

MUR69



WHO Collaborating Centres | Access to data

Signal detection | Substandard medicines | China dictionary



Marie Lindquist
Director
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Some time ago I watched a fascinating film, called Stories we tell. In addition to being cinematographically innovative, it told a very moving story about a woman – the film director – discovering a major family secret, through gentle, but persistent interviews with relatives and friends of the family. Bit by bit, as the interviewees opened up and started talking about the past and what they had observed, a picture emerged of what had happened during those months many years ago when her mother was away from home, and gradually the truth was unravelled about who her biological father really is.

For me, this film is a vivid illustration of how little we often know about people around us, even those nearest and dearest to us; and how important it is to cover all angles and go beyond what is immediately apparent in order to get a complete picture, and understanding, of complex events.

We need stories, and good story-telling, in pharmacovigilance, too. And I'm not talking about stories like in fairy-tales or film dramas now, but the clinical case history: the narrative account of a sequence of events. I believe there is a good level of agreement that pharmacovigilance is about providing the best available knowledge so that patients and health professionals can make wise therapeutic decisions in their use of medicines. Good quality data is a fundamental building block in this process. To verify and quantify overall population effects of adverse medicines reactions, we no doubt need statistical evidence from epidemiological studies, and other sources of data. But, to truly learn about the real life effects of medication on the individual level, including how it affects patients' well-being and quality of life, we also need to make sure that we hear, and listen to, their stories.

The gathering of good clinical data starts with the patient; and with the willingness to share information. Only if we believe that our story will make a difference will we go through the effort of making it known. This applies to the dialogue between the patient and their health professional; to the decision by a health professional to report a suspected adverse reaction; and to a story told in

a patient's own words – be it on a web forum, or submitted on a case report form.

One of the problems with our current reporting systems is that the structured data forms used (particularly paper forms) do not lend themselves well to capturing a complete clinical picture (who can fit a complete clinical history in a space that is just about enough for a 'twitter'?). If, on the other hand, we employ tools that allow easy capture of a narrative description of the course of events, we are in a much better position to determine the likelihood of causative drug effect in each individual case, which means that we can avoid unjustifiable scare and unnecessary patient suffering due to false signals.

It must be a top priority to encourage and facilitate collection of good quality case data! Reducing time and effort spent on re-entry of already existing data will help. As we heard in the recent conference in Edinburgh on the UK Yellow Card Scheme 50th anniversary, some electronic health record (EHR) systems today allow automatic extraction of patient and medication data to generate an ADR report, which can then be completed with relevant details and submitted electronically. I wish all EHR systems had this facility! It was also encouraging to hear about an initiative in the Netherlands to concentrate data entry on relevant clinical information by implementing context-sensitive on-line data entry forms, with follow-up questions generated automatically based on the information entered.

The key is to maximise the use of IT technology – where it will help us! – and concentrate our minds on the critical assessment needed to make sense of all the information and turn it into the knowledge that will bring us closer to the ultimate goal of good therapeutic decision making – and safer patients.

A handwritten signature in black ink that reads "Marie Lindquist".

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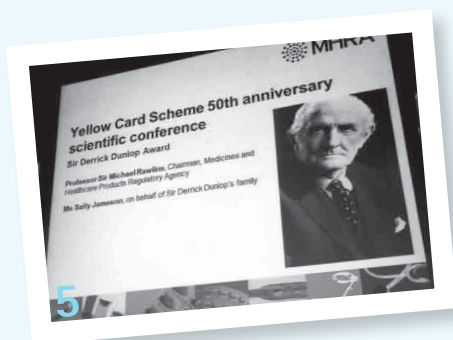
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We review several recent publications to add to the pharmacovigilance bookshelf



Bangladesh joins WHO Programme

Md. Akter Hossain

In the field of drug safety, Bangladesh has just joined other countries in the world. Pharmacovigilance is now one of the important functions of the Directorate General of Drug Administration (DGDA), which is the Bangladesh regulatory authority.

Early struggles

In Bangladesh, pharmacovigilance started in 1999, but became dormant due to a lack of legislation, motivation, inadequate knowledge and attitude, as well as a lack of coordination and communication between stakeholders, resulting in many ADRs not being properly reported.

A fresh start

In January 2013, the United States Agency for International Development (USAID) 'Systems for Improved Access to Pharmaceuticals and Services' programme (implemented by Management Sciences for Health) provided support to DGDA to revive the programme. For this purpose, a monitoring cell, known as Adverse Drug Reaction Monitoring (ADRM) was established and designated as the National Drug Monitoring Centre by the Ministry of Health & Family Welfare, Bangladesh. An Adverse Drug Reaction Advisory Committee (ADRAC) has also been formed to evaluate, analyze and make recommendations on adverse drug events.



Hospitals and companies

As a result, the ADRM cell and ADRAC have become fully functional, with meetings taking place at regular intervals. At present, 30 public and private teaching hospitals in Dhaka city have been selected as sentinel sites for pharmacovigilance activities. More recently, we have extended the programme to two divisional teaching hospitals (Chittagong and Rajshahi Division). We have also circulated an

executive order from DGDA to all local pharmaceutical manufacturing companies and pharmaceutical importers to monitor the ADRs of their products through their own channels and to report to the national centre. We have a plan to phase in pharmacovigilance activities across the entire country.

Into the Programme

It was our pleasure to be informed in December 2014 that WHO had accepted Bangladesh as the 120th member of the WHO Programme for International Drug Monitoring. We have established links to the Uppsala Monitoring Centre, Sweden and wish to have cooperation and assistance from other stakeholders, in order to maintain a good relationship with WHO-UMC.

Md. Akter Hossain is the Assistant Director, Directorate General of Drug Administration and Focal Point, National Pharmacovigilance Center, Bangladesh.

Afghanistan

The Regulation of Medicines and other Health Technologies department at WHO has arranged for Afghanistan to become an Associate Member of the WHO Programme, following receipt of information from the Director of the General Directorate of Pharmaceutical Affairs in Kabul about the development of a national system for reporting of adverse reactions.

2015 Programme meeting

Geoffrey Bowring

The early preparations for the 2015 meeting of the WHO Programme for International Drug Monitoring, from 3-6 November in India, continue.

Official invitations from WHO Headquarters, together with a provisional agenda for the three days, are planned to be sent out to heads of national pharmacovigilance centres towards the end of April.

The hosts, the Indian Pharmacopoeia Commission are in regular discussions with WHO HQ and



Indian Pharmacopoeia Commission (IPC)

the WHO Country Office, and the meeting venue in New Delhi will be confirmed soon.

Getting to the meeting should be straightforward for national centre representatives. Indira Gandhi International Airport is about 15 kilometres from the metropolis with good links to the centre. One of the busiest airports in the world it has direct connections from many countries, using the Terminal 3, opened in 2010.

Anniversaries – and challenges ahead

Marie Lindquist

The future is yellow

The UK Medicines and Healthcare Products Regulatory Agency (MHRA) celebrated 50 years of the UK Yellow Card scheme with a scientific conference on 20 March at the Royal College of Physicians in Edinburgh.

The conference looked at how the Yellow Card scheme is evolving, and discussed

developments and scientific innovation in medical technology in healthcare.

Following the keynote speech by Dr Aileen Keel, Acting Chief Medical Officer of Scotland, the Chairman of MHRA, Professor Sir Michael Rawlins, introduced the roadmap for the future, which takes into account the widening scope of pharmacovigilance, extended to include incident reporting for

medical devices, and defective and counterfeit medicines. Four major strategic themes have been identified:

- Improving patient safety through systematic and cultural change
- Embedding Yellow Card into the healthcare system
- Making the best scientific use of Yellow Card data
- Sustainability into the future through collaboration.

Along with these themes, there were panel discussions, presentations on scientific developments, parallel workshops, and a lively debate in classic British style (for and against the motion that "health professionals' role in Yellow Card reporting will diminish in the era of electronic media?").

In his concluding remarks, Dr Ian Hudson, Chief Executive of MHRA, thanked all contributors who had travelled from around the UK and joined guests from other parts of the world, and said that this conference will have a very positive and tangible impact, in that many of the ideas and comments raised by the participants will be incorporated into the finalisation of the roadmap for the future of the Yellow Card scheme.



Dr Aileen Keel in Edinburgh

EMA aims high

In March several hundred people gathered in the impressive glass-ceilinged East Wintergarden building, a few hundred metres walk from the new EMA offices in London, to celebrate that 20 years have passed since the European Medicines Agency was created.

The purpose of the anniversary conference, entitled 'Science, Medicines, Health: Patients at the heart of future innovation', was to serve as a forum for stakeholder dialogue to discuss how EMA should best continue to deliver its mission to foster scientific excellence in the evaluation and supervision of medicines for the benefit of public and animal health.

After the introductory congratulatory remarks by distinguished speakers, the ensuing presentations and a panel discussion touched on a range of challenges and

opportunities for the future, with a focus on how EMA will contribute to improved public health by being the enabler of public access to innovative medicines therapy.



EMA Chief Medical Officer Hans Georg Eichler and the audience in London

UMC at the FDA

Antonio Mastroianni

In January 2015, Antonio Mastroianni, Anki Hagström, and Helena Sköld braved a major snow storm in Washington DC (4 centimetres of snow!) to visit the Center for Drug Evaluation and Research within the United States Food and Drug Administration (US-FDA). Not only is the US-FDA the largest contributor of ICSRs (Individual Case Safety Reports) to VigiBase® (the WHO global ICSR database), it is also a key UMC partner in several scientific initiatives,

ultimately wisdom, via analysis and understanding of adverse reactions within VigiBase.

Improving the quality of FDA ICSRs improves the overall vigiGrade completeness score of VigiBase, which has a large impact on the value of this data for analysis purposes (both internally at UMC and externally for all countries in the WHO Programme for International Drug Monitoring).

UMC, the WHO Programme and US-FDA as a leader in international pharmacovigilance, to around 50 senior staff at the Center for Drug Evaluation and Research (CDER). This was much appreciated, as the staff at CDER learned how their actions impact on other countries in the WHO Programme, and the responsibility of the FDA to explain their regulatory decisions to other members of the WHO Programme. They also heard how effective communication around regulatory decisions have an impact in other countries.

The staff were very pleased to learn about the outreach efforts by FDA and to see the positive impacts on capacity building throughout the WHO Programme. The audience showed particular interest in VigiLyze, which was rewarding for us, since it is a tool of great value for all national centres, from the developing to the advanced.

Multiple impacts

After lunch Gerald and Dr. David Martin, Division Director, Office of Biostatistics and Epidemiology (CBER), met with UMC to discuss collaboration efforts, teaching and training opportunities, and to hear about the research priorities of the UMC for the coming year.

Overall it was a very productive visit and feelings were positive due to the achievements seen in 2014 regarding data quality. FDA staff saw the importance of their participation in UMC/WHO events, as FDA decisions impact on other countries in unexpected ways. In addition, FDA staff reaffirmed their understanding that ill effects on public health in one country can have potential to impact US shores and the FDA can protect the US population by continuing to work closely with UMC and member countries of the WHO Programme.



Suranjan De, Gerald Dal Pan, Anki Hagström, Helena Sköld and Antonio Mastroianni.

and senior staff from the FDA regularly teach at UMC training events and at the WHO National Centres meeting.

Impact of US quality

Dr. Gerald Dal Pan, Director of the Office of Surveillance and Epidemiology (OSE) and Suranjan De, Division Director (OSE) hosted the UMC and were eager to understand how recent changes to the US-FDA data feed sent to UMC will impact the overall analytical value of VigiBase data. UMC is always striving to improve VigiBase data and to better convert this data to information, knowledge and

US-FDA implemented their new ICSR reporting system FAERs in 2012, and since then UMC has advised FDA on what ICH E2B fields should be included to provide more information in their reports and how to improve their vigiGrade completeness score. By end of 2014 FDA confirmed that four out of six recommendations from UMC would be implemented in the first half of 2015.

Interaction with FDA staff

In addition to these important discussions around data quality improvement, Antonio and Anki made a presentation about the

Lusophone missions

Hilda Ampadu

Alex Doodoo and Hilda Ampadu of the WHO Collaborating Centre in Accra, Ghana visited two Portuguese-speaking African countries in the Atlantic in late February.

Cape Verde has made major progress since it became a Full Member of the WHO Programme for International Drug Monitoring in 2012. Head of the national regulatory agency is Carla Djamil Monteiro Reis.

Suggestions for further advances included the incorporation of pharmacovigilance policy into associated pharmaceutical legislation, research in pharmacovigilance using local population data, and providing leadership and human resources for the development of pharmacovigilance in Portuguese-speaking African countries, with workshops in Portuguese.

The Republic of **São Tomé and Príncipe** is not yet a Programme member, but the team met Ministry of Health Pharmaceutical Department and WHO Country Office officials. There is a keen awareness of the need to restart previous medicines safety work.

Recommendations for São Tomé and Príncipe included ensuring that the draft National Strategic Plan for the Pharmaceutical Department with emphasis on pharmacovigilance is approved, designating the Pharmaceutical Department as the National Pharmacovigilance Centre and applying for membership of the WHO Programme, as well as applying for start-up funds to key global donors. Getting healthcare workers on the two islands to participate in pharmacovigilance is a major aim.

A big step in patient safety: WHO opens its global database

Paula Alvarado

VigiAccess™ is here

VigiAccess™ was launched with the aim of improving patient safety, increasing transparency and encouraging the reporting of adverse reactions to medicinal products. In an event organised at the Press Club in Geneva, WHO and Uppsala Monitoring Centre (UMC) presented VigiAccess on April 17th.

VigiAccess is a new web-based application that will allow anyone to access information on reported cases of adverse events related to over 150,000 medicines and vaccines. More than ten million cases from over 120 countries are held in VigiBase®, the WHO database of suspected adverse reaction reports which is maintained by the UMC.

"VigiAccess is a global public good," said Marie-Paule Kieny, WHO Assistant Director-General for Health Systems and Innovation. "By promoting open access and transparency, we hope that we will also promote drug awareness and save lives."

Introducing VigiAccess

VigiAccess (www.vigiaccess.org) allows us to search VigiBase and retrieve statistical data on medicines' and vaccines' side effects – suspected adverse reactions – reported to the WHO Programme for International Drug Monitoring. VigiAccess offers us an opportunity to understand better how our bodies interact with medicines and enables us to learn more about possible side effects. The more we know about suspected adverse drug reactions and the more information we share, the more we can contribute to a global culture of patient safety and well being.

A spontaneous reporting system provides very important information on potential risks and helps to identify groups of patients or situations in which particular attention or special monitoring might be needed. The information gathered from a spontaneous reporting system is unique as it covers all populations treated as long as a medicine is available on the market. It is also very cost effective.

What can we find in VigiAccess?

VigiBase has over 10 million reports and it is the biggest dataset on side effects in the world, and the only one with such a global coverage. Nevertheless, this number is not as big as it seems. Spontaneous reporting is influenced by many factors and only a small percentage of the occurring adverse drug reactions are being notified.

The screenshot shows the VigiAccess™ web interface. At the top, there is a search bar with 'alvedon' entered and a search button. Below the search bar, a message states: 'alvedon contains the active ingredient(s): Paracetamol. Result is presented for the active ingredient(s). Total number of records retrieved: 7.' Underneath, there is a 'Distribution' section with several expandable categories: 'Adverse drug reactions [ADRs]' (expanded), 'Geographical distribution', 'Age group distribution', 'Patient sex distribution', and 'ADR reports per year'. The 'ADRs' section lists: 'Congenital, familial and genetic disorders (1)', 'Hepatobiliary disorders (1)', 'Investigations (3)', and 'Neoplasms benign, malignant and unspecified (incl cysts and polyps) (3)'.

www.vigiaccess.org

"VigiAccess is not the answer to all patient safety issues," said UMC Chief Medical Officer, Pia Caduff-Janosa MD, "but it certainly points us in the right direction; one of sharing information, promoting knowledge and encouraging patients to be more in charge of their own well-being".

"We encourage patients to talk to their doctors if they experience a side effect, not to discontinue their medicine, or to change their doses. We need to have more dialogue between patients and healthcare professionals", Caduff-Janosa added.

Also, these reports refer to a suspected causal relationship between a drug and a reaction, without this relationship being proven. There might be other reasons for a patient to develop the condition reported.

Tell me about pharmacovigilance

VigiAccess is a tool you may use if you want to see if the side effect you are experiencing has been previously reported. It is a starting

point towards a more empowered attitude and behaviour in relation to medicines. The information is organised with a focus on clear visual components and patients can easily find what they are looking for.

"The user interface for VigiAccess has intentionally been kept simple in order to let the data play the main part and to avoid confusion", said Helena Sköld, UMC Product Manager responsible for VigiAccess. "We have used responsive techniques in the development in order to make it accessible from tablets and phones as well".

As part of an effort to broaden the knowledge of pharmacovigilance among patients, UMC has launched 'Take & Tell' online campaign (www.takeandtell.org). 'Take & Tell' has a very simple message on the importance of monitoring our experience when taking medicines and encourages patients to talk to their doctors. It is a small change in our behaviour with a big impact in our health.

Benefit and risk

Knowledge plus information in one place is a good combination, but it is very important to emphasize that the reports in VigiBase result from suspicions of a relationship between a drug and a reaction, no causal relationship having been proven. The balance between benefit and risk of a medicine is not the same for all patients and individual decisions must be taken.

UMC encourages patients to seek the advice of their health care provider if experiencing an unexpected side effect. Medication should not be discontinued, or doses changed, unless advised by the health care provider.

In order to guarantee that neither patients, nor health care professionals reporting or treating institutions can be identified we have chosen not to make national data available as a small number of reports in a country might lead to a breach of privacy.

Agile signal detection – 2014, a year of change

Tomas Bergvall and Lovisa Sandberg

Signal detection is a core scientific activity directly related to the WHO Programme's mission of discovering and communicating potential medicine safety issues. Up until 2013 the UMC signal detection process followed stable and standardized procedures, largely established in the early 2000s. The routine screening of VigiBase® data relied on disproportionality analysis and long-established triages.

As described in UR65, the former signal analysis team, responsible for the routine signal detection, and the research department, responsible for the methodological research, merged and formed a new Research section in 2014. The reorganization paved the way for a revision of the routine signal detection process, both in terms of screening methodologies and the work process.

Novel analytical methodologies

The main aim of bringing the two teams together was to shorten the lead time between development of novel analytical methods and their introduction to practice. The first novel method to be implemented in the routine signal detection was *vigiRank*¹ (see UR67 p12-13). The algorithm ranks drug-adverse drug reaction (ADR) combinations according to the strength of evidence of being a signal. Disproportionate reporting is one component of *vigiRank* but it also accounts for the quality and content of the reports. *vigiRank*, together with a set of selection criteria, is currently the basis for identifying and prioritizing which associations to focus on. The selection criteria are flexible and can be adjusted ad hoc, and enable us to focus on specific medicine safety areas of interest.

Agile process

The merger of the two teams brought different competences together and opened a window of opportunity for changes also in the signal detection work process. A completely new way of working, inspired by agile methods like scrum (see box on page 9 for explanation) was integrated in several parts of the process.

In line with methodologies like scrum, the routine screening of drug-ADR combinations in VigiBase is now performed in so called 'sprints'. The aim of a sprint is to identify potential signals from the list of drug-ADR combinations based on *vigiRank*. The process

involves literature review and analysis of the case series in VigiBase, in order to assess which combinations merit in-depth assessment – typically performed by a review panel of international experts.



A UMC scrum team working

A sprint is limited in time, i.e. between one to two weeks, and is conducted two or three times per year. The whole UMC Research section is engaged and gathers four to five people in each project room, distributing competences across the groups. Each morning all participants meet to very briefly recount, one by one, what was done the previous day, what is planned for the coming day and if any obstacles have been encountered. The meeting is kept to 15 minutes.

Multi-disciplinary approach

The purpose of engaging the whole research section, i.e. research engineers, statisticians, pharmacists, nurses and medics, is to reduce the distance between method development and routine signal detection. Bringing these different competences together opens up for knowledge sharing between staff and integrates method research as a natural part of the routine process.

The interdisciplinary work has made it possible to raise questions with the medical experts in close connection with the drug-ADR assessment. Previously, potential signals were suggested by a pharmacist and later confirmed or refuted by a medical expert, often resulting in the pharmacist having to answer further questions and hence a need for re-opening the investigation, which is not as time efficient.

The goal in sight

In line with the agile process, each sprint has a pre-set goal, i.e. a certain number of potential signals to be identified. There are many reasons for this decision. First, a clear goal is one of the main features of the agile process and brings the group together with the aim of achieving it. Second, we believe that aiming to find a pre-defined number of potential signals raises the quality of the signals, in contrast to going through a set number of combinations as in the previous approach. The approach has shifted focus from quantity to quality and allows more time to be spent on combinations that are likely to become signals. Third, we have limited resources to take on large quantities of potential signals, as all of them require further in-depth analysis of the literature and the individual cases.

Limiting the number of potential signals may sound harsh but in reality it would be impossible to handle a large number of potential signals after each sprint. The sprint is closed either when the goal is reached or when the time for the sprint is up.

Review and improve

A major aspect of the agile methodology is to continuously improve the process. To support that, a retrospective meeting is held with the sprint team, to gather experiences and reflections on how the sprint was performed; what we want to keep as is, what we want to stop doing, and what would we like to start doing. In the meeting each person is encouraged to give their view of the sprint. The main purpose of this retrospective is to identify improvements for how to conduct future sprints.

The agile way of working has also been adopted in the planning and preparation process for a new sprint. After the medical focus area and dates for the next sprint have been defined, the preparation work starts. Depending on the scope of the sprint, this work starts four to eight weeks before a sprint. A dedicated team of about five persons is responsible for the preparation.

The team collects the experiences from the last sprint together with adjustments needed for the defined focus area and any new ideas for improvements, and compiles a list of

requirements. The requirements are prioritized, with an estimation of time needed, in order to make sure we focus on what we think will offer the most benefit. Using this list of requirements, the weeks preceding the sprint are used to make adjustments to the drug-ADR combinations list criteria, to comply with the specific focus area. The user interface used in the sprint work is also adjusted accordingly.

A signal review guideline, serving as the basis for a common view on the work process, is updated for each sprint and all research staff are informed about the changes made for the sprint.

A kick-off meeting is held a few days before the sprint starts, in order to gather the staff, provide a unified message, and give in-depth information about the specific focus area.

A trio of sprints

Up to March 2015 three sprints have been performed in this new format. The first sprint focused on serious reactions to new drugs and

Scrum

Scrum is an iterative and agile framework, used most often in software development projects, to manage a team-based work environment. Some details are described below but for in-depth information please see <https://www.scrumalliance.org/>

1. Add new ideas to the product requirements and prioritize them according to business value and estimated resource requirements.
2. Select the requirements that provide the highest business value and lowest resource requirement and plan them in detail.
3. The heart of scrum is the sprints which usually take about two weeks and are where the actual work happens. Progress is measured every day to enable the team to quickly adjust to any problems.
4. A retrospective meeting is held after each sprint to gather thoughts about how to improve team work and processes. The work starts again at step 1.

was kept as close as possible to previous signal detection triages to be able to evaluate the new process, including the implementation of *vigiRank*. The two other signal detection sprints have been on the paediatric population and on vaccines. The experiences from these will be published in a future issue of *Uppsala Reports*.

In general, the experiences from this new way of working have been very satisfying and we believe this is a concept we will continue with and develop further in coming years.

1. Caster O, Juhlin K, Watson S, Norén GN. Improved Statistical Signal Detection in Pharmacovigilance by Combining Multiple Strength-of-Evidence Aspects in *vigiRank*. *Drug Safety*, 2014. 37(8):617-628.

Save the date for *Let's talk PV!*

3rd November 2015

Join a team of international experts during the UMC pre-meeting day preceding the 2015 WHO National Centres meeting in New Delhi, India. *Let's talk PV!* offers a day on interactive learning, dialogue and discussion of leading themes in pharmacovigilance.

- Latest scientific developments in the field of signal detection
- Impact communication: how do we tell the pharmacovigilance story?
- Pharmacovigilance in focus – how do we develop it in challenging scenarios?
- Sustainability of pharmacovigilance data management



Let's talk PV! faculty consists of speakers from national pharmacovigilance centres, regulators, academia and UMC. Take this opportunity to learn, share and network with pharmacovigilance colleagues and experts from all over the globe.

Let's talk PV! is open to all member countries of the WHO Programme for International Drug Monitoring.

At the heart of things

The International Society of Pharmacovigilance gathers from 27th to 30th October 2015 in Prague, at the heart of the European continent.

Czechoslovakia was one of the pioneer countries in the development of spontaneous reporting systems that joined the WHO Programme in 1968. Hosted by the Charles University in Prague in the Czech Republic, and the Czech Pharmaceutical Society, the 15th Annual Meeting of ISoP promises serious science in a historic setting.

The call for abstracts is open until 1 June 2015, and 'Early bird' registration rates apply before 31 July.



Cubism in Prague

Topics concerning pharmacovigilance education, drug safety in special populations, the role of pharmacists in patient safety and direct patient reporting will be featured. There will be a discussion about new methodologies in pharmacovigilance, and 'hot topics' around the 'Cube'.

For more details visit the conference website <http://www.isop2015prague.org/> where you can register online.

Secretariat: info@isop2015prague.org.

The code to China

Madeleine Krig

China, which is expected to soon become the world's third-largest prescription drug market, has an extensive domestic product mix that includes synthetic chemicals and drugs, biopharmaceuticals, herbal remedies and locally-prepared traditional medicines. International pharmaceutical companies and CROs (contract, or clinical research organizations) seeking to locate their product development and clinical trials in China face a dilemma: how to deal with the thousands of concomitant medicines being taken by patients whose product names they do not recognize and which they cannot code in the WHO Drug Dictionary Enhanced™ (WHO DDE).

A coding solution

Since December 2013, the Uppsala Monitoring Centre (UMC) has had a new product available, the WHO Drug Dictionary China™ (WHO DDC). By converting Chinese character medicinal product names into the unique WHO DDE global coding system, WHO DDC solves this problem and can reveal information vital to pharmaceutical development projects.

Search results – achieved in just a few seconds – give international companies access to a broad array of up-to-date information and analytical tools needed to progress and understand drug development projects in this huge marketplace.

Simplified coding for Chinese market

The main function of the WHO Drug Dictionary China (WHO DDC), as with UMC's WHO Drug Dictionary Enhanced (WHO DDE), is to help CROs and pharmaceutical companies identify, code and analyze concomitant medication that appears in clinical trials.



Unlocking the code

WHO DDC translates Chinese character medicinal product names into the WHO DDE coding system used worldwide by commercial organizations as well as national regulatory bodies. This simple conversion gives non-Chinese speakers access to the up-to-date medicinal product information and analytical tools contained within WHO DDE for drugs used in China, including Traditional Chinese Medicines.

Broad information

WHO DDC thus helps international companies collect and analyze information about drugs likely to appear as concomitant medication in clinical trials being carried out in China. This information includes trade names, the names of the active ingredients, a hierarchical classification of the intended therapeutic use, and the chemical classification.

Comparing Chinese medicinal product data with that from other countries follows exactly the same structure and methodology as found

in WHO DDE. The Chinese dictionary also converts medicinal product names found in WHO DDE into Chinese characters if the entry in WHO DDE also exists in WHO DDC.

Benefits to users

More and more companies, both international and domestic, are realizing the value of being able to code Chinese character drug information, especially for Traditional Chinese Medicines. By using WHO DDC to improve data management they are increasing their understanding of the impact that medicines taken by Chinese patients can have in clinical studies and within pharmacovigilance.

For more information about WHO Drug Dictionary China please contact sales@umc-products.com

WHO DD in US

Malin Jakobsson

The US Food & Drug Administration (FDA) has submitted a recommendation, 'Electronic Study Data Submission; Data Standards; Recommending the Use of the World Health Organization Drug Dictionary' in the official US Federal Register (published daily with proposed rules and public notices of federal decisions.) The FDA is encouraging the use of WHO Drug Dictionaries variables in investigational study data provided in regulatory submissions to the Center for Drug Evaluation and Research and the Center for Biologics Evaluation and Research.

WHO Drug Dictionaries is used to code and analyse the impact of concomitant medications used by subjects during clinical trials and contains unique codes for identifying drug names, active ingredients and drug classes. WHO DDs will be listed in the FDA Data Standards Catalog (see <http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm> <<http://www.fda.gov/forindustry/datastandards/studydatastandards/default.htm>>). The UMC welcomes and acknowledges the recognition by FDA of the contribution WHO DDs can make to identify where wise therapeutic decisions can be made in the development and use of medicines.

Reference for the Notice: Federal Register / Vol. 80, No. 61 / Tuesday, March 31, 2015 / Notices, page 17047.

有备无患

A Chinese translation of the UMC's crisis management guide 'Expecting the Worst' was published in January. This was through a collaboration between the UMC and staff at the Institute of Executive Development of the China FDA. The Institute in Beijing have taken Bruce Hugman's text about anticipating, preventing and managing medicinal product crises and translated it for a Chinese audience.

This valuable translation of the book is obtainable from the Institute, with a price of 50 Yuan, and is obtainable from http://train.sfdaied.org/book_cd/book_cd/ProductDetail.asp?id=813.



Mr Jiang Deyuan, Director of the Institute

WHO Collaborating Centres for Safety and Vigilance

Noha Iessa and Shanthi Pal, Medicines Safety, Safety & Vigilance, WHO

The World Health Organization (WHO) is the United Nation's specialist agency for health. Amongst a range of health issues, it covers safety and vigilance of medicinal products via the WHO Programme for International Drug Monitoring, which was set up in 1968 following the thalidomide tragedy. The 16.36 resolution from the 16th World Health Assembly (1963) called for "a systematic collection of information on serious adverse drug reactions during the development and particularly after medicines have been made available for public use". WHO pharmacovigilance activities are coordinated by the Safety and Vigilance (SAV) team which forms a sub-unit of the Essential Medicines and Health Products Department at WHO Headquarters in Geneva.



Charlotte Williams, Shanthi Pal, Leticia Megias-Lastra, Noha Iessa, Gauri Deoras & Daisuke Tanaka - Safety & Vigilance Team

Collaborators supporting WHO

In advancing its global health priorities and strategies, WHO works with a network of more than 700 Collaborating Centres (WHO CCs) that support implementation of mandated work. Academic, scientific and government institutions can be designated as WHO CCs provided they meet a number of

criteria, for example, high scientific and technical standing. A work plan and terms of reference are jointly agreed, planned and implemented to ensure activities are designed to support WHO strategies and operational plans. These activities may not necessarily be the institute's standard activities.

WHO SAV works with four Collaborating Centres to advance pharmacovigilance in countries. These are, in the order of establishment, the WHO Collaborating Centre for: International Drug Monitoring, Uppsala, Sweden; Advocacy and Training in Pharmacovigilance, Accra, Ghana; Pharmacovigilance, Rabat, Morocco, and Pharmacovigilance in Education and Patient Reporting, Lareb, the Netherlands. The four are responsible for research and scientific development, capacity building and technical support to countries. A fifth Collaborating Centre, the WHO CC for Drug Statistics Methodology, located in the Norwegian Institute of Public Health in Oslo, Norway, supports WHO/SAV by developing and training countries in the use of the Anatomical, Therapeutic and Chemical Classification system for medicinal products and their Defined Daily Doses (ATC/DDD).

WHO and the WHO Programme

The WHO overall vision is that health is a fundamental human right, and everyone has the right to the highest possible level of health. The primary role of WHO is to direct and co-ordinate international health. In alliance to the overall roles, the WHO aims to define norms and standards of pharmacovigilance internationally, provide leadership and strategic guidance to pharmacovigilance centres, monitor trends and articulate policy options. [Figure 1 below](#) illustrates the application of WHO roles to PV through activities run by WHO/SAV and its Collaborating Centres.

Centres that support WHO/SAV

WHO Collaborating Centre for International Drug Monitoring
(The Uppsala Monitoring Centre)



Marie Lindquist, Director of the Uppsala Monitoring Centre

The Uppsala Monitoring Centre (UMC) was the first WHO Collaborating Centre to be established for pharmacovigilance when, in 1978, the scientific and technical responsibility of the WHO Programme for International Drug Monitoring was transferred to Sweden. The Centre is an independent, self-funded, non-profit organisation.

The UMC holds and maintains the largest global database of individual case safety reports (ICSRs), known as VigiBase®, on behalf of WHO and its Member States. Scientific principles are applied to data from VigiBase for the identification, interpretation and communication of important drug safety signals and signal strengthening. Leadership in scientific development and methodological research is evident through the formation and exploration of data mining techniques and on-going research for early detection of signals.

Figure 1

Roles of WHO	Application to pharmacovigilance
Provide leadership on matters critical to health	* Lead strategic development in pharmacovigilance * Advocate and integrate pharmacovigilance as a standard of care, provide the platform and framework for its implementation
Shape the health research agenda	* Develop and promote PV policies, new approaches and methodological developments in pharmacovigilance * Convene regular meetings of the Member States and other stakeholders, to support information exchange, networking and knowledge sharing in PV
Define norms and standards for health	* Convene expert committees and working groups to develop and adapt norms, guidelines and standards for best practices in pharmacovigilance * Provide a standard international system for the classification of medicinal products and drug utilization research
Articulate policy options for health	* Communicate safety signals on a global scale, to influence regulatory decisions and policies on pharmacovigilance * Drive the integration of pharmacovigilance in public health programmes.
Provide technical support and build capacity	* Establish and co-ordinate a network of experts and Collaborating Centres to provide technical support in pharmacovigilance * Contribute to building and strengthening PV capacity and infrastructure to achieve international standards
Monitor health trends	* Develop indices and metrics to monitor PV systems and practice * Guide countries in the monitoring and evaluation of PV systems and practices against standard indices and benchmarks

The UMC provides technical support and guidance to national centres in pharmacovigilance practice. They facilitate information exchange between national centres through portals such as Vigimed, an online web-based platform. In addition the UMC develops and supports countries with reporting and data management tools such as VigiFlow, a web-based system that integrates international standards to record and manage ICSRs at many national centres. Furthermore the UMC conducts training sessions and publishes scientific articles, books, newsletters and periodicals in pharmacovigilance and risk communication.

WHO Collaborating Centre for Drug Statistics and Methodology

The Norwegian Institute of Public Health



Hanne Strøm, Director of the Oslo centre

This Centre forms part of the pharmaco-epidemiology department at the Norwegian Institute of Public Health in Oslo. The Centre was established in 1982, and is funded by the Norwegian government. It is responsible for developing and maintaining the ATC/DDD classification system for medicines. The ATC/DDD classification ensures organized standardisation and harmonization of drug utilization statistics across a range of users and disciplines, such as manufacturers, academics and national pharmacovigilance centres. To ensure that the system is representative of current practices, it is also responsible for keeping classifications up to date.

In 1992, the decision to globalize the ATC/DDD classification led to the formation of the WHO International Working Group for Drug Statistics Methodology. This group contains 12 experts nominated by WHO and drawn from the WHO Expert Advisory Panels for Drug Evaluation and for Drug Policies and Management. The Working Group meets twice a year to revise and make decisions on ATC classifications or DDD assignments.

The Norwegian WHOCC also functions to stimulate and influence the practical use of ATC systems by interacting with users. They provide technical support, training courses and lectures to member countries using the ATC/DDD codes within their pharmaco-vigilance systems. They also publish guidelines of ATC classification and DDD assignment.

WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance

The Centre for Tropical Clinical Pharmacology and Therapeutics, University of Ghana Medical School



Alex Dodoo, Director of the Accra centre

The Centre in Accra was designated as a WHO Collaborating Centre in 2009. The Accra Centre focuses on providing pharmacovigilance training in African countries, building capacity, promoting advocacy and strengthening reporting.

As part of the training function, the Accra Centre has organised fellowship and internship programmes, attracting fellows from several African countries. They also run courses for regulators, such as 'Data management training for clinical and regulatory affairs'.

Activities to support countries and promote communication and advocacy of pharmacovigilance include: hosting annual workshops, visiting countries to assess national centres, and developing high-level training material and risk management plans.

The Centre develops, hosts and maintains a pharmacovigilance Toolkit. The Toolkit is a collection of resources and information needed for the practice of pharmacovigilance. It aims to ensure that practitioners have easy access to information on processes and activities from a trusted source. The Toolkit provides links to publications, handbooks, e-learning courses, and guidelines. There are specific tool-kits for pharmacovigilance in HIV, malaria and immunization programmes. The Accra Centre works with the WHO/SAV to provide support for countries conducting cohort event monitoring (CEM) and other active surveillance studies of new medicines and vaccines.

WHO Collaborating Centre for Pharmacovigilance

Centre Anti poison et de Pharmacovigilance du Maroc

In 2011, Centre Anti poison et de Pharmacovigilance du Maroc, in Rabat, Morocco, became a WHO Collaborating Centre. With the global expansion of pharmacovigilance and growing number of member countries, the Rabat centre assists WHO by building capacity in the eastern



Rachida Soulaymani, Director of the Rabat centre

Mediterranean, francophone and Arabic countries. They facilitate regional and national training courses in this geographical area and also support normative functions to promote patient safety. Their annual training course covers topics such as VigiFlow, causality assessments, pharmaco-vigilance of herbal medicines, patient safety, vaccines, and medication errors.

The Rabat Centre is also involved in projects aimed at integrating patient safety reporting systems across different types of health facilities; and pharmacovigilance in public health programmes such as multi-drug resistant TB treatment programmes. The Rabat Centre supports WHO in developing appropriate guidelines, tools and methods to detect and minimize medication errors through pharmacovigilance. The Centre also surveys and evaluates performance and development of pharmacovigilance systems in Africa.

WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting

The Netherlands Pharmacovigilance Centre Lareb



Agnes Kant, Director of Lareb

The Lareb Centre in the Netherlands is a specialised national centre which focuses on the process and scientific evaluation of patient spontaneous reporting. In 2013, it was designated the WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting. Its role is to assist WHO in training member countries on how to handle patient reports. It holds workshops and hosts visitors at the Centre to share their experiences of patient reporting. Support is provided to countries with patient reporting by providing information and feedback. The Lareb Collaborating Centre training on practical aspects of collecting information about adverse drug reactions and on patient reporting.

The Centre conducts research on the contribution of patient reports to pharmacovigilance. The research is conducted in collaboration with the University of Groningen and has several publications in the pipeline. Further to the work involving patient reports, the Centre promotes pharmacovigilance education in academia by developing and maintaining a curriculum for medical, pharmacy and paramedical students. A project collecting information on the content of pharmacovigilance core curricula is in process and the Lareb Centre will organize workshops for Member Countries within the WHO Programme for International Drug Monitoring to discuss the curriculum.

Table 1 describes the terms of reference and activities of the five Collaborating Centres. We provide an overview of the establishment of these Centres, their roles and contributions to WHO programmes.

Going forward

While WHO/SAV and the UMC are mandated to develop and implement pharmacovigilance, the other WHO CCs that support SAV do this as an additional task, on top of their 'day-jobs', and without compromising their national responsibilities. This is a remarkable distinction and underlines the commitment and nature of engagement of the individuals within these WHO CCs. Their support to WHO and the global patient community is invaluable.

Table 1

Name, institution date of designation, website	Place	Terms of reference
WHO Collaborating Centre for International Drug Monitoring 1 January 1978 http://www.who-umc.org	Sweden (Uppsala)	Lead scientific development in the WHO Programme for International Drug Monitoring particularly regarding: <ul style="list-style-type: none"> • Identification and explanation of important safety signals related to medicinal products. • Develop best practices in pharmacovigilance. • Improve the visibility and status of pharmacovigilance globally. Provide useful, high-quality and cost-effective pharmacovigilance products and services to member countries of the WHO Programme for International Drug Monitoring (PIDM) for local applicability building on international standards. Contribute to capacity building in WHO PIDM member countries in establishing and supporting sustainable, high quality pharmacovigilance systems and evaluating their performance.
WHO Collaborating Centre for Drug Statistics Methodology 1 November 1982 http://www.whocc.no	Norway (Oslo)	To classify drugs according to the ATC system. To establish DDDs for drugs which have been assigned an ATC code. To review and revise as necessary the ATC classification system and DDDs. To stimulate and influence the practical use of the ATC system by cooperating with researchers in the drug utilization field. To organize training courses in the ATC/DDD methodology and to lecture in such courses and seminars organized by others. To provide technical support to countries in setting up their national medicines classification systems and build capacity in the use of medicines consumption information.
WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance 1 October 2009 http://who-pvafrica.org/	Ghana (Accra)	Training in pharmacovigilance in African countries for building and strengthening spontaneous adverse drug reaction reporting systems. Advocacy for pharmacovigilance across Africa either alone or in collaboration with WHO Promoting the integration of pharmacovigilance into public health programmes. Technical support to national pharmacovigilance centres. Support in communication and crisis management to national pharmacovigilance centres. Acquisition (from WHO, UMC) and distribution of needed literature and technical tools to national pharmacovigilance centres and governments by hosting and maintaining a Toolkit. Research in pharmacovigilance including cohort event monitoring of specified medicines. Assisting countries to develop and maintain pregnancy registers.
WHO Collaborating Centre for Pharmacovigilance 1 November 2011 www.sante.gov.ma www.capm.ma	Morocco (Rabat)	To conduct and facilitate regional and national pharmacovigilance training courses for Francophone, Eastern Mediterranean and Arabic countries. To support the WHO normative functions related to pharmacovigilance and promote patient safety. To assist WHO in pharmacovigilance assessments and in the provision of technical support to Member States in pharmacovigilance and patient safety.
WHO Collaborating Centre for Pharmacovigilance in Education and Patient Reporting 1 May 2013 www.lareb.nl	The Netherlands ('s-Hertogenbosch)	To work with WHO in the development and maintenance of a core pharmacovigilance curriculum to be part of the university curriculum for pharmacy, medical and paramedical professions. To assist WHO in the promotion of the pharmacovigilance core curriculum. To assist WHO and the member countries of the WHO International Drug Monitoring Programme in the development of patient reporting systems. To work with WHO in providing training to member countries of the WHO International Drug Monitoring Programme in handling patient reports. To contribute to research in pharmacovigilance, to identify and investigate the value of additional data sources such as reports submitted by patients.

The WHO Programme has existed for nearly 50 years, but has grown slowly, especially in resource limited settings (RLS) because of insufficient engagement of all stakeholders, the perception in many RLS that pharmacovigilance is a luxury; lack of strategy to support its growth in non-Anglophone countries; and inadequate developments to address the growing needs of low- and middle-income countries (LMIC) with their special disease demographics. WHO's strategy to establish additional Collaborating Centres closer to the point of care in LMICs, with a focus on public health programmes and local language needs is paying off.

Growth

The WHO Programme has been growing steadily in membership and in scope of work these last 15 years, especially in those regions with weak infrastructure but a high burden of diseases. The WHO CC in Ghana has been instrumental in integrating pharmacovigilance in malaria and immunization programmes in sub Saharan Africa and will continue to support WHO in developing relevant methods for monitoring in HIV, TB and other priority programmes. The Morocco centre has helped bring pharmacovigilance to francophone and Arabic language countries; the Centre also supports WHO in expanding the scope of pharmacovigilance, to detect and prevent medication errors and the harmonization of reporting systems across health facilities. Lareb, the latest to join the fleet of WHO CCs is especially important in bringing patients to the network and integrating pharmacovigilance in mainstream curricula.

Shared responsibilities

Going forward, WHO will continue to exploit the WHO CC model and will join hands with other groups and initiatives to support global pharmacovigilance. For example, WHO/SAV will work with the Pan American Health Organization and the Pan American Network for Drug Regulatory Harmonization to support Latin American countries; it will work with regional centres of regulatory excellence in Ghana and in Zimbabwe, to provide a regulatory framework for LMICs; with the Asia-Pacific Economic Cooperation forum and ASEAN (Association of Southeast Asian Nations) networks in Asia and Pacific regions; with professional organizations such as ISO, to influence global best practices, to name a few.

Global pharmacovigilance is a shared responsibility of many stakeholders: it requires the commitment and engagement of health professionals, regulators, patients and civil society, academics and researchers, inter-government agencies and their Member States, global health initiatives, donors, industry. Working through WHO CCs and other partners, we are enlisting a global participation in pharmacovigilance, one stakeholder at a time.

Medication use in pregnancy

Kristina Star and Lovisa Sandberg

The EUROmediCAT consortium and the Poznań University of Medical Sciences in Poland organized a European conference on 'Safety of Medication use in Pregnancy' on 2-4 February 2015. The EUROmediCAT is a



Safer medicine use in pregnancy in Poznań

research project financed by the European Union's 7th Framework Programme and runs between 2011 and 2015. The initiative aims to build a European system to evaluate the risk for congenital anomalies in relation to medication use in pregnancy. The EUROmediCAT database, used for the research in this project, is based on the EUROCAT central congenital anomaly database with information on medication use during the first trimester of pregnancy.

New findings

Research findings and final results from the project were presented at the conference in February: the central database and software development; prescription data linkage; internet use and risk management; safety and utilization of antiepileptics, antidiabetics, antidepressants and antiasthmatics in pregnancy and signal detection in the EUROmediCAT registry. The findings in the signal detection session were particularly

interesting since this was the first time broad exploratory analysis was conducted on this type of data. The conference concluded with a discussion on the recommendations for reproductive pharmacovigilance in Europe.

Highlighting the issue

Several publications have been and will be visible in the scientific literature based on the EUROmediCAT initiative, which will benefit pharmacovigilance work in the reproductive area. The conference was very well attended and the Polish hosts did a great job to promote the importance of the subject. We hope that the researchers will receive funding to continue this important work to protect pregnant women from teratogenic drugs.

Further information can be found on the following sites: <http://euromedicat.eu/> and <http://www.eurocat-network.eu/>.

A rich palate in Mysore

Rebecca Chandler

The International Society of Pharmacovigilance (ISoP) and the Uppsala Monitoring Centre (UMC) agreed in 2014 to collaborate in training efforts to increase education and to harmonise safety reporting requirements and systems in Asia. The 2nd International ISoP/UMC training course, 'Risk Management through Fostering Good Pharmacovigilance Practice in Emerging Markets' was held between January 12 – 14, 2015 in Mysore, India.

Expert guidance on offer

The course focus was to provide a multi-coloured guide and expert perspectives on the essentials of pharmacovigilance, including safety data management, signal detection/causality assessment, and risk management/risk minimization. Speakers were an international group: members of the ISoP Executive Committee, UMC staff, pharmacovigilance leaders in India, representing government, academia and industry.

The 50 participants, predominantly from the JSS College of Pharmacy, but also working at industry and regulatory agencies, came mainly from India, but some travelled from Singapore and Thailand.

The meeting opened with a ceremonial lamp lighting by YK Gupta from the All Indian Institute of Medical Sciences (AIIMS) New Delhi, B Suresh, G Parthasarathi, both from the JSS University in Mysore; with Andrew Bate (representing ISoP) and Marie Lindquist (UMC).

The first day included lectures describing the current status of pharmacovigilance in India/Asia from the perspectives of industry, academia, and regulators. Other highlights were a session on the history and importance of pharmacovigilance by YK Gupta and a talk on counterfeiting and quality defects by former Deputy Drug Controller in India, Dr D Roy.



Sensorial brilliance in Mysore

The second day featured presentations of a more 'bread and butter' flavour: signal detection basics, causality assessment, disproportionality statistics. There was also a much-appreciated, interactive and 'hands-on' session introducing VigiLyze by Anders Viklund.

Day 3 focused on risk management, with presentations on the EU Risk Management Plan, methods of risk minimization, and studies to measure the effectiveness of risk minimization activities. Ralph Edwards and Marie Lindquist explored considerations in risk/benefit assessment and the importance of risk communication with an entertaining tag-team session.

Scents and colours

The city of Mysore provided a feast for all the senses: the brilliance of the illuminated Mysore Palace and the colour of the harvest festival Makar Sankranti; the smells of sandalwood incense and warm curries; the constant beep-beeps of the tuktuks and explosions of night-time/early morning fireworks; and of course the incredible, mouth watering buffets of curries, naan, chapati, and fresh papaya and pineapple.

Much activity in Chile

Juan Roldán Saelzer

There was a lot for Elki Sollenbring to observe and get involved in when we welcomed her to Chile in early March. The National Pharmacovigilance Centre of Chile (CNFv) within the Instituto de Salud Pública (ISP) was the centre of her busy stay. As the regular UMC contact person with the CNFv team we had plenty to discuss with her about technical management issues and guidelines of the WHO Programme, an essential aspect of the daily work at the Centre.

Hospital visit

The opportunity to visit two hospitals in Santiago (one paediatric, the other for adult patients), gave Elki a chance to discuss issues with the Clinical Pharmacist in charge of their pharmacovigilance activities and with other professionals. A significant number of ICSRs (Individual Case Safety Reports) are generated there and managed via the new on-line notification system developed by the CNFv.

Vaccines

A meeting of the 'Proyecto Multicolaboración Multi-país' on vaccines safety on 4–5 March in Santiago was attended by experts from eight countries in the region. The project concerns building signal detection capacity in the field of vaccine safety.



José Luis Castro (PAHO), Elki Sollenbring (UMC), Adiel Saldaña (ISP), Deok-Ryun Kim (IVI), David Mena (ISP), Juan Roldán (ISP) in Santiago

Data transmission tool

The following day a workshop involving experts from the International Vaccine Institute (IVI), the Pan American Health Organization (PAHO) and the CNFv team examined the development of a tool to permit data transmission of ICSRs from Chile to VigiBase, with the emphasis on vaccines. Again Elki's presence at these meetings

allowed us to gain advice on essential technical elements of the proposal submitted by IVI and PAHO. All this will be taken into account during the next stages of the development of the tool and help determine its final characteristics, including the data structure used in the current CNFv ICSR database.

Symposium in West Bengal

Sten Olsson

A two-day symposium on medicine safety and pharmacovigilance was organized at the School of Tropical Medicine, Kolkata, West Bengal, India, on 2–3 March 2015. The main organizer was Santanu K. Tripathi, Professor of Clinical and Experimental Pharmacology.

Several lectures were devoted to the need and challenges of introducing pharmacovigilance in public health programmes (PHP), particularly those against tuberculosis and HIV/AIDS.



S. K. Tripathi, Kolkata

Sten Olsson from UMC, representing the WHO Programme, talked about WHO norms and standards in pharmacovigilance and the methods recommended by WHO to complement spontaneous reporting in PHP. Sessions were devoted to the progress of the Pharmacovigilance Programme of India and how to use VigiFlow for data management. An engaging talk was given on the promising future of stem cell therapy and its potential risks. Young researchers also competed in orally presenting adverse reaction case reports in the most enlightening and engaging manner.

Arab meeting report

An article describing the first Arab/EMR PV meeting in Rabat last year has appeared in the journal *Drugs – Real World Outcomes*. It includes reports from the working groups and examples of harmonised Arab pharmacovigilance terms. The link is: <http://link.springer.com/article/10.1007/s40801-015-0015-8>

Bilal Bham. The First Eastern Mediterranean Region/Arab Countries Meeting of Pharmacovigilance. *Drugs – Real World Outcomes* (2015) 2:111–115. DOI 10.1007/s40801-015-0015-8.

Ebola Crisis in Liberia: a pharmacovigilante reflects

Hasipha C. Tarpeh

Background

Ebola is a deadly haemorrhagic disease with an incubation period of 21 days and signs and symptoms similar to diseases such as cholera, malaria and typhoid. Despite several attempts since its discovery in 1976, to date there is no scientific evidence of a cure for the Ebola Virus disease (EVD).

The EVD broke out in Liberia in March 2014 when an individual infected with the virus travelled from Guinea to Liberia. The outbreak paralyzed the health system in Liberia, and major health institutions and activities, including the pharmacovigilance programmes in the schools, hospitals and the regulatory authority, came to a standstill. The crisis greatly affected pharmacovigilance activities due to the nationwide closure of the health facilities.

The period between July and November 2014 witnessed the shutdown of several businesses in the country, departure of investors and loss of jobs. The government declared a state of emergency, ordered the closure of schools and entertainment centres, and quarantine measures. Restrictions were imposed on social activities aimed at breaking the transmission and stabilizing the disease, such as a restriction in the number of persons riding vehicles (rather than the usual practice of passengers sitting on each other's laps). All these measures, though difficult to enforce 100%, brought some level of sanity in the struggle to fight the disease.

Challenges

Some of the major problems which impacted safety monitoring:

1. A total collapse of the health system due to the outbreak of the EVD presenting as a strange disease in the country. Many health workers died from lack of experience in its management.
2. Deaths of health workers due to the lack of protective equipment, and the abrupt closure of major hospitals reporting adverse drug reactions (ADR).
3. The circulation of fake and substandard medicines due to the slowdown of regulatory activities.
4. To date only a few health facilities are returning to full operation. Focal persons for spontaneous reporting of ADRs in hospitals are yet to return to work, posing a question about training new people for reporting.
5. More than 3,000 persons, including many health workers died; unconfirmed reports

indicate that some deaths were due to unauthorized, self-designed treatment.

The outbreak of the EVD also affected pharmacovigilance activities when the expert committee ceased, as there were no cases to be verified in any manner and form.

Lessons learned

The greatest lesson learned as a result of the Ebola epidemic is that Liberia has a very weak health system; a system with no capacity to contain the EVD or similar disease. This is in terms of manpower, infrastructure, equipment and logistics. Most health facilities have very poor laboratory facilities and there are few specialists – for example the lack of clinical pharmacists. Most health practitioners, especially physicians, are only general practitioners. This weakness was blamed by Health Minister Dr. Walter Gwengale on inadequate budgetary allotment. The health system needs to be improved and strengthened to be able to contain future outbreaks of diseases. There needs to be a clearly defined treatment protocol for the EVD management.

One positive outcome is the display of Ebola awareness messages on private residential buildings, public buildings, vehicles, bus-stops, etc. As a result of persistent and continuous public awareness activities, the state of denial no longer exists. Public awareness of safety issues is of course vital in pharmacovigilance too.



Ebola awareness messages on a bus stop on street leading to Monrovia from the airport.

Another success was the establishment of an Incident Management System headed by Assistant Minister of Health, Tolbert Neyenswah (a public health specialist).

On-going coordination

Currently, there are close to 1,000 survivors who were admitted into Ebola Treatment Units (ETU), tested positive, given supportive

treatment and later discharged because they were tested negative after the supportive treatment. Many survivors are children whose parents lost their lives to the EVD.



United Nations military personnel seen immediately after washing his hands to enter a pharmacy store in Monrovia – 6 year-old boy holds certificate stating that he is now Ebola-free.

The construction of ETUs around the country helped solve the lack of secure bed space which initially led to rejection of patients and many deaths. Monrovia city and its environs has six ETUs, and at least one is to be constructed in each of the other 14 counties; nine already have been.

Donations from all walks of life in cash and kind created a good atmosphere and a balance to effectively fight the disease. These came from the international community as well as local groups, banks, individuals and the like. The international response saw the USA playing a leading role in providing financial support and manpower, followed by the Economic Community of West African States, the African Union, other friendly governments and groups.

Current disease trends

July 2014 witnessed hundreds of daily deaths at the Ebola Treatment Units (ETU), street corners, in communities, churches, mosques, etc. The entire country became terrified between July and November 2014, with over 3,000 persons losing their lives to Ebola in Liberia.

As a result of the experience in the fight against the disease, Liberia has seen the need to share success stories with the other countries to the extent of sending some health workers to Sierra Leone. Unless neighbouring countries are free of Ebola, Liberia risks experiencing cases again, as our borders with our sister countries are very porous.

Asia Pacific Training

Anki Hagström

The First Asia Pacific Pharmacovigilance Training Course was arranged in Mysore, India from 16-28 February 2015. This two-week training programme was organized by JSS University Mysore and Uppsala Monitoring Centre in collaboration, with the objective of sharing knowledge and skills in pharmacovigilance to healthcare professionals and regulators across the Asia Pacific region.

Advocacy

Countries in this part of the world face increasing awareness of adverse drug reactions among health care professionals and the public, placing demands on effective communication to reach a large and diverse audience. Another challenge is to establish sustainable safety surveillance systems, which requires purposeful advocacy towards ministers of health and other stakeholders to secure funding and resources for pharmacovigilance activities. Training is closely related to equipping pharmacovigilance experts in addressing those challenges and to building capacity for patient safety in relation to the use of medicines. UMC and JSS University offered the Asia Pacific training course to meet pharmacovigilance training needs and to help support the advancement of pharmacovigilance in the region.

Barbara Muller (Medicine Safety Unit Pharmacist, Vanuatu) explained that pharmacovigilance is known as "problems with medicines" in Vanuatu and the training in Mysore certainly covered many of those problems. "The designing of a relevant and simple-to-use ADR reporting form, the training in why, how and when to use it, and the importance of how to communicate

within a culture are the most important 'take home' messages for me."

Practical sessions

The course provides solid practical foundations on the principles of drug safety and covers topics essential to effective capacity building in the field. Sessions included pharmacovigilance best practices, signal detection, reporting culture, pharmacovigilance in drug development, benefit/harm assessment and pharmacovigilance tools, communications and risk management.



The joint training course students and teachers

Dr. Shanthi Pal from the WHO Safety and Vigilance Group, UMC, JSS University and pharmacovigilance experts from universities, academic institutions and pharmaceutical industry across the region contributed to the training.

Chaitanya Kulkarni (Drug Safety Associate, Lupin Ltd, India) commented that the programme had "an excellent adapted curriculum which touches base with almost all the aspects of global pharmacovigilance practices", finding the speakers very professional with in-depth knowledge of different subjects. He was also "amazed to see that the passion and enthusiasm in the trainers and speakers about pharmacovigilance", and felt that one would be able to develop a similar passion for pharmaco-

vigilance. "I strongly recommend people to attend this training as once-in-a-life-time opportunity."

Open environment

Training is built around lectures, workshops and hands-on exercises, in an open and interactive environment. There is plenty of opportunity for participants to interact with JSS staff, UMC staff, faculty experts and fellow course participants. Social activities comprised an official course dinner and sightseeing tours.

"I really enjoyed the multicultural class, fruitful workshops, and amazing advice. It has been a pleasure to attend the course, which made us feel so empowered" enthused Mark Tyan A Lirasan (Regulation Officer, FDA, Philippines).

Sixteen participants from eight countries participated, and the success of the training was confirmed both by faculty and course participants. At the end of the course Chuon Vibol (Pharmacovigilance Technical Officer, Department of Drugs and Food, Cambodia) told us that "Upon completion of this training and my return, I have strong confidence that I will be able to get involved more actively in developing and also enhancing pharmacovigilance activities, and in particular aspects in the health care system in Cambodia."

The establishment of this joint training course shows UMC's and JSS University's dedication to contribute to the advancement of pharmacovigilance. The challenges and training needs in the Asia Pacific region apply to many other countries and participants from other regions are welcome to apply for the next course, on 18-29 January 2016.

Conclusion

A return to full healthcare services is a major challenge to government and all stakeholders. President of Liberia Madam Ellen Johnson Sirleaf commented "The restoration of health services depends on the economic recovery of the country". Restoration of the health system therefore, is a concern for all residents and donors alike. The government of Liberia with the support of partners has the challenge of human resource development. Liberia will experience a great deal of sanity in the years

ahead if the human resource challenge is adequately addressed.

Clearly the EVD has had a major impact on our work in pharmacovigilance but the crisis has shown that reliable funding, a good infrastructure and committed individuals are as essential in combating a major public health crisis as in routine safety monitoring to protect the public. The other lessons relate to the merits of crisis planning and decisive action at the early signs of a crisis.

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Finding substandard medicines in VigiBase®

Kristina Juhlin & Maria Andér

The Uppsala Monitoring Centre in collaboration with the National Centres in Malaysia, Singapore, South Africa, South Korea, the UK and the USA have just published the results of a pilot study on the potential to identify substandard medical products in VigiBase®. The study is published as open access in Drug Safety.

Background

Substandard medicines, whether the result of intentional manipulation or of lack of compliance with good manufacturing and distribution practice (GMP/GDP), pose a significant potential threat to patient safety. The effects of substandard products can be severe; patients can suffer adverse reaction to additives and substitute products or a lack of therapeutic effect leading to worsening of the disease and possible death. Substandard products made with the main intent to mislead or deceive patients for financial gain, also lead to loss of money, productivity, and confidence in health systems worldwide.

Identifying substandard medicinal products

In 2011, the Uppsala Monitoring Centre (UMC) developed an algorithm to identify reporting patterns suggestive of substandard medicines in the WHO global ICSR database, VigiBase™. The initial research was performed within the Monitoring Medicines collaboration, and included a limited evaluation of a restricted set of highlighted clusters. In order to thoroughly evaluate the effectiveness of the algorithm the assessment of potential clusters should be done as near as possible to the original sources of information, as assessment often requires that additional details are gathered from the original reporter. Therefore, this pilot study was set up as a collaborative project between UMC

and selected pilot country sites to perform the assessments on the suspected clusters of substandard medical products.

The participating countries were Malaysia, Peru, Singapore, South Africa, South Korea, UK and US, which were chosen based on prevalence of highlighted clusters and with respect to having a good geographical spread.

The algorithm for identifying substandard medical products highlights clusters of reports based on a higher than expected prevalence of MedDRA terms indicative of lack of effect or directly suggesting product quality issues. To capture local occurrences of substandard products, clusters are defined as 'reports on a product with the indicator terms from a single country and year'.

Empirical evaluation

From the clusters of suspected substandard products identified by the algorithm, 147 were randomly selected by the UMC for evaluation by the participating national centres. Out of these, 8 clusters were classified as 'confirmed' and 12 as 'potential' substandard medicines. 57 of the clusters were classified as 'indecisive', which reflects the difficulty of evaluating suspected substandard products retrospectively when additional information from the primary reporter as well as samples may no longer be possible to obtain.

Potential for future use

The UMC also investigated the status of prerequisites for effective routine use of the algorithm through interviews with specialists at the pilot country sites. The responses show that these prerequisites are not fulfilled today. Most importantly, the current lead times in the reporting to VigiBase are

too long, and would need to be decreased to approximately 30 days to enable a meaningful follow-on investigation. Increased awareness, and hence increased reporting of adverse events related to substandard medical products, is also needed, especially in regions where substandard medical products are known to be a significant problem and where pharmacovigilance systems are still maturing.

Prerequisites for effective routine use of algorithm

- 1) Reporting of lack of effect and quality issues established within the country
- 2) Time efficient reporting process to VigiBase guaranteed - from occurrence of AE to ICSR available in VigiBase
- 3) Reporting occurs on product name level
- 4) NCs need necessary capacity to perform investigations and follow-up

However, the interviews confirmed an interest in a routine use of the algorithm among five of the seven countries. Provided that prerequisites are met, there may be a potential benefit of putting the algorithm into routine use for resource limited countries or for countries where limited monitoring for substandard medical products is done today, to help highlight suspected cases and to guide initial investigations.

Next steps

Since effective investigation and follow-up of potential cases of substandard medicines is not possible with the current reporting lead times, it is not yet the time to introduce the algorithm into routine use. UMC is recommending that actions are taken by UMC, WHO and countries with an interest in routine use of the algorithm to improve current pharmacovigilance processes, to move towards fulfilling the prerequisites for better detection of substandard medical products.

Article available in *Drug Safety* online: <http://link.springer.com/article/10.1007/s40264-015-0271-2>

This study has been conducted with financial support from the FDA in the United States.



Medical record data as reference source in signal work

Kristina Star

The paper 'Longitudinal medical records as a complement to routine drug safety signal analysis' was recently published online ahead of print by *Pharmacoepidemiology* and *Drug Safety*. The UMC authors explored the feasibility of using longitudinal electronic medical records as a source of reference in the early phases of signal detection and analysis of individual case safety reports in VigiBase®. The original idea for this study was suggested by Dr Marie Lindquist.

We used The Health Improvement Network (THIN) database of electronic medical records from UK general practice, on which a previously published temporal pattern discovery method with a self-controlled design, *vigiTrace*,¹ had been applied. *vigiTrace* on THIN was used as a source of reference during manual review of 458 drug-adverse reaction combinations generated from VigiBase during the third quarter of 2011.

Accessing THIN during signal detection in VigiBase provided a useful clinical context for the drug-adverse reaction combinations under review. However, the paucity of data in THIN for many of these combinations, meant that only a small number of potential signals from VigiBase could be evaluated in the electronic medical records. Data was particularly sparse for newly marketed drugs reported with serious reactions as defined by the WHO Adverse Reaction Terminology (WHO-ART) critical terms.

Another challenge was matching medical event terms recorded using the 'Read' code terminology in THIN with adverse reactions coded using WHO-ART in VigiBase. The main value of using THIN data in this study was the opportunity to view drug-event patterns in *vigiTrace* displayed in the chronographs, i.e. a specific medical event displayed monthly three years before and after a specific prescription. This particularly helped

in identifying drug-adverse reaction combinations that were most likely to be associated with the underlying or concomitant disease.

This study has added one more piece to the puzzle of knowing how to best use electronic medical records in the context of signal detection and analysis. The full list of authors is Kristina Star, Sarah Watson, Lovisa Sandberg, Jeanette Johansson and I Ralph Edwards.

The paper is published open access via the following link: <http://onlinelibrary.wiley.com/doi/10.1002/pds.3739/epdf>

Reference

1. Norén GN, Hopstadius J, Bate A, Star K, Edwards IR. Temporal pattern discovery in longitudinal electronic patient records. *Data Min Knowl Discov* 2010; 20:361–387.

ADRs for cardiometabolic drugs from Sub-Saharan Africa

Kristina Star

This was a collaborative study between researchers in the Netherlands, Ethiopia, South Africa and Sweden (UMC). Peter GM Mol, Assistant Professor at the Department of Clinical Pharmacology, University Medical Center Groningen, Netherlands, and his PhD student Derbew Fikadu Berhe from Ethiopia initiated the investigation on adverse drug reaction (ADR) reports with cardiometabolic drugs from Sub-Saharan Africa (SSA). Since the majority of the reports in the study originated from South Africa, and clarifications to questions on these reports were needed during our analysis, Mukesh Dheda also got involved in the writing up of the study.

The burden of cardiometabolic disease is increasing rapidly in SSA. Berhe and his co-authors aimed to identify key features in ADR reports on cardiometabolic drugs from SSA. Individual case safety reports entered in VigiBase® from 1992 to 2013 were included in the study. Key features were identified using *vigiPoint*, which is a logarithmic-odds ratio-based method used to compare covariate values (e.g., age, gender, reporter, drugs and adverse reactions) in a selected subset of reports of interest with one or several comparators.¹ In this analysis, reports with cardiometabolic drugs from SSA were the subset of interest and reports with the

same group of drugs from the rest of the world constituted the primary comparator.

In SSA, 9% of the reports concerned cardiometabolic drugs compared with 18% in the rest of the world. In the SSA subset of reports on cardiometabolic drugs, 79% were from South Africa, and 81% had been received after 2007. Drugs acting on the renin-angiotensin system were reported disproportionately more frequently in SSA (36%) than in the rest of the world (14%). Lip swelling, cough, angioedema, face oedema, swollen tongue and throat irritation were more frequently reported in SSA, most likely reflecting the known ADRs of ACE-inhibitors. This finding is in line with prior knowledge that ACE-inhibitors seem to be less tolerated in the black population.

This is probably the first study to focus on ADR reports with cardiometabolic drugs across countries in SSA. The findings emphasize the importance of continuing pharmacovigilance efforts in this part of the world in order to increase our understanding of the benefits and risks of medicines in the population of SSA. The paper is published online ahead of print and the abstract is available at: <http://www.ncbi.nlm.nih.gov/pubmed/25704305>

The authors are Derbew Fikadu Berhe, Kristina Juhlin, Kristina Star, Kidanemariam G Michael Beyene, Mukesh Dheda, Flora M Haaaijer-Ruskamp, Katja Taxis and Peter GM Mol.

Reference

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Antimicrobial resistance: UMC joins global initiative

Antonio Mastroianni

On June 2 and 3, decision-makers, opinion leaders and experts from politics, industry, academia and civil society at the Uppsala Health Summit will discuss how research results and innovations can tackle a major health challenge (www.uppsalahealthsummit.se). The Summit will provide a critical opportunity to discuss consequences of actions and non-actions for people, animals and the planet in relation to antibiotic resistance, one of the great global health threats that needs urgent coordinated action on a global scale. Importantly, this will be one of the first major international venues following the World Health Assembly in May 2015, where WHO is expected to present a formal global action plan against antimicrobial resistance, to be coordinated by WHO.

UMC is supporting the Summit because this issue is not only a key component in effective pharmacovigilance, but also in patient safety. We see antimicrobial resistance as part of the broad scope of pharmacovigilance, which also includes medication errors, bad quality drugs, etc.

Burden ahead

As underlined in the WHO 2014 report, 'Antimicrobial Resistance – Global Surveillance', anti-microbial resistance will result in ordinary infections becoming lethal

if it is not addressed in a global and coordinated fashion. A growing burden of antimicrobial resistance will increase the mortality among frail groups such as patients with pre-existing conditions and vulnerable populations in unsanitary environments lacking access to regular medical services. As a result, routine medical interventions may again become interventions of high risk. One problem. Different perspectives.

Dialogue

The 2015 Uppsala Health Summit will rely on frank and open dialogue on how the current state of knowledge and innovations can lead to action on global, national and local levels, to reduce the threat from antibiotic resistance. It will cover:

- measures for rational use of antibiotics for human and veterinarian purposes
- environmental issues
- business models for innovation and release of new antibiotics
- prevention of infections.

The Uppsala Health Summit series was started by local, regional and national governmental and academic institutions to create a natural meeting point in Sweden to tackle pressing health-related issues facing the world. Sweden has a thriving life

sciences community with hands-on international experience in many of today's most important healthcare issues. Uppsala has a strong science base with two leading academic institutions, Uppsala University and the Swedish University of Agricultural Sciences, internationally competitive research in several fields, and clinical research at Uppsala University Hospital. The research infrastructure, including platforms for large-scale biomedical research, biobanks, patient registries and resources for advanced computational science, open up many new possibilities to improve healthcare worldwide.

In addition, Uppsala is home to two regulatory authorities, the Medical Products Agency and the National Veterinary Institute, and a wide network of international organizations, such as ReACT and Uppsala Monitoring Centre – the WHO Collaborating Centre for International Drug Monitoring. This ecosystem contributes to the overall ability to put research results into practice to improve health and health outcomes.

2014 WHO report, 'Antimicrobial Resistance – Global Surveillance'
www.who.int/drugresistance/documents/surveillancereport/en/

Be part of the Summit

The Uppsala Health Summit (June 2-3 2015) aims to bring together decision-makers, opinion leaders and experts to discuss consequences of actions and of non-actions for people, animals and the planet in relation to antibiotic resistance, which is one of the great threats to health globally, a threat that needs urgent coordinated action on a global scale. Antibiotic resistance is a key component of pharmacovigilance and the irrational use of these medicines and lack of awareness by those that abuse them have the potential of cataclysmic consequences for the entire world.

The WHO underlines in its 2014 report "Antimicrobial Resistance – Global Surveillance", that if not dealt with, ordinary infections that we today consider treatable will kill again. The growing burden

of antimicrobial resistance will increase the mortality among frail groups as patients suffering from other diseases, and even simple surgical interventions will once again become interventions of high risk. During the World Health Assembly it



Uppsala congress centre, the Summit venue

is expected that WHO will outline a global action plan against antimicrobial resistance, to be coordinated by the WHO.

Uppsala Health Summit is a by invitation only event, that can host only up to 200 persons. If you have yet not received an invitation, but have a distinct role forming the future healthcare sector, as decision maker, opinion leader or expert from private sector, academia, public sector or civil society, The Organizing Committee is happy to add you to their list of invitees. Please contact info@upsalahealthsummit.se.

More information about the Uppsala Health Summit can be found at <http://www.uppsalahealthsummit.se/antibiotics-antibiotic-resistance-2-3-june-2015/>

Medicines for Women

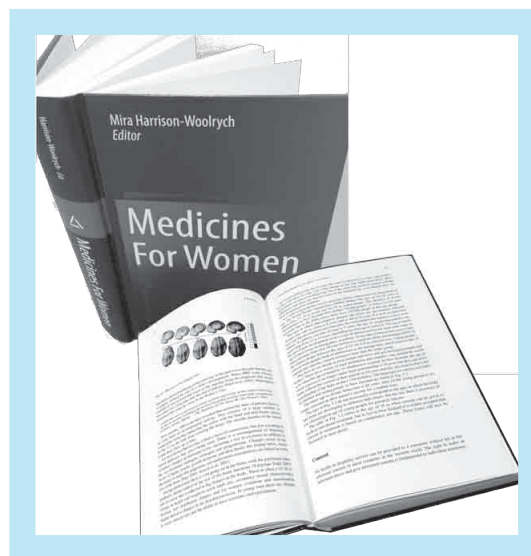
Geraldine Hill

This comprehensive new 627-page publication* brings together in one volume many issues that relate to the use of medicines by women. While much has been written separately on the various topics covered in the book, this valuable resource sharpens the focus on women and their specific needs in relation to medicines. It examines the intricacies of prescribing to women: from the distinctive pharmacokinetics of medicines in women to the socio-cultural understandings that form the context in which medicines are used by women.

The book comprises three parts. Part I, Prescribing Medicines for Women: General Principles and Consideration of Special Sub-populations, starts with a brief history of the use of medicines in gynaecology and notes how the history of contraception has been closely linked to the socio-cultural and economic position of women over time. The personal account by Elizabeth Claire Hooper of her experiences with diethylstilboestrol (DES) and the poster promoting DES to pregnant mothers are powerful reminders of how the health needs of women have been exploited by the commercial interests of pharmaceutical companies, with little thought to the safety or efficacy of these products. Topics covered in Part I include the peculiarities of drug pharmacokinetics in women and how they affect drug safety and efficacy, special considerations when prescribing to adolescent women, and medication use in pregnancy.

Part II, Specific Medicinal Products for Women: Benefits and Risks, deals with medicines used either exclusively or predominantly by women. It includes chapters on the risks and benefits of oral contraceptives, with a separate chapter dedicated to the risk of venous thromboembolism, emergency contraception and contraceptive devices. The development of the two HPV vaccines is discussed in Chapter 9 and concludes that their safety and efficacy are well established; the challenge now is to ensure that the vaccine is accessible to all girls in the target age-group (9-14 years). Chapter 10 discusses medicines used in the treatment of Chronic Pelvic Pain (CPP) and emphasizes the need to take a holistic approach to managing the pain, noting that the evidence for effective treatments is lacking. A chapter on Menopausal Hormone Therapy (MHT) summarises the current evidence that

supports targeted, short-term use of MHT specifically for the treatment of menopausal symptoms, and emphasizes the need for women to be fully informed of the risks and benefits associated with this treatment. Chapter 12 addresses the use of bisphosphonates for the prevention of fractures in osteoporotic women: it describes the pharmacology and mechanism of action of this group of drugs and discusses the efficacy and safety of each of the currently available drugs in this class. The final chapter in Part II provides an overview of the use of



herbal and complimentary medicines for women's health and notes that while these remedies now form the basis of a multi-billion dollar industry, there is a lack of evidence for the efficacy and safety of many of these products, and they remain largely unregulated.

Part III, International Perspectives on Medicines for Women and Risk Communication starts with a chapter on prescribing for women in the primary care setting, which notes that information on dosing, efficacy and safety of medicines is often not available specifically for women, yet women are more likely to be prescribed medicines. The chapter on medicines regulation goes on to highlight the need for strong evidence to support a positive benefit:risk evaluation for medicines such as contraceptives that are used by healthy women. Chapter 16 provides a fascinating discussion on political and religious perspectives regarding the risks and benefits of women's medicines. Weak health systems, lack of access to qualified health workers, poor quality medicines and a largely

unregulated drug market with widespread over-the-counter availability make women in developing countries particularly vulnerable to the potential harms of medicines, as is discussed in Chapter 17. The final two chapters address risk communication and emphasise that information on the risks and benefits of medicines must be communicated in a way that is relevant and understandable, and that personal, social and cultural factors will influence how that information is processed by women.

A key message in this book is that 'a holistic approach that values women and considers their socio-cultural environment is important when prescribing medicines and in all stages of medicines regulation and monitoring'. Women are not a minority group, but there are important differences between men and women that influence the efficacy and safety of medicines that should be considered specifically during drug development, prescribing and monitoring. There is still room to improve the evidence and communication of the benefits and potential harms to women for all medicines, not only those developed specifically for women.

This book will be of interest to clinicians, nurses and pharmacists (and students of these professions) who provide health care to women. It will also be important reading for regulators, pharmacovigilance colleagues, the pharmaceutical industry and others with an interest in women's health. The text is accessible to a wide audience, with easily understood language and clear take-home messages for each chapter.

** Editor*

Mira Harrison-Woolrych

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As an eBook it can be purchased from springer.com/shop

Staff news

Jonas Avelin, born in Hallstahammar and raised in Västerås in central Sweden, moved to Uppsala at the age of 20. After his PhD in mathematics, he worked as a university lecturer for a couple of years before starting



a new career in software development. He has been working in that field for more than 15 years, both in industry and in government organizations. His previous employer was the Swedish National Food Agency.

Jonas joined PDQ-IT (Production, Development and Quality – IT) at the beginning of this year, and is currently working on development of the next generation Vigilize system.

"During the fall of 2014, I visited UMC a couple of times and was very glad when Jonas Ahlkvist offered me a position in IT. My impression so far is that everyone is really friendly, and also passionate about their jobs. The competence is high, and I consider myself privileged to work here."

Departures

Over the last few months we have said farewell to Ulrika Rydberg, Ola Strandberg,

Ingrid Johansson and Yvonne Thomson. Anneli Lennartsson, who joined the UMC as Team Support and P.A. back in September 1999, has now taken well-earned retirement. We wish them all the best in the future.

After two years working in our research team in Uppsala, Geraldine Hill moved back to New Zealand in December. However, she will fortunately not be lost to the WHO Programme and will be working directly with WHO Headquarters providing expertise in pharmacovigilance in public health programmes and supporting countries running CEM studies. We look forward to collaborating with Gendie in her new role, thank her for all the work done and the good time we had together at UMC and wish her and her family all the best back in their home town Dunedin.

Books received

Pharmacoinformatics

Pharmacoinformatics and Drug Discovery Technologies: Theories and Applications

We did not mention the publication in 2012 of a book which may be of interest to some UR readers. This 440-page book from IGI Global (ISBN 13: 9781466603097) is mainly concerned with maximizing the benefits from the use of information systems and technologies for the provision of decision support tools necessary for improved drug management, use, and administration practices.

It includes a chapter on pharmacovigilance (by Jimmy Jose, University of Nizwa, Oman) which focuses on the application of pharmacoinformatics in the practice of pharmacovigilance and covers experiences in industry, regulatory, and hospital settings.

The book also has a chapter entitled 'The Humane Dimensions of Effective Communication' by Bruce Hugman, and a chapter from Sudan on the work of the national pharmacovigilance centre. Individual chapters may be purchased separately from the IGI website.



Cardiovascular drugs

Cardiovascular drugs and the risk of systemic autoimmune diseases – Pharmacovigilance and experimental approaches.

This is a book based on the thesis by Hilda de Jong. It covers:

- Signal detection for statin-associated autoimmune disorders in spontaneous reporting systems
- Cardiovascular drug use and the incidence of autoimmune diseases in electronic health records
- Statin use and autoimmunity
- Causal relationship, statin use and autoimmune diseases.

Among the distinguished co-authors may be noted H.G.M. Bert Leufkens, Ronald H.B. Meyboom and Frank de Vries, and the book can be read on-line at the digital archive of Maastricht University.

Spinning to give hope

Saturday 28th of March saw the annual Swedish event Spin of Hope – an event where companies or private teams can sponsor a spinning cycle for 12 consecutive hours to raise money for cancer research in children. UMC sponsored one cycle and 11 participants from UMC staff kept the cycle running throughout the day.

The event is nation-wide and this year over 4.2 million SEK was raised – a new record!

UMC's participants were (in order of appearance): Helena Sköld, Anna Mattsson (pictured), Madeleine Krig, Jenny Adamsson, Malin Zaar, Camilla Westerberg, Cecylia Wojcik, Damon Wallin Fahimi, Jessica Avasol, Emma Rofors and Thomas Vidinghoff.



DATES	TITLE	PLACE	ORGANISER/CONTACT
18 May 2015	A practical guide to writing risk management plans	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 E-mail: registrations@management-forum.co.uk www.management-forum.co.uk
18-29 May 2015	17 th International Pharmacovigilance Training Course	Uppsala, Sweden	Uppsala Monitoring Centre www.who-umc.org
20-21 May 2015	Global Regulatory Pharmacovigilance Environment	Hammersmith, London, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 www.dsru.org/trainingcourses E-mail: jan.phillips@dsru.org
1-12 June 2015	9 ^{ème} Cours Francophone de Pharmacovigilance	Rabat, Morocco	Centre Anti Poison et de Pharmacovigilance du Maroc www.capm.ma/
1-19 June 2015	The WHO Collaborating Centre Vaccine Pharmacovigilance Fellowship	Accra, Ghana	WHO Collaborating Centre for Advocacy & Training in Pharmacovigilance Tel: +233 302 268 746 / +233 289 014 000 E-mail: training@who-pvafrica.org www.who-pvafrica.org
9-11 June 2015	Signal Detection Conference	London, UK	Drug Safety Research Unit (See above for contact details)
10-11 June 2015	Medical Approach in Diagnosis and Management of ADRs	Paris, France	DIA Europe www.diahome.org/en-GB/Meetings-and-Training/
14-18 June 2015	DIA 2015 : 51 st Annual Meeting	Washington, DC, USA	DIA www.diahome.org/Home/Flagship-Meetings/DIA-Annual-Meeting.aspx
24-26 June 2015	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (See above for contact details)
27-30 June 2015	12 th Congress of the European Association for Clinical Pharmacology and Therapeutics (EACPT 2015)	Madrid, Spain	EACPT http://www.eacpt2015.org/
22-26 August 2015	31 st Annual Conference ICPE	Boston MA, USA	International Society for Pharmacoepidemiology (ISPE) www.pharmacoepi.org
9-10 September 2015	Back to Basics in Pharmacovigilance	Fareham, UK	Drug Safety Research Unit (See above for contact details)
14 September-9 October 2015	The WHO Collaborating Centre Pharmacovigilance Fellowship	Accra, Ghana	WHO Collaborating Centre for Advocacy & Training in Pharmacovigilance (See above for contact details)
30 September-1 October 2015	Pharmacovigilance Planning and Risk Management	Fareham, UK	Drug Safety Research Unit (See above for contact details)
13-14 October 2015	9 th Annual QPPV Forum	London, UK	DIA Europe (See above for contact details)
14-15 October 2015	Case Narrative Writing for Reporting Adverse Events	Fareham, UK	Drug Safety Research Unit (See above for contact details)
21-22 October 2015	Risk Benefit Assessment in Pharmacovigilance	Fareham, UK	Drug Safety Research Unit (See above for contact details)
27-30 October 2015	ISoP 2015 Annual Meeting	Prague, Czech Republic	International Society of Pharmacovigilance E-mail: administration@isoponline.org www.isop2015prague.org/
3-4 November 2015	Benefit/Risk Management	Paris, France	DIA Europe (See above for contact details)
5-6 November 2015	Signal Management in Pharmacovigilance	Paris, France	DIA Europe (See above for contact details)
24 November 2015	4 th Nordic Pharmacovigilance Conference	Stockholm, Sweden	Läkemedelsakademin www.lakemedelsakademin.se/templates/kurs/kurstillfalle.aspx?kld=6101&tid=6102
25-27 November 2015	2 nd African Society of Pharmacovigilance (ASoP) conference 'Pharmacovigilance In Africa : New Methods, New Opportunities, New Challenges'	Accra, Ghana	ASOP 2015 www.asop2015.com



– Building a global safety culture

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 120 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 VigiLyze™ and VigiFlow®, for data entry, management, retrieval and analysis.

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

Communications information

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About UMC > UMC staff – on our website.

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