

# MUR71



**Indicators | International partnerships**

**Integration in Rabat | Improvements for VigiLyze**



Marie Lindquist  
Director  
Uppsala Monitoring  
Centre

*At this time of the year, when the summer has inevitably moved into autumn, the morning light gets softer and the spiders' webs show clearly against the grass which is wet from the morning dew; and there is a crispness in the air as a sign of the chilly days to come. Going for my morning walk I feel a brief sadness coming over me, like a waft, lingering in the air for a moment.*

*But September is also a good time for rekindling ideas for the future. There are lots of things to look forward to; exciting prospects of new achievements in the months to come, stimulating and challenging discussions with colleagues to improve and fine-tune work processes and collaborations, and meetings across the globe which all contribute, in one way or another, to drive the pharmacovigilance agenda onwards.*

*One reflection: in a world where there is so much cruelty, forcing millions of people to leave their homes and flee for their lives; and millions again face yet another day when they cannot even hope to have enough to eat: how can we keep optimistic and continue to believe that it is possible to make this world a better place? Well, maybe it is as simple as 'we have to'. I don't believe that human capacity to do evil will ever be extinct; but neither is our capacity to do good! Instead of feeling powerless about the many horrible things going on around us, I think the only way to stay sane and positive is to keep going, doing something useful, and telling ourselves that every genuinely positive contribution makes a real difference, no matter how small it may seem in the big scheme of things.*

*The very purpose of the UMC is to do good: to support and promote patient safety through building sustainable and effective pharmacovigilance practices globally. In other words, what we do is to build pharmacovigilance capacity.*

*All UMC core activities together make up our capacity building portfolio: delivering our baseline services to the WHO Programme for International Drug Monitoring, providing state-of-the-art technical and scientific developments and support, and bringing together people from different parts of the world in training activities.*

*Some perhaps associate the term 'capacity building' primarily with training; but it is much more than training. According to WHO, "capacity building has typically been defined as the development and strengthening of human and institutional resources"; and community capacity building is defined in Wikipedia as "the process of developing and strengthening the skills, instincts, abilities, processes and resources that organisations and communities need to survive, adapt, and thrive in the fast-changing world".*

*United Nations Development Programme (UNDP) recommends a five-step approach, which makes very good sense:*

- 1. Engage stakeholders in capacity development*
- 2. Assess capacity needs and assets*
- 3. Formulate a capacity development response*
  - a. Institutional arrangements*
  - b. Leadership*
  - c. Knowledge*
  - d. Accountability*
- 4. Implement a capacity development response*
- 5. Evaluate capacity development.*

*For me, sustainable development and a dialogue among equals are two key aspects of capacity building: developments need to cover institutional and legal frameworks as well as human resources and organisational improvements, and the principle of mutuality in teaching and training is essential.*

*As always, when people get together, there will often be differences of opinion, sometimes ending up in serious conflicts. We all know what this can lead to in its extreme form. Therefore, we must always do our best to resolve those conflicts, as and when they occur. This requires a genuine will to understand each other; that we talk openly with one another; that we are prepared to admit errors; and that we will make reasonable concessions and compromises which we will embrace gladly and not grumble about or even ignore later.*

*It is not about 'us' and 'them'; it is 'us' – full stop!*

A handwritten signature in black ink that reads "Marie Lindquist". The signature is written in a cursive, flowing style.

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20-21

# Pharmacovigilance bolstered in Lao PDR

*Soulyvanh Keokinnaly*

Lao People's Democratic Republic (PDR) is a small landlocked country in South East Asia bordering Myanmar, Thailand, Cambodia, Vietnam and China, with a population of 6.7 million. In recent years, three major milestones have been reached that could be the turning-point for pharmacovigilance in our country.

Targeted Spontaneous Reporting (TSR) covered two antiretroviral (ARV) drugs, namely nevirapine and zidovudine.

Then, in 2014, the FDD created a division that will focus on pharmacovigilance, among other topics. This initiative to bolster pharmacovigilance was stimulated by the

## A strong legal basis

Lao PDR's National Medicine Policy (2003), and the Law on Medicines, and Medical Products (2011) already provide a strong legal basis for the creation of a centre to collect and assess ADRs. In July 2015, in order to implement the legislation related to pharmacovigilance work, an international consultancy was initiated in Lao PDR to provide technical assistance to strengthen the regulatory system in order to develop and maintain a strong pharmacovigilance system. The main objective of this technical assistance is to develop draft regulations and guidelines and revise the ADR form.

## Consultation and training

As part of this, WHO offered a contract to Dr. Syed Rizwanuddin Ahmad, who is a pharmacovigilance consultant with a special interest to strengthen national systems in resource-limited settings. Dr. Ahmad visited Lao PDR for two weeks in July 2015 to have consultative meetings with key concerned stakeholders to discuss the draft regulations and guidelines, and start the process of revising the ADR form.

## Support from above

In addition, Dr. Ahmad conducted hands-on training/workshops for the different stakeholders including staff of the FDD on the importance of pharmacovigilance and on causality assessment. Dr. Ahmad stated that "higher-ups in FDD have shown strong support for pharmacovigilance and sometimes you need a champion to be your advocate to raise awareness and promote pharmacovigilance in a country".



## Three key steps

Firstly, in 2012, with funding from the Bill and Melinda Gates Foundation, the Food and Drug Department (FDD), an agency under the Ministry of Health whose responsibility includes regulation of medicines and vaccines, started a pilot project on pharmacovigilance with the support of WHO. This project of

successful TSR pilot project. The new division will monitor additional ARV drugs, medicines to treat opportunistic infection, and second-line tuberculosis (TB) medicines, especially in multi-drug resistant TB (MDR-TB) patients. Our third milestone was passed in July 2015 when Lao became the 122<sup>nd</sup> nation to become a full member of the WHO Programme for International Drug Monitoring.

## New Associate

We are happy to welcome Chad as a new associate member of the WHO Programme for International Drug Monitoring. The Bureau de Pharmacovigilance has been formed within the Ministère de la Santé Publique, Direction Générale de la Pharmacie et des Laboratoires.

The national centre and UMC are currently establishing the collaboration needed for Chad to become an full member.

## Delhi-bound

As we go to press, the local hosts are putting the final touches to the arrangements for the 38<sup>th</sup> meeting of national centres participating in the WHO Programme for International Drug Monitoring. We hope to see many old friends in India, and make new acquaintance with centres staff who have not before attended this important annual meeting.

# Creating a platform for dialogue

Therese Lundin

Keeping the bigger picture in mind, and where your piece of the puzzle fits in, can be a challenge in any situation. During the lengthy drug development process, from an entirely new chemical substance to a marketed drug used in regular patient care, the steps are many and you may lose sight of the ultimate goal – safer and healthier patients.

Bringing researchers together from all phases of drug development and surveillance is one of the main goals of the upcoming Uppsala Forum, arranged by UMC on 30–31 May 2016 in Uppsala, Sweden. To learn more, I talked to Professor Ralph Edwards, Senior Advisor to the UMC.

*So, what is the Uppsala Forum really about?*

"There is a need to talk more about the impact of the research we do – and the other way around as well!" says Ralph Edwards. "We want to create a space for dialogue and discussion around current patient safety issues: about what problems "out there" need to be solved."

*How does it connect to the research conferences previously organized by UMC?*

"Previous years' research conferences started out of a desire to showcase our research as

well as to arrange an in-depth research meeting in the pharmacovigilance area. Uppsala Forum aims to develop this concept and broaden the audience to engage a wider community concerned with patient safety and its scientific underpinning."

*What is the profile of participants and speakers?*

"The target audience is really people interested in the future of pharmacovigilance. People with any interest in research and who want to contribute to the debate and discussions, both formally and informally. We want to create a forum for true dialogue, not just one-way presentations.

We aim to have speakers who will cover areas from basic sciences of drug development to drug safety economics, highlighting different angles of the main theme."

*Could you tell us something about the conference theme?*

"There is a lot to be learnt about the relationship between pre-marketing safety and what we do in pharmacovigilance. It is particularly important for risk management planning, and even more so with more rapid drug access demands. The future of

pharmacovigilance is bound to incorporate links to early pre-clinical research as well as health information systems and social media."

*What does UMC expect to achieve with the conference?*

"We want to stimulate a good and active debate about the current issues of drug benefits and harms, particularly considering rapid access to new medicines. I hope we will create new links between people with different views on safer and more efficient therapeutics, as well as create awareness of the research we already do at the UMC. We want to show that we are an approachable party and a partner for dialogue in the area of patient safety."

*Look out for more information about Uppsala Forum, and don't forget to mark the dates in your calendar!*



# GlnAS gather in Uppsala

Malin Jakobsson

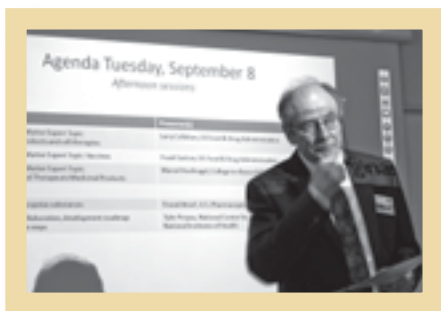
UMC was the proud host of the 5<sup>th</sup> GlnAS workshop on 7-8 September. The meeting had over 80 registrants from all over the world present, plus another 50 'remote' participants listening from afar.

## Towards ISO standards

GlnAS stands for Global Ingredient Archival System, an initiative which aims to deliver a substance registration tool based on the requirements of the ISO (International Organization for Standardization) IDMP (Identification of Medicinal Products) 11238 Substance Standard (EN ISO 11238:2012), and Health Informatics, Identification of Medicinal Products (IDIMP) standard 'Data



Paolo Alcini (EMA), Frank Switzer (FDA), and Vado Perkins (FDA) at GlnAS in Uppsala



Herman Dietrich, College ter Beoordeling van Geneesmiddelen

elements and structures for unique identification and exchange of regulated information on substances!

## Global aims

In the GlnAS Project Group, regulators and collaborating expert scientists have made significant progress in developing a system and data model to implement the ISO IDMP 11238 Substance Standard that could be used by regulators throughout the world to

register substances, and exchange critical information related to substances. This database will also provide all stakeholders with global ISO IDMP-Identifiers for substances used in medicinal products.

Uppsala Monitoring Centre very much welcomes the initiative of standardising substance data in order to improve pharmacovigilance research and surveillance.

Photo credits: idmp1.com

# Towards poison control in Eritrea

Elsa Mekonnen Afewerki and Selamawit Ghebrihiwet Teklmariam

Exposure to a poisonous or toxic substance can be intentional or accidental and can lead to acute or chronic poisoning. This issue is common worldwide and is among the leading causes of death. In Eritrea, cases of poisoning are treated in hospitals as emergencies, where victims receive supportive care as well as maintenance therapy. However, identification of the poisoning agent based on objective analysis does not always occur, and depends mainly on subjective criteria.

A study was undertaken to estimate the incidence of poisoning cases in Eritrea (accidental or due to attempted suicide) and to explore the profile of the targeted population, and identify the most common poisoning agents.

## Orotta hospital study

Data was collected from patient cards for the period January 2012 to August 2013 at the emergency department of Orotta

hospital. A total of 257 cases of poisoning were documented over the 20-month period involving 12 types of poisoning agents. The male to female ratio was 37.36% to 62.64%. Clorox (a commonly-used household detergent) followed by snake bite occurred most frequently. Snake bite, followed by carbon monoxide, were the main causes of accidental poisoning, while Clorox, and other drugs, were used in the suicide attempts. Reasons for the high incidence of Clorox are its powerful toxicity, ease of availability and relatively low cost.

Evaluation of this data also revealed:

1. two cases of death with known causative poisoning agents (organophosphate insecticide) where the specific antidote (pralidoxime) was not used, and
2. more than 21% of poisoning cases in adults and 7% of cases in children caused by unknown drugs.

## Start of a strategy

According to international guidelines and the results obtained from this work, there is a need to establish a National Eritrean Poison Control Center. Our hope is that this centre should be entrusted with multidisciplinary functions:

- Treatment of poisoning cases according to international guidelines.
- Enhancement of public awareness by providing information and advice on individual poisoning agents.
- Strengthening the technical capability of personnel working in the relevant areas of analysis, statistics and interpretation.
- Understanding and applying the standard protocol methods for the identification and safe storage of toxic agents.

# Cissi takes a bow

*Sten Olsson*

My colleague and friend Cecilia Biriell (Cissi) has decided that working for the UMC and the WHO Programme for International Drug Monitoring for 37 years will be enough. She started her retirement in September 2015, having worked for us since August 1978. This would be considered enough by any standard but we will certainly miss having her around.

I remember interviewing her for the pharmaceutical officer position in 1978 and I'm very happy with the choice we made then. Cissi is a very diligent and conscientious person with an eye for detail. She has managed to keep us, her colleagues, on the agreed path, following SOPs and standards, and delivering on time with high quality. This she has done from all of the positions she has held at the UMC, and they are many.

During the first ten years there were only three persons working for the WHO Collaborating Centre (still not called the Uppsala Monitoring Centre); Cecilia, Marie (our current director) and me. All of us had to do and know all aspects of the work to cover for each other, and we got to know the WHO Programme and each other very well.

We then also realized that each of us had a different personality with different strengths and weaknesses – which was an overall strength for the Centre. The gang of three is now splitting up; it was bound to happen one day.

Cecilia has made major and important contributions to the growth and sustenance of the UMC and the WHO Programme. She



*A strawberry cake for Cissi on her leaving day.*

has combined her critical mind with good humour and a good heart. She always wants to do the right thing. I hope enjoying retirement is the right thing for her now and I wish her many pleasant experiences when, as far as I understand, she will be travelling the world, not connected to work. Fortunately I know that we will keep in touch.



*The original three - in 1980 and 2015*

# Student-run pharmacovigilance education

*Rike van Eekeren, Tim Schutte*

In the July edition of Uppsala Reports (UR70 p18) we wrote about the national programme for pharmacovigilance education for medical students in The Netherlands. Alongside this national programme, we started an innovative extracurricular pharmacovigilance project in a local university hospital (VUmc Amsterdam).

This initiative is part of the student-run pharmacotherapy project in which medical students have full responsibility for projects aimed at improving patient treatment and pharmacotherapy. This programme is student-run and is a novel educational approach in which students learn mostly by doing. Within this project, the pharmacovigilance initiative concerns the assessment of reported adverse drug reactions on causality and pharmacology.

## Student assessments

Every week undergraduate medical students assess three ADR reports that were recently reported to the Netherlands Pharmaco-

vigilance Centre Lareb. The anonymous reports are selected by Lareb staff on suitability regarding sufficiency of documentation, relevance and the possibility of a pharmacological mechanism.

The students handle the pharmacovigilance assessment just as regular Lareb staff would have done: they assess causality of the adverse drug reaction and investigate a scientific or pharmacological explanation. Consequently, they write a feedback letter to the reporter (either a healthcare professional or a consumer) and a summary of the report for pharmacovigilance databases. The assessment and feedback letter are returned to the Lareb assessor for final checking and submission of the report to the database and for sending out the feedback letter to the reporter.

## Dual benefits

The major benefit for students is real-life experience in pharmacovigilance, using practice in pharmacology together with an

experience with adverse drug reactions. For the Netherlands Pharmacovigilance Centre Lareb the benefit is to provide future health care professionals with attitudes, knowledge and skills regarding the importance, recognition and reporting of adverse drug reactions to pharmacovigilance centres.

## A good experience

The programme has been active for a year now, and our experiences are very positive. The students assessments are very useful and scientifically sound. Only a few corrections are needed in the feedback letters to the reporters. Overall, the project cost Lareb staff no more time effort than a regular assessment of ADR reports.

*Rike van Eekeren, The Netherlands Pharmacovigilance Centre Lareb and Tim Schutte, Research and Expertise Centre In Pharmacotherapy Education (RECIPE of VU medical centre Amsterdam)*

# Holding a stake in SCOPE

*Marie Lindquist*

The elegant surroundings of the Royal Society of Medicine in London W.1 were the very central setting to welcome the stakeholders into the Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) project.\* (See UR64 page 20 for an introduction to this major international project.)

Packages, including results from surveys, proposed recommendations and tools to be developed. The Forum will also provide opportunities for SCOPE partners to meet and interact. In this context 'stakeholders' consist mainly of medicines agencies within the European Union.

## Pointing forward

The meeting on 21 September began with an introduction and welcome from June Raine, Director of Vigilance and Risk Management of the MHRA, who reiterated the purpose of SCOPE: to share expertise and practice, deliver practical tools and guidance and operate pharmacovigilance in the EU.

This was followed by presentations on aspects of SCOPE's work so far and future prospects from Helen Lee, European Commission, and Mick Foy, MHRA. François Houyez of the NGO the European Organization for Rare Diseases (EURORDIS) raised interesting points about patient reporting with particular reference to Croatian and Dutch initiatives.

We then heard about systems for managing ADRs and signals, after which risk benefit

assessment and quality management systems were put under the spotlight. Speakers representing all the work packages came from a complete cross-section of EU countries.

\* For more: <http://www.scopejointaction.eu/aims/>



*June Raine, addressing SCOPE stakeholders in London*

## Sharing and delivering

This Stakeholder Forum will provide an opportunity to receive updates on progress achieved across the eight SCOPE Work



# Integrating pharmacovigilance

*Magnus Ekelo*

Organized by the WHO Eastern Mediterranean Regional Office (EMRO), the second Arabic/Eastern Mediterranean regional meeting on pharmacovigilance 'Strengthening Pharmacovigilance Systems in the EM Region' took place in the Moroccan capital, Rabat, on 7-10 September 2015.

## The road to integration

The first Arabic/EM regional meeting in September 2014 recommended that an annual regional meeting be arranged, to enhance collaboration and the sharing of best practices between countries. The 2014 delegates had also recommended that national centres harmonize and coordinate all 'vigilances' and introduce and sustain the concept of an integrated vigilance system. This meeting therefore aimed to push forward the concept of an integrated pharmacovigilance system and to provide guidance by constructing a roadmap for future development. This roadmap contained advice to existing and new pharmacovigilance programmes and to WHO.



*A workshop in full flow*



*Madhava Balakrishnan, WHO vaccines, talking to the EMRO group in Rabat*

## Country experience

The first two days were devoted to the integrated vigilance approach and to providing background information. Countries with different experiences and areas of expertise were invited to share their knowledge and practices. Presentations showed the many different approaches to pharmacovigilance, from the very clinical to robust regulatory systems. From resource-poor environments to well-funded programmes. From centres with decades of experience to new initiatives.

The recently published WHO pharmacovigilance indicators were introduced. An assessment using these indicators to measure the pharmacovigilance status in each country of the region has been undertaken and was presented at the conference.

## Walking the talk

As this year's meeting was organized by the EMRO office, which has a strong focus on vaccine vigilance and AEFIs (Adverse Events Following Immunization), half of the agenda was devoted to vaccines, and the ratio of participants from vaccine and medicines

vigilance was also 1:1. While this mix of people was good as a stimulus for integration, it also exposed some of the major challenges in harmonizing the two worlds in terms of concepts, procedures and terminologies.

## At the sharp end

To focus discussion in the reality of daily practice, delegates were also offered four site visits – to the Moroccan Pharmacovigilance Centre, the Anti-Poison Centre, a hospital setting and a pharmaceutical company, followed by a plenary debriefing. Robert Pless (Canada) joined the meeting by remote connection to discuss topics such as methods for monitoring/conducting AEFI surveillance and vaccine safety signal detection.

To enhance communication between the countries in the region, a new online communication platform will be constructed and launched later this year. The platform will be administered by the WHO Collaborating Centre in Rabat although the ownership will be shared among all the countries in the region.

## Geographical spread

Approximately 50 participants took part, from Afghanistan, Djibouti, Egypt, Iran, Jordan, Kuwait, Lebanon, Morocco, Oman, Palestine, Qatar, Somalia, Sudan and Tunisia. Representatives of WHO Headquarters, EMRO, WHO Collaborating Centres in Morocco, Ghana, Netherlands (via Skype) and Sweden were also present.

# Fellowship in vaccine safety

Sten Olsson

In support of the vision of the WHO Global Vaccine Action Plan that there should be "effective vaccine safety systems in all countries", the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, Accra, Ghana, conducted a vaccine pharmacovigilance training course from 7–18 September 2015. Thirteen senior health professionals from nine countries, representing different parts of Africa, were admitted to the training.

## Interactive content

The curriculum was divided into 11 modules covering subjects specific to immunization programmes, but also methodology applicable to pharmacovigilance in general. Both theoretical sessions and hands-on practical exercises were included as well as field visits to the regulatory authority and immunization centres. The faculty included experts from WHO, Geneva (delivering lectures through remote communication), the Uppsala Monitoring Centre, the Ghana Food and Drug Authority, the University of Ghana, School of Public Health and the WHO Collaborating Centre hosts themselves.



No passive learning for the vaccine fellows...



The inaugural Fellowship group

Participants came with a lot of field experience and knowledge from their various professional backgrounds. As a result, the input from participants led most sessions into an interactive discussion guided by the assigned facilitator. Throughout this process the participants learned a lot from each other and from the valuable experiences of other African countries.

## A hot topic – malaria vaccine

The expected imminent introduction of the new and complex RTS,S malaria vaccine, recently approved for use by the European Medicines Agency, was the subject of an in-depth discussion about the challenges of detecting unexpected problems among the exposed in an environment without an established reporting culture. The complexity of active monitoring of a large number of

people vaccinated led participants to call for inter-country collaboration. The need for extensive education of the public was noted, for instance to ensure the continuous use of impregnated bed nets, considering the limited efficacy of the malaria vaccine.

It was agreed that in many situations even the best experts do not have all the answers to what is good pharmacovigilance practice, but that such practice has to be developed locally with the assistance of community leaders.

It is hoped that the course participants, with their newly-acquired knowledge in vaccine safety surveillance, can form a core competence pool to support further development of vaccine pharmacovigilance in Africa in the coming years.

# WHODrug™ in Japan

Malin Jakobsson

In a recent announcement, 'Notification on Practical Operations of Electronic Study Data Submissions', the Japanese medicines authority, the PMDA (Pharmaceuticals and Medical Devices Agency) strongly recommends the use of WHODrug dictionaries (WHO DD).

PMDA states that in submissions for new drug approvals:

*WHODrug is a global standard for organizing and standardizing drug information in pharmacovigilance and clinical trial data. WHODrug is maintained by Uppsala Monitoring Centre and is released four times per year and contains a standardized structure and classification of nearly 400,000 drugs on the global market, including conventional drugs, biologics, herbals and Kampo and Traditional Chinese Medicines.*

The notification can be found on the PMDA home page at <http://www.pmda.go.jp/files/000206451.pdf>.

The UMC welcomes and acknowledges the recognition by PMDA of the contribution WHO DD can make to safer medicines for patients.

# Making tracks in Boston

*Kristina Juhlin*

This year's meeting of the International Society of Pharmacoepidemiology (ICPE) was held in Boston, US. As a first-time visitor to the city, I was struck by the historical and modern nestling side by side. Walking from my hotel to the conference venue I passed 19<sup>th</sup> century churches as well as 21<sup>st</sup> century sky-scraping office complexes.

## Hive of activity

As always, the meeting was bursting with people, posters and presentations. In addition to the six to seven parallel sessions with presentations on different topics, meeting attendants were kept busy by the vast range of posters and by the many exhibitors present. To help navigate the conference, ICPE had created 16 session tracks based partly on the special interest groups; I particularly welcomed the pharmacovigilance/regulatory track.

## UMC presence

UMC participated with contributions both to the scientific and the exhibition sides of the meeting. At the UMC booth Helena Sköld was ready to answer questions about UMC, the new WHO Drug tool and the newly-launched Take&Tell campaign, as well as provide demonstrations of VigiLyze™ and other UMC tools.

On the research side, UMC presented three posters; on the characteristics of vaccine reports in VigiBase®, on signal detection performance in spontaneous reports compared to electronic health records, and an evaluation of switching from using IC values to using vigiRank™ in our signal detection work. Professor Parthasarathi Gurumurthy of the JSS College of Pharmacy in Mysore also attended the conference and joined Helena at the booth to promote the Asia Pacific pharmacovigilance course taking place in Mysore in January.

## Perspectives

A highlight of the meeting was the plenary session 'The eye of the beholder' in which different aspects of an adverse reaction were discussed from the perspective of the patient, prescriber, manufacturer, regulator and lawyer.

The patient representative gave a compelling perspective on his relationship to warfarin

and handling the choice between GI bleeding and stroke. He stressed that his decisions were based on his life, personal interests and family situation, and that the choices of another patient might be different.

Next, Professor Jerry Avorn – in the role of the prescriber – explored the difficulty of keeping up to date with the constant stream of new drug safety findings while tackling the persuasive messages from drug companies, often with no formal training in performing benefit-risk assessments. He suggested evidence-based reviews of drug benefits and risks together with better system incentives to reward good prescribing as possible ways forward.

## Mingling without the Red Sox

The conference dinner took place at Fenway Park, home venue of the baseball club Boston



*Making tracks for ICPE 2015*



*Trinity church reflected in an adjacent glass-plated building*

Red Sox. Unfortunately for us, the Red Sox were away playing in Chicago that evening, but we all enjoyed mingling with their mascot while enjoying American finger food and the live band.

# The WHO Pharmacovigilance Indicators

Ambrose Isah

## Why indicators?

The growth of pharmacovigilance in the last five decades has been enormous and the recent publication of a practical manual for the assessment of pharmacovigilance systems elaborating a set of indicators is an additional step in this trajectory.\* The need existed to establish indices to delineate the baseline status and allow for the measurement of growth and level of performance of pharmacovigilance activities.

This much-needed tool for the assessment of the status of pharmacovigilance enables comparison within and between pharmacovigilance establishments, such as national or regional centres, hospital facilities, and public health programmes. The tool can monitor pharmacovigilance activities in the immediate and the trends over time, as well as measuring the impact of interventions. The indicators provide information for governments and other stakeholders to enable them to take appropriate actions in ensuring drug safety.

## Categories and types

There are a total of 63 indicators, categorized into Core (27) and Complementary (36). Core indicators (C) are those considered to be highly relevant, important and useful in characterizing pharmacovigilance, while Complementary indicators (T) are those additional measurements considered to be relevant and useful. They serve to further characterize the pharmacovigilance situation in the chosen setting but need not be used in all instances.

## A comprehensive tool

Each category is further classified into three types: Core indicators – structural (10), process (9) and outcome/impact (8) and Complementary indicators – structural (11), process (13) and

outcome/impact (12). Briefly, the structural indicators assess the existence of key pharmacovigilance structures, systems and mechanisms in the setting being studied. The process indicators assess the extent of pharmacovigilance activities which describe the mechanism of pharmacovigilance – the collection, collation, analysis and evaluation of ADR reports. The outcome and impact indicators measure the effects (results and changes) of pharmacovigilance activities. They measure the extent of the realization of the pharmacovigilance objectives. Notably, the entire scope of pharmacovigilance is addressed.

There is also need to obtain some background information (itemized in Annex 2) which defines and describes the milieu where the pharmacovigilance activities are taking place and other factors likely to impact on pharmacovigilance. The information covers demographics, economics, the healthcare system and the pharmaceutical scenario. Thus they provide the denominator for calculating most of the indicator values.

Lastly, nine pharmacovigilance indicators cutting across the three classes were selected for Public Health Programmes (PHP) to enable the monitoring and evaluation of pharmacovigilance following the large-scale deployment of medicines in a PHP where a large number of persons are exposed to medicinal products (see Table 1).

## Historical perspective

The development of this set of indicators commenced in 2007 following its conceptualization at a meeting in Accra, Ghana attended by African pharmacovigilance consultants and staff from WHO, UMC and WHO African Regional Office. The over-riding philosophy was to develop a set of indicators

for the assessment of pharmacovigilance with the participation of stakeholders and by building consensus (see Figure 1).

The development of the indicators was based on an adequate understanding of the pharmacovigilance system and on principles defined by the WHO Advisory Committee on Safety of Medicinal Products (ACSoMP). The identification of candidate indicators and their categorization was carried out through questionnaires to national pharmacovigilance centres, the results presented and discussed at subsequent meetings of the African Pharmacovigilance Consultant Group and annual meetings of representatives of national centres participating in the WHO Programme for International Drug Monitoring.

Table 1

<b>PART 1: CORE INDICATORS</b>
Core structural indicators
Core process indicators
Core outcome/Impact indicators
<b>PART 2: COMPLEMENTARY INDICATORS</b>
Complementary structural indicators
Complementary Process Indicators
Complementary Outcome/Impact Indicators
<b>PART 3: INDICATORS FOR PUBLIC HEALTH PROGRAMMES (PHP)</b>

A significant input into the process indicators also came from the pharmacovigilance landscape assessment study by WHO, UMC and the University of Washington, USA. At a 2010 meeting in Lomé, Togo, the relevance of, and need for a set of indicators for PHPs was suggested and thus incorporated. The set of indicators were validated by a team of experts from ACSoMP.

Figure 1



ACSoMP kicking off indicators in 2008, with Ambrose Isah, far right

## Characteristics and use

These indicators are robust, simple to understand, and it does not require great expertise to conduct the evaluation or monitoring, or to interpret the findings. Findings are likely to be reproducible irrespective of investigator. Again, the specificity and sensitivity of the indices will enable the detection of pharmacovigilance problems requiring attention as well as changes occurring in the pharmacovigilance systems.

It is intended that the indicators will be integrated into the healthcare system providing at a glance the pharmacovigilance perspectives. This can be achieved by periodic assessment which should range from monthly, annual and – for the more intensive outcome/impact indicators requiring surveys – every five years.

Importantly, there is a need for objectivity in assessment to provide objective measures to describe the pharmacovigilance situation in a country. The stakeholders are advised to read the manual and understand the contents in the sections on 'How to Use the Manual' and 'Description of Core Indicators'. The annex on the Assessment Checklist provides a ready-to-use template for collecting and reporting the value of each indicator.

## Where next?

This publication is version one, which implies an intention to have subsequent versions which will address any shortcomings observed in the present one. Improved future versions will depend on feedback from all stakeholders notably the national centres, who are urged to share their experiences. Further enquiries should be addressed to Dr Shanthi Pal ([pals@who.int](mailto:pals@who.int)).

It is also of interest that, even as the WHO indicators were being finalized for publication, the Indicator-based Pharmacovigilance Assessment Tool was published by Management Sciences for Health (MSH) / United States Agency for International Development (USAID). Both sets of indicators may provide information on pharmacovigilance in developing country settings. However, some basic differences remain in the number of indicators, and the mode of assessment; furthermore, and given the fact that the WHO pharmacovigilance indicators were shortlisted by the national centres themselves, the WHO indicators may be better suited for countries in their periodic self-evaluation of the pharmacovigilance systems and impact.

The painstaking effort of the entire WHO and UMC team, members of ACSoMP and the National Pharmacovigilance Centres of Member States in the process of consensus building, validation in the development and subsequent publication of this important pharmacovigilance tool is most commendable.

- \* A practical manual for the assessment of pharmacovigilance systems (accessible via [http://www.who.int/medicines/areas/quality\\_safety/safety\\_efficacy/en/](http://www.who.int/medicines/areas/quality_safety/safety_efficacy/en/))

The indicators described in Professor Isah's article have already been tried out by the medicines agencies in Kenya and Morocco. In addition, the indicators formed the basis of a Master dissertation on the pharmacovigilance system in Oman (see right column).

## Assessing a national system using the indicators

Madiha J. Almaskari

The purpose of my study was to assess the structure of a pharmacovigilance (PV) system in a developing country, namely Oman. The primary aim of this study was therefore to investigate the structure of Oman's pharmacovigilance system, and the secondary aim was to compare it with systems in developed countries in order to identify gaps and strengths in Oman and suggest solutions for any shortcomings. At the time of this study nothing had been published on the WHO PV indicators. In addition, this was the first study to compare the structure of a developing country's system with that of a developed country.

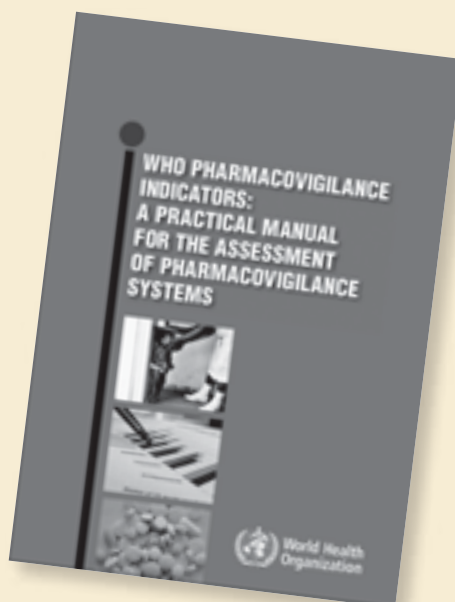
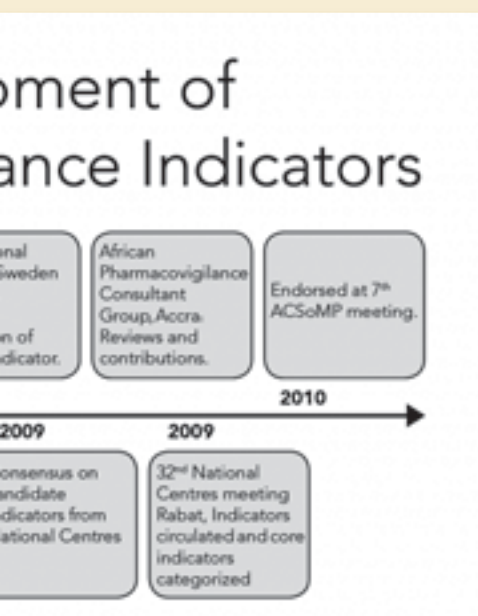
In this study, only the component assessing pharmacovigilance structure was used, consisting of two different types of questions: the core structure indicators (CSTs) and the complementary structure indicators (STs). A survey was conducted to investigate the pharmacovigilance structure in Oman and two developed countries were selected as comparisons, the Netherlands (Lareb) and Ireland (Health Products Regulatory Authority, HPRA), due to their different organisational structures. Oman's system is based on its Medicines Regulatory Authority (MRA), the same as in Ireland, but Lareb in the Netherlands is independent from the national MRA.

The pharmacovigilance system in Oman was found to operate with 35% of the CSTs, compared with 75% and 70% in HPRA and Lareb respectively. Moreover, 50% of the STs were found to be available, compared with 78% and 71% in HPRA and Lareb. Oman differs from Ireland and the Netherlands in the way these required structures are implemented. The results suggest that Oman's system has deficiencies and this confirms previous studies, which have identified similar challenges to the establishment of pharmacovigilance systems in developing countries.

The WHO PV indicators helped in detecting missing pharmacovigilance structural elements in Oman, and the comparison with developed countries' systems highlighted deficiencies and gaps.

Following implementation, the structure and outcomes of a pharmacovigilance system should be routinely measured with a validating tool, such as the WHO PV indicators to ensure the establishment of an effective, up-to-date system.

- \* An analysis of pharmacovigilance (PV) system structure in Oman using WHO PV indicators: comparisons with developed countries. Madiha J. Almaskari, School of Life Sciences, University of Hertfordshire, UK. E-mail: [madiha.juma@gmail.com](mailto:madiha.juma@gmail.com)



## Focus on harmony in Seoul

*Anki Hagström, Magnus Wallberg*

The 2015 APEC (Asia-Pacific Economic Cooperation) Harmonization Center ran a Pharmacovigilance Workshop and Training Program on 14–18 September 2015 in Seoul, Republic of Korea. The event was arranged as part of the on-going activities of the APEC Regulatory Harmonization Steering Committee Roadmap to Promote Regulatory Convergence on Pharmacovigilance.



*From left: Magaly Tito Yopez (Peru), María De La Luz Lara Méndez (Mexico), Hye ran Jang (APEC), Yeonjoo Lee (APEC), with Anki, Magnus and Malin (UMC) and Nahum Vergara Salazar (Chile) enjoying a traditional Korean dinner.*

### Workshop for all stakeholders

For the workshop on 14–15 September, regulators, industry representatives, and experts from academia were invited, and approximately

150 persons attended. The focus was on providing a forum to review the challenges and opportunities faced in regulatory harmonization, and the current status of pharmacovigilance within the APEC economies.

### System strengthening

The aim is to build and strengthen capacity for improvement of pharmacovigilance systems. Among others, the US-FDA, Health Sciences Authority (HSA) of Singapore, the Federal Commission for the Protection against Sanitary Risk (Comisión Federal para la Protección contra Riesgos Sanitarios, COFEPRIS) from Mexico, and national centres from Indonesia and the Philippines all contributed as speakers.

### Pilot training

The training programme on 16–18 September was intended to serve as a pilot programme, to train experts drawn from regulatory authorities, government-affiliated institutions, and international organizations in the APEC region. Anki Hagström, Magnus Wallberg and Malin Jakobsson contributed from UMC. Outcomes and feedback from the participants will be evaluated to plan for future training.

### Relaxing after work

The workshop and training did also leave some room in the evenings for excursions in the very interesting, high-tech city of Seoul. Modern art and buildings were combined with historical sites and traditional foods. We would like to send a big thanks to our hosts (especially Hye ran Jang, and Yeonjoo Lee from APEC Harmonization Center Secretariat) who showed us some secrets of Seoul and a small glimpse of the Korean way of life.

## Bustling paediatric meeting in Belgrade

*Kristina Star*

The 15<sup>th</sup> biennial congress of the European Society for Developmental, Perinatal and Paediatric Pharmacology (ESDPPP) was held in Belgrade, Serbia, from 23–26 June 2015. The scientific programme included reports from different paediatric networks, and covered the challenges of paediatric pharmacotherapy in different parts of the world and within different paediatric age groups, as well as the results from pharmacokinetic and other research studies.

While ESDPPP is a European society, it also raises awareness of the worldwide need for improving rational use of medicines for children. One such example was Dr Facundo Garcia Bournissen from Argentina, who presented the current situation for neglected paediatric diseases, such as Chagas disease, leishmaniasis and sleeping sickness. There is a lack of available drugs for some of these diseases, and the safety profile for the paediatric population is not always well-defined.



*The original and amusing programme cover for the ESDPPP congress in Belgrade*

I attended from the UMC and was delighted to chair one of the sessions. Despite the many challenges in the area of paediatric pharmacotherapy, the enthusiasm and optimism of the presenters and participants shone through, with the prospect of hope and progress in this field.



*The ultra-modern Dongdaemun Design Plaza, Seoul; from left: Shusen Liu (Merck Research Labs), Hye ran Jang (APEC), Anki, Yeonjoo Lee, (APEC) and Magnus.*

## One summer: four countries

*Elki Sollenbring*

Visiting our colleagues in their national centres is one of the great privileges we have in UMC's Global Services. To exchange knowledge and experiences and to meet face-to-face with people with whom we have communicated for a long time only through e-mail, is invaluable. To learn about their daily activities is the best way to understand their work and the importance of pharmacovigilance in each country.



*Discussions at a sentinel hospital in Guatemala*

During the Swedish summer (from June to August) I had the opportunity to visit four national centres; Costa Rica, Guatemala, Nicaragua and Mexico. Each country has a different way to manage its pharmacovigilance activities, the countries are at different levels of development, but the enthusiasm, commitment, delight and knowledge in our shared work is very similar.

### Always reaching out

One common activity for these countries is to raise awareness on the importance of



*Entrance lodge to the ministry of health in Nicaragua*

pharmacovigilance and reporting ADRs, still low for them, so they are constantly organizing workshops and meetings with health care professionals across their countries.

Mexico and Costa Rica have had a well-established centre for over 15 years, but it's still a big challenge to develop a system that covers the whole country. The centres in Guatemala and Nicaragua are newer but they are working hard to build up more stable national systems.

### Staffing

It was impressive that one of the centres has 25 staff, but unfortunately this is not the



*Staff of the national centre, Costa Rica*

I had the honour to be invited to visit sentinel hospitals in Guatemala, Nicaragua and Costa Rica to learn about their activities. It's fantastic how clinical pharmacists take part in the development of pharmacovigilance in these four countries.

I also participated in a four-hour workshop in Guatemala, which around 70 health professionals attended. This was also a wonderful occasion to exchange experiences and to present the WHO Programme.

### Data handling problems

Of course many things need to be improved, and a big challenge centres still have in Central America and Mexico is how to comply with international standards for ICSR (individual case safety reports) transmissions. The lack of safety databases that allow for seamless exchange of pharmacovigilance data between different organizations and stakeholders (health care professionals, patients, market authorization holders, public health programmes, immunization programmes, etc.) is still a major issue to be solved in this region.

norm in all countries. Pharmacists, physicians and secretaries are however present in most of the centres, the ideal scenario for a good, functioning centre in the region.



*Greetings from the pharmacovigilance staff in Mexico!*

## Coming back to Macau

*Sten Olsson*

Nine years after my first visit in Macau SAR (Special Administrative Region of China) for a pharmacovigilance training course I was delighted to be invited back by the Chief of Pharmaceutical Affairs, Dr Terry Choi.

### Herbals

A training workshop on drug safety and pharmacovigilance was organized by the Health Bureau and WHO on 22–23 August. WHO-HQ was represented by Dr Zhang Qi, Coordinator, Traditional and Complementary Medicine.



*Dr Zhang Qi*

He made a presentation on safety monitoring of herbal medicines against the background of the Macau Health Bureau recently being appointed a WHO Collaborating Centre for Traditional Medicine.



*Dr Terry Choi*

### Weekend study

The remaining sessions during the two days were shared between me and Dr Martin Huber from the German Federal Institute of Drugs and Medical Devices. We covered a wide range of subjects from consumer involvement, causality assessment, signal analysis, regulatory functions, medication errors, risk assessment, and good communication practice, to the global pharmacovigilance scenario.

The audience of 250 health professionals from Macau SAR gave up their weekends to update themselves on patient and drug safety.

### Reports from Macau

Discussions were held with representatives of the Department of Pharmaceutical Affairs about the formal requirements for connecting the Macau SAR pharmacovigilance programme to the WHO Programme for International Drug Monitoring. It was concluded that additional information needs to be acquired from WHO and the pharmacovigilance programme of mainland China before the issue can be resolved.

## Encore in Brazil

*Elki Sollenbring*

The ISO-P Latin-American chapter held its second symposium of 2015 in early September in the Public Health School, São Paulo University adding further to the considerable growing cross-continental dialogue. With speakers from Brazil, Argentina, two members of the ISO-P Executive Committee and Pia Caduff and myself from the UMC, practical topics of pharmacovigilance, as well as the most recent challenges in drug regulation and use were discussed.

### Keen focus

The current position of spontaneous reporting as well the potential use of patient registries received particular focus. Over a hundred participants attended from Brazil, Venezuela, Argentina, Paraguay, Guatemala, Panama and Colombia.

## Anniversaries in Mexico

*Miriam Sánchez Arroyo*

Since its foundation in May 2005, the Mexican Pharmacovigilance Association (AMFV) has contributed to enhancing pharmacovigilance and technovigilance activities in Mexico. Our associates are a multi-disciplinary group of healthcare professionals who are interested in the safety of medicines and medical devices for the benefit of Mexican patients and consumers.

Since 2007 an annual congress has taken place and in this, our tenth anniversary year, the Association held its 9<sup>th</sup> National Congress in June at the World Trade Center in Mexico City, in collaboration with the national pharmacovigilance centre at the Federal Commission against Sanitary Risks (COFEPRIS). There were 371 participants, 19 invited speakers (including Elki Sollenbring of the UMC) and 24 posters.

A broad range of topics went beyond popular subjects to include the safety of biotech products, technovigilance, safety in hospitals and inspections. We were also introduced to the video of Take&Tell, which offered us a simple but clear message for all to be active about our own health and wellbeing.

Take a look at our website (Spanish) : [www.amfv.org.mx](http://www.amfv.org.mx)





# VigiLyze improvements

Monica Plöen, Anders Viklund

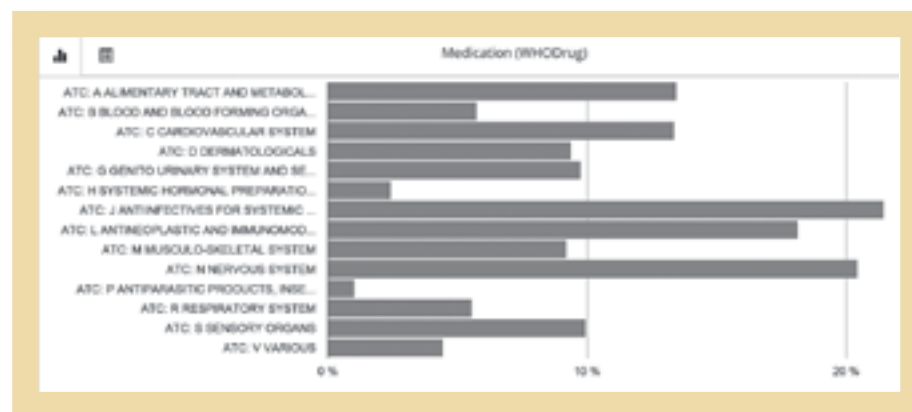
UMC is currently working on a new version of VigiLyze™. The release is planned for late 2015 or early 2016. With this release, VigiLyze will get a brand new appearance that uses the computer screen width more optimally.

The Silverlight plug will not be needed any more. The new version is built on a modern platform compatible with most common browsers. Searches will now be more exact since the result may be displayed on the lowest level terms in both WHO-ART and MedDRA.

Equally, when drilling down in the reaction graph users can now do the same for the drugs, from ATC down to trade name.

In the upcoming releases we are planning to implement Standardised MedDRA Queries (SMQs) and disproportionality data. Watch out also for webinars hosted by UMC to get a quick start to the new version of VigiLyze.

Background information on VigiLyze is available at the UMC's website: Public Services > Pharmacovigilance > Tools > VigiLyze.



New look and new searching in VigiLyze



## Asia Pacific training

Uppsala Monitoring Centre and JSS University Mysore are pleased to announce that following the successful Asia Pacific pharmacovigilance training course in Mysore, India in 2015, the next course will take place from 18 to 29 January 2016 in Mysore.

This course provides solid practical foundations for those working in drug safety as well as updates for experienced staff. The aim of the course is to develop pharmacovigilance knowledge and skills among health professionals in Asia Pacific.

For more information go to <http://jsspharma.org/node/502>

## Ministerial visit

The UMC received a visit from a delegation from the Swedish Ministry of Health and Social Affairs (Socialdepartementet) at the beginning of October.

have the opportunity to introduce our visitors to UMC's work, and we look forward to finding new ways to collaborate in the future!

The delegation came to discuss the best way for the two parties to exchange knowledge and share information. We were happy to



Swedish Ministry of Health and Social Affairs visitors and UMC managers

# A woman is not like a man

Why sex differences and disparities matter so much in healthcare and risk communication

Bruce Hugman

Few readers of Uppsala Reports are likely to argue with the title of this article, though many might be surprised at the extent to which differences between the sexes are often ignored or downplayed in medicine and patient safety; they might also be shocked at the dangerous disparities in healthcare access and quality between the sexes in many parts of the world.

## Health and sickness

We know, for example, that women with chest pain or other urgent heart symptoms are often treated less effectively than men and that they have worse outcomes. On the whole, women do live longer than men, but they suffer from more illness and disability, report more pain and suffer from a higher incidence of adverse reactions to medicines. Women's bodies process and eliminate drugs in quite different ways from men's; many physical experiences and conditions are unique to women and some of them – menopause, pregnancy and eating disorders, for example – are neglected in research and poorly understood by men.

Even when women are represented equally in clinical trials, there may be no specific recommendations for prevention and treatment for them. The absence of pregnant, lactating and elderly female subjects from almost all trials contributes to women's greater risk in general of exposure to unsafe medications and drug interactions.

These are all issues that regulators and health professionals must factor into their understanding of what they are doing and into the communications they have with women about medicine in general and about risk in particular. Everything needs to be subject to a gender-based analysis that may turn up alternatives for understanding or action quite different from those suggested by routine – and gender-blind – data, information or practice.

## The context of women's lives

The purpose of risk communication in clinical practice is to inform and protect; to support wise, balanced and rational decisions that match patients' wishes and needs. The risks that women face, and the assessments they must make about benefit and harm, exist in a complex psycho-socio-politico-cultural

context which those communicating with them must understand if they are to be effective.

Women have wide-ranging preferences about the source of their risk information and those they regard as trustworthy (mothers, women or medics of their own ethnic group, female providers, other peers, for example); they also have strong views

Differences between the sexes are often ignored or downplayed in medicine and patient safety

Women have wide-ranging preferences about the source of their risk information and those they regard as trustworthy

about consultation and decision-making style (participative or delegated, for example). They are very sensitive to individual or institutional gender-bias and may, even to their own disadvantage, avoid services they perceive as lacking in respect or empathy (such services often male-dominated). Given choices, women have very particular and divergent preferences in contraception and in benefit-harm assessments that affect, for example, their physical appearance and their self-image.

## Suffering and abuse

Women everywhere are subject to male oppression and violence on a scale that is astonishing. Male dominance in some cultures will mean women may not seek medical services without permission or an accompanying relative, if at all; women may have no say in family planning matters and maybe no respite from multiple pregnancies; many women will sacrifice their own health needs to care for their homes or land. Young brides may be fattened up in fulfilment of male fantasies of female beauty while others will threaten their health in the pursuit of unnatural body-image or skin colour that follows the current trend.

Suffering of this kind, as well as physical abuse or more elusive anxiety or depression, may not be talked about at all; we know that only a small percentage of women report abuse and that young people, engaged in all

kinds of risky activity, rarely tell their health providers or anyone beyond their peers about it. Many more young women than young men plan to kill themselves and do so.

## What does it mean for practice?

Women face a number of categories of risk that professionals, in every aspect of regulation and practice, must take account of. First, the risks of all medicines and medical interventions, with the additional dimension of insufficient account being taken of the differences between men and women. Second, the risks inherent in a deficient and gender-biased healthcare system, including its individual agents. Third, the impact of the overt and hidden risks of women's lives that impinge radically on their health, freedom and happiness, in ignorance of which no effective healthcare or meaningful communication can be provided.

Risk communication for women requires an extraordinary degree of knowledge, commitment, empathy – and determination to provide service that is uniquely targeted to women and at least as good as that offered to men.

*This article is based on Bruce's two chapters (18 and 19) in Harrison-Woolrych (Ed.), Medicines for Women, Adis Press, 2015 (see review in UR69 p21). Extensive references can be found at the end of the two chapters.*

*The topic is also featured in this year's ISoP annual meeting in Prague.*

# ACC: in Accra for Africa

Alex Dodoo

Remarkable progress has been made in pharmacovigilance on the African continent, to the extent that current discussions have shifted from whether pharmacovigilance is needed at all in Africa to how best to ensure optimum deployment of pharmacovigilance systems on the continent. All pharmacovigilance stakeholders in Africa including the WHO, the UMC and the African Union are aware of the potential for Africa to "leapfrog" some of the evolutionary problems that were encountered in ICH countries.

## Key milestones

African countries are already talking of "longitudinal datasets", "outcomes of PV", "metrics for measuring PV activity" and "integrated PV systems" to name but a few. To ensure that the traction so far gained is sustained, it is important to outline some of the key developments that have led to success so far including, but not limited to, the following:

1. The training and capacity-building activities undertaken by the World Health Organisation in Africa in the 1990s, but more actively from 2000 either alone or in collaboration with the Uppsala Monitoring Centre and the Moroccan National PV Centre (CAPM)
2. The establishment in June 2009 of the African hub of the Uppsala Monitoring Centre (dubbed UMC-Africa) with dedicated funding and support to spread the PV message in Africa and bring more countries into the WHO Programme for International Drug Monitoring. (The name UMC-Africa is no longer used since the activities of UMC-Africa have been merged with those of the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, Accra, Ghana.)
3. The designation in October 2009 of the University of Ghana as a WHO Collaborating Centre (WHO-CC) for Advocacy and Training in Pharmacovigilance. The WHO-CC has clear terms of reference in line with WHO procedures and worked very closely with UMC-Africa to promote PV in Africa. It has subsequently taken over all the activities of UMC-Africa which no longer exists as a separate entity
4. The designation in November 2011 of Morocco's national centre as a WHO Collaborating Centre for Pharmacovigilance. The terms of

reference of this centre includes among other things "to conduct and facilitate regional and national pharmacovigilance training courses for Francophone, Eastern Mediterranean and Arabic countries", an activity it has been undertaking for several years and which has benefited many Francophone African countries

5. The designation in May 2014 by the African Union's 'African Medicines Regulatory Harmonisation' project ([www.amrh.org](http://www.amrh.org)) of the University of Ghana Medical School as an African Regional Centre of Regulatory Excellence (RCORE) in pharmacovigilance. This is part of a consortium including the WHO-CC, Quintiles plc and the national centres of the medicines regulatory agencies of Ghana (Ghana FDA), Nigeria (NAFDAC), Tanzania (TFDA) and Zimbabwe (MCAZ).

The birth of the ACC gives a platform for the various players to engage with each other and to take forward the science and practice of pharmacovigilance. The individual initiatives and designated centres will continue to work as normal but ACC will be a key point for pharmacovigilance in Africa, especially sub-Saharan Africa. This prevents the challenges associated with meeting the designation requirements and rules of the different global agencies like the World Health Organisation and the African Union.

Governance and leadership of the ACC involves not just Ghanaians but also all stakeholders in Africa, including external and African experts, as well as African and international organisations and agencies. For pharmacovigilance in Africa, look for the new name: ACC – African Collaborating Centre for Pharmacovigilance.



*The African Collaborating Centre for Pharmacovigilance*

## Enter a new centre

With so many players and partners, and with so many acronyms, designations and recognitions, it is easy for anyone to get lost in the myriad of institutions, initiatives, players, roles and activities. To prevent redundancies as well as foster sustainability and prevent the obvious confusion associated with all the good things going on in Africa, the African Collaborating Centre for Pharmacovigilance (ACC) has been established as a legal not-for-profit entity in Accra (airport code: ACC), Ghana as a convening and converging point for "all things PV in Africa".

## Varenicline and abnormal sleep-related events

Ruth Savage

Varenicline is used as an aid for cessation of tobacco smoking. This case series study from Vigibase™ was initiated by one of the authors who observed that a number of reports of somnambulism and nightmares associated with varenicline use included ADR terms indicating harm or potential harm to the patient or others. It was unclear if these actions occurred during sleep or wakefulness. The national centres who submitted the reports kindly supplied additional details.

The authors identified 10 adults who became aggressive during sleep and almost or actually assaulted their bed partner, usually in the context of violent dreams. The descriptions were similar to conditions known as rapid eye movement sleep disorder and nonrapid eye

movement sleep parasomnias in some adults. Another seven adults were not aggressive but their activities included apparently deliberate self-harm, moving a child, driving and lighting a stove. The patients were often very distressed and some developed psychiatric symptoms because of these experiences.

A causal relationship between varenicline and these abnormal sleep-related events was supported by the observations that comorbidities and concomitant medicines did not suggest an alternative cause and nine of the seventeen patients had recovered or were recovering after stopping varenicline. Furthermore, sleep-related aggression and other harmful activities are not recognised symptoms of nicotine withdrawal.

Some patients had several nights of distressing or violent dreams before they became active during sleep. The authors concluded that patients who develop very disturbing or violent dreaming while taking varenicline should be advised to consult their health care providers.

The authors were Dr Ruth Savage from the New Zealand Pharmacovigilance Centre, University of Otago, and the UMC, and Alem Zekarias and Dr Pia Caduff-Janosa from the UMC.

Savage, R.L., Zekarias A. and Caduff-Janosa P. Varenicline and abnormal sleep related events. *Sleep*, 2015. 38(5): 833-7.

## Resource-limited pharmacovigilance

Sten Olsson

This open access review article starts by briefly describing the context in which pharmacovigilance is operating in resource-limited countries. Examples are given of how existing pharmacovigilance systems have been established in the environment and the specific challenges they are facing. The importance of political commitment to patient safety, expressed in a supportive regulatory framework and a sustainable budget for pharmacovigilance is discussed.

The article refers to the different stakeholders that need to be engaged and their roles, e.g., academic institutions for capacity building, public health programmes, and marketing authorization holders for data acquisition and information. Methods suitable for pharmacovigilance in public health programmes are explored and concern about the inadequate exchange of safety information between national immunization programmes and medicine regulatory authorities is noted.

Suggestions are made for how to leverage modern technology such as mobile phones and electronic health records, to improve the collection of safety data, and the importance of engaging not only healthcare professionals but also the general public and traditional therapists in the collection and interpretation of relevant safety information.

The importance of research in documenting the burden of medicine-related harm in local communities is emphasized. The authors also propose that the WHO pharmacovigilance indicators be used to document the status and gaps of pharmacovigilance programmes and the effects of investments in development.

The supportive role of the WHO Programme for International Drug Monitoring and its WHO Collaborating Centres for the development of pharmacovigilance in resource-limited countries is described. The

benefit for pharmacovigilance of regulatory harmonization activities that are currently taking place in different regional fora is also mentioned.

Olsson S., Pal S.N., Dodoo A. Pharmacovigilance in resource-limited countries. *Expert Review of Clinical Pharmacology* (2015) DOI 10.1586/17512433.2015.1053391

## Statistical signal detection

The UMC research team have recently also been involved in a study to compare statistical methods used in signal detection.

The full paper is available as a free open access document via <http://link.springer.com/article/10.1007/s40264-015-0345-1>

Candore, G., K. Juhlin, K. Manlik, B. Thakrar, N. Quarcoo, S. Seabroke, A. Wisniewski and J. Slattery, Comparison of statistical signal detection methods within and across spontaneous reporting databases. *Drug Safety*, 2015. 38(6): p. 577-87.

## 'Drugs and Bugs' explains big issues to small readers

*Alexandra Hoegberg*

Why do people get sick? What's a virus? Who invents medicine, and what do they put in it? 'Drugs and Bugs – A little book about medicine' is a children's book that sets out to answer those questions in a fun and engaging way, without skipping any of the important facts about medicine, diseases and the human body.

We sponsored the reprint of 'Drugs and Bugs', as we believe that enhancing children's understanding of medicine and health can only have a positive impact. The book is provided free of charge; send a request to [info@who-umc.org](mailto:info@who-umc.org) for more information.



*In the world of 'Drugs and Bugs', bacteria are illustrated as dragon-like creatures and white blood cells are tiny police officers guarding the body.*

# Accra gears up for ASoP

Haggar Hilda Ampadu

It is beginning to appear that the "must be" PV event in any low or middle-income country (LMIC) in 2015 is the 2<sup>nd</sup> African Society of Pharmacovigilance (ASoP) conference being held in Accra, Ghana from 25-27 November 2015.

Under the theme "*Pharmacovigilance in Africa: New Methods, New Opportunities, New Challenges*" ASoP-2015 has confirmation of attendance by key global leaders including the Deputy Director-General of WHO, Dr Anarfi Asamoah-Baah and Chairperson of the EMA's Pharmacovigilance and Risk Assessment Committee (PRAC), Dr June Raine.

Other speakers, in addition to industry experts, include the Director of the Uppsala Monitoring Centre, Dr Marie Lindquist; the

Coordinator for Safety and Vigilance, WHO, Dr Clive Ondari, the Head of PV, WHO, Dr Shanthi Pal, as well as Lead Expert for pharmacovigilance at the Bill and Melinda Gates Foundation, Dr Raj Long.

As well as the hectic and intellectually stimulating scientific discussions there is also a busy and exciting social programme, including a street party and a conference gala dinner / beach party on the Gulf of Guinea in sizzling temperatures accompanied by fine cuisine and excellent entertainment.

ASoP-2015 is open to all stakeholders in pharmacovigilance across the globe. Official languages are English and French, and interpretation services will be available. The registration portal is extremely easy and fully secure so participants can pay the

conference fees and/or hotel expenses directly by credit or debit cards or by wire transfer.

Accra is ready for the world at the end of November. Is there any reason why anyone will miss this opportunity to network, improve public health and contribute to making everyone safer in relation to the use of medicines, vaccines and all other medical products? The World Bank Group, WHO, the African Union and the global pharmacovigilance community will be there.

Further information on ASoP-2015 is available from [www.asop2015.com](http://www.asop2015.com) or directly from the Chairperson of the Organising Committee: Ms Haggar Hilda Ampadu ([haggar.ampadu@who-pvafrica.org](mailto:haggar.ampadu@who-pvafrica.org)).

## Time to sign up!

UMC is pleased to announce its 18<sup>th</sup> international pharmacovigilance training course, which will take place in Uppsala, Sweden, 16-27 May 2016.

The aim of the course is to further develop sustainable and effective pharmacovigilance in countries, by creating a space of learning and collaboration. Participants will benefit from theoretical and practical knowledge essential to initiate and develop pharmacovigilance plans in their own countries. The interaction among participants will provide an ideal platform to improve pharmacovigilance and build important relations at a local, regional and global level.

The course focuses on topics essential to effective pharmacovigilance including sessions to strengthen the overall WHO Programme: pharmacovigilance best practices, signal detection, regulatory aspects, reporting culture and pharmacovigilance tools.

The programme also includes a management component designed to help participants improve their capacity to influence sustainable change in their countries. Issues related to health economics, pharmaco-epidemiology, communications, fundraising and risk management will be covered.

More detailed course information and application details will be available on the UMC website in October: [www.who-umc.org](http://www.who-umc.org). Due to the limited number of places we would recommend you to sign up early.

Questions regarding the course can be sent to: [pvtraining@who-umc.org](mailto:pvtraining@who-umc.org)

We are looking forward to receiving your application!

## Cup winner

Not many UMC staff compete in sports at a global level, but **Anette Sahlin** achieved a superb 2<sup>nd</sup> place in the World Football Golf Championships in Rumburck (Czech Republic) in August. Playing with Simon Bruce from Alunda, Sweden, they overcame fierce opposition to raise the runners-up cup. Congratulations to Anette!



*Anette and Simon on the podium in Rumburck*

DATES	TITLE	PLACE	ORGANISER/CONTACT
5-6 November 2015	Signal Management in Pharmacovigilance	Paris, France	DIA Europe <a href="http://www.diahome.org/en-GB/Meetings-and-Training/">www.diahome.org/en-GB/Meetings-and-Training/</a>
9-10 November 2015	Post-marketing drug safety and pharmacovigilance	Philadelphia, USA	DIA <a href="http://www.diahome.org/en-GB/Meetings-and-Training/">www.diahome.org/en-GB/Meetings-and-Training/</a>
10-12 November 2015	Monitoring the Effectiveness of Risk Minimisation	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 <a href="http://www.dsru.org/trainingcourses">www.dsru.org/trainingcourses</a> E-mail: <a href="mailto:jan.phillips@dsru.org">jan.phillips@dsru.org</a>
14-16 November 2015	The ISPE 9 <sup>th</sup> Asian Conference on Pharmacoepidemiology	Bangkok, Thailand	ISPE <a href="http://www.pharmacoepi.org/">http://www.pharmacoepi.org/</a>
16-17 November 2015	New EU Pharmacovigilance Legislation	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 <a href="http://www.management-forum.co.uk">www.management-forum.co.uk</a> E-mail: <a href="mailto:registrations@management-forum.co.uk">registrations@management-forum.co.uk</a>
18-19 November 2015	6 <sup>th</sup> Annual Pharmacovigilance Asia 2015	Singapore	Tel: +65 6722 9388 E-mail: <a href="mailto:enquiry@iqpc.com.sg">enquiry@iqpc.com.sg</a> <a href="http://www.pharmacovigilanceasia.com/">www.pharmacovigilanceasia.com/</a>
18-19 November 2015	Pharmacovigilance 2015 : 'Ensuring Drug Safety, Ensuring Life'	London, UK	IQPC <a href="http://www.recunnect.com/pharma-events/pharmacovigilance-2015/">http://www.recunnect.com/pharma-events/pharmacovigilance-2015/</a> E-mail: <a href="mailto:info@recunnect.com">info@recunnect.com</a>
18-19 November 2015	Pharmacovigilance in Products Subject to Licensing Agreements	London, UK	Drug Safety Research Unit (See above for contact details)
24 November 2015	4 <sup>th</sup> Nordic Pharmacovigilance Conference	Stockholm, Sweden	Läkemedelsakademin <a href="http://www.lakemedelsakademin.se/templates/kurs/kurstillfalle.aspx?kld=6101&amp;tid=6102">www.lakemedelsakademin.se/templates/kurs/kurstillfalle.aspx?kld=6101&amp;tid=6102</a>
25-27 November 2015	2 <sup>nd</sup> African Society of Pharmacovigilance (ASoP) conference 'Pharmacovigilance In Africa : New Methods, New Opportunities, New Challenges'	Accra, Ghana	ASOP 2015 <a href="http://www.asop2015.com">www.asop2015.com</a> E-mail: <a href="mailto:info@asop2015.com">info@asop2015.com</a>
7-9 December 2015	Pharmacovigilance	London, UK	Management Forum Ltd (See above for contact details)
18-29 January 2016	Asia Pacific pharmacovigilance training course	Mysore, India	JSS University, UMC <a href="http://jsspharma.org/node/502">http://jsspharma.org/node/502</a> E-mail: <a href="mailto:pvtraining@jssuni.edu.in">pvtraining@jssuni.edu.in</a>
20-22 January 2016	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (See above for contact details)
24-27 January 2016	Pharmacovigilance and risk management	Washington DC, USA	DIA <a href="http://www.diahome.org/en-GB/Meetings-and-Training/">www.diahome.org/en-GB/Meetings-and-Training/</a>
24-25 February 2016	Back to Basics in Pharmacovigilance	Fareham, UK	Drug Safety Research Unit (See above for contact details)
14-16 March 2016	Advanced Pharmacovigilance	London, UK	Management Forum Ltd (See above for contact details)
9-20 May 2016	10 <sup>ème</sup> Cours Francophone de Pharmacovigilance	Rabat, Morocco	Centre Anti Poison et de Pharmacovigilance du Maroc <a href="http://www.capm.ma/">www.capm.ma/</a>
16-27 May 2016	18 <sup>th</sup> International Pharmacovigilance Training Course	Uppsala, Sweden	Uppsala Monitoring Centre <a href="http://www.who-umc.org">www.who-umc.org</a>
30-31 May 2016	Uppsala Forum 2016 – Inspiration in the science of pharmacovigilance	Uppsala, Sweden	Uppsala Monitoring Centre (See above for contact details)
8 - 9 June 2016	Global Regulatory Pharmacovigilance Environment	London, UK	Drug Safety Research Unit (See above for contact details)



**Uppsala  
Monitoring  
Centre**

– Building a global safety culture

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

Many of our services and products have been developed as a result of our responsibility – as a World Health Organization Collaborating Centre – for managing the WHO pharmacovigilance network of over 120 countries and the WHO global individual case safety report database, VigiBase®. A core function is the screening and analysis of data with the aim of detecting potential issues of public health importance in relation to the use and safety of medicines. Other services include technical and scientific support to WHO and its member countries, and provision of tools, such as VigiLyze™ and VigiFlow®, for data entry, management, retrieval and analysis.

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

## Communications information

### Visiting address

Uppsala Monitoring Centre  
Bredgränd 7  
SE-753 20 Uppsala  
Sweden

### Mail Address

Box 1051  
SE-751 40 Uppsala  
Sweden

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

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

### E-mail:

General enquiries: [info@who-umc.org](mailto:info@who-umc.org)

Personal e-mail messages may be sent to any member of the team by putting their name (e.g. [sten.olsson](mailto:sten.olsson@who-umc.org)) in place of info

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

A 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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