and Louise Andersson from the Swedish government. Unfortunately Marie Lindquist, Director of UMC, was out of office, so the high-level delegation was received by Sten Olsson, Pia Caduff-Janosa and Antonio Mastroianni from UMC.

Sten Olsson gave a brief presentation of the history of the WHO International Drug Monitoring Programme and the role of the UMC in supporting, developing and expanding it in close collaboration with national pharmacovigilance centres, WHO-HQ and other WHO Collaborating Centres. An open discussion followed.

Antonio Mastroianni, Sten Olsson, Louise Andersson, Marie-Paule Kieny, Pia Caduff-Janosa, Kees de Joncheere

The current challenges facing the WHO and the Programme were identified as well as opportunities for resource mobilization for the WHO Programme to maintain its leadership in the global movement for safer use of medicines. It was agreed that the open dialogue between WHO-HQ and the UMC should continue and develop for the WHO Programme to attain its full impact.

CEM Training

Geraldine Hill

During the week 11-15 March we welcomed to the UMC Adam Fimbo, Alambo Mssusa and Alex Nkayamba from the Tanzania Food and Drug Authority for training on cohort event monitoring (CEM) data assessment and data analysis. At the same time, Adela Gwira and Irene Frempong from the Ghana Food and Drug Authority came for training on CEM data entry using CemFlow. Both countries are currently undertaking CEM programmes for antimalarial medicines.

The week's programme started with an overview of CEM to highlight the objectives for this type of monitoring. Each of the parties then shared their experience of implementing CEM programmes in their respective countries. Over the first two days, our visitors heard presentations on the assessment of individual events, the structure of the CEM Dictionary, CEM data analysis and the principles of signal detection. During the week, there were also presentations on the use of VigiFlow, the importance of quality ICSR data and an introduction to VigiLyze. Much of the week was also filled with 'hands-on' sessions using CemFlow to enter and extract data. On the last day, we had a very productive brain-storming session on the types of analyses we would like to be able to do with the data. We identified the analyses that can be performed using tools already available in CemFlow, those that can be done by exporting the data from CemFlow to Excel, and those that we would like to make available through further development of CemFlow.

Uppsala welcomes CEM visitors

By the end of the week, the team from Tanzania had been able to assess each of the events in their dataset and write a report describing their observations. At the same time, the team from Ghana were able to resolve the difficulties they had been experiencing with access to CemFlow and were able to proceed with data entry and the assessment of individual events.

Unfortunately our visitors struck a particularly cold week here in Uppsala, with morning temperatures down to around -12 to -15 degrees Celsius; however, we were delighted to be able to introduce some of our visitors to snow for the first time!

New medical staff

Pia and Geraldine

Pia Caduff-Janosa

I am a Swiss anesthesiologist with an exquisite southern European temper now living and working with one foot in Uppsala and the other one in Bern. I spent 15 happy years in operating theatres in Switzerland and New Zealand before taking up a position as clinical reviewer at the Swiss regulatory authority in 1999.

After heading the Vigilance Unit at Swissmedic for 4 years from 2009 to 2012, I joined the UMC as their Chief Medical Officer in January 2013, with the responsibility to act as the final opinion on all medical matters in the UMC and to provide support to UMC and WHO on medical matters relating to pharmacovigilance. This new post in part presents the challenge of stepping into the shoes of Ralph Edwards, whose vast medical experience and wisdom has been put at the service of the WHO Programme and UMC for over 20 years - and which I hope will continue. My differing background and perspectives will enable the UMC team to build further on that foundation. In the near future I will be able to say more about some projects we are working on which pharmacovigilance colleagues around the world should find interesting.

In my more private life I can be seen as a passionate but not necessarily proficient harpist, reliable wife and mother, avid reader and keen world traveller.

Geraldine Hill

Geraldine is from New Zealand and has lived and worked in many parts of the country, although for the past 10 years, Dunedin was her home.

"I joined the Pharmacovigilance Services Department in January 2013 as a 'Medical Doctor/ CEM specialist' and will be involved in the on-going development of Cohort Event Monitoring (CEM) and the CemFlow data management tool, with a particular focus on the analysis of data from CEM projects. I will be working with the Analysis Team to provide clinical input on potential drug safety issues arising from VigiBase and with the Research Department to support their research activities from a clinical perspective.

I graduated from the University of Otago Medical School in 1990 and worked in hospitals in New Zealand and Australia for 5 years before undertaking training in general practice. I worked as a General Practitioner for a further 5 years in rural and urban practices. From 2002 until 2008, I held a position as Research Fellow at the Intensive Medicines Monitoring Programme (IMMP), part of the New Zealand Pharmacovigilance Centre. During this time I completed a Masters in Public Health. In 2008, I worked on a project which aimed to examine the legal, ethical, social and policy implications of emerging genetic technologies; I focused on the current place of pharmacogenetic technology in clinical practice. Following this I took up a teaching position at the University of Otago Medical School, teaching clinical skills to undergraduate medical students. In November 2009, as the result of a chance conversation with the former head of the IMMP, Dr. David Coulter, about the work he was doing with WHO to develop the CEM method (which is based on the method used by the IMMP), I was invited to attend a WHO training on CEM for ARVs in Tanzania. Since then, I have contributed to the development of CEM and have provided technical support to countries where CEM programmes are being implemented. I have also facilitated at a number of pharmacovigilance training workshops focusing on CEM.

This is an exciting opportunity that enables me to bring together my experience in clinical medicine, pharmacovigilance, public health and medical teaching.

Outside work I enjoy swimming, cycling and running, and since moving to Uppsala, my family and I have taken up cross-country skiing – and we are hooked! While many in Uppsala are looking forward to spring, we're hoping the snow will last a bit longer so that we can continue to hone our technique!"

Ralph at 70

Former UMC Director Ralph Edwards recently celebrated a birthday which was featured in the regional newspaper UNT. You may be able to access the link still at http://www.unt.se/familjeliv/njuter-av-en-lugnare-tillvaro-2321414.aspx

We should add for those who can read the Swedish text that his life is not as idle as reported...

UMC spins for kids

Mats, Anna, Sten, Madeleine after a lot of pedalling

For the third year running UMC staff participated in a national charity event 'Spin for Change' at gym in Uppsala. The beneficiary of this year's spinning (indoor endurance cycling) was the Swedish Childhood Cancer Foundation (Barncancerfonden). On Saturday 9 March a lot of UMC perspiration was offered for the cause, and in addition 2,500 euros were donated.

Farewell

Annika Wallström, Chief Marketing Officer and responsible for UMC's commercial operations for several years recently left her employment. In thanking her for all her contributions to the development of the organization we also wish her well for the future.

DATES	TITLE	PLACE	ORGANISER/CONTACT
9-10 May 2013	XII Jornadas de Farmacovigilancia	Tenerife Island, Spain	Spanish Medicines Agency & Regional Centre of Canary Islands www.jornadasdefarmacovigilancia2013.org/
13-14 May 2013	Benefit/Risk Management	Zurich, Switzerland	DIA Europe Tel.: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org www.diahome.org/en-GB/Meetings-and-Training.aspx
15-16 May 2013	Introduction to Pharmacoepidemiology	Fareham, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org/trainingcourses
4-5 June 2013	Impact of the New Pharmacovigilance Legislation on Regulatory Affairs	London, UK	DIA Europe (Details as above)
10-11 June 2013	Signal Management in Pharmacovigilance	Nice, France	DIA Europe (Details as above)
10-12 June 2013	Pharmacovigilance – Basic Training for those working on drug safety monitoring in the EU, USA and Japan	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 E-mail: registrations@management-forum.co.uk www.management-forum.co.uk
11 & 12-13 June 2013	7th Biennial Signal Detection Conference	London, UK	Drug Safety Research Unit (Details as above)
17-28 June 2013	7th annual francophone pharmacovigilance training course	Rabat, Morocco	Moroccan Pharmacovigilance Centre E-mail: louammi@gmail.com
19-20 June 2013	4th Annual Pharmacovigilance Asia 2013	Singapore	IQPC Worldwide Tel: +65 6722 9388 Fax: +65 67203804 E-mail: enquiry@iqpc.com.sg
19-20 June 2013	Periodic Safety Update Reports (PSURs)	Southampton, UK	Drug Safety Research Unit (Details as above)
1-2 July 2013	Pharmacovigilance	London, UK	SMi Group Ltd Tel: +44 (0)870 9090 711 E-mail: events@smi-online.co.uk www-pharmacovigilance-event.com
3-4 July 2013	Changing Global Regulatory Pharmacovigilance Environment	London, UK	Drug Safety Research Unit (Details as above)
7-26 July 2013	48th Graduate Summer School in Epidemiology (includes Pharmacoepidemiology and Risk Management, and Global Health Issues)	Ann Arbor, USA	University of Michigan School of Public Health www.sph.umich.edu/epid/GSS
17-19 July 2013	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (Details as above)
25-28 August 2013	29th International Conference on Pharmacoepidemiology and Therapeutic Risk Management	Montréal, Canada	ISPE E-mail: ISPE@paimgmt.com www.pharmacoepi.org/meetings
4-5 September 2013	Back to Basics in Pharmacovigilance	Winchester, UK	Drug Safety Research Unit (Details as above)
10-12 September 2013	World Drug Safety Congress (Europe 2013)	London, UK	Health Network Communications Tel: +44 (0)20 7608 7054 www.healthnetworkcommunications.com/
1-4 October 2013	13th Annual ISoP Meeting 'The Renaissance of Pharmacovigilance'	Pisa, Italy	International Society of Pharmacovigilance www.isoponline.org | http://isop2013pisa.org/
21-25 October 2013	20mo Congreso Latinoamericano de Farmacología y Terapéutica (5to Congreso Iberoamericano de Farmacología)	Havana, Cuba	Nacional de Sociedad Cubana de Farmacología - Asociación Latinoamericana de Farmacología E-mail: rdelgado@infomed.sld.cu or eventosfarmacologia@finlay.edu.cu | www.latinfarma.com
6-7 November 2013	Signal Management in Pharmacovigilance	Paris, France	DIA Europe (Details as above)

the UPPSALA MONITORING CENTRE

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.

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Editors: Sten Olsson and Geoffrey Bowring

Uppsala Reports ISSN 1651-9779

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