

# MUR64



**Regional trends: Africa, Asia-Pacific, Eastern Europe, Latin America**

**Genetic markers | SCOPE launched | WHO Technical Briefing**



Marie Lindquist  
Director  
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Centre

*After all these years as an international traveller, I'm still not comfortable on board an aeroplane. Before take-off, I fret in my seat; once in the air I constantly listen for unexpected sounds suggesting that the engines are about to stall or something equally awful; and when there is a sudden change in either speed or direction I am convinced that my last moment has come.*

*But does this agonising stop me flying? No, because I have made my risk assessment, and come to the conclusion that the benefits to me far outweigh the risks. There is obviously a probability that I may one day die in a plane crash, but the risk is much lower than the risk of injury or death on my daily drive to work. I also recognise that my emotional responses have no rational relationship with the actual risk. Besides, conquering one's fears is one of the many challenges in life, and the rewards are plentiful when one succeeds!*

*In some circumstances, and for some people, not knowing about the real risk may be a good thing. But on the whole, I believe that the best approach in risk management is to be open; to acknowledge that there is a risk associated with a particular activity, but at the same time make sure that it is put into the relevant context and neither exaggerated nor underestimated; to gather and provide the best evidence to characterise and quantify the risk; to distinguish between the perception of risk versus real risk; and to make it clear that the overall, statistical population risk may or may not apply to a certain individual, or an individual situation.*

*Risk management, and risk communication, are particularly challenging when the level of risk is not well known. Things are even more difficult if the potential negative outcome is one that seriously affects people's health and well-being. Medicines safety is a case in point, and I am glad that so much time and effort now is put into developing better methods for risk management and risk communication in pharmacovigilance. Nevertheless, we have a long way to go in developing truly effective methods that patients and health professionals can make good use of.*

*The risk of 'medicines scares' has been used as an argument for keeping medicines safety data out*

*of the public domain. Many are the times I've heard that immunization and other public health programmes will be jeopardized if we are not extremely careful about who has access to what data. I fully appreciate the importance of a high level of compliance with life-saving treatments, and I do not doubt that high-profile safety issues, real or perceived, may undermine public confidence in medicines – if they are not handled well.*

*But I do believe that people in general do understand the basic concepts of risk, and are willing to accept some risk, provided that the benefits are understood and acceptable to them. What they have the right to expect is that there are mechanisms in place allowing prompt, scientific evidence-based responses to medicines safety issues whenever these occur; and the availability of competent and empathetic help to those affected. In the long run, I am sure that this is what instils public confidence in our work. I am equally convinced that being seen, rightly or wrongly, as sweeping uncomfortable truths under the carpet will have the opposite effect.*

*Far from being damaging, openness is a recognition of people's right to know and of their capacity, with help, to manage difficult issues positively. If we provide data, we have to make sure that we also offer appropriate support to enable good understanding of it, and what it signifies for the population and the particular individual. We must also see that we distinguish between facts and hypotheses, making clear what we know and what is uncertain. It is a big responsibility, and we must accept accountability for the consequences. If mistakes are made, we must be open about them, too, and do our best to correct them and learn from them. George Bernard Shaw once said: "a life spent making mistakes is not only more honourable, but more useful than a life spent doing nothing". For me, doing nothing is not an option.*

*Wishing you all a prosperous and productive new year 2014!*

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

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What's happening in the regions?

In this issue we take a trip around four regions of the world to look at their priorities and views on advancing pharmacovigilance in their area: Africa, Asia-Pacific, Eastern Europe and Latin America



ISoP

A bright Tuscan sojourn for ISoP members



At the sharp end

A UMC member of staff finds out about life in three national centres: Indonesia, Viet Nam and Cambodia

Singapore annual report

Making reports more involving





## Angola joins

*Isabel Margareth Malungue*

The National Pharmacovigilance Department of Angola has about eight employees of which two are pharmacists and six are pharmacy technicians. With a population of 20 million, Angola is situated in south west Africa, and has 18 provinces. We have implemented pharmacovigilance in ten of these.

Last September, after the visit of UMC-A staff, the National Pharmacovigilance Department submitted through VigiFlow its first case reports, and we became a full member of the WHO Programme for International Drug Monitoring in mid-October 2013. Our next goal is to hold our first national meeting of pharmacovigilance in October 2014. The head of the National pharmacovigilance Department is Isabel Margareth Malungue.



*The Angola national pharmacovigilance team*

## More countries

During the last quarter, United Arab Emirates became member number 116 of the WHO Programme, and Qatar became an Associate.

### 2014 dates

The dates and city of the 2014 meeting of the WHO Programme for International Drug Monitoring have now been confirmed. The Chinese Food and Drug Administration (CFDA) will host the meeting in the city of Tianjin from 14–17 October 2014. The annual meeting of the International Society of Pharmacovigilance will immediately follow the WHO Programme meeting, also in Tianjin.

## A sad end for IMMP

*Sten Olsson*

We learnt in late 2013 that the search for sustainable funding for the Intensive Medicines Monitoring Programme (IMMP) in New Zealand had failed. The IMMP closure took place in December and pharmacovigilance around the world has lost a small but important cog in its wheel.

### Leader in PEM

The IMMP was established in 1977, the first Prescription Event Monitoring (PEM) programme in the world. During the 1970s, the NZ Ministry of Health and its advisory committees became aware of the limitations of spontaneous reporting ('yellow card schemes') for detecting and quantifying adverse reactions to medicines. Physicians were encouraged to report 'suspected' adverse reactions, but the system aspired to detect new, unknown reactions, very difficult for physicians to suspect as being caused by a medicine.

The logical step was to record all 'medical events' happening to patients while exposed to a new medicine, whether suspected to be caused by the medicine or not, and then to compare event profiles between similar medicines, or before and after exposure. This early awareness of the need for additional methods for post-marketing pharmacovigilance was a major step forward. Subsequent international pharmacovigilance guidelines have recommended methods which the IMMP had carefully developed over many years.

### 36 years, 130 papers

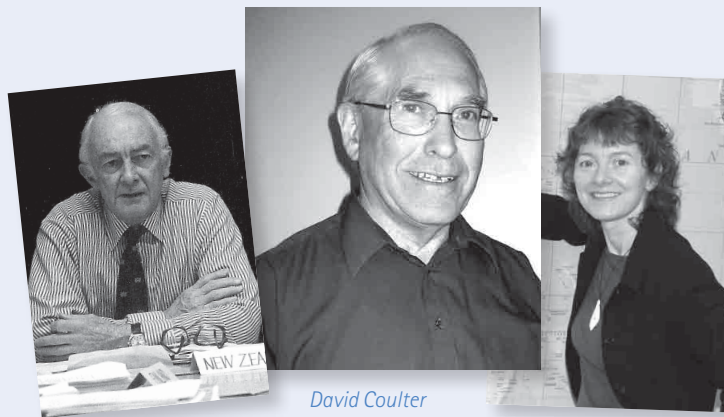
IMMP was the vision of Garth McQueen, who engaged David Coulter as its director. For 36 years the IMMP carried out monitoring studies and published its results in New Zealand and around the world, contributing to public health and patient

safety. This amounted to over 130 research papers. IMMP received considerable support from health professionals in New Zealand and recognition internationally as a leading pharmacovigilance programme. One weakness of IMMP was that it was established in a country with a limited population (currently 4.5 million), making it difficult to enrol the target number of patients (normally 10,000) in the exposed cohorts. Had the population been larger, results could have been generated more quickly. The stimulus from the IMMP programme did mean that New Zealand had the highest ICSR reporting rate per population in the world for many years, only recently overtaken.

Although IMMP's demise had been anticipated for some time, it was no less painful when it finally happened. Mira Harrison-Woolrych, its director since 2003, expressed her sadness at seeing the world's first PEM programme fold in this way, but in the end it did not have the support it deserved or funding it needed to continue. A final summary booklet of the work of the IMMP may be available from the University of Otago website (<https://nzphvc.otago.ac.nz/immp/>).

### Model for the future

However, the IMMP has been the model for the Cohort Event Monitoring (CEM) method WHO is recommending for active surveillance of medicines introduced in public health programmes. David Coulter was the main author of the three handbooks on pharmacovigilance in malaria, HIV/AIDS and tuberculosis, available from the WHO web site. Pilot CEM programmes have been established in several countries, allowing the survival of the philosophy of IMMP.



*Garth McQueen*

*David Coulter*

*Mira Harrison-Woolrych*

# GVSI sets priorities

Sten Olsson

The 2<sup>nd</sup> annual meeting of the Global Vaccine Safety Initiative (GVSI) stakeholders was held in New Delhi, India, on 19–20 November, followed by a meeting of the GVSI planning group on 21–22 November. Around 70 delegates from over 20 countries attended the stakeholders' meeting. Delegates represented UN agencies, academic institutions, funding agencies, pharmaceutical companies and other partners with an interest in GVSI activities. Updates on GVSI actions since the previous meeting and case studies on safety challenges encountered in connection with new vaccine introductions were presented.

## Reporting and collaboration

Breakout sessions discussed how to increase AEFI reporting, and how to improve collaboration between national immunization programmes and regulatory authorities responsible for pharmacovigilance. The first working group proposed guiding principles and strategies to attain higher reporting

rates and identified areas in which further support is needed from governments and international agencies. Output from the second breakout session consisted of a set of challenges, identified best practices and suggested actions for better collaboration.

## IVI and UMC input

The second day included a presentation of a vaccine adverse event management system (VAEIMS) being developed by the International Vaccine Institute, in technical collaboration with WHO-HQ and UMC (see also article below). An update from UMC included a brief demonstration of how the VigiLyze tool can be used for retrieval of vaccine data from VigiBase and introduced the new module in VigiFlow allowing direct web-based reporting from health professionals and patients. Vaccine topics discussed by national centres at the 2013 WHO Programme meeting in Rome were reviewed. The development status of new vaccines against malaria and dengue fever was presented.

The Day 2 breakout sessions were devoted to vaccine risk communication, and enabling factors to strengthen national regulatory authorities. The first group identified audiences for safety communications on vaccines, confounding factors, and made proposals on how GVSI may engage in improving conditions and facilities for good communication practices. The second working group produced a set of functions and facilities that may need to be strengthened for national regulatory authorities to perform better.

## New priorities

The GVSI planning group met for two days following the stakeholders' meeting. They reviewed the outcome of the main meeting and then focused on prioritization of pharmacovigilance activities and projects which have been proposed for GVSI funding. Professor Gurumurthy Parthasarathy, from Mysore, India was introduced and welcomed as a new member of the group.

# Getting to know IVI

Antonio Mastroianni and Ola Strandberg

During our visit to Korea in November for the APEC Harmonization Workshop (see p8–9), we took the opportunity to visit the International Vaccines Institute (IVI), based at Seoul National University. We were keen to learn more about IVI's active participation in the Global Vaccine Safety Initiative, and its efforts to build a vaccine adverse event information management system to collect AEFIs for submission to VigiBase at the UMC.

## A global mission

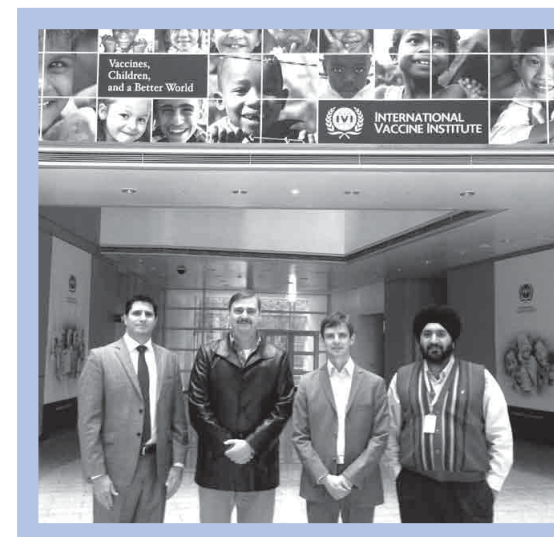
IVI's mission is to "discover, develop, and deliver safe, effective and affordable vaccines for the world's developing nations". It is an international non-profit-making organization founded on the belief that the health of children in developing countries can be dramatically improved by the use of new and improved vaccines. Working in collaboration with the international scientific community, public health organizations, governments, and industry, IVI is involved in all areas of vaccines – from new vaccine design in the laboratory, through vaccine development and evaluation in the field, to facilitating sustainable introduction of vaccines in countries where they are most needed.

## Clear focus

IVI was created as an initiative of the United Nations Development Programme (UNDP), and began formal operations as an independent international organization in 1997 in Seoul, Republic of Korea. Currently, IVI has partners in 35 countries, along with WHO, which are signatories and/or state parties to its Establishment Agreement (a memorandum of understanding). The Institute has a unique mandate to work exclusively on vaccine development and introduction specifically for people in developing countries, with a focus on neglected diseases affecting these regions.

## Fruitful discussions

During the visit it became clear there were many similarities with the origins of IVI and UMC. Discussions took place with Dr. Tom Wierzba, Deputy Director General for Development and Delivery, and Ajit Pal Singh, Senior Research Scientist, on sustainable approaches for vaccine safety training and capacity building through collaborative pharmacovigilance education and training programmes. Although no conclusions were reached it is clear that synergies toward sustainable efforts exist



Antonio Mastroianni, Tom Wierzba, Ola Strandberg and Ajit Pal Singh at IVI

and further investigation to take them forward will be required.

International Vaccines Institute (IVI) : [www.ivi.int](http://www.ivi.int)

WHO have now posted information about the recent reorganization of the Medicines department.  
[http://www.who.int/medicines/about/emp\\_reorg2013/en/](http://www.who.int/medicines/about/emp_reorg2013/en/)

# Commonwealth summit in Ukraine

Sten Olsson

The shared recent history of the Commonwealth of Independent States (CIS) provides an understanding that the countries concerned will benefit from collaborating in pharmacovigilance and learning from each other. Alongside regional collaboration though, there is also a manifest desire to be part of the global patient safety movement, which in turn requires adoption of current international standards and practices.



Olena Matvieieva

## Together in Kiev

The State Expert Center of Ministry of Health of Ukraine organized a conference in Kiev on 23 and 24 October 2014 'Safety and Legal Support of Medicinal Products: From Development to Medical Use'. The conference attracted approximately 500 delegates, mainly from Ukraine, but also from Armenia, Azerbaijan, Belarus, Kazakhstan, Kyrgyzstan, Moldova and Russia. After the first plenary session, separate programmes were offered in three parallel tracks. Excellent Russian-English simultaneous translation was offered in two of the meeting rooms.

R.M Bogachev of the Ukraine Ministry of Health, Ukraine opened the conference, explaining how medicine safety is a part of the national public health policy. The role of pharmacovigilance in public health programmes was described by Olexandr Polishchuk (WHO EURO office), and I presented on the economic burden of medicine-related harm. Ulf Bergman, Sweden gave a talk on the use of ATC/DDD methodology in pharmacovigilance.

## Legal harmonization

The rest of the plenary session focused on harmonization of legal requirements for monitoring of efficacy and safety of

medicinal products. The new Good Vigilance Practice (GVP) guidelines established by the European Union (EU) were often quoted as a reference standard. Olena Nagorna, General Director of the drug regulatory authority, explained how Ukraine has worked to adapt to the international standards. Later presentations discussed adaptations to the ICH Common Technical Document and techniques for health technology assessments.

## Evaluations presented

Contributions were also made by delegates from Management Sciences for Health (MSH) representing the USAID 'Systems for Increased Access to Pharmaceuticals and Services' (SIAPS) programme. O. Lebege presented an evaluation of the Ukraine pharmacovigilance system, using indicators developed by MSH, which show that the Ukrainian system is relatively well developed except in the area of active surveillance. Jude Nwokike gave an overview of surveillance methods focusing on the merits of active surveillance. Svetlana Setkina from the pharmacovigilance centre in Belarus set out the active surveillance activities in Belarus, including the HIV/AIDS cohort event monitoring pilot supported by WHO and UMC through the Monitoring Medicines project.

## Round table

A round table session was held on *Pharmacovigilance requirements in CIS countries: challenges and achievements*

◆ **Sergey Glagolev**, Russia, of the state agency Roszdravnadzor, gave a brief account of the present pharmacovigilance situation in Russia. Reporting rates from the constituent states of the vast country are very uneven – ranging from very good to nothing. The regulatory situation regarding responsibility for safety monitoring in the country is not quite clear. Dr Glagolev mentioned the potential of regulatory collaboration between the countries of the Customs Union, a political coalition currently consisting of Kazakhstan, Russia and Belarus. Belarus is the appointed lead in pharmacovigilance within the Customs Union.

◆ **Svetlana Setkina** presented a broad picture of pharmacovigilance in Belarus in addition to active surveillance activities (mentioned above). Rapidly improving statistics in ICSR submissions have been noted.

◆ **Raisa Kuzdenbaieva** spoke about the present pharmacovigilance situation in Kazakhstan. She emphasized the need to involve public health programmes (TB and HIV/AIDS) and to monitor the safety and quality of products used in them. The intent is to initiate active surveillance methods in these programmes in Kazakhstan.

◆ Pharmacovigilance developments in Moldova were outlined by **Elvira Istrati**. She cited the recent introduction of VigiFlow as their data management tool, and how that has allowed uploading of E2b files from marketing authorization



Jude Nwokike





*Svetlana Setkina and Sergey Glagolev*

holders (MAH) and also easy submission of ICSRs to WHO and others.

### The future

In the closing session, Olena Matvieieva, head of pharmacovigilance in Ukraine and the main organizer of the conference, summarized the strategy for future pharmacovigilance in Ukraine. She referred to the legal harmonization with EU GVP which will lead to MAHs being required to submit expedited ICSRs, PSURs and risk minimization plans. She stressed the need to undertake active

surveillance in public health programmes, and to engage clinical pharmacologists, clinical pharmacists and patients in safety monitoring. She also highlighted the necessity of identifying medication errors and of limiting the costs associated with patient harm.

### Collaboration

The conference demonstrated that CIS countries can benefit from collaborating in all branches of pharmacovigilance. Their belief in participating in global patient safety initiatives and use of international

### Commonwealth of Independent States (CIS)

*Nine countries are full member states of the Commonwealth of Independent States*

Armenia  
Azerbaijan  
Belarus  
Kazakhstan  
Kyrgyzstan  
Moldova  
Russia  
Tajikistan  
Uzbekistan

*plus two 'participating states'*

Turkmenistan  
Ukraine

standards will lead to expectations on not only WHO and UMC but also MSH and EU, for example, to provide support for human and technical capacity-building.

## New UMC analysis method achieves top results

*Hanna Lindroos*

The second phase of the Observational Medical Outcomes Partnership (OMOP) comparing methods to screen de-identified patient records and insurance claims for suspected adverse drug reactions was recently published\*. The Temporal Pattern Discovery method developed by the Uppsala Monitoring Centre achieved top performance across tens of millions of patients within nine databases across the United States and Europe.

In November, 200 representatives from regulatory agencies, research organizations, and pharmaceutical industry got together at the OMOP-IMEDS 2013 Symposium hosted by the Reagan-Udall Foundation in Washington DC. UMC Chief Science Officer Niklas Norén participated in a panel discussion on the OMOP Findings with representatives of the Regenstrief Institute, Harvard School of Public Health, and the US Food and Drug Administration (FDA).

Generally, identification of unknown side-effects relies on observant health professionals reporting their suspicions to national authorities. The spontaneous reporting systems remain critically important, but in recent years scientists have begun to explore alternative data sources, including insurance claims and electronic patient records that collect comprehensive clinical data over extended periods.

Since 2007 the FDA has secured access to data from 100 million patients to screen for harmful effects of medicines, leading to a number of new research projects. OMOP is one such, testing a variety of analytical methodologies in a range of data types to look for drug impacts that are already well-known. The goal was to identify one model to accommodate both administrative claims and electronic health records.

UMC was one of the first organizations to explore the possibilities of electronic patient records for pharmacovigilance, in a pilot study with IMS Health started in 2004 and published in 2008. Since 2009 UMC leads the Signal Detection work-package in the Innovative Medicines Initiative public-private partnership PROTECT, in which further research on this topic is performed.

For details of the study  
OMOP evaluation <http://omop.org/>

*\*Empirical Performance of the Calibrated Self-Controlled Cohort Analysis within Temporal Pattern Discovery: Lessons for Developing a Risk Identification and Analysis System*

G. Niklas Norén, Tomas Bergvall, Patrick B. Ryan, Kristina Juhlin, Martijn J. Schuemi and David Madigan <http://link.springer.com/article/10.1007/s40264-013-0095-x/fulltext.html>

# On the road to APEC harmony

*Antonio Mastroianni and Ola Strandberg*

Asia-Pacific Economic Cooperation (APEC) is an inter-governmental forum set up in 1989 for 'member economies' to promote free trade and economic cooperation in the Asia-Pacific region. It is now turning its attention to pharmacovigilance as an economic and public health factor to improving economies within the region.



*Antonio Mastroianni at the podium, Sun-Hee Lee (MFDS) and other speakers*

APEC accounts for 40% of the world's population, around 54% of the world's gross domestic product and about 44% of world trade. It operates on the basis of non-binding commitments, open dialogue and equal respect for the views of all participants. Decisions made within APEC are reached by consensus and commitments are undertaken on a voluntary basis.

## On the road for drug safety

On 20-21 November, Ola Strandberg and Antonio Mastroianni from the UMC, and Shanthi Pal (Medicines Safety Programme

Lead, WHO, Geneva) attended by invitation the APEC Pharmacovigilance Workshop hosted by the APEC Harmonization Center (AHC) in Seoul, Korea. This workshop was part of the first step in the APEC Regulatory Harmonization Steering Committee (RHSC) Roadmap, aimed to promote regulatory convergence for pharmacovigilance within all APEC economies through:

1. Harmonized pharmacovigilance systems across APEC by 2020
2. Strengthen pharmacovigilance systems for public health improvement
3. Protect and enhance public health through systematic pharmacovigilance
4. Streamline mutual inter-country medicines approval process.

These are being pursued through four stages:

1. Assessment of APEC economies (2012-2015)
2. Training/workshops (2014-2017)
3. Assessment of training/workshops (2016-2017)
4. Training/workshops to reach the goals, and recommendations for regulatory convergence (2017-2020).

## Coordination vital

As an economic-geographical community, APEC needs to have a coordinated system in place to ensure that safety information on all available medicines is adequately collected, impartially evaluated in the context of benefits and risks, and made accessible to all participating economies. Due to the public safety and the economic

importance of this effort a champion country was nominated by the RHSC – the Republic of Korea – with the specific task of facilitating the harmonization of regulatory requirements and pharmacovigilance standards through active communication among the APEC economies.

The importance of this workshop was reflected in the active participation and representation by the Korean Minister of Food and Drug Safety, the Chairman of the Korean Pharmaceutical Manufacturers Association and the Director General of the Korean Pharmaceutical Safety Bureau. There were roughly 300 participants from across APEC region.

## A broad overview

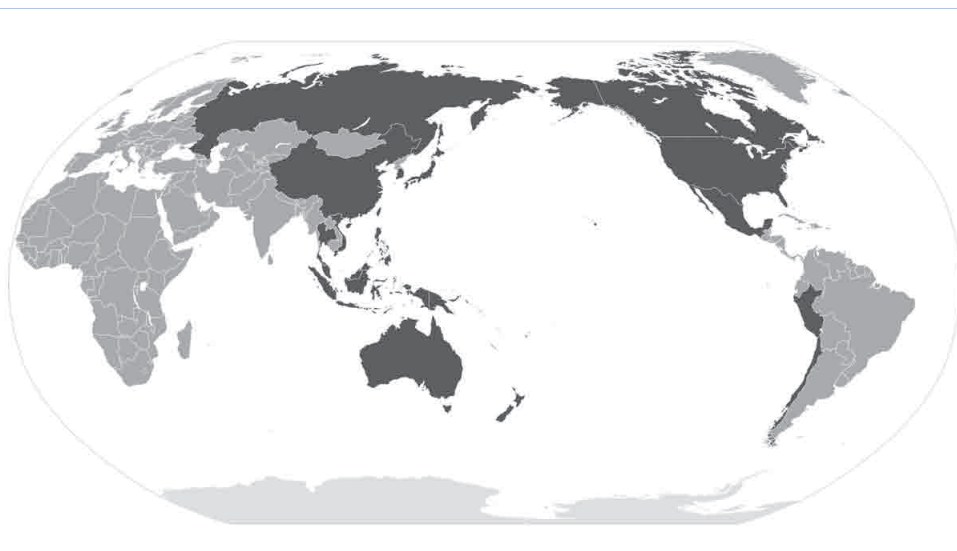
The first day of the workshop focused on providing an overview of the Harmonization Roadmap, and looking at issues, challenges, current status and perceived gaps of the pharmacovigilance systems within APEC. The programme chairs were Gerald Dal Pan, Director of the Office of Surveillance and Epidemiology within the Center for Drug Evaluation and Research (US FDA) and Dr. Don-Woong Choi, Director – Drug Information Evaluation, Ministry of Food and Drug Safety (MFDS), Korea.

The first session was chaired by Prof. Byung Joo Park (Korean Institute of Drug Safety & Risk Management – KIDS) and Wimon Suwankesawong (Thai FDA) and focused on pharmacovigilance harmonization efforts within APEC. Shanthi Pal and Gerald Dal Pan presented during this session, describing WHO and ICH activities respectively.

## Harmonization across the board

Chairs of the second session were Antonio Mastroianni (Chief Operations Officer, UMC) and Dr. Sun-Hee Lee (Director General, Drug Evaluation Department, MFDS) and examined 'Issues and Challenges towards Pharmaco-

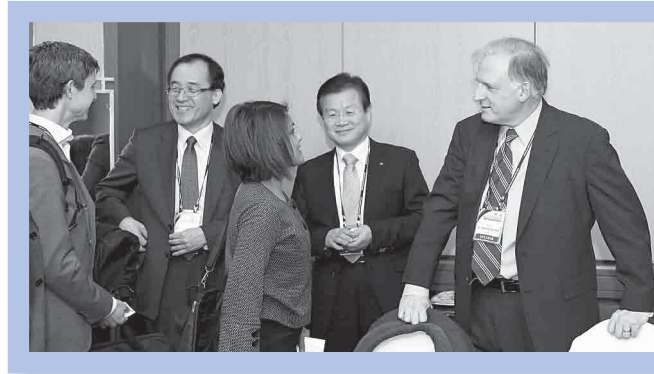
APEC has 21 members - referred to as 'member economies': Australia ~ Brunei Darussalam ~ Canada ~ Chile ~ People's Republic of China ~ Hong Kong, China ~ Indonesia ~ Japan ~ Republic of Korea ~ Malaysia ~ Mexico ~ New Zealand ~ Papua New Guinea ~ Peru ~ the Philippines ~ Russian Federation ~ Singapore ~ Chinese Taipei ~ Thailand ~ United States of America ~ Viet Nam.



*Map showing the members of APEC in darker shading*



vigilance Harmonization'. A clear theme was the importance of structuring data through the use of international dictionaries, terminologies, classifications and adherence to standards such as ICH-E2B for effective communication and analysis of medicines safety data. There were presentations on the WHO Programme for International Drug Monitoring, the APEC questionnaire and issues and challenges faced by Indonesia, Thailand, China, and in industry and academia.



*Ola Strandberg (UMC), Professor Byung Joo Park (KIDS), Dr Shanthi Pal (WHO), Professor Jin-Ho Lee (Dongguk University Ilsan Hospital), Gerald Dal Pan (US FDA) in discussion*

### Are there gaps?

Next Gerald Dal Pan and Siti Addoellah (Indonesia) chaired a panel on the current status and gaps of pharmacovigilance systems within APEC economies. The contributors were Maria Francisca Aldunate Gonzalez (Chile), Ola Strandberg (UMC), Dr. Zhang Li (China), Dr. Don-Woong Choi (Korea), Rokiah Isahak (Malaysia), Cecilia Beltran Noblega (Peru) and Wimon Suwankesawong (Thailand). In the session's closing discussion Shanthi Pal pointed out that the situation where countries are catching up with leaders in the field can be addressed as long as they share the same foundation. She stressed that WHO and UMC are keen to work with others at both a country and a regional (e.g. APEC) level, and requested that APEC submit a wish list, promising that UMC would work with APEC to deliver cost-effective tools and support a sustainable approach in training efforts to meet the needs of the APEC economies.

### Risk communication lessons

The day closed with a lecture on risk communication, chaired by Jin-Ho Lee (Dongguk University Ilsan Hospital) and Jean-Christophe Delumeau (Bayer). Gerald Dal Pan explored safety communication and what lessons could be learned from FDA experiences. One key success factor was finding unbiased information based on data alone, without judgment, and trying to find the balance between under warning or over-warning. Gerald Dal Pan also shared that FDA is doing significant research on the impact of its product warnings by interviewing health care professionals to see what happens after FDA issues them.

### A way forward for the region?

Chaired by Gerald Dal Pan and Don-Woong Choi, the second day was a 'Regulators Only' session, with representatives from Viet Nam, Thailand, Malaysia, Indonesia, Chinese Taipei, Singapore, Korea, China, Brunei Darussalam, Philippines, Chile, Peru and

Mexico. The agenda focused on four key points concerning the Roadmap:

1. Whether vaccines are to be included on the Roadmap
2. Cooperating with WHO-UMC and preparing for the alternatives
3. Priority in the second phase of the Roadmap
4. Other efforts for regulatory harmonization between APEC economies.

The Republic of Korea, as the appointed APEC champion for pharmacovigilance, facilitated the discussions. Korea recommended an AHC and WHO/UMC collaboration to provide benefits, especially with training, curriculum development, and E2B understanding. During 2014 Korea will finalize the situational analysis, gap analysis and the consensus-forming process.

### Working effectively with reports

There was much focus on how to improve public health by increasing the effectiveness of analysis of ICSRs. The working group discussed the importance of determining a desired E2B set of fields to add to the Roadmap and getting WHO/ICH guidance on those fields. More importantly, primary healthcare reporting and analysis tools were requested. The goal of these efforts is to develop pragmatic ways of collecting, analyzing and communicating information about the safety of medical products.

### Meeting training needs

The need for training, especially in signal analysis and causality assessment, was a common theme. WHO/UMC and AHC discussed how best to utilize existing curricula and to incorporate WHO/UMC training on pharmacovigilance tools, while involving AHC regulatory training capacity and ensuring E2B compliance. Training around proactive risk-benefit management

planning and pharmacovigilance tools, as well as measuring the effectiveness of these tools, will provide additional opportunities for regulators and industry together to protect public health.

Vaccines were recommended to be included in the Roadmap. VigiBase was put forward as the one repository of combined data for medicines and vaccines. In this respect WHO informed the working groups about efforts to apply the E2B standard to vaccines. WHO/UMC will continue discussions with AHC on these initiatives to ensure

that processes around E2B adoption are developed collaboratively for medicines and vaccines and not as parallel, separate activities.

### Important first steps

The UMC has good contact with most of the national pharmacovigilance centres in this region and the APEC Harmonization Center. Many APEC economies are reliable contributors to the WHO Programme and the determination to achieve more by working together provides a valuable model which UMC will definitely encourage and utilize in the future.

## Banned medicines on the web

The Philippines FDA recently negotiated the removal of illegal unregistered health products from an internet trading platform, in a 'translational pharmacovigilance' initiative.

A website advertising several banned medicines and health supplements sold by internet pharmacies and other sellers was targeted. Acting Director General Kenneth Hartigan Go said that internet pharmacies are now within the scope of the agency's 'pharmacovigilance'.

# Looking around Latin America

*Elki Sollenbring*

Visits to Latin America in the last quarter of 2013 illuminated the concerns of pharmacovigilance professionals in the region at the moment. While systems are established in the majority of settings, countries are striving to work together more



*Pharmacology and therapeutics in Havana*

on several issues. Now that countries have collected sufficient data, analysis of data for signals has become paramount, and training and tools are at the forefront of work across the region. Harmonizing the management and analysis of vaccine safety reports is also urgent; indeed, the general issue of data management of ICSRs is a hot topic for many in Latin America.

## Biotherapeutic medicines

The conference Biotherapeutic Medicines: Sharing Experiences and Best Practices in November was organised by IFPMA (International Federation of Pharmaceutical Manufacturers & Associations). The 200 delegates were mostly from the pharma industry but some were from academia, regulation, health care and patient organizations. It gave updates on regulatory aspects of biotherapeutics and biosimilars, development, interchangeability, pharmaco-vigilance, and the views of patients on the subject. Malin Fladvad and myself from UMC spoke on the WHO Programme for International Drug Monitoring and focused on capacity building, signal process, WHO Drug Dictionaries and pharmacovigilance for biotherapeutics.

Speakers came from different countries and organizations, Raffaella Balocco (International Nonproprietary Name (INN) Programme, WHO), Barry Cherney and Gustavo Grampp (Amgen), Karin Heidenreich (Novartis), Thomas Schreitmueller and Fermin Ruiz de

Erenchum (Roche), Maurice Mayrides (Esperanta, a non-profit patient organization), regulatory authorities from Latin America plus Italy and Canada, and academia (Colombia, Argentina, Mexico and Costa Rica).

## Progress

Different countries are developing their own regulations concerning development and approval of biotherapeutics and biosimilars. Brazil has already implemented theirs, while Peru and several other countries are still getting them approved. There is no harmonization of such regulations within the region, and some countries have had biological products comparable to an original biological drug approved without biosimilar regulations in place. There were interesting discussions on biosimilar interchangeability by health professionals, on immunogenicity and extrapolation of indications. Pharmacovigilance was mentioned in most sessions as a key factor in monitoring biosimilars. However, many countries in the region lack resources to undertake such pharmacovigilance work.

## Signal detection

As an indication of the emerging concern for improved signal detection at national and regional level, a workshop was requested by the Head of the Peru National Centre on how to analyze the data in their national database, which contains over 30,000 reports. Elki Sollenbring and Geraldine Hill from the UMC gave presentations and facilitated the three-day workshop, and Pia Caduff (UMC) contributed via Go-To-Meeting.

The presentations and practical hands-on sessions covered basic principles, UMC signal detection process, causality assessment (practical), use of Vigilize (practical), signal

detection at a national level (practical), regulatory action, benefit/risk assessment, and which pharmacovigilance method to use when. Elki and Geraldine spent the following day at the national centre learning about their processes and providing technical support.

## Lively mixed audience

The majority of the 20 participants were pharmacists but there were also several medical doctors from hospitals in Peru; Romina Heredia, from the national centre in Argentina (ANMAT) also took part. Everyone was actively engaged in the workshop, asking questions and participating enthusiastically in the practical sessions, and we look forward to hearing what impact this has had nationally.



*Cuban national centre staff with Elki Sollenbring*

## Barranquilla bound

Magnus Wallberg and Elki attended the X International PV Latin American congress organized by the National University of Colombia, Pan American Health Organization (PAHO), Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA) and the Ministry of Health of Colombia in November. Ranging from pharma industry,

regulators, academia, hospital staff, to a pharmacist association, students, etc, 200 people gathered in Barranquilla, Colombia. The speakers also had different backgrounds: Mariano Madurga (AEMPS, Spain), Albert Figueras (European Programme of PV and PE, Spain), Björn Wettermark (Karolinska Institute, Sweden), Héctor Izurieta (FDA, USA), Maribel Salas (Pfizer, USA), Nancy Huertas (Ministry of Health, Colombia), Carlos Sánchez (INVIMA), Juan Erviti (Drug Information and Advice, Navarro, Spain).



*Winners of the PAHO online training competition, with José-Luis Castro, right*



Main topics were:

- How to register, evaluate and monitor the clinical investigation of safety and efficacy of drugs.
- Use of clinical information to take regulatory decisions for drug coverage.
- Coverage of decisions and the reality of the drug in the market (interaction between agencies of technology evaluation and healthcare).
- Social networks which might complement regulatory decision-making.

During the congress Magnus and Elki spoke about WHO networks, training, publications, patient reporting, E2B, dictionaries (DD and WHO-ART), VigiLyze and signals.

### Diversity together

As usual you learn a lot during this kind of conference and from the different experiences you encounter. Many speakers pushed the need for active pharmacovigilance, especially in relation to vaccines. A number of presentations referred to the pharmacovigilance related networks in Latin America. There seems to be some good collaboration already!

### Bursary prize

The last session was awards to the poster presentation winners. Eighty people had displayed posters on projects that have been undertaken in the different regions of Colombia and in other Latin American countries. The award was a bursary to attend the UMC training course.

### Regional vaccine concerns

Magnus and myself also attended a three-day vaccine workshop in Barranquilla, organized by PAHO, the Ministry of Health of Brazil (ANVISA) and the Global Alliance for Vaccines and Immunization (GAVI). The purpose of the workshop was:

- to strengthen cooperation between the regulators and the Expanded Programme on Immunization (EPI), as part of the AEFI monitoring system and national vaccine safety committees.
- to complement virtual training and strengthen competence in critical evaluation of clinical trials of new vaccines and in the implementation of epidemiological studies.
- to develop a protocol for the monitoring of new vaccines and a 2014 plan to expand a sentinel hospital network, including AEFI reporting.

Core participation was one person from the national pharmacovigilance centre, one from the national AEFI group and one from the national regulatory authority from 15 countries in Latin America. Most were participating in a virtual vaccine training course organized by PAHO.



*Enthusiastic participants in the Lima signals course*

Practical sessions, such as how to evaluate post-marketing studies, signal detection in vaccine safety, planning an observational study post-commercialization to introduce a new vaccine, formed an integral part of the meeting.

### Sentinel collaboration

Some countries presented their experiences in the Multi Country Collaboration project (MCC) headed by WHO. MCC's goal is to provide the framework for a global collaboration among sentinel sites to verify vaccine safety signals and test hypotheses related to rare events associated with vaccine administration. The intention is that the majority of Latin American countries will contribute to this project. They also discussed the necessity to harmonize their vaccine databases so they can interchange information both with PAHO and VigiBase.



*A local delicacy : causa*

Most Latin American countries have separate organizations responsible for AEFI and pharmacovigilance. A big focus during the workshop was to strengthen the bi-lateral working between each pair of organizations.

### Latinfarma in Havana

The 20<sup>th</sup> Latinoamerican Congress on Pharmacology and Therapeutic and the 5<sup>th</sup> Iberoamerican Congress on Pharmacology was organized by PAHO and other societies and associations. This big congress had more than 700 people, both from Latin America and further afield. Its aim was to give an overview about new drug entities and major therapeutic breakthroughs.

### Broad level workshops

The congress was organized in workshops and symposia combining basic and applied pharmacology with therapeutics. One workshop was on pharmacovigilance, which covered the WHO Programme, drug safety in Cuba, regulatory requirements for safety reports in clinical research, low-frequency ADRs in the Cuban surveillance system, competence in reporting ADRs and medication errors by nurses in a Spanish teaching hospital, patient reporting, ADRs to antimicrobial agents, ADRs and non-steroidal anti-inflammatory drugs in the elderly in Colombia, Cuban pharmacovigilance system, and so on.

### Cuban system

The pharmacovigilance system in Cuba is very interesting; the pharmacovigilance curriculum for health care education is already implemented in most universities. This ensures that professionals already know something of the subject when they start work. The system works very closely with other important fields such as pharmaco-epidemiology and pharmaco-economics. Some current PhD research on pharmaco-economics aims to measure the burden of ADRs in Cuban hospitals. Visiting the regulatory agency, I met the three national centre staff, receiving a lot of information on how the centre works, and their future plans.

### Pleasant experiences

PAHO, especially through the efforts of Dr José Luis Castro, continues to support and co-ordinate regional activities with attention to individual countries needs while keeping the international picture in mind. We thank the organizers of all these activities, both for the meetings and the social activities. All these countries are so beautiful and the people are so friendly and cheerful that visiting and learning is a great pleasure.



# Recognising that Africa is different

Western assumptions and rules about PV don't always work south of the Sahara

*Bruce Hugman, in Accra, Ghana*

Leading pharmacovigilantes from across Africa know that they have to find regional and local solutions to the challenge of creating a sustainable system for patient safety on the continent. They are not short of ideas. Discussing them face-to-face brings the continent's unique pharmacovigilance perspective into focus and highlights both the challenges and the successes.



*Media training: Raja Benkirane (Morocco), with professional journalists*

One such get-together recently was the sixth annual meeting of WHO African pharmacovigilance consultants in Accra, Ghana, 25-29 November 2013. Around thirty participants, from nearly twenty countries spent the week discussing how pharmacovigilance could be pushed forward in Africa, capitalizing on the considerable progress made in the last decade.

## Raising profile and impact

A high priority for all countries was for effective advocacy of pharmacovigilance to be given greater national priority and increased human

and financial resources. A serious deficiency in making the case for pharmacovigilance in Africa was identified in the absence of studies showing the economic burden of ADRs and other medicine-related problems. Morocco alone had made some progress in such research but elsewhere, except for a new project in Eritrea and methodological proposals emerging from Ghana, there was nothing yet to match the major projects in the West (still limited to hospitals as most of them are) that had measured the rates and costs of reported harm to patients.

Detecting signals relevant to Africa was a further hot issue: were signals based largely on Western reporting data useful and credible in building the case for pharmacovigilance in Africa? Probably not was the answer, in an environment where newer, expensive drugs were not widely available; where disease profiles were quite different; where a different range of drugs were in use; where injections, often administered without clinical prescription, were widespread; where counterfeit or sub-standard drugs and irrational combinations were prevailing problems. A rise in the rates of reporting of known ADRs to well-established drugs could be an important indicator of emerging problems of a kind the West would probably not experience or wish to pay attention to.

## Analogue to digital

Everyone recognised that the worldwide drive for digital communications demands that pharmacovigilance keeps pace and provides credible, modern methods for reporting and all aspects of managing patient safety. Kenya's recently introduced web-based, electronic reporting system for ADRs and poor quality drugs (see UR62 page 11) was a good example of the kind of progress that can be achieved with adequate financial and technical support: already the number of reports and the range of those reporting have improved. Nevertheless, unpredictable power-supply, limited internet access, unreliability of service or high charges (US\$2000 per month in Kenya) in African countries meant that a parallel paper system would remain essential for some time.



*Participants gather at the cathedral bus before departure*

## Longitudinal data

Few African countries have electronic health records (EHRs) of any kind in the public sector, except for some public health programmes, and a few other specialised purposes, such as a cancer registry in Sierra Leone, some immunisation data in Zimbabwe and HIV medication records in Morocco and South Africa. Private sector hospitals and health insurance companies often have comprehensive EHRs, including pharmacovigilance data, for their own business, but these are not integrated with each other nor designed for integration with any possible national system in mind.

It was commonly acknowledged that EHRs were a vital step in improving the management of patient care and in providing essential longitudinal data for research into patient safety issues and many other questions at the heart of pharmacovigilance. Nigeria and Ghana had electronic health management systems, but they provided only aggregated data, of little use for pharmacovigilance purposes. Ghana, however, has begun development of the use of EHR data as a potential new tool in pharmacovigilance; course members saw this as a promising method. The group saw advocacy for national EHR policies, such as that in Kenya (not yet implemented), with pharmacovigilance built in from the beginning, as a high priority for strengthening healthcare systems and enriching the contribution of pharmacovigilance.

## What are we trying to achieve?

One African member of the group expressed the feeling that pharmacovigilance in Africa had, in some respects, lost the sense of vision and purpose that were so strong and bright in the early days. Individuals were still passionate and



*George Muthuri (Kenya), Mulugeta Russom (Eritrea), Shanthi Pal, WHO; Haggai Hilda Ampadu and Adwoa Anima Ohene, UMC-Africa*

committed but systems had, in some places, become rigid and bureaucratic with a paper-shuffling mentality replacing the urgent purpose of preventing harm to patients. Some examples of work, including cohort event monitoring (CEM), had become a kind of



ore a reception on the edge of the Atlantic

procedural priority without clarity about the questions to be answered by research or about the desired outcomes, and with some methodological confusions. In some places large numbers of CEM paper reports were awaiting transfer to electronic databases while reporters and others waited for results: such a situation was demoralising and raised questions about the rationality of planning and choice of method.

The point was emphasised that tools and methods had no kind of universality of application: each specific, carefully formulated safety research question needed its own unique planning and selection of methods and tools. Targeted Reporting (TSR), was a further available method and the example of Zimbabwe's pilot project on monitoring ARVs, anti-TB drugs and essential medicines was presented, showing the extra depth and detail possible beyond passive reporting methods.

### Looking ahead

The meeting was privileged to hear an account of Nigeria's ten-year strategic pharmacovigilance plan (see UR61 page 8). It was an impressive model of intelligent strategic thinking and comprehensive planning, not least in the clarity of its policy and goal and its detailed targets, performance indicators and outcome measures for every aspect of the plan. The national authority (NAFDAC) and the pharmacovigilance centre had dedicated considerable time and resources to embedding very serious intentions and activities at the very heart of their work.

### Be bold!

Priorities that underpinned all the discussions were those common to almost all countries in

the world: to raise the profile of pharmacovigilance and patient safety among health professionals, policy makers and the general public; to ensure pharmacovigilance was taught on all professional courses; radically to improve reporting rates and report quality. Amongst many other measures necessary, it was agreed that pharmacovigilance needed to venture boldly into the world of modern communications and to show the creativity and appeal of so much of the largely commercial material that already competes for public attention.

The profound differences between African and most developed countries coloured much of the discussion. This led to the ambition to ensure that systems and solutions in Africa really were fit-for-purpose and to the abiding reservation that assumptions and systems based on practice in the EU or the US, or anywhere else, should be adopted only with the greatest caution.



Ndinda Kusu, Technical Advisor at MSH

The WHO African pharmacovigilance consultants meeting was organised and funded by WHO, Department of Essential Medicines and Health Products, financially supported by MSH, and hosted and staffed by UMC-Africa. Members of the Uppsala UMC team were also present.

## Africa Congress Declaration

The First African Congress of Pharmacovigilance, attended by 340 participants from 34 African countries, hosted by the Centre Anti Poison et de Pharmacovigilance du Maroc and organized by the Moroccan Society of Pharmacovigilance and the African Society of Pharmacovigilance (ASoP) deliberated on: 'An efficient partnership for an efficient pharmacovigilance in Africa', on 12-13 December 2013.

*'We, the participants, hereby declare that pharmacovigilance needs to be developed in all African countries to promote the safety of health products so as to ensure patient safety. In this regard, we urge the authorities of all African countries to:*

- *make available the necessary structures and resources (human and financial) and put in place regulation for the development of pharmacovigilance for all health products including herbals and traditional medicines*
- *integrate pharmacovigilance activities into the public health programmes*
- *promote pharmacovigilance collaboration between African countries and encourage further participation in the international pharmacovigilance network*
- *note the commitment of WHO-UMC, WHO Collaborating Centres in Ghana and in Morocco for their support to African countries in pharmacovigilance activities*
- *encourage the important role of pharmaceutical industry as a key partner to enhance the safe and effective use of quality medicines and the need for continued support to these activities*

- *encourage donors, the international community and development partners to provide the necessary resources for annual meetings of ASoP since ASoP intends to provide a forum for discourse, networking and exchange of information including providing practical solutions and sharing research findings on pharmacovigilance activities in Africa.'*

*For all participants, the President of ASoP Pr Rachida Soulaymani-Bencheikh.*



Preparing the Declaration: the audience



and the speakers in Rabat.



# Linking Pharmacovigilance with Pharmacogenetics to Improve Patient Safety: the HSA experience

*Pharmacogenetics Team, Vigilance Branch, HSA, Singapore*

Cutaneous adverse drug reactions (cADRs) is the most common category of ADRs reported to Health Sciences Authority (HSA). Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are of particular concern due to the severity, unpredictability, high morbidity and mortality of these ADRs. More than 600 such reports, including at least 21 fatal cases, have been reported to HSA over the past 10 years, of which 15-20% were suspected to be associated with carbamazepine (CBZ).

In 2004, Chung et al provided evidence of a strong genetic association between CBZ-induced SJS and the HLA-B\*1502 allele among Han Chinese patients in Taiwan; the HLA-B\*1502 allele was present in all 44 patients with CBZ-induced SJS/TEN, but only in 3% of CBZ-tolerant patients.<sup>1</sup> However, the genetic association did not extend to other types of cADRs (e.g. maculopapular eruption and hypersensitivity syndrome).<sup>2</sup> Furthermore, although the HLA-B\*1502 association was observed among Han Chinese in Hong Kong and in the Thai population, this association was not replicated in Caucasians or Japanese.<sup>3-7</sup>

In 2008, HSA embarked on an initiative to investigate possible pharmacogenetics associations of serious cADRs in the major ethnic groups in Singapore – Chinese, Malays and Indians – to help formulate a nationally relevant policy on pharmaco-genetics testing. This initiative includes recruitment, collection, banking and genotyping of DNA samples from patients who had experienced serious cADRs, as well as from drug-tolerant controls in participating public hospitals. High resolution HLA-B typing was performed on 13 CBZ-induced SJS/TEN cases and 26 CBZ-tolerant controls. All 13 cases, but only 3 controls, tested positive for HLA-B\*1502 for an odds ratio of 181 (95% CI 8.7 to 3785,  $p=6.9 \times 10^{-8}$ ).<sup>8</sup> This is consistent with the recently published meta-analysis of studies in Asian patients that reported a pooled odds ratio of 113.4 (95% CI 51.2 to 251,  $p<1 \times 10^{-5}$ ).<sup>9</sup>

Concurrent with the pharmacogenetics association case-control study, a cost-effectiveness analysis of genotyping for HLA-B\*1502 prior to selecting a drug for treatment of newly diagnosed epilepsy patients in Singapore was initiated. The analysis concluded that genotyping new

epilepsy patients in Singapore for HLA-B\*1502 is more cost-effective than prescribing or avoiding usage of CBZ without knowledge of the genotype.<sup>10</sup> Hence, a one-time HLA-B\*1502 test will help to differentiate high-risk patients who should avoid CBZ from low-risk patients who are able to take this low-cost yet effective medicine. Additional consultations with physicians highlighted costs and turnaround time as barriers to adoption of genotyping. These were resolved through the establishment of a centralized

induced SJS/TEN and 44 controls (matched by gender and ethnicity) have been collected. The initiative has now expanded recruitment to other ADRs, particularly drug rash with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), and drug-induced liver injury (DILI).

There are complex challenges facing the translation of pharmacogenetics research findings into routine clinical practice. By setting up infrastructure for collection of DNA and associated clinical information of ADR cases and holding consultation sessions with relevant stakeholders, HSA was able to formulate a nationally relevant genotyping recommendation with genotyping facilities and financial support in place. The implementation of genotyping for the HLA-B\*1502 allele prior to the initiation of CBZ therapy in new patients of Asian ancestry in Singapore provides a model for how a pharmacovigilance centre can improve patient safety by promoting collaboration in the scientific and clinical community towards a common goal of reducing the unpredictability of serious cADRs.



*HSA pharmacogenetics project investigators and collaborators*

HLA-B\*1502 genotyping facility. The costs were further reduced for subsidized patients in public clinics and hospitals through a 75% subsidy provided by the Ministry of Health (MOH). This is the first genetic test locally to receive subsidy funding from MOH, which was based on the strong local and international data supporting an association between HLA-B\*1502 and CBZ-induced SJS/TEN as well as the favourable findings from the cost-effectiveness study.

After further consultation with stakeholders, MOH and HSA issued a joint Dear Health Care Professional Letter on 30 April 2013 to inform HCPs that "genotyping for HLA-B\*1502 allele prior to initiation of CBZ therapy in new patients of Asian ancestry is now considered the standard of care".<sup>11</sup> As of 1 November 2013, a total of 307 blood samples were sent for HLA-B\*1502 genotype testing, and 30 (9.8%) samples were tested positive for the presence of HLA-B\*1502 allele. It is noteworthy that HSA received an average of 15 reports of CBZ-induced SJS/TEN per year over the past 10 years. After the implementation of HLA-B\*1502 genotype screening, HSA has not received any reports of SJS/TEN associated with the use of CBZ in patients screened for the HLA-B\*1502 allele.

The initiative for accrual of SJS/TEN cases continues and to date, 54 cases of any drug-

## Acknowledgements

We wish to thank our collaborators from National University Hospital, Singapore General Hospital, Changi General Hospital, NUH Molecular Diagnosis Centre, NUHS Tissue Repository, Singapore Immunology Network and Duke-NUS Health Services and Systems Research Program.

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# Indian safety trail

The last few months have been busy for pharmacovigilance professionals in India with many national and international meetings in different parts of the country and with different focus, but all dealing with the issues of making medical treatment and immunizations safer.

## Economics with added vigilance

*Sten Olsson*

The Indian chapter of the International Society of Pharmacoeconomics and Outcomes Research (ISPOR) conference in New Delhi 9–10 October 2013 included a two-hour educational symposium on *Pharmacovigilance & Drug Safety Monitoring in Patients*. Many of the leading experts involved in the development of the Pharmacovigilance Programme of India (PvPI) took part in the conference but also many active young health professionals. My contribution was a key-note lecture on The Economic Burden of Medicine Related Patient Harm.

## Calling IPC

In connection with the conference I also visited the coordinating centre of the PvPI, located at the Indian Pharmacopoeia Commission (IPC) at Ghaziabad, outside of New Delhi. This was to inaugurate a toll-free telephone line which any health professional

may use to ask questions about adverse reactions and how to report them. He or she will then be called up by a representative of one of the current 90 adverse reaction monitoring centres spread around the country to follow up on the case details.

A brief meeting was held with representatives of the national TB and immunization programmes and opportunities for future collaboration and harmonization were discussed. Finally a question and answer session was organized with the pharmacovigilance staff at IPC.

## In Anand

*Ruth Savage, New Zealand Pharmacovigilance Centre*

The XIII Annual Conference and International Symposium of the Society of Pharmacovigilance, India was held in November in the lovely setting of Anand, the 'milk city' of India. It was organised by Professor Barna Ganguly and staff of the Department of Pharmacology at nearby Pramukshwami Medical College, Karamsad, Anand, Gujarat.

I was privileged to deliver the K.C. Singhal oration in honour of Professor K.C. Singhal who has worked so hard to make pharmacovigilance a reality in India. The conference highlighted the enormous enthusiasm amongst academics and students for many aspects of pharmacovigilance with a dedication to developing

effective teaching of this topic at undergraduate and postgraduate levels particularly evident.

## Ayurveda, Unani and Siddha drugs

Guest lectures also included presentations on children and the elderly, pharmacovigilance in vector-borne diseases and tropical and neglected diseases and a National Pharmacovigilance Programme for Ayurveda, Unani and Siddha drugs.

The progress of the Pharmacovigilance Programme of India (PvPI) at the India Pharmacopoeia Commission (IPC) since its establishment in 2011 was described by Dr V. Kalaiselvan and an analysis of reporting from India in VigiBase was shown using VigiLyze.

## Good memories

I also visited the PvPI in Ghaziabad and met with an enthusiastic team to discuss some principles of data mining and causality assessment. I have taken home good memories of welcoming and stimulating colleagues, beautiful surroundings in Anand with parakeets among the trees and the delight of being plied with tasty dishes both at the conference and at IPC.



*From left: Dr. S. Z. Rahman, Dr. Clara Marr (England), Dr. Ruth Savage (New Zealand), Prof. K. C. Singhal, Prof. Govind Mohan and Prof. Anurag Tomar outside the main building of Amul Dairy Industry, Anand*

We have received the sad news of the recent deaths of Ronald Mann, Peter Jacobs and Laurie Mashford. We hope to have some reflections on their achievements in pharmacovigilance in our April edition of Uppsala Reports.

## Extended time in Addis Ababa

*Kristina Star*

I spent October and half of November away from the UMC Research department, at the Food, Medicine and Healthcare Administration and Control Authority (FMHACA) of Ethiopia.



*Elizabeth Woldemariam, Aida Arefayne, Assefa Ejamo of the Ethiopian centre*

My husband was on an assignment in Ethiopia for some months so I joined him there and took the chance to work at FMHACA. The aim was to exchange experiences and to enhance UMC's understanding of the daily routines and challenges of an African national centre, and to gain insight into how UMC methods and services are utilized.

The pharmacovigilance representatives at the FMHACA work within the Regulatory Standards Setting and Information Delivery Directorate. The importance of pharmacovigilance has successfully been promoted during past years. One goal has been to hold at least two face-to-face meetings per month at health facilities. Suspected ADRs as well as medication errors and product quality defects are collected by the centre. Safety signals detected in 2012 primarily concerned product quality defects that had

been investigated and confirmed by the FMHACA laboratory. Recent pharmacovigilance initiatives have been to agree and publish a strategic framework for the country, a guideline on how to monitor Adverse Events Following Immunizations, a teaching manual to be used in health teaching institutions, and a strategy for preventing antimicrobial resistance.

Representatives at the authority graciously hosted me and showed great hospitality during my stay in Ethiopia. I learned to eat and enjoy injera bread for lunch and was privileged to be informed about its nutritional value by the authority's food experts. I was fortunate to experience and feel the energy of the developments taking place in Addis Ababa. The national high activity level also applies to our dedicated and enthusiastic colleagues working for pharmacovigilance in Ethiopia.

## Korean mission

*Antonio Mastroianni*

During the APEC meeting (see p8-9) there was an opportunity for delegates to make site visits to the Korean Institute of Drug Safety and Risk Management (KIDS) and to a Korean regional pharmacovigilance centre at Seoul National University Hospital.

Professor Byung-Joo Park, President of KIDS, gave us an overview of the institute, officially opened in April 2012. Since its inception KIDS has developed the Korean Adverse Event Reporting System (KAERS) and submitted over 100,000 ADRs to VigiBase.

### Role in Korea

KIDS has a mission to collect, analyze, evaluate, and manage ADR data. It also develops drug utilization criteria and medication guidelines for health professionals through causality assessments on ADR data collected via the national monitoring system which covers regional centres, societies and organizations, healthcare providers, patients and the pharmaceutical industry. It also makes use of claims data, mortality data, and hospital data. In addition, KIDS plays a vital role in offering drug safety education and in raising awareness on the importance of pharmacovigilance among the public and within the Korean government. These activities are carried out in collaboration with the Ministry of Health and Welfare, Health



*At KIDS, from left: Ian C.K. Wong (Hong Kong), Jun Li (Johnson & Johnson, Singapore), Antonio Mastroianni (UMC), Byung-Joo Park (KIDS), Ola Strandberg (UMC), Shanthi Pal (WHO), Soo-Youn Chung (KIDS)*

Insurance Review and Assessment, and the Ministry of Food and Safety, as well as via a network of 22 regional centres.

### Safety in hospital

After the presentation, and lively discussion about how KIDS developed their infrastructure and staff competency, obtained funding, and acquired key political support, the delegation

went to see a regional centre at Seoul National University Hospital Drug Safety Monitoring Centre. There was a lecture about the university and how pharmacovigilance is incorporated in the structure and operations of the hospital.



## TBS highlights

*Johanna Stenlund*

In October Anna Hegerius and myself from the UMC had the pleasure of travelling to Geneva to attend the WHO Technical Briefing Seminar (TBS). The course was an excellent event for networking with participants from all over the world (Nepal, Micronesia, Jordan, Singapore and Afghanistan, to mention just a few) as well as to meet colleagues at WHO Headquarters. Some highlights from the very intense TBS agenda:

**WHO vision and strategy** – an overview of the new Essential Medicines and Health Products (EMP) structure given by Kees de Joncheere, along with the vision and strategy for WHO as a whole. This session set out the many complex topics handled by WHO and the broad scope of the organization.



*'On-the-spot' profiles created by the TBS participants*

**National Medicines Policies and World Medicines Situation** – Richard Laing on how high-income countries (18% of the world)

consume 80% of the global pharmacy market, while low-income countries (11%) consume only 0.5%.

**Medical Devices Policy and Access** – Adriana Velazquez-Berumen spoke about what WHO does in terms of medical devices. There are over 10,000 types of medical device, and from the age of 60 you should expect to use an additional one every decade (glasses, hearing aid, stick, etc). A problem is often that a country may have a budget to buy equipment but not for maintenance.

**UN Life-Saving Commodities** – Lisa Hedman talked about 13 commodities that would save lives if access was improved (e.g. oxytocin, injectable antibiotics, zinc, oral hydration solution).

**Health and access to medicines as a human right** – Hans Hogerzeil on health and access to medicines as a human right; and that everyone has the right to the highest obtainable standard of health.

**WHO strategy for working with countries** – Gilles Forte stated that EMP has 30 Collaborating Centres (UMC being one), six regional offices and 150 country offices in their network.

Clive Ondari, the new coordinator for Safety and Vigilance (SAV) within EMP, led a session where Shanthi Pal talked about new challenges



*Richard Laing with an attentive group*

within pharmacovigilance, Madhava Balakrishnan about the Global Vaccine Safety (GVS) blueprint and Michael Deats gave an update on current work in substandard/spurious/false-labelled/falsified/counterfeit (SSFFC) medicines.

The EMP Information Portal (<https://apps.who.int/medicinedocs/en/>), demonstrated by Claude Da Re. All kinds of documents can be found (guidelines, essential medicines lists, etc); anyone can contribute by uploading documents from their country or organization.

**Poster session** – new for TBS in 2013, and highly appreciated by both participants and WHO staff who were able to mingle and discuss a broad range of topics presented by participants. Great initiative!

Interested to read more about the TBS topics? Go to: [www.who.int/medicines/technical\\_briefing/tbs/en/index.html](http://www.who.int/medicines/technical_briefing/tbs/en/index.html)

## Iraq: challenges and progress

*Maytham H A Al-Amiry, IPhvC*

The Iraqi pharmacovigilance center (IPhVc) consists of four units: the ADR unit, medication errors unit, communication unit, and vaccines and serum unit.

In 2012, the first guidelines for the pharmacovigilance system were issued and pharmacovigilance units were introduced in each health directorate, except in three provinces in the north (Kurdistan). These pharmacovigilance units, three in the capital (Baghdad) and one in each province, consist of two pharmacists. Their main duties are to raise pharmacovigilance awareness in their province and help the national centre to follow up the reports coming from that region. The staff of these units participated in an intensive training course by the IPhvC in order to prepare for this work. The result

has been a significant increase in the number of ADR reports received. In October 2013, a training course for health care professionals in Erbil province in Kurdistan set the basis



*Training course in Erbil, with lecturers Dr. Amjed A. Mahmood and Dr. Maytham H.A. Al-Amiry from the IPhvC*

for creating pharmacovigilance units in this region.

Our main concern, both at IPhvC and in the regions, was to raise awareness among health care professionals. The ADR reporting form (in English) was updated many times to meet the local requirements, and a form was adapted in Arabic to meet the reporting requirements of nurses, pharmacy technicians, etc, and (in future) of patients. Brand drug companies (as a first step) are obliged to provide Periodic Safety Update Reports and inform us about any serious ADRs. The Iraqi centre is about to launch a national campaign in collaboration with some brand drug companies to raise awareness of pharmacovigilance in the whole community.



# PV in Pisa

*Ghazaleh Karimi*

Pisa is an old city but with a vibrant feel, probably helped by the large university population. ISoP's annual meeting there in early October was well attended – 400 people – for the many and varied sessions. The Palazzo dei Congressi is located adjacent to the university department of economics, providing nostalgic glimpses of student life.



*Opening ISoP 2013: President, Hervé le Louet, Professor Corrado Blandizzi, Dr Marco Tuccori, and Mayor of Pisa Marco Filippeschi*

## On the agenda

The first day featured invited talks and plenary sessions, sandwiched between parallel sessions from contributing researchers. New this year was a separate Junior Pharmacovigilance session, well-attended despite coming last in the afternoon.

The second day offered insights into the emerging areas of biotechnological therapies and biosimilars, in parallel to psychotropics, and a miscellaneous French language session. Afternoon sessions included PRAC (EMA Pharmacovigilance Risk Assessment Committee), ISoP general assembly and Signal detection analysis, including highlights from several programmes.

The short third day closed at lunchtime, but included two-times-two parallel sessions and a plenary lecture on the role of media in pharmacovigilance.

## Presentations of note

*Characterization of adverse reaction reports associated with adulterated health products: the Singapore pharmacovigilance database 1993 to 2012* by W.C. Tan from the Health Sciences Authority, presented work on the reporting of adulterated health products.

Based on WHO-ART preferred terms, they had retrieved and characterized 392 reports (0.3% of dataset) within their national ADR database. The results showed drugs for sexual enhancement, general well-being and slimming as the most frequently reported indications.

*Safety of immunotherapies* by Michele Maio of the Italian network of biotherapy of tumours, introduced a comprehensive session on pharmacovigilance of biotechnologicals and activation immunotherapies. A review of available classifications of immunotherapeutics led on to the mechanism of action of the major classes. Immunotherapy in general requires time, in contrast to chemotherapy, the alternative in many cancer treatments. However, with immunotherapy survival has been observed to increase significantly. ADRs highlighted included cutaneous rashes/pruritus, colitis/diarrhea, liver toxicity and hypophysitis.

*Disease-related Adverse Events following Non-live vaccines: Analysis of the WHO Global ICSRs Database* was by Giuseppe Roberto. He pitched the case of the suspected reporting bias for non-live vaccines, reported with signs and symptoms of the infection itself (as they should not be able to cause infections to the patient). Giuseppe not only made a good case out of the study, but also took the opportunity to remember Jerry Labadie, who was thanked in his absence.



*Celtic Harp Orchestra*

## UMC reports

There were six posters from the UMC, the three from Research being: Juhlin et al, *Pinpointing Key Features of Case Series in Pharmacovigilance - a Novel method*, Bergvall et al, *Great Case Reports, Where do they come from?*, and Caster et al, *A Paradigm*



*Alex Dodoo speaking, Ian Wong in the chair*

*Shift for Screening Individual Case Reports: Accounting for quality and content.* One drawback of the otherwise excellent facilities was the circulation space for posters, cramped and located away from coffee service, limiting their natural exposure. (We can supply pdfs of our posters – apply to [info@who-umc.org](mailto:info@who-umc.org).)

My oral presentation on the characterisation of lack of effect reports in VigiBase was well attended and received positive feedback. It was noted how our results on the disproportional reporting of drugs used for life-style issues corresponded to those presented for a characterisation of reporting of adulterated medicines in Singapore earlier. A member of a German pharmacist association interested in the topic, informed us of related work they do by testing drugs reported with lack of effect against measures derived from pharmacopoeias.

Niklas Norén presented selected results from PROTECT in the Signal detection analysis session, mainly focusing on outcomes of the use of existing terminologies, some results from the prospective screening in THIN, and the duplicate detection project. Pitched to an audience with limited experience of methodological development, it was well received.

## People

I had the opportunity to meet several speakers and attendees who made an impression on me, such as Priya Bahri and Gunilla Sjölin-Forsberg, as well as old acquaintances such as Ronald Meyboom. The organizers provided delightful social settings for relaxing and meeting colleagues. At one, the Celtic Harp Orchestra led by Fabius Constable performed in the Church of Santa Caterina d'Allessandria.

# Learning from the East

Helena Wilmar

## Secondment at Badan POM

During 2013 the UMC put special focus on Asia and specifically the ASEAN region by supporting harmonization efforts around safety reporting requirements and systems. The goal was to ensure stakeholders in the region can collect, share, analyze, and act upon suspected medicines-related safety problems.



*A VigiFlow training session in Jakarta*

To better understand working processes, daily routines and challenges of pharmacovigilance centres in the region I had a two-week secondment in August at the Indonesian national centre (Badan POM). The objective was to learn about Indonesia's pharmacovigilance processes and interaction with other organizations in the ASEAN region.

Indonesia was part of the WHO Programme in 1975 – the only developing country of the 18 Programme members at the time. Initially a pilot project in six public hospitals, it progressed over the years, but a specific pharmacovigilance unit was not established until 2004, within the National Agency of Drug and Food Control (Badan POM). In 2012 mandatory reporting by pharmaceutical industry came in and Badan POM staff have trained industry in how/what to report.

The collaboration and interactions between the pharmacovigilance unit and other directorates within Badan POM (as well as global organizations) are successful, and there is a political mandate and support from higher management.

I attended the AEFI national committee and national launch of a pentavalent vaccine (for five major childhood diseases: diphtheria, tetanus, pertussis, hepatitis B and Haemophilus influenzae type B) produced in Indonesia (Bio Farma) which demonstrated just how important collaborations are in pushing forward pharmacovigilance in a country.

Indonesia is large geographically, with over 250 million people, and to succeed in all provinces is a major task. With its own systems, including an electronic ADR reporting for HCPs 'e-MESO' UMC is supporting them in implementing VigiFlow as part of the handling of case reports from both industry and HCPs. With 31 regional offices VigiFlow could enhance the PV unit's collection of case reports from as many provinces as possible.

My time with Head of Pharmacovigilance Ms Siti Asfijah Abdoellah and her dedicated team was truly awarding. I had the great pleasure to spend time with everyone in the team and gained a clear picture how they work and useful insights into how UMC services and tools are implemented (or not) and why.

## On to Viet Nam

Vietnam joined the WHO Programme in 1999, but the first pharmacovigilance centre in Hanoi was established in 1994. Since 2009 the National DI & ADR Centre has undertaken all PV activities on behalf of the



*Dr. Nguyen Hoang Anh (Technical Vice Director DI & ADR Centre), Dr. Vo Thu Thuy (Administrative Vice Director DI & ADR Centre), Helena Wilmar (UMC), Comfort Suku (Global Fund)*

Regulatory Authority (DAV) and is now located at Hanoi's University of Pharmacy (HUP). The NC's dedication and target-oriented work has led to great progress. An independent centre that combines expertise from both academia and hospitals, it also has a close collaboration with DAV. 15 staff, mainly pharmacists, support the NC's core job to ensure rational use and effective drugs by:

- Data collection, analysis and evaluation
- Feedback on ADRs, substandard drugs and irrational drug use
- Information to HCPs and the public
- Under/post-graduate training

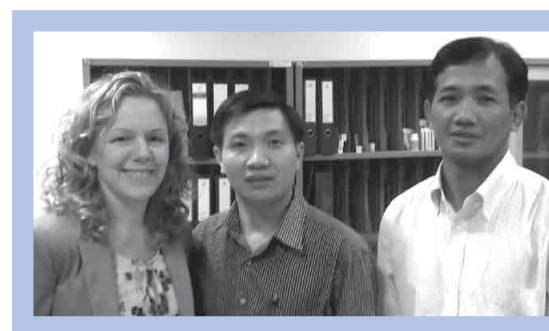
- Research projects
- Consultation services
- International cooperation (WHO, UMC, MSH, ISO, other NCs).

Close collaboration with public health programmes is ongoing and projects involving CEM on ARVs and second-line anti-tuberculosis drugs as well as targeted spontaneous reporting (TSR) of ARVs are part of the centre's scope.

The Vietnamese DI & ADR Centre is in many ways already functioning effectively. However, as well as creating a national system based on local requirements, there is also a need for global harmonization of ICSRs data. National Centre-UMC discussions on how to share data from the newly-launched Vietnamese database on a regular basis with VigiBase are on-going.

## Potential in Cambodia

The Pharmacovigilance Center in Cambodia is part of the Essential Drug Bureau, Department of Drugs and Food (DDF). DDF consists of 75 staff in five Bureaus; Drug Regulation, Pharmaceutical Trade, Drug Registration, Food Safety and Essential Drug. Cambodia joined the WHO Programme in 2012 and since then has received around 400 ADR reports. They use VigiFlow to send reports to the UMC, but the complete version of VigiFlow is desired, to both collect and manage all Cambodian case reports.



*UMC's Helena Wilmar, PV Head Mr. Sea Thol and Dr. Cheap Thon Vuthy*

Mr. Sea Thol, Deputy Chief of the Essential Drug Bureau and the Head of CPVC, has a tough mission (with his tiny staff team) trying to make medicines safer for more than 15 million people in Cambodia. Guidelines and SOPs are already in place; funding and a political mandate are yet to be fully realized.



# EU pharmacovigilance Joint Action launch

Mick Foy, MHRA

On 18 November 2013, delegates from 23 EU countries met in Luxembourg for a workshop to mark the launch of SCOPE (Strengthening Collaboration for Operating Pharmacovigilance in Europe). SCOPE is a €7 million Joint Action (see <http://ec.europa.eu/eahc/health/actions.html> for more information) funded to 70% by the European Agency for Health and Consumers (EAHC), an executive agency of the European Commission. SCOPE will last for the next three years with the aims of improving the abilities of EU medicines regulators to operate the new 2012 pharmacovigilance legislation effectively. It will be led by the UK Medicines and Healthcare Products Regulatory Agency (MHRA).



Mick Foy, June Raine and Viola Macolić Šarinić, in Luxembourg

definition of risk communication and its objectives, as well as emphasising the importance of measuring the impact & effectiveness of communications.

that patients are key stakeholders in SCOPE, which would benefit from involving patient organisations in communication packages.

There were lively discussions and incisive questions throughout the day, many relating to the position of SCOPE alongside other on-going European public health initiatives. It was established that SCOPE aims to raise standards across the EU, and there are opportunities for synergy with these projects. Further, there are several aspects of operating pharmacovigilance not covered by any kind of guidance, hence the need for SCOPE to focus on areas where development is needed.

Dr June Raine, Chair of the Pharmacovigilance Risk Assessment Committee (PRAC) and Director of the Vigilance and Risk Management at the MHRA opened the day. She outlined its aims: to inform, enthuse, and motivate the attendees to help deliver the Joint Action objectives. Mick Foy and Paul Barrow, both of the MHRA, then spoke about the coordination of the Joint Action. The structure of SCOPE was summarised, and emphasis was placed on delivering on target, on time, and on budget.

## Work Packages

SCOPE is made up of five core work packages, each designed to focus on a key area of pharmacovigilance to deliver best practice guidance and practical tools for national competent authorities. Throughout the day presentations given by each work package (WP) lead provided a brief overview of their WP.

Viola Macolić Šarinić (Croatia) outlined the deliverables and approach of WP4 - Adverse Drug Reaction reporting. These include an audit of national reporting systems, creating and proposing procedures for patient reporting, and raising awareness levels amongst health professionals and patients of national reporting systems.

For WP5, Signal Management, Sabine Straus (Netherlands) highlighted how this is a key process in pharmacovigilance, and any gains made in this area have a direct impact upon public health.

Risk Communications is WP6. Miguel-Ángel Maciá (Spain) provided the meeting with a

Júlia Pallós (Hungary), outlined the rationale behind WP7 Quality Management Systems, and provided initial process and outcome indicators, including the need for standardised SOPs and audit procedures. Carmela Macchiarulo (Italy) spoke about WP8, Lifecycle Pharmacovigilance. This focusses on lifecycle pharmacovigilance management and strengthening the capabilities for benefit risk assessment including a competency framework underpinned by effective training programmes.

The importance of evaluating the Joint Action was discussed by Margarida Guimarães (Portugal), who set out the parameters for how the deliverables across all core work packages will be reviewed.

## Collaborating Partners

SCOPE will also feature contributions from collaborating partners – external organisations who are not directly involved with national regulatory authorities.

Marie Lindquist of the Uppsala Monitoring Centre outlined the UMC priorities for the coming years, and set out to inspire SCOPE partners with the thought that the Joint Action can make a positive impact across the world. Marie will also sit on the SCOPE General Advisory Board, well positioned to ensure we link in with other interested stakeholders. Solvejg Kristensen, representing the Patient Safety and Quality of Care Joint Action, urged SCOPE partners to communicate between work packages as much as possible. François Houyez of the European Organisation for Rare Diseases (EURORDIS) told attendees

Dr Raine concluded the day by returning to the three objectives she had set out in her opening presentation and delegates resoundingly agreed that the workshop had been informative, enthusing, and motivating.

*One of our key aims throughout the project is to provide high quality and relevant information to stakeholders, within and outside the EU. We will produce a newsletter and build a website as well as hold stakeholder meetings. Colleagues are asked to register interest in receiving updates by contacting us at [scope@mhra.gsi.gov.uk](mailto:scope@mhra.gsi.gov.uk)*

## EMA definitions

The 2<sup>nd</sup> revision of the definitions annex of the Good Pharmacovigilance Practices (GVP) was published on the EMA's GVP webpage in January ([www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document\\_listing/document\\_listing\\_000345.jsp&mid=WC0b01ac058058f32c#section4](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c#section4)).

This includes a number of definitions for GVP Module XV on safety communication and for the GVP Considerations P.I on vaccine pharmacovigilance, as well as from the previously adopted revised EU Regulatory Network Incident Management Plan for Medicines for Human Use. The vaccine definitions are in line with the CIOMS-WHO definitions. There are also amendments to existing definitions, in particular those for missing information and safety concern.

# Who is at risk?

Hanna Lindroos

UMC is preparing for its next bi-annual research conference. The theme for 2014 is safety of medicines and the challenges of shifting focus from identifying risks to determining who is at risk. It will take place on May 22-23 in Uppsala, only 30 minutes direct by train from Stockholm Arlanda, Sweden's international hub.

groups are at risk for suffering from adverse events? And how does the genetic make-up of an individual affect the outcome of the drug intake?

## Historical dinner

A Viking conference dinner will take place at Odinsborg restaurant in Old Uppsala, near

drug/ADR signals but also broader risk scenarios, and which methods are available?

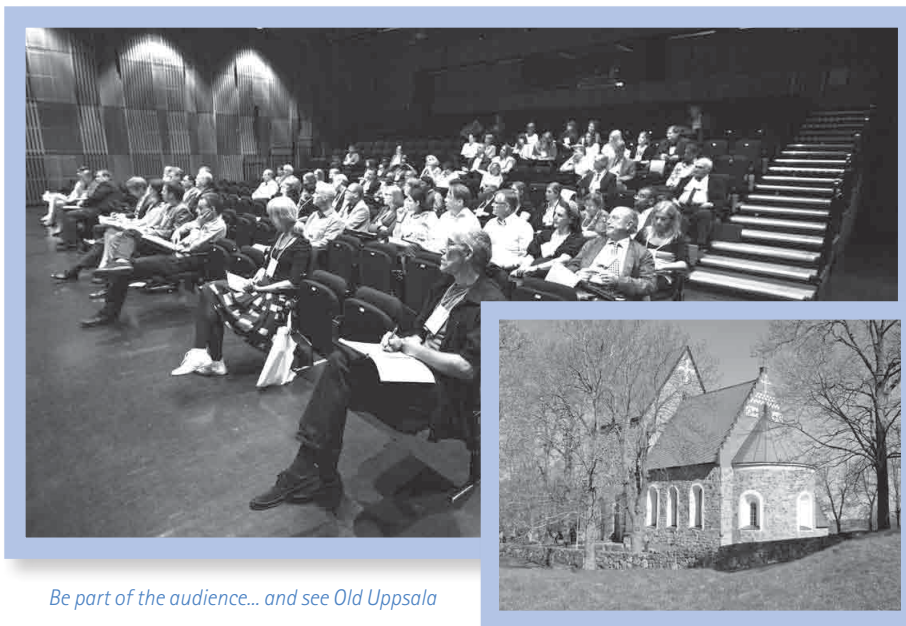
What about individualized benefit-risk assessment? Some drugs affect women in different ways from men; some affect children more than adults. Coincident health conditions may also affect the way drugs are absorbed, distributed and excreted. When a doctor examines a patient – how does he/she determine which drug will be appropriate and which is too risky?

A panel drawn from patient organizations, pharmaceutical industry and regulatory agencies will discuss the opportunities and challenges to reduce risk to individual patients from drugs, alongside patients and health care practitioners, with audience participation.

## Want to talk for 5 minutes?

We are accepting abstracts for 'rapid fire' talks on the theme of risk – each five minutes long and consisting of 20 slides that auto-advance every 15 seconds. So join us in Uppsala in May 2014: registration is open now at [www.who-umc.org/research](http://www.who-umc.org/research).

Your participation and contribution are warmly invited!



Be part of the audience... and see Old Uppsala

## Can we predict patients?

After a buffet lunch the scientific programme begins by focusing on patient groups at risk and how the molecular structure of drugs affects patients, depending on their genetic background. ADRs do not occur randomly in all patients who have all been treated with the same drug. This is because the vast majority of medical products interact with biochemical pathways which are not the primarily intended target and these are subject to genetic variations. How can we predict such interactions? Which population

huge burial mounds for three Norse rulers dating back to the 6th and 7th centuries. According to ancient mythology and folklore, the three gods Thor, Odin and Freyr lie in the mounds.

## Decision-making dilemmas

The second day will tackle difficulties with the detection and confirmation of signals. Extensive information on adverse events is available in large datasets collected by regulatory authorities and drug manufacturers. Can we use the data to identify not only

## Rapid fire talks

To see how the 'rapid fire' format works, we recommend viewing a video of Niklas Norén at DigDisDet 2013 which illustrates how it should be done: <http://www.youtube.com/watch?v=ADfXwCjdMVM>

## Do warnings attract us?

Sten Olsson

A recent article from *Harvard Business Review* goes against our usual perceptions and practices. It claims that, under certain circumstances, product related warnings may increase product sales rather than reducing them. The explanation is that "the mere inclusion of a warning builds trust, because consumers feel that the seller is being honest – and over time trust becomes more prominent, while the substance of the warning fades".

This concept warrants a serious discussion among pharmacovigilance professionals and regulatory authorities. Do we have observations or data confirming or refuting this thesis? Should we research, to find out if safety warnings related to medicines indeed lead to increased exposure to the very medicines whose safety we are concerned about? Do we have the tools to follow drug utilization patterns in a population once a warning has been issued by the pharmacovigilance centre or regulatory authority? Can we adhere to the

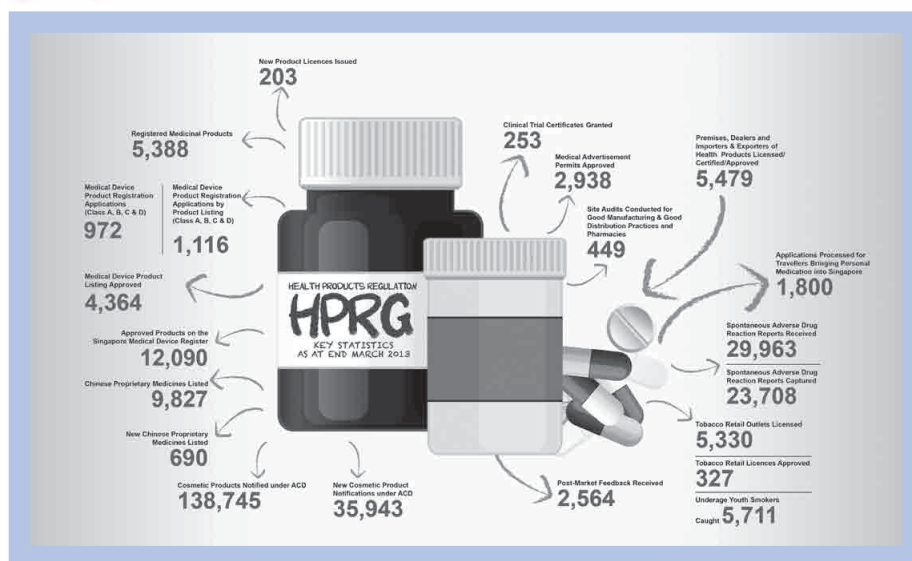
final advice of the article: "Those who genuinely wish to warn consumers should ensure that the message is conveyed-or repeated- shortly before the relevant event?"

'Scary Health Warnings Can Boost Sales' by Ziv Carmon, Yael Steinhart, and Yaacov Trope: October 2013, *Harvard Business Review*.



## A report to enjoy

Many of us at the UMC office were very impressed with the latest annual report from the medicines agency in Singapore, the Health Sciences Authority. A huge amount of care, effort and imagination has gone into making the document attractive and accessible throughout. How many annual reports that arrive on desks or in e-mail inboxes get the recipient to immediately stop and read them? The design, layout and quality of photographic material from the Singapore did just that. Having caught our attention it also held it with the wealth of accessible information it contained. There are naturally several references to the well-recognised work of colleagues in the Pharmacovigilance Branch of HSA.



Health Sciences Authority of Singapore Annual Report 2012/13

## Commune visitor



Stefan Hanna

In December, UMC received a visit from Uppsala's Deputy Mayor, **Stefan Hanna**. The visit was part of an effort by UMC to engage better with the city of Uppsala and to highlight the important role of decision makers to ensure political support for pharmacovigilance. During his visit, the UMC executive team

explained the origins and history of modern pharmacovigilance, and the creation of the WHO Collaborating Centre for International Drug Monitoring in 1968. We discussed the rationale of moving the centre to Uppsala in 1978, the creation of the Uppsala Monitoring Centre to provide technical and scientific operations to the WHO Programme, and its progress since then in promoting the scientific, economic, and social importance of improving patient safety.

## Books update

Two sample chapters from **Expecting the Worst** (2<sup>nd</sup> edition), the UMC publication about anticipating, preventing and managing medicinal product crises, are now available in print-protected format to show examples of the book's content. Chapters 1 (Introduction) and 2 (The Framework for Planning) may be viewed in pdf format (700 Kb).



The UMC's publications online also now have current French and Spanish pdf versions of **Viewpoint** to download or print.

## Colombian pharmacist

In November **Mauricio Duque Arrubla**, a pharmacist and Master's Programme in Public Health Sciences student (Specialization in Health Economy, Policy and Management) at Karolinska Institute, Stockholm came to visit. Mauricio has worked as a pharmacovigilance contact person for pharmaceutical companies in Colombia and since he heard a lot about the UMC he wanted to take the opportunity to visit us when he was in Stockholm. I gave him an overview of the WHO Programme with special focus on Latin American countries, and he appreciated his time here.



Mauricio Duque Arrubla with Elki Sollenbring

DATES	TITLE	PLACE	ORGANISER/CONTACT
11 February 2014	Essential Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008   E-mail: registrations@management-forum.co.uk   www.management-forum.co.uk
26-27 February 2014	Back to Basics in Pharmacovigilance	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621   www.dsru.org/trainingcourses   E-mail: jan.phillips@dsru.org
3-5 March 2014	Advanced Pharmacovigilance	London, UK	Management Forum Ltd (see above for contact details)
13 March 2014	Meeting of the Swiss-Austrian chapter of ISoP 'From data analysis to better health care'	Zurich, Switzerland	Swiss-Austrian chapter of ISoP E-mail: isop.chat@intranets.ch
24-28 March 2014	Data Management for Clinical & Regulatory Affairs	Accra, Ghana	UMC-Africa www.umcafrica.org/index.php/training-alerts   E-mail: info@umcafrica.org   +233-302-268-746 / +233-289-014-000
3-4 April 2014	Proactive Pharmacovigilance and Risk Management in the Era of Personalized Medicine	Zagreb, Croatia	International Society of Pharmacovigilance www.isoponline.org   E-mail: administration@isoponline.org
5-8 April 2014	ISPE Mid-Year Meeting	Rotterdam, The Netherlands	ISPE www.pharmacoepi.org/meetings   E-mail: ISPE@paimgmt.com
9-11 April 2014	4 <sup>th</sup> Bordeaux Pharmacoeppi Festival	Bordeaux, France	Université Bordeaux Segalen https://www.pharmacoepi.org/pub/A0FA2A3D-C7A0-7503-6F25-DAAA386F48DB
22-24 April 2014	IX <sup>ème</sup> Congrès de Physiologie, Pharmacologie et de Thérapeutique	Poitiers, France	Société Française de Pharmacologie et de Thérapeutique http://congres-p2t.fr/
7-21 May 2014	Uppsala Monitoring Centre 16th international pharmacovigilance training course	Uppsala, Sweden	UMC www.who-umc.org
21-22 May 2014	Signal Management in Pharmacovigilance	Prague, Czech Republic	DIA Europe www.diahome.org/en-GB/Meetings-and-Training/
22-23 May 2014	Uppsala Monitoring Centre Research Conference 2014 – Risk: What risk? Whose risk?	Uppsala, Sweden	UMC www.who-umc.org
4-5 June 2014	Constantly Changing Global Regulatory Pharmacovigilance Environment	London, UK	Drug Safety Research Unit (see above for contact details)
16-27 June 2014	8 <sup>eme</sup> Cours Francophone de Pharmacovigilance	Rabat, Morocco	Centre Anti Poison et de Pharmacovigilance du Maroc www.capm.ma/
25-27 June 2014	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (see above for contact details)
4-5 July 2014	Introduction to Pharmacovigilance	Accra, Ghana	UMC-Africa www.umcafrica.org/index.php/training-alerts   E-mail: info@umcafrica.org   +233-302-268-746 / +233-289-014-000
13-17 October 2014	Excellence in Pharmacovigilance: Clinical trials and post-marketing	London, UK	DIA Europe www.diahome.org/en-GB/Meetings-and-Training/
18-22 October 2014	ISoP 2014 Annual Meeting	Tianjin, China	International Society of Pharmacovigilance www.isoponline.org   E-mail: administration@isoponline.org
24-27 October 2014	30 <sup>th</sup> Anniversary ICPE	Taipei, Taiwan	ISPE http://pharmacoepi.org/abstracts/
14-17 October 2014	37 <sup>th</sup> Annual Meeting of representatives of national centres participating in the WHO Programme for International Drug Monitoring	Tianjin, China	





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

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

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A list of UMC staff may be found via –  
About UMC > UMC staff – on our website.

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

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## Time to sign up!

The UMC PV course 2014 is now open for applications. Please visit the UMC website for further details and contact [pvtraining@who-umc.org](mailto:pvtraining@who-umc.org) if you have any questions regarding the course.

Navigate to: Pharmacovigilance > Education & Training on the UMC site [www.who-umc.org](http://www.who-umc.org) for more.

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