

MUR67



vigiRank | New collaborations in Africa

Complete reports | Medication errors guide



Marie Lindquist
Director
Uppsala Monitoring
Centre

*Can an organisation – be it Google, your local shop, or UMC – have a soul? Or, perhaps more importantly, does an organisation **need** a soul? My answer to both questions is “yes”.*

“Is she losing her mind now?” you may wonder, talking about an organisation as a living being. Yes, that’s exactly what I am talking about! And as far as I know, my head is still screwed on properly. My purpose is to argue that an organisation must have something in addition to its tangible assets in order to thrive. This, to me, is ‘soul’. The Oxford dictionary offers one relevant definition: “A person’s moral or emotional nature or sense of identity”. If we exchange ‘person’ for ‘organisation’, this definition describes pretty well what I am after: the spiritual dimension, the essence of a being, that depends on meaning and values as well as on the lifeblood of an organisation – its people – but which goes far beyond seeing them as mere resources or assets on a balance sheet.

*Only when every staff member is acknowledged and genuinely valued for **what they are**, and when they feel that the vision and values of their organisation are right **for them**, do we have the seeds from which a good soul may grow and be sustained. This requires a management with empathy and humanity, the ability both to understand and appreciate each individual; and employees with maturity and insight into who they are and how they can positively contribute to the soul of the organisation.*

Many leaders today are determined that their organisation should contribute something good to society, and create ‘core value’ statements intended to reflect the soul of their organisation in a positive light. If done in the right way, this activity can build a good spirit among staff and help communicate the depth and breadth of what an organisation stands for. But, unless each individual in the organisation truly encompasses the expressed values – as part of their own soul – there is an obvious danger:

*producing a value statement becomes just a token exercise, something that can be ticked off as part of dutiful adherence to some notion of Good Management Practice. It may well have the opposite effect to the one intended; we are all familiar with buildings and businesses that are **soulless**. Employees may end up alienated and frustrated by yet another wordy pronouncement enforced upon them from above, and customers and clients lose trust in, and respect for, an organisation that has pretensions and makes promises it does not live up to.*

Working to implant an organisation’s values must never be a one-off project – there needs to be constant dialogue, both within and outside the organisation; asking questions such as who we are, why we are here, for whom, and how we should conduct ourselves with colleagues, partners, and customers. The internal reality must set and match external expectations – otherwise we have a big

problem! We need to define what the core values mean in practice, translating them to acceptable behaviours that everyone agrees to, and lives by, day to day. Every staff member can, and should, contribute to this work in their own unique way. Whilst I believe it is critical to have shared core values in any group of people working together, there must also be plenty of room for individuality in terms of personality,

creativity, skills and experience.

Personally, I am very attracted by the thought of the brick-layer who said he was building a cathedral (see text box); but we do need people who will be content laying bricks and building walls as well as the visionaries. What I cannot accept is a person who is interested in neither the cathedral, nor in doing a good job with the bricks!

A man came upon a construction site where three people were working. He asked the first, “What are you doing?” and the man replied: “I am laying bricks.” He asked the second, “What are you doing?” and the man replied: “I am building a wall.” As he approached the third, he heard him humming a tune as he worked, and asked, “What are you doing?” The man stood, looked up at the sky, and smiled, “I am building a cathedral!”

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

UMC's vision and its approach to communications appear on page 22.

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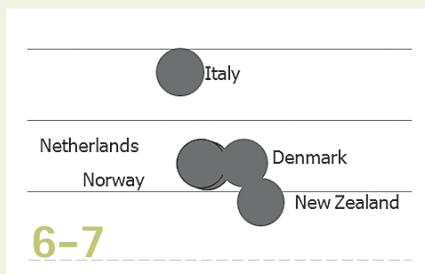
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ADR statistics

A closer look at completeness versus reporting rate.

Major advance in signals

A new method will help identify risks to patients that would otherwise go undetected, or be delayed.



The role of Collaborating Centres

Centres with interest in drug safety meet for the first time.

Recent new books

Publications from WHO and CIOMS are new on the bookshelf this quarter.



New associate member

Following a mission by staff of WHO Collaborating Centre-Africa, the Ministry of Health of the Kingdom of Swaziland applied to the WHO in September for the Swaziland National Pharmacovigilance Centre at the Ministry of Health to become a member of the WHO Programme for International Drug Monitoring. They have now been accepted as an associate member of the Programme.

The key persons at the Swaziland National Pharmacovigilance Centre are:

Ms Fortunate Fakudze, Chief Pharmacist
Mrs Nomsa Shongwe, Pharmacovigilance Focal Person



The WHO Country Representative Dr Owen Laws Kaluwa, his staff, a representative from the Ministry of Health and the mission team in Swaziland.

WHO and open access

A new policy on open access came into force at WHO on 1 July 2014 making work by WHO authors, or funded by WHO, that is published in external journals or books, fully accessible to readers free of charge.

The information that WHO publishes is freely available on WHO's website www.who.int. The objective of the new WHO policy on open access is to ensure that articles or chapters published in non-WHO publications authored or co-authored by WHO staff, or

produced by individuals or institutions funded in whole or in part by WHO, are now also freely available to the public.

To allow WHO staff to publish in open access journals, WHO together with other major intergovernmental organizations has negotiated with Creative Commons a special licence appropriate for them (CC 3.0 IGO) http://www.wipo.int/pressroom/en/articles/2013/article_0026.html

All WHO-authored and WHO-funded work produced under the terms of the policy will be deposited in Europe PubMed Central. Such work will also be available in WHO's Institutional Repository for Information Sharing (WHO IRIS). See also <http://www.who.int/about/policy>

Ebola – the safety angle

Sten Olsson

Ebola virus disease (EVD) is currently in the general news and consuming much time and effort in the medical fraternity to slow and stop the human suffering in several parts of Africa. The virus, transmitted to people from wild animals, spreads in the human population through human-to-human transmission. At present WHO considers the average EVD case fatality rate to be around 50%.

The current outbreak in West Africa is the largest and most complex Ebola outbreak since the virus was discovered in 1976. More cases and deaths have occurred in this outbreak than all others combined. The situation is compounded by weak health systems and infrastructure in some of the countries affected.

A range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. No licensed vaccines are available yet, but two potential vaccines are undergoing human safety testing.

On 5 September 2014 WHO issued a Statement on the WHO Consultation on Potential Therapies and Vaccines.

The Statement noted the possibility of adverse side effects when potential therapies and vaccines are administered. It opined that study design for these should be based on the aim "to learn as much as we can as fast as we can without compromising patient care or health worker safety, with active participation of local scientists, and proper consultation with communities", and this would demand that:

- appropriate protocols must be rapidly developed for informed consent and safe use
- a mechanism for evaluating pre-clinical data should be put in place in order to recommend which interventions should be evaluated as a first priority
- a platform must be established for transparent, real-time collection and sharing of data
- a safety monitoring board needs to be established to evaluate the data from all interventions.

The main WHO website has a growing amount of useful information to read and download. www.who.int

Forms, Apps, Electronic records

Marie Lindquist

The 2014 meeting of the Advisory Committee for Safety of Medicinal Products (ACSoMP), which provides expert advice to the Safety and Vaccines department at WHO, took place in May in Geneva. The Committee's twelve members are drawn from national pharmacovigilance centres and WHO Collaborating Centres (see box). As ever, wide-ranging discussions filled the three days.

Forms and formats

A major area of discussion concerned ADR reporting forms, the type of data fields on them and the formats of those fields. The existing comprehensive document (Sten Olsson and Bruce Hugman, *Drug Safety*, 2008) was reviewed, and the importance of emphasizing the broadening scope of pharmacovigilance in any guidance was agreed.

Likewise, forms are not static – they need to reflect current scope and practices, and the Committee felt that it should aim to meet user requirements and reflect reality. Questions about whether ADR forms collect the right information, and striking a balance between national 'ownership' of each form and there being a model form with the 'WHO stamp' were considered.

Apps

Methods for communicating reports have to keep pace with evolving technology use. Experiences from the use of mobile apps for ADR reporting in the UK, Ghana, USA, New Zealand and Kenya were shared and discussed. A wider look at the research-based evidence for development of appropriate policy and technology solutions is needed.

The technical considerations in app use – E2b compatible, dictionaries, identification of sender, feedback to sender, commercial vendors or in-house development? – all need to be carefully weighed up. One of the UMC's aims is to make sure that patient-generated data will eventually be channelled into VigiBase.

My vision is to have an intelligent feedback system, linking data collection at the point of care (for example using apps) to data in VigiBase. Not so much statistical as tailored information based on the real patient.

Electronic Health Records

Electronic medical records can provide valuable data in the pursuit of patient safety.

A concept note describing the usefulness of EHR was proposed. The possibility to improve patient care, with responsive systems that ask relevant questions at the point of data entry has the potential to assist clinical decision-making, although there are barriers to the implementation of EHR in low- and middle-income countries.

There are also possible links with data collected as part of cohort event monitoring studies. There may be limitations in EHR further along at the stage of signal detection (of rare reactions) unless they include many more patients than today's systems.

Risk minimization policies

We had a presentation outlining the pharmacovigilance centre view on risk minimisation actions.

Public health systems should build risk minimisation plans to complete those produced by industry; roles around patient safety objectives should be reinforced; proactive pharmacovigilance should be developed to minimise harm; and guidance is needed for pharmacovigilance centres.

Regional issues

The Committee heard about database harmonization initiatives in Africa (African Medicines Regulation Harmonization, AMRH). Those on the table at Asia-Pacific Economic Cooperation (APEC) for Asia-Pacific countries were mentioned (see UR64 p8-9). The desire for signal detection tailored for LMICs (low- and middle-income countries) led to a wider examination of where signals are going.

UMC reports

The UMC's input to two ACSoMP-related projects was presented. The pilot project evaluating an algorithm for detecting SSFFC products through pharmacovigilance data had been able to take into account unexpected geographical and time clusters. UMC tools were also able to compare a local spike in reactions with global data.

A second project, looking at possible dependence-causing drugs had been undertaken and the data analysis could be incorporated in UMC signal detection processes.

Advisory Committee on Safety of Medicinal Products members 2014

Gerald Dal Pan
Office of Surveillance and Epidemiology/CDER
US FDA

Kenneth Hartigan-Go
Food and Drug Administration
The Philippines

June Raine
Medicines and Health Care Products Regulatory Agency (MHRA)
United Kingdom

Gunilla Sjölin-Forsberg
Council for International Organizations of Medical Sciences (CIOMS)
Switzerland

Peter Arlett
European Medicines Agency

Claudia Vaca-Gonzalez
Universidad Nacional de Colombia

Li Fang
Division of Drug Monitoring and Re-evaluation
Department of Drug and Cosmetics Supervision
China

Gugu Mahlangu
Medicines Control Authority of Zimbabwe

Ananda Amarasinghe
Epidemiology Unit, Ministry of Health
Sri Lanka

WHO Collaborating Centres

Marie Lindquist
The Uppsala Monitoring Centre

Alex Dodoo
Centre for Tropical Clinical Pharmacology & Therapeutics
Ghana

Rachida Soulaymani-Bencheikh
Centre Anti Poisons et de Pharmacovigilance
Morocco

Reporting trends

Cecilia Biriell

Quantity and quality matter

Every six months the overall reporting of Individual Case Safety Reports (ICSRs) to the WHO Global ICSR database is presented in *Uppsala Reports*. Case reports from all over the world continue to come in to the database at a steady pace. In the last UR we could report about passing the milestone of 9 million ICSRs, and by September 1st the number had already increased to 9,383,954.

During the last few years almost one million case reports have been reported each year, and with the backlog of case reports from both China and France soon to enter VigiBase we can expect the 10 million milestone to be reached around the end of this year.

Quantity and quality

UMC is constantly repeating that both quantity in reporting and quality of the individual case reports are important to make the WHO database a useful information resource. A third factor is also timeliness – that case reports are entered into the national databases as soon as possible and regularly forwarded to UMC. There can be various reasons why this does not always happen.

So far we have only described in graphs how regularly national centres have submitted batches of case reports to VigiBase (see for example UR63), but not how long a time it takes from the onset of an adverse reaction until it is available for analysis by the world pharmacovigilance community in the global database. There are of course several factors that influence the timeliness; how speedily the reporter sends in the case report to the national centre (NC) (where access to reporting forms or the possibility to do electronic reporting are factors), how effective the routines at the NC are, how much can be spent on updating the databases and how often case reports are forwarded to UMC. We hope to be able to come back to an analysis of the timeliness of reporting.

Completeness and reporting rate

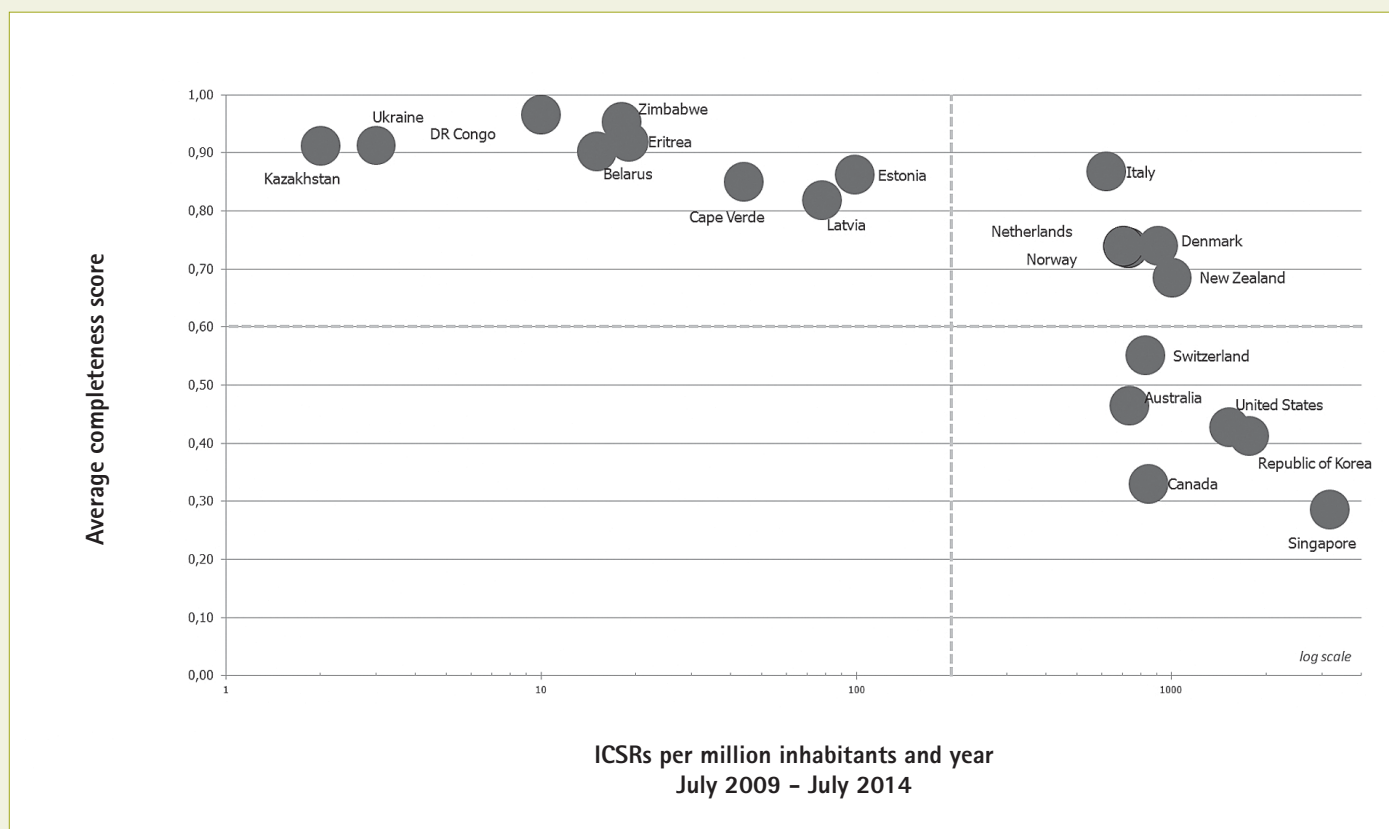
In this quarter's description of reporting trends we introduce a new type of graph with number of ICSRs per million inhabitants per year plotted against the average completeness score of the case reports for the ten countries with the highest value on each of these axes (for more on quality of reports, see UR65, page 6). Note that the x-axis has a log scale; with a linear scale it

would not be possible to distinguish the countries with a low reporting rate from one another. The data covers reporting during the last five years.

On the horizontal axis (at far right) we can see that the top 10 reporting countries all have more than 700 case reports per million inhabitants per year, which is a very high figure, and not achievable for many others. Countries with around 100 case reports per million are usually regarded as having a functional national pharmacovigilance system.

At the top of the vertical axis are the ten countries with the highest average completeness score for their case reports. It is encouraging to see that many of the newer countries submit well filled-in reports, although their number of reports is still rather low.

There are only a few countries that have both a high number of case reports per million inhabitants and a high completeness score of their reports and we would of course like to see more countries in the upper right-hand corner of the graph, together with Italy, Netherlands, Norway, Denmark and New Zealand.



Streamlined ICSR processing

Helena Sköld

VigiBase processing improved

VigiBase®, the WHO Global ICSR Database, have experienced an increase of a million Individual Case Safety Reports (ICSRs) on a yearly basis during the last five years. To meet the steady increase in the number of ICSR, and changes in regulatory environments around the world, comprehensive technological improvements and process enhancements have been made to the VigiBase ICSR Processing System.

Developments include faster processing, improved follow-up handling, quality validation (data type, field lengths, etc), completeness score calculation, and content validation such as automatic mapping of drugs and ADR terms and other predefined calculations (e.g. patient age, fatal case).

Changes to VigiLyze as a result

As a result from these improvements, to ensure consistent data handling and getting the most value from the ICSR in VigiBase, reprocessing of all ICSR was inevitable. This will also impact some of the data displayed in the search and analysis tool for National Centers, VigiLyze™.

One of the more notable changes will be that more information may be available in some fields. An example of this is Reporter qualification (Physician, Pharmacist etc.) which is a repeatable field in ICH-E2B; previously only one reporter was displayed in VigiLyze, but from the next release all reporters listed in the original report will be displayed.

In some cases adjusted calculations will cause changes to individual values on

individual ICSR. An example is Patient age; if no age is reported this value is calculated from patient's date of birth and date of the reaction. If incomplete dates are given, like '2004-06', the calculated result may look different after the reprocessing due to changes in the functions used.

Implementation

These improvements will be implemented in late 2014 and will require a delay in the regular ICSR processing and monthly updates of VigiLyze for a short period (up to a month) but after that all VigiLyze users will be able to benefit from the improved information handling.

Any questions regarding the reprocessing of ICSR in VigiBase and its implications may be directed to vigibase@who-umc.org. Your feedback is greatly appreciated.

WHO-ART major revision

Helena Sköld

After a period with very few revisions, the content of the WHO adverse reaction terminology, WHO-ART, has now been thoroughly updated and modernized. The main changes include fewer System Organ Classes, more High Level Terms and rearrangement of some terms to better suit today's needs in pharmacovigilance.

The mapping from WHO-ART to MedDRA has also been updated, enabling more of the Individual Case Safety Reports (ICSRs) in VigiBase® to be searched and analysed using either of these terminologies.

The French, Portuguese and Spanish translations of WHO-ART have been updated

and a new translation to Chinese has been added. A decision was made to exclude Italian and German translations from future releases due to very low demand for these translations.

There will be no structural changes to the text files released to subscribers of WHO-ART and documentation of all changes will accompany the updated version as it is released.

These updates will be implemented in UMC systems at the end of 2014, and the first release to subscribers will be 1 March 2015.

Table 1. The WHO-ART revision in numbers

	WHO-ART 14:4	WHO-ART 15:1
System Organ Classes	32	23
High Level Terms	189	340
Preferred Terms	1988	2125
Included Terms	3627	3928
Total terms	5804	6053
PTs with no HLT	1324	335

Centenarian

Sten Olsson

In July Frances Kelsey celebrated her 100th birthday. One of the most notable scientists in pharmacovigilance – a pharmacologist and medical doctor – she joined the US FDA as a medical officer in 1960. A month later she was assigned the review of a new drug application for thalidomide. Despite pressure from the manufacturer to approve the application, and the popularity of the

drug in other parts of the world, Dr Kelsey refused approval due to lack of adequate evidence that the drug was safe, supported by her FDA colleagues.

Many lives were saved by her decision, but laws and routines in drug safety were also profoundly affected. As a result of her blocking approval of thalidomide, Kelsey was awarded the President's Award for Distinguished Federal Civilian Service by John F Kennedy.

Kelsey devoted the rest of her working life to the FDA, becoming responsible for directing the surveillance of drug testing, finally taking her well-earned retirement in 2005. We wish Dr Kelsey many belated happy returns and sincere thanks for her work.

Capacity building through education

News from Lareb, WHO Collaborating Centre for Pharmacovigilance Education and Patient reporting

Spontaneous reporting relies on the voluntary reporting of adverse drug reactions (ADRs) from health care professionals and patients. It is therefore essential that reporters gain knowledge in recognizing, managing and reporting ADRs. For most pharmacovigilance centres, the number of health care professionals to train wildly exceeds the resources available. Choices have to be made on which groups to focus.

one of the aims of the education was not only to provide information about ADRs but also encourage the GPs in training to actually report, we introduced a reporting assignment. GPs in training were required to submit at least one ADR report during their GP training. By actually submitting a report, they become aware of what the reporting procedure entails and when they receive the individualised feedback from Lareb, they

method has an impact on the documentation level of the reports and on the number of unlabelled events. The reporting assignment resulted in significantly more and better-documented reports and more often concerned unlabelled events than the lecture-based method. This effect persisted and did not appear to diminish over time.¹ Since then the reporting assignment has spread to include all pharmacy students in the Netherlands, and at the moment it is being implemented for medical students. Our experience is that students submit well documented reports. Every year, we also choose the best student report, both concerning documentation and relevance. Last year the report concerning a decrease of HDL cholesterol when using interferon beta.²

Next: medical students

This year a new initiative was started with one of the universities in the Netherlands. Medical students doing their Masters are offered the possibility to assess real ADR reports submitted to our pharmacovigilance centre. This assessment is of course supervised and if necessary completed by an assessor of our pharmacovigilance centre. By assessing a report the student becomes familiar with how to search for information about ADRs, what elements are necessary for a good causality assessment, etc. The hope is that this knowledge will in the future contribute to increased awareness of ADRs in clinical practice and contribute to more and better documented reports.

1. Gerritsen et al. Effectiveness of Pharmacovigilance Training of General Practitioners. A retrospective Cohort Study in the Netherlands Comparing two methods. *Drug Safety* 2011; 34(9):756-62.
2. Van Grootheest et al. Teach students to recognize ADRs. *Medisch contact* 2014; 4:150-153.



Clinical pharmacologists on Lareb training.

At the Netherlands Pharmacovigilance Centre Lareb, we believe that it is important to train health care professionals as early as possible in their career: it is easier to teach a student a certain behaviour than to change the behaviour of an older health professional.

For trainee GPs

A few years ago we started to give workshops to general practitioners (GPs) in training. As

(hopefully) also see the added value of reporting.

Did it work?

To find out if the introduction of a reporting assignment leads to an increase of reported ADRs after completion of this traineeship, we conducted a study comparing this method with a lecture-based method. We also investigated whether the applied training

Manila brings UMC and ISoP together

Anki Hagström, Hervé le Louet

Following the signing of a Memorandum of Understanding in February this year between ISoP and UMC, the first joint training course on 5-7 June 2014 in Makati (Manila), the Philippines clearly presented the opportunity to showcase the synergy between UMC's scientific and technical strengths toward capacity building, combined with the regulatory, scientific and academic expertise of ISoP. The Philippines FDA, under Acting Director-General Kenneth Hartigan Go,

generously contributed in making the arrangement of the course possible.

The three-day training course **Ensuring Safe Medicines: How harmonization underpins international pharmacovigilance** engaged pharmacovigilance professionals from regulatory, industry, hospital, university and community settings with Asian and international expert speakers. 74 participants from 12 different countries attended:

Philippines, Singapore, Malaysia, Thailand, Indonesia, Bangladesh, China, Australia, Pakistan, Korea, France and Sweden.

The programme was set up to incorporate basic to advanced knowledge, starting with appreciation of the landscape of pharmacovigilance in government and in industry, leading to the need for good quality information and the principles and concepts of risk minimization and management.

Pharmacovigilance methodologies in industry were shared.

Data best practice

This training served as an opportunity for UMC to stress the principle of converting data to wisdom and the importance of structuring data through terminologies, dictionaries, and international standards.

The course included traditional lectures, webinar lectures, workshops and hands-on sessions, with ample opportunity to exchange views and ideas. Panel discussions facilitated a lively dialogue where participants shared their comments and questions, and actively participated with the faculty.

use and the role of consumers/patients were also raised. This educational experience exposed the audience to new ideas and scientific methods concerning pharmacovigilance, ensuring that academia are able to provide input regarding new methods and present their vital role in advancing pharmacovigilance.



Participants from twelve nations in Manila for UMC-ISoP training.

Innovative scientific methods and improvements to products and services that advance pharmacovigilance were covered. It also showed how to submit quality data, analyze data and undertake causality assessment.

Sessions included case studies, causality assessment, risk management and crisis communication. Practical experience on how regulators make decisions based on available pharmacovigilance data was presented. The place of mobile technology

The course served as an open and collaborative forum for local, regional and global industry representatives, regulators and academia to share ideas, experience, concerns, goals, and their real life experiences, contributing to a successful course.

Core Elements for teaching pharmacovigilance

Jürgen Beckmann and Ulrich Hagemann

With the growing need for pharmacovigilance capacity-building, professional training through high-quality courses with different focuses and levels of detail are essential. Experts working in various fields of medicine safety around the world have taken the initiative and collaborated in creating a comprehensive, detailed and balanced curriculum for pharmacovigilance. Some of the experts are members of committees associated with the World Health Organization (WHO) or working at its Collaborating Centres. Others are members of the Executive Committee of the International Society of Pharmacovigilance (ISoP) or its Education and Training Project (ETP) group, or work in institutions dedicated to pharmacovigilance.

The initiative hopes to elaborate a systematically-structured pharmacovigilance

curriculum covering the breadth of pharmacovigilance and recent developments of relatively new topics. The development of practical training for a wide range of audiences and settings was considered useful.

Using existing packages

The group use several relevant existing national and international packages of pharmacovigilance topics and concepts of pharmacovigilance teaching from various institutions. It also drew upon extensive printed material, overviews, textbooks and guidelines developed by international organisations.

A core with flexibility

The core curriculum includes a main component of 15 chapters for theoretical lecture-based training and a minor component

with suggested hands-on exercises. The structure and content allow in-depth focus on specific issues, while maintaining overall context. It offers opportunities to tailor courses specifically to the needs of an audience and intensive or short overview courses or addressing specific narrow topics in perspective.

The full article, with the title 'Teaching Pharmacovigilance: the WHO-ISoP Core Elements of a Comprehensive Modular Curriculum', is published with open access and available from <http://link.springer.com/search?query=teaching+pharmacovigilance>

Vaccine safety in pregnancy

Sten Olsson



Dr Jan Bonhoeffer, chairing in Geneva.

In 2013, the WHO Strategic Advisory Group of Experts on Immunization (SAGE) requested that a process and a plan be developed in support of an increased alignment of safety evidence, public health needs, and regulatory processes in the context of maternal immunization. The evidence of safety of vaccines given in pregnancy and to newborn children is still limited. There is a critical need to support

development of standardized data collection methods including definitions of adverse events to be monitored in clinical trials and after marketing approval of vaccines.

WHO, together with the Brighton Collaboration, carried out an inventory and assessment of maternal immunization adverse events and identified events of special interest in obstetrics and paediatrics. A consultation was held on 24–25 July 2014, with the objectives of:

- reviewing adverse event definitions of pregnancy and the newborn period
- recommending maternal immunization case definitions for use in clinical trials and post-licensure surveillance

- establishing a core data set to be collected for continuous safety monitoring.

Around 50 delegates, observers, WHO consultants, representatives of WHO and its regions took part in the consultative meeting. Material presented by the WHO consultants, responsible for the inventory, was discussed during intense interactive sessions. The process was successful in producing a consensus list of events of special interest, interim consensus definitions and data sets to be collected.

Monitoring vaccines in Montenegro

Nemanja Turković and Maja Stanković

The Agency for Medicines and Medical Devices of Montenegro (CALIMS), in cooperation with the Institute for Public Health of Montenegro (responsible for immunization) has a legal responsibility to monitor the safety of vaccines that are marketed in Montenegro.

Reporting of AEFI

CALIMS receives reports concerning vaccines (and other medicines) by spontaneous reporting by healthcare professionals and representatives of medicine manufacturers (marketing authorization holders). Montenegrin law states that healthcare professionals must report adverse events following immunization (AEFI) to CALIMS and/or the Institute for Public Health of Montenegro.

In 2013 the possibility of reporting through the information system of primary healthcare institutions and general hospitals was introduced. Reports filed this way are received by both CALIMS and the Institute for Public Health. This is expected to be the principal method when it comes to AEFI reports, because it is an easy, safe and fast way to transfer data from a healthcare institution to CALIMS and the Institute.

Expert group

An expert group for monitoring vaccine safety has been formed, modelled on those in countries with advanced systems of vaccine side effect monitoring. Our Expert

conducts numerous activities promoting pharmacovigilance. The Institute for Public Health, along with CALIMS and the Clinical Center, hosts annual professional educational seminars on immunoprophylaxis. In these seminars healthcare professionals conducting the immunization programme are introduced to basic pharmacovigilance terms, classification of adverse reactions, and how to fill out and submit the vaccines adverse reaction reporting form.



Professional educational meeting, Kolašin, April 2014.

Group for Vaccines, consisting of CALIMS, the Institute for Public Health and the Clinical Center of Montenegro representatives, makes decisions on seriousness, expectedness and causality and meets several times annually.

Professional education

The success of pharmacovigilance systems in every country depends on healthcare professionals' participation, and CALIMS

International cooperation

CALIMS participated in an international meeting on monitoring of vaccine safety and actions of anti-vaccination groups (movements), on 10–11 June in Bar. The meeting gathered together professionals running immunization programmes, as well as those responsible for control, supervision and evaluation of efficiency and safety of vaccines used in these programmes. They came from the Institutes for Public Health of Montenegro, Serbia, and Croatia, the Agency for Medicinal Products and Medical Devices of Croatia, healthcare professionals involved in the process of immunization, academics, and representatives of vaccine manufacturers.

The meeting resolved to:

- Consider the possibility of creating a data repository ('Questions Et Answers') on controversial immunization issues, in order to provide a common responses to the major issues and concerns of

healthcare professionals and the public (primarily concerned parents)

- Create an international, regional group tasked to deal with key issues connected to vaccine safety.

Proactiveness, competence and joint action by all institutions responsible for implementation of immunization are the key to success in the system of safe immunization, a field that constantly improves in Montenegro.

GACVS – 15 years old

Patrick Zuber

On the occasion of its 30th meeting, on 11–12 June 2014, the Global Advisory Committee on Vaccine Safety (GACVS) also celebrated its 15th anniversary. WHO's vaccine safety advisory committee first met on 14–15 September 1999 and has since met twice a year and has also been convened by telephone conference when needed.

The Committee's regular reports are published soon after each meeting in the WHO's Weekly Epidemiologic Record, while urgent reports are posted separately online, and a compendium is available on the GACVS website maintained by WHO. Since the committee was established, it has produced over 100 reports related to vaccine safety

issues. GACVS's role is primarily to assess risks related to vaccine use in order to assist policy-makers in establishing benefits and risks as part of evidence-based vaccination policies. GACVS risk assessments are regularly used by the WHO Strategic Advisory Group of Experts (SAGE), the Expert Committee on Biological Standards (ECBS) as well as regional technical advisory groups related to immunization.

A total of 39 experts have served on GACVS to date, the current committee being composed of 15 members. Current and past members represent all WHO regions, although a majority (26) do originate from industrialized countries in Europe, North America or Australia.

They provide expertise in multiple fields related to vaccine safety including epidemiology, statistics, clinical medicine, pharmacology and toxicology, infectious diseases, public health, immunology, vaccinology, pathology, ethics and health product regulation. GACVS members, in addition to participating in bi-annual in-person meetings also contribute to the work of the committee through various sub-groups that develop statements on selected topics between regular meetings.

A full report appeared in the GACVS Bulletin June 30, 2014.

International Pharmacovigilance Course

Register now! Limited spaces available!

Uppsala Monitoring Centre (UMC) is pleased to announce its 17th international pharmacovigilance training course, which will take place in Uppsala, Sweden, 18–29 May, 2015.

The purpose of the course is to further develop effective and sustainable pharmacovigilance for member countries of the WHO Programme for International Drug Monitoring by creating a unique opportunity for learning and collaboration.

The course focuses on topics essential to effective pharmacovigilance, including sessions to strengthen the overall WHO Programme, e.g. pharmacovigilance best practices, signal detection, regulatory aspects, reporting culture, benefit/harm assessment 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, communications, fundraising and risk management will be covered.

For a detailed programme and how to apply, please visit our website: www.who-umc.org

Looking forward to receiving your application!

Introducing vigiRank : Promise for more ef

Ola Caster

The Uppsala Monitoring Centre (UMC) has developed vigiRank, a novel method to screen databases of individual case reports for possible new safety signals with medicines. For over a decade screening has relied on disproportionality analysis, which is based solely on aggregate numbers of reports. vigiRank incorporates disproportionate reporting as one component, but additionally considers several aspects related to the quality and the content of reports. Initial results suggest that vigiRank can help uncover more signals than disproportionality analysis alone; while reducing the number of false leads. vigiRank promises more complete and effective safety information on marketed medicines, all in the interest of pharmacovigilance professionals, physicians, and patient safety worldwide.

Numbers are a problem

The need for pharmacovigilance is widely acknowledged. This need stems from the incomplete knowledge about the safety profile of a medicine as it enters the market. Pre-marketing trials are too short and

include too few patients from groups that are not sufficiently heterogeneous.

Individual case reports of suspected harm from medicines are the most important source of information to detect previously unknown risks with marketed medicines, so called signals. Individual case reports describe observations reflecting concerns that a medicine may have caused an adverse reaction. Such observations are made by healthcare professionals and patients alike.

A practical issue for many organisations performing signal detection, including UMC, are the vast numbers of reports collected. This makes the use of triages* to guide clinical assessment a necessity. A common criterion for such triages is strength of evidence.

Improving on disproportionality

Since the end of the 1990s, disproportionality analysis has formed the mainstay for automated evaluation of strength of evidence. Disproportionality analysis has fundamentally changed the conduct of signal detection. It is

now a mainstream activity recommended by major regulatory guidelines. UMC substantially contributed to this development by devising the Information Component (IC) in 1998. The IC is one of the common measures of disproportionality, along with the Proportional Reporting Ratio (PRR).

There is one major weakness with disproportionality analysis: all case reports count equally. The only thing that matters is the number of reports on a drug together with an adverse reaction, in relation to the numbers of reports on the drug and the reaction overall. It does not matter whether the reports contain any useful information to support a causal association. In fact they may contain nothing more than the names of the drug and the reaction.

Report Quality factored in

However, the quality and content of individual case reports are essential in the ensuing clinical assessment, which is a necessary step in the signal detection process. The idea behind vigiRank is to bridge that gap by simultaneously taking into account several strength-of-

When using vigiRank, a score is computed for each drug-adverse reaction pair. A higher score is intended to imply a higher likelihood of a safety signal. Consequently, all pairs are ordered according to their score, and clinical assessment ensues from the top of the list and downwards. The number of drug-adverse reaction pairs that are clinically assessed may be decided based on the available resources.

The figure illustrates how the score is computed. This example is for a fictional drug-adverse reaction pair with eight reports, depicted in the box to the far left. For example, the top left report is from Switzerland, was entered in 1995, attains a vigiGrade completeness score of 1.0 (this score measures how informative the report is, one being the highest score), and it contains a free-text case narrative.

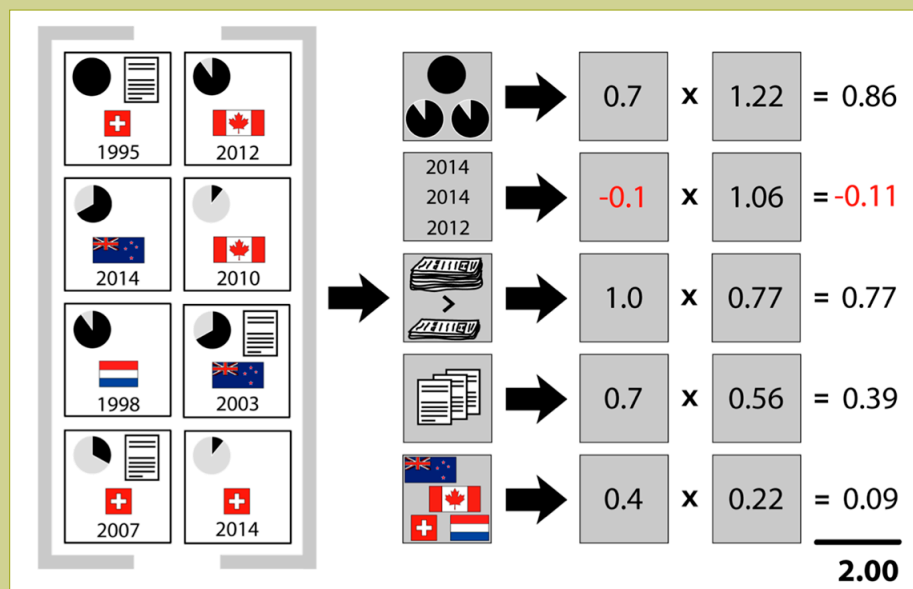
In the first (left) column of grey boxes, the relevant aggregated data for this drug-adverse reaction pair are displayed. From top to bottom: there are three informative reports, i.e. reports with a vigiGrade completeness score of 0.9 or higher; there are three recent reports, i.e. reports submitted during the past three years; there is disproportional reporting; there are three reports with free-text descriptions; and the geographical spread is four countries for which there are more reports than expected.

In the second (middle) column of grey boxes the raw aggregated data for each component is

replaced by a corresponding numerical value. This value is between 0 and 1 for all five components except recent reporting, whose value is between 0 and -1. For example, this drug-adverse reaction pair has three informative reports, which is replaced by the value 0.7. To obtain the maximum value 1, at least five informative reports would have been required. As another example, the three recent reports incur a small negative value of -0.1. To avoid any penalty, at least four recent reports would have been required.

In the third (right) column of grey boxes, the respective weight of each component is displayed. The higher the weight, the greater the general contribution of the component to vigiRank. In the figure, the weights decrease from top to bottom.

The numbers to the far right are the results obtained from multiplying the specific values for this drug-adverse reaction pair with the general weights of the corresponding components. The sum of those products forms the score used to rank drug-adverse reaction pairs for clinical assessment.



Effective signal detection

evidence aspects as part of the automatic screening that precedes clinical assessment.

While *vigiRank* does take disproportional reporting into account, it simultaneously considers the numbers of informative reports, recent reports, and reports with free-text descriptions, as well as the geographic spread of reporting. For a descriptive example of how *vigiRank*, please see the diagram. It is noteworthy that the five components of *vigiRank*, as well as their respective contributions to the algorithm, were chosen empirically rather than subjectively. This selection was based on the features of emerging safety signals and non-signals, respectively, in the past.

vigiRank has been scientifically evaluated using a retrospective experimental setup. The results suggest that *vigiRank* increases first-pass screening performance in signal detection compared to disproportionality analysis as much as the shift from crude report counting to disproportionality analysis once did. Therefore, taking *vigiRank* into routine use as a replacement of disproportionality analysis

alone is expected to uncover more signals and to reduce the number of false leads.

Early evidence promising

So far *vigiRank* has been used in one intensive effort at UMC to detect signals from *VigiBase*[®], the WHO global individual case safety report database. Our experiences were positive and largely matched the expectations based on the retrospective evaluation. As of 1st September, eight signals out of that effort had been decided and 14 more potential signals had not been fully assessed. Clinical assessors generally agreed that use of *vigiRank* resulted in potential signals whose reports were of higher quality than that experienced previously with disproportionality analysis.

The long-term impact of *vigiRank* remains to be seen. It promises to lead towards more complete safety information on marketed medicines with less effort required, all in the interest of greater knowledge and of patient safety.

The UMC believes that *vigiRank* as presented here may be the first step towards a new

paradigm for screening individual case reports. However, further evaluations and calibrations of the algorithm must follow.

The approach of *vigiRank* is generic, although adaptations are likely to be needed in order to obtain the highest possible performance on other databases. An interesting prospect would be to develop a similar algorithm for other types of data such as longitudinal health records.

For a complete description of *vigiRank*, please see the full paper published in peer-reviewed journal *Drug Safety*. It is freely downloadable at: <http://linkspringer.com/article/10.1007/s40264-014-0204-5>

Questions, comments, or ideas are welcome. Please direct them to ola.caster@who-umc.org

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

* Triage is any process that attempts to determine priorities by assessing major elements of a situation or problem without sifting through every smallest detail.

UMC's Chief Science Officer Niklas Norén responds to questions about *vigiRank*

*1. How will the *vigiRank* approach improve UMC's signal analysis performance compared to the previous UMC methodology, eg. earlier identification of possible signals, identification of signals that would have previously been missed or same outcome but more resource efficient?*

"All of the above! We expect that *vigiRank* will help uncover signals that would be missed by disproportionality analysis alone, and at the same time reduce the number of false leads. In practice, we have found its focus on case series with geographic diversity and informative reports to be very well aligned with the ensuing manual review; preliminary results suggest that a larger proportion of its potential signals eventually end up as signals."

*2. How will national centres, and ultimately patients, benefit from *vigiRank* as the main basis for UMC signal analysis?*

"It will help identify risks to patients that would otherwise go undetected, or be delayed."

*3. Can the *vigiRank* method be applied to any ICSR database or is it meaningful only for global and very big datasets?*

"*vigiRank* has been developed for and evaluated

in *VigiBase*, but to account for multiple aspects of strength of evidence in first-pass screening should be beneficial in any setting. The benefits of a method such as *vigiRank* that focuses on the content and quality of individual reports may in fact be more pronounced for smaller and less diverse databases, in which disproportionality analysis can be problematic. With that said, an implementation of *vigiRank* for another database would require careful thought and some adaptation. Ideally, *vigiRank* should be rebuilt for the database in question, but this would be a substantial research effort. One might consider using our *vigiRank* implementation also in other databases, after adaptation of some of the variables (geographic spread in a national dataset could e.g. be measured in terms of states or regions etc). However, the performance of such an implementation would need to be evaluated against emerging safety signals in the database at hand."

4. Do you see risks in applying statistical methods to simulate and replace analyses previously made by clinical experts?

"It is important to distinguish between the statistical screening and the manual clinical review. *vigiRank* cannot and should not replace the clinical review, but aims to focus the attention of our experts on the most likely signals."



*Using *vigiRank* in a signal detection sprint.*

*5. The *vigiRank* article invites researchers to suggest variations to the methodology and parameters used. How do you foresee the *vigiRank* approach developing in the next few years?*

"I would hope to see adaptations of *vigiRank* to other collections of individual case reports as well as to longitudinal observational databases, and perhaps their combination. I would like to see the incorporation of other aspects of strength of evidence such as suggestive time-to-onset or (lack of) alternative explanations to the suspected adverse drug reaction, including concomitant medicines and the underlying disease."

New Partnership to lift African pharmacovigilance

Alex N. O. Dodoo and Haggard Hilda Ampadu

Pharmacovigilance in Africa is receiving a major boost from a completely unexpected source – the New Partnership for Africa's Development (NEPAD). NEPAD, an African Union strategic framework for pan-African socio-economic development, is both a vision and a policy framework for Africa in the twenty-first century. It is a radically new intervention, spearheaded by African leaders, to address critical challenges facing the continent: poverty, development and Africa's marginalisation internationally and provides unique opportunities for African countries to take full control of their development agenda, to work more closely together, and to cooperate more effectively with international partners. One of NEPAD's initiatives is the African Medicines Regulatory Harmonization (AMRH), which, amongst other things, provides support for harmonizing pharmacovigilance requirements across the continent (www.amrh.org).

Harmonization

The AMRH programme works with Regional Economic Communities (RECs) to fulfil the vision of the Pharmaceutical Manufacturing Plan for Africa. The aim is to support African countries to improve public health by increasing access to good quality, safe and effective medicines through harmonizing medicines regulations, and expediting registration of essential medicines.

Regional collaboration

Across the continent, regional initiatives (the RECs) are pursuing a path to better cross-border collaboration: the East African Community (EAC) (see page 15), Southern African Development Community (SADC), Economic Community of West African States (ECOWAS), Economic and Monetary Community of Central Africa (CEMAC), Community of Sahel and Saharan States (CEN-SAD) and the Arab Maghreb Union (AMU). Some countries belong to more than one of these groups.

Key plans

In view of limited human resources in many African medicines regulatory authorities, AMRH hopes to assist regulatory harmonization and build capacity. With regional bodies and partners it will:

- establish Regional Centres of Regulatory Excellence (RCOREs)
- conduct training in regulatory science

- engage RECs and medicines authorities in establishing a pool of regulatory expertise in Africa
- carry out performance assessments.

Centres of excellence

Two established units have already been designated as RCOREs in pharmacovigilance by NEPAD/AMRH in the first such tranche of nominated bodies; the WHO Collaborating Centre (WHO-CC) for Advocacy and Training in Pharmacovigilance at the University of Ghana Medical School, Accra, Ghana, and the Pharmacy and Poisons Board in Kenya. A further eight organizations have received designation for other elements of regulatory function.

Consortium

The RCORE for Pharmacovigilance at the WHO-CC in Accra, Ghana is a consortium consisting of various partners including the national pharmacovigilance centres of Ghana, Nigeria, Tanzania and Zimbabwe as well as a clinical research organisation (Quintiles plc.) and a health technology provider Sante-Afrique International Limited. Consortia like these hold the promise of sustainability if the rules governing them are clear, transparent and accepted by all partners, and offer another model for attracting the needed human and material resources for capacity building in pharmacovigilance. By including various pharmacovigilance centres, the consortium can also facilitate the acceptance of harmonized approaches towards pharmacovigilance across Africa since each national centre can champion the cause of harmonization and the adoption of the harmonized guidelines.

Global partners

Partners in the AMRH initiative include, in addition to NEPAD, the following: the World Health Organization, the Pan African Parliament, the Bill & Melinda Gates Foundation, the UK Department for International Development (DFID), The Clinton Health Access Initiative (CHAI), the African Development Bank, the African Union Commission, the World Bank and UNAIDS.

On the ground in Zimbabwe

Alem Zekarias

In recent years, UMC has seen Africa as a key region and focussed on the continent by supporting national centres in building functional pharmacovigilance systems. Our overall goal has been to ensure that all stakeholders in the region can rapidly collect,

seamlessly share, effectively analyze, and quickly act upon suspected medicines-related safety problems.

An increased number of African countries have joined the WHO Programme with on-going pharmacovigilance activities. In order for the UMC Global Services department to be able to provide adequate support, we need to better understand the working processes, environment and challenges in African pharmacovigilance centres. During July and August 2014 I spent a three-week secondment at the Medical Control Authority of Zimbabwe (MCAZ), in the capital Harare, and then a two-week secondment at the National Department of Health in Pretoria, South Africa. The objective was to learn more about pharmacovigilance processes in Zimbabwe and South Africa, and to interact with stakeholders there.



Discussing the fields in an ADR report with the pharmacist, Rusape Hospital, Zimbabwe.

To observe two different centres that are working in different ways gave me as a pharmacist and as a Global Services staff member, excellent knowledge, experience and lessons that will be valuable in my future work. Working together with national centre staff in their workplace I had the opportunity to build relationships and get a better understanding of how they operate. I was also able to identify gaps and improvements that can be enhanced with support, training and regular collaboration between UMC, UMC-A and the national centres.

MCAZ responsibilities

The MCAZ, through the pharmacovigilance and clinical trials division (PVCT) is the national centre for pharmacovigilance for Zimbabwe, and an active member of the WHO Programme for International Drug Monitoring since 1998. MCAZ is a statutory body established by the Medicines and Allied Substances Control Act (MASCA) and an autonomous National Drug Regulatory Agency (NDRA) which means that it has the legal mandate for regulation of clinical trials of medical devices, medicines and vaccines in Zimbabwe.

The PVCT division provides a number of different services and programmes in collaboration with other divisions at the centre. These include the monitoring of medicines, medical devices and vaccines and product defects; conducting product recalls, training in cohort event monitoring (CEM) of anti-malaria and anti-tuberculosis medicines in line with WHO recommendations, targeted spontaneous reporting of adverse events following immunizations (AEFIs) and evaluation of clinical trial protocols.

Working with others

Collaboration and interaction between PVCT and other directorates within MCAZ, as well as with global organizations (WHO, Global Fund, UNICEF, UMC) are considerable and successful. In addition, the support from the Director-General at MCAZ creates a solid ground for the pharmacovigilance unit's achievements.

Zimbabwe has over 13 million people spread over eight provinces and two cities with a provincial status. For pharmacovigilance to succeed in all provinces is a major task. Current in-house systems including training in targeted spontaneous reporting and regular follow-ups in each province have been successful.

Rewarding time

My three weeks with pharmacovigilance head Priscilla Nyambayo and her dedicated team were rewarding in many ways. I had the great pleasure to spend time with all the team, giving me a clear picture of how pharmacovigilance is dealt with on a daily basis. I got useful insights into how UMC services and tools are implemented (or not) and reasons why. This experience will assist my work with national centres in the future.

East African harmonization

Bernice Owusu-Boakye

The aim of the East African Community (EAC) Medicines Regulatory Harmonization project (MRH) is to improve access to safe, efficacious and good quality medicines by harmonizing medicines regulatory systems within the Community, in agreement with national and international policies and standards.

World Bank sponsorship

In order assist the implementation, six participants from EAC Partner States – namely Burundi, Kenya, Rwanda, Tanzania, Uganda and Zanzibar – were sponsored by the World Bank to undergo a 4-week 'PV fellowship' programme at the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance in Accra,

Ghana. This training fostered experience-sharing and capacity-building among the EAC Partner States.

How to harmonize: theory

The participants were taken through the theory and practice of pharmacovigilance as well as harmonization. The broad theoretical component covered areas such as integrating pharmacovigilance into public health, regulatory aspects, pharmacovigilance audits, PSURs, signal detection and communication and crisis management.

...and practice

Practical aspects included a hands-on session on statistical software, VigiFlow and Vigilyze, PV toolkits and indicators. The participants went on field visits to see real-life practice of pharmacovigilance in a hospital and an industrial setting. Topics covered under harmonization concentrated on practical steps achievable within the EAC.

The participants also had the opportunity to present the perspective on harmonization in the EAC from their respective countries. They shared the strengths and weaknesses of their systems and opportunities for harmonization.

Looking forward

Opportunities identified were:

1. access to internet technology by all health facilities
2. use of e-LMIS (e-Learning Management Information System) software to help detect poor quality products
3. use of health professional councils to provide training to the private sector.

Future plans include:

1. Finalizing EAC pharmacovigilance guidelines
2. Establishing an EAC medicines and food safety commission by 2016
3. Stakeholder sensitization and advocacy at EAC regional and national levels
4. Active pharmacovigilance component in research
5. Resource sharing among EAC partner states.

Arab congress

As we go to press, the first First Arab Congress of Pharmacovigilance organized by the Centre Anti Poison et de pharmacovigilance du Maroc has drawn to a close. We will present a full report, and the meeting declaration, in January's *Uppsala Reports*.



Antiretroviral safety coaction

Kalaiselvan Vivekanandan

Since the introduction of antiretroviral therapies (ART) in 2004, the Indian national treatment programme has scaled-up provision of ART to about 796,200 people. In order to make treatment more accessible, ART centres are located in tertiary/district hospitals and medical colleges. For many antiretroviral medicines, outcomes from long-term use are still not known. Lack of information may lead

to loss of patient confidence that in turn may cause suboptimal levels of adherence to the treatment. To ensure the safety of ARV medicines used in the programme, the Indian Pharmacopoeia Commission (National Coordination Centre for Pharmacovigilance programme of India) and the National AIDS Control Organization (NACO) formally agreed on 15 September 2014, to collaborate and set

up systems and processes for reporting, analysis and monitoring of ADRs due to antiretroviral medicines used in the programme.

Memorandum signed

A Memorandum of Understanding (MoU) was signed between NACO and the Indian Pharmacopoeia Commission at the NACO office in New Delhi, under the chairmanship of Mr R K Jain (Additional Secretary, Director General of Health Services, Ministry of Health & Family Welfare). Dr A S Rathore (Deputy Director General, Care, Support & Treatment Division), and Dr G N Singh (Secretary-cum-Scientific Director, Indian Pharmacopoeia Commission), signed the MoU on behalf of their respective organizations. Mr Jain highlighted that both the organizations need to work with clear milestones and timelines.

Phased training

In the first phase, 30 Antiretroviral Therapy Centres would be identified and training will be provided to them before 1 January 2015, and the process scaled up in a phased manner through 2015. Mr Jain also appreciated the important role being played by WHO India in these endeavours, as a key partner for technical support.



Meeting to sign the MoU between Indian Pharmacopoeia Commission and National AIDS Control Organization in New Delhi.

Chinese audio-visual materials

Zhurong Liu

In recent years, there has been a rapid development in adverse drug reaction monitoring in China, especially in terms of building an institutional framework. There are 2,500 people engaged in adverse drug reaction monitoring at present, and the constantly growing monitoring team brings great challenges in training on adverse drug reaction monitoring and rational drug use.

The National Center for ADR Monitoring has always attached great importance to publicity and taken measures to achieve practical, targeted and effective training and publicity, with scientific and standardized teaching materials.



Videos launched

At the end of 2013, a series of video training materials were designed and completed, in three parts:

Part 1: the collection, evaluation and analysis of adverse drug reaction reports, as well as basic knowledge of laws and regulations, epidemiology and statistics.

Part 2: relevant background to medical device adverse event monitoring.

Part 3: popular science knowledge of safe medication and rational drug use, for the public.

The training materials have been made into CD-ROM equipped with text notes and self-test questions after training, which will be provided to all provincial ADR centers. The public may also obtain them via the website of the National Center for ADR Monitoring, China.

Safety at the highest level

Brian Edwards

Background

The UK scandal of Mid-Staffordshire Hospital, where there was a systematic breakdown in safe healthcare, resulted in many patients suffering avoidable severe, even fatal, harm. This led to a public enquiry and the resulting Francis report was published in February 2013. The report stressed the lack of safety culture and how systematically the National Health Service (NHS) had paid little attention to this. The UK Government invited US healthcare safety expert Donald Berwick to advise on how patient safety could be enhanced, and his report was published in August 2013.

Meanwhile, since about 2008 the Clinical Human Factors Group (CHFG) in the UK has been working to stimulate dialogue and demonstrate through concrete action a better understanding of the significant impact of human factors on safety, quality and productivity in healthcare. The NHS Concordat is a unique initiative which resulted from the coalescence of all these activities. The aim is to make the NHS run both more efficiently and safely within existing resources.

Signatories

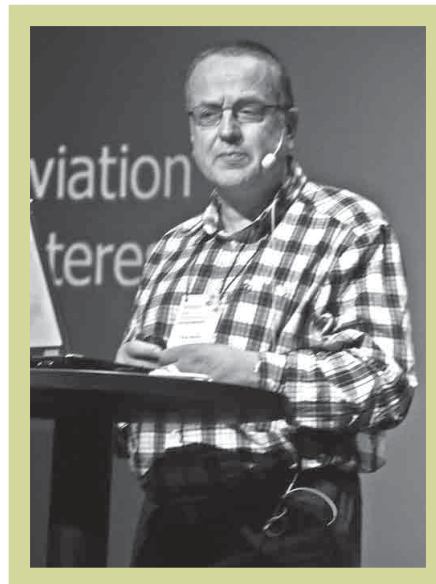
The signatories to this Concordat consist of healthcare bodies that directly interact with the NHS. Although it is difficult to verify the complete and current list, there is a noticeable absence of pharmacy and pharmaceutical organizations. Indeed, clinical research is not covered at all by the concordat.

The reality is that patient safety in the UK is managed in various 'silos'. Although the current focus of the Concordat is on the NHS, there are other sectors with their own regulations and cultures such as pharmacy, pharmaceutical industry, clinical research, devices and private medicine. If not all patient safety sectors are engaged in a concerted effort to develop human and organizational factors in the design of safe processes, we believe this will interfere with or significantly hold back progress in the NHS.

Human factors – a speciality

Human factors training needs to be fully integrated into medical, pharmaceutical, nursing and other healthcare professional curricula in the teaching and training of tasks and activities. It is NOT an add-on as a 'soft-skill' which is 'nice to have'. An effective

human factors approach must similarly apply to all relevant regulatory bodies. Systems and organizational science should be developed as a healthcare speciality, with sponsorship of research into systems science for safety of healthcare products. Adoption of human factors needs top-down and bottom-up buy-in and to be embedded in all aspects of healthcare. Initial training for the current workforce is required in the short-term, to then be totally integrated into training of all healthcare workers from the start. Learning from other industries, it is clear that training and assessment will also need repeating every year thereafter – it is not a one shot fix.



Brian Edwards, speaking at the 2014 UMC Research Conference.

Concordat and pharmacovigilance

What can we do in 'pharmacovigilance'? In the UK, in reaction to the Concordat, Chris Seal, who was previously a pharmacist and is now Chair of the UK Air Safety group, and I have set up the Pharmaceutical Human Factors Group (PharmaHuF) in LinkedIn. This is an independent campaign group in UK & Ireland linked to CHFG, which similarly aims to stimulate dialogue and demonstrate through concrete action how a better understanding of the role of human factors can have a significant impact on safety, quality and productivity in all areas of the pharmaceutical sector including pharmacy.

PharmaHuF is a broad coalition of pharmaceutical professionals (447 as of September) who have joined experts in

human factors from healthcare and other high-risk industries to campaign for change in the pharmaceutical sector in UK & Ireland at the level of individuals, teams and organizations.

International applicability

Our approach is all about the system, the product and all the individuals and how human factors affects the functioning of all. It is internationally applicable. The fewer your resources, the more important human factors are, as you cannot literally afford to be unsafe. Human factors is a science-based discipline (not a 'collection of factors about humans'), which is why we don't answer the question "What are human factors?"; human factors encompasses all those factors that can influence people and their behaviour in a work context.

The way ahead

To our knowledge, there has been little emphasis on system design and sciences in pharmacovigilance curricula and training. Training in industry is focused solely on SOPs, but this is only part of the process and learning to work in complex systems is critical for efficient pharmacovigilance. There is an urgent need to optimise human performance within the pharmaceutical sector for patient safety and efficiency.

Further references can be found here:

Heath Foundation have been working on measurement and monitoring of safety
<http://patientsafety.health.org.uk/?gclid=CMO6q5vnIroCFQnpwgodl44A9g>

National Advisory Group on Patient Safety
<http://www.hsj.co.uk/Journals/2013/03/12/k/k/z/ Terms-of-Reference.pdf>

NPSA Handbook – design for safety
<http://www.nrls.npsa.nhs.uk/resources/collections/design-for-patient-safety/>

ICDRA in Rio

Anki Hagström

This year, the 16th International Conference of Drug Regulatory Authorities (ICDRA) was hosted in Rio de Janeiro, Brazil. The Brazilian Health Surveillance Agency, ANVISA – celebrating its 15th anniversary this year – helped coordinate the event, making us all feel very welcome.

Pre-ICDRA

The pre-meeting offers an opportunity for the pharmaceutical industry to engage in discussions with drug regulatory authorities. The theme this year was: 'Ensuring Quality and Safety of Similar Biotherapeutic Products for Patients Worldwide'. With a number of originator biological product patents soon to expire, attention is on the need for national, regional and worldwide harmonization, as well as understanding the challenges facing regulatory authorities in evaluating, approving and monitoring biosimilars. Experiences from

several drug regulatory authorities, as well as industry, were shared.

In relation to pharmacovigilance, workshop 2: 'Pharmacovigilance for biotherapeutic products' was of special interest. Malin Fladvad of the UMC moderated, and also presented on 'Reporting Systems: UMC experience'.

ICDRA itself

ICDRA provides a strategic opportunity for drug regulatory authorities to discuss trends and challenges, but also to share solutions found in different parts of the world. The conference, on 26–29 August, was well attended by representatives from regulatory authorities from across the globe.

The conference was opened by Dirceu Barbano, Director Chairman of the Brazilian

Health Surveillance Agency, Arthus Chioro, Minister of Health, Brazil and Carissa Etienne, Director, Pan American Health Organization.

WHO presented the resolutions from the 67th World Health Assembly of principal interest to ICDRA: regulatory system strengthening and ensuring quality, safety and efficacy of biotherapeutics. A status report from the 15th ICDRA meeting recommendations was made.

Key safety discussions

From a pharmacovigilance perspective, of particular note were two workshops:

- Workshop A on 'Best practices in pharmacovigilance' with papers from India, Switzerland, Kenya (the East African Community) and Republic of Korea.
- In workshop G on the topic 'Preventing and reducing the risk to public health from SSFFC (Substandard/spurious/false-labelled/falsified/counterfeit) medical products', presentations were given by Argentina, USA and Tanzania. I spoke in this session on 'Pharmacovigilance as a tool to detect SSFFC medical products'.

Overall, this year's meeting in Brazil once again shows the value of having a forum to determine priorities for action in regulation of medicinal products, contributing to regulatory convergence and the improvement of the quality, efficacy and safety of medicinal products globally.

Full Pre-ICDRA and ICDRA programmes are available at: <http://www.icdra.com.br/content/programmes-pre-icdra>

Recommendations from the 16th ICDRA will be published in the quarterly WHO Drug Information journal.



Dirceu Barbano, Director Chairman of Brazilian Health Surveillance Agency, performing with the opening day's brief cultural presentation surprise – a local Rio de Janeiro band.

Indian guidance released

Kalaiselvan Vivekanandan

In a strategic move aimed at strengthening the Pharmacovigilance Programme of India (PvPI), the Indian Pharmacopoeia Commission (IPC) has brought out a guidance document to cater exclusively for the 150 ADR monitoring centres. Henceforth, this document will act as a point of reference to

ensure best practice with respect to ADRs, and help to streamline the process in a uniform manner.

Its key features focus on modalities of reporting ICSRs that will be helpful in developing and implementing a uniform

reporting culture in the Programme. It also describes the collaborative efforts between IPC and UMC, Sweden, to promote medicines safety. Interestingly, one of the recommendations of WHO assessment of the national regulatory authority was to have a guidance document of this kind for PvPI.

How can Collaborating Centres collaborate?

Sten Olsson

An unusual and innovative gathering recently took place in Groningen in the far north of the Netherlands. Representatives from ten past and present WHO Collaborating Centres for pharmacovigilance, drug statistics, pharmaceutical policy, regulatory sciences along with representatives from WHO Headquarters and the European Office in Copenhagen met on 26 August 2014. UMC was represented by Alem Zekarias, Johan Ellenius and myself.

pursue their shared interests outwith the full group, and better circulation of reports and relevant information between the Centres was agreed. Everyone welcomed ways of increasing face-to-face meetings (such as satellite meetings at conferences related to drug utilization, safety or policy, and, in particular, to take advantage of the presence of people at the World Health Assembly), liaison on student placement requests and considering possible research partnerships.

Collaborating Centres present in Groningen

WHO CC for Drug Statistics Methodology, Oslo, Norway

WHO CC for International Drug Monitoring, Uppsala, Sweden

WHO CC for Research and Training in Pharmacoepidemiology, Barcelona, Spain

WHO CC for Pharmacovigilance in Education and Patient Reporting, 's-Hertogenbosch, Netherlands

WHO CC for Pharmaceutical Pricing and Reimbursement Policies, Vienna, Austria

WHO CC for Pharmaceutical Policy and Regulation, Utrecht, Netherlands

WHO CC in Pharmaceutical Policy, Boston, USA

WHO CC for Pharmaceutical Policies, Rio de Janeiro, Brazil

WHO CC for Pharmaceutical Research and Science Policy, San Francisco, USA



A pause in the discussions...

Finding out about other CCs

The meeting explored ways in which the very diverse set of WHO Collaborating Centres, with WHO, could work together for mutual benefit, develop some joint short-, medium- and long-term goals and create an action plan for collaboration. Through sharing of background information prior to the meeting and very brief presentations from each Centre at the meeting, we learned about each other's core activities.

Lively idea sharing

The afternoon exploited the face-to-face nature of the meeting by offering three parallel breakout groups. These 'brainstormed' about some themes that had been raised during morning presentations and added more ideas to take forward. Although many of us had only met for the first time, discussions were free and lively.

Positive outcomes

By the close of the very positive day a new communication mechanism was agreed, sub-groups were formed (safety and policy) to

Some Centres have large data sets that may be of interest to other Centres as well as to WHO HQ and Europe; this also deserves serious attention.

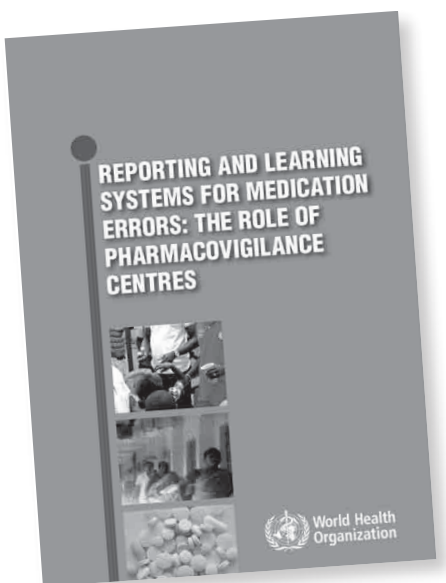


... of a happy group of collaborators in Groningen.

WHO medication errors booklet

A new document developed as part of the 'Monitoring Medicines' project has just been published. The booklet *'Reporting and learning systems for medication errors: the role of pharmacovigilance centres'* provides a framework for advancing the application, coordination and optimal use of pharmacovigilance evidence and dealing with medication errors. It also explores best practice for sharing that evidence and for strengthening the links between pharmacovigilance centres and other patient safety networks, in order to minimize preventable harms from medicines.

Background and technical guidance are provided on the principles and methods of medication error incident reporting and learning. This information is intended to assist stakeholders to begin to use the same philosophy, terminology and processes in undertaking this work.



Key project partners were representatives from the National Pharmacovigilance Centre, Morocco, the National Patient Safety Agency, England, WHO (Department of Essential Medicines and Health Products, Switzerland) and the Uppsala Monitoring Centre. The WHO Advisory Committee on Safety of Medicinal Products was consulted throughout the development of the publication for advice and critical review.

The booklet may be obtained via the Publications section of the WHO website.

Risk minimisation from CIOMS

CIOMS (the Council for International Organizations of Medical Sciences) has announced the publication of the report of CIOMS Working Group IX entitled: *'Practical approaches to risk minimisation for medicinal products: Report of CIOMS Working Group IX'*.

The CIOMS IX report provides guidance on how to determine which risks need additional risk minimisation beyond the routine risk minimisation measures of labelling and package inserts in the United States of America or patient information leaflets and summaries of product characteristics in the European Union. It addresses how to select the appropriate tools, apply and implement such tools globally and locally, and measure if they are effective and valuable. A CIOMS framework for the evaluation of effectiveness of risk minimisation, a discussion of future trends and developments, an annex on vaccines, and examples from real life, also feature.

This report included the consulting of a group of patients, sometimes overlooked in similar reports. Feedback obtained from these stakeholders regarding the role of the patient in the area of risk minimisation planning is incorporated.

Hard copies or electronic pdf files may be ordered by e-mailing to info@cioms.ch or via the CIOMS website www.cioms.ch.

Therapeutic Risk

Therapeutic Risk Management of Medicines, 1st Edition

Stephen J. Mayall and Anjan Swapu Banerjee

ISBN 9781907568480

This new 448-page book offers:

- an up-to-date practical guide on conceiving, designing, and implementing global therapeutic risk management plans for medicines
- a number of useful frameworks which add impact to RMPs (Risk Management Plans), together with regional specific information (European Union, United States and Japan)
- a comprehensive guide for performing risk management more effectively throughout a product's life-cycle.

The book aims to complement current regulatory guidance, by exploring key areas and practical implications in greater detail. Its chapters encompass a background to therapeutic risk management, strategies for developing RMPs, implementation of RMPs, and the continuing evolution of the risk management field.

The topic is of critical importance not only to the pharmaceutical and biotechnology industries, but also regulators and healthcare policymakers.

EMA updates

The regular and dynamic evolution of EU Good Pharmacovigilance Practices (GVP) continues.

Recent updates on the EMA GVP webpage (www.ema.europa.eu/ema/ > [Pharmacovigilance](#) > [Good pharmacovigilance practices](#)) have seen:

- the GVP Module VI on adverse reaction reports revised to reflect clarifications requested from stakeholders, in particular to align adverse reaction reporting from non-interventional post-authorization safety studies with study objectives.
- the GVP Module III on pharmacovigilance inspections revised to include a link to new EU procedures for such inspections.

New staff

We asked three new members of staff to introduce themselves

Yvonne Thomson

I was born in Fagersta and raised in Västerås, but have since spent most of my life in the Stockholm area, with the exception of some time in France and the US.

I started working as a physiotherapist, but after a few years went back to study and took a Master of Science from Stockholm School of Economics. My working experience in the pharmaceutical industry began in 1991 and has focused on marketing and sales, business development, market access, and lifecycle management. As head of department I have been involved in many therapy areas, cross functional groups as well as leadership teams.

I enjoy travelling with my husband and two children, but also relaxation closer to home; skiing, walking the dog, or horse riding.

At the UMC I will work as a section manager at Sales and Customer Relations. With Mats Persson and the team we will develop both the department and the collaboration within UMC. Focus will of course be on customer



Ingrid, Jonas and Yvonne.

needs and satisfaction, but always striving to reach sales targets.

Jonas Fransson

I was born and raised in Landsbro in Småland. Most of my adult life I've lived in Växjö in southern Sweden where I went to university. In June my girlfriend and I moved to Stockholm where we live for now.

I started academic studies to become a teacher, but after reflection I changed paths. I hold an MSc in Education, but more

importantly for my UMC job, an MSc in Mathematics which I finished in June 2014. I will be working as a Research engineer here at UMC with data extraction and computations. Prior to this I've been working in education, teaching at various places, and as a developer for educational applications in my own company.

Ingrid Johansson

I come from Lillhärda, a village in the forest in southern Härjedalen (bordering Norway). My interest in mathematics took me to Danderyd and an upper secondary school with a special mathematics focus. I continued to move

south and received my MSc in Engineering Mathematics from Lund University in June 2014. An interest in statistics, a wish to come closer to home and some fortunate circumstances has given me a position as a UMC research engineer.

When not working, I spend my time with friends, going out to dance salsa, practicing pilates, reading books and perhaps also going home to join the annual moose hunt.

Adjö to Bill and Sven

Sten Olsson

UMC is losing two of its pillars in software design to retirement, Bill Dagerus and Sven Purbe. Having access to dedicated experts in software development has contributed majorly not only to the stability of the software tools used internally and by all clients, but also to the stability of UMC itself.

Although not directly employed until the last decade, Bill was part of the IT development team from the first day of UMC's establishment in 1978. Initially he was based at the University Data Centre, UDAC, later at software service providers like PharmaSoft.

Sven has been the SQL 'guru' at UMC for almost 15 years. In times of very high

demand for IT developers it has been a privilege to for us to be able to keep our experienced and specialized IT experts.

Losing these pillars will not make UMC or its IT tools fall apart but we will be considerably weaker in many other aspects e.g. knowledge of classical music and its composers and engagement by the pool table!

We wish Bill and Sven all the best for their life in retirement.

UMC's vision is a world where all patients and health professionals make wise therapeutic decisions in their use of medicines



UMC's Vision and Mission

Our Vision, "A world where all patients and health professionals make wise therapeutic decisions in their use of medicine", reflects our organisation's soul and helps all of us keep our mind focused on a clear goal. With that aim in mind we intend to make our communications even stronger and reach a wider audience. To achieve that goal, we have established a global communications team that will lead our efforts to step up our impact in the development of pharmacovigilance.

We know that challenges, risks, opportunities and solutions need to be communicated more effectively. We are now working on developing different dialogue and information platforms that will bring us closer. We intend to offer communications trainings to national centres and build partnerships that will help us disseminate more knowledge on patients' safety. We aim for impact and sustainable changes.

Every brick counts on the construction of a great building. Every communication matters when we work towards a wiser use of medicine.

SAFER visitor

Vassilis Koutkias, Senior Researcher, Marie Curie Fellow at INSERM* in Paris, was a visitor with a challenge. He spoke to UMC staff in September about the need for increased drug surveillance through the synthesis of all possible information sources.

His research, being conducted in the scope of the SAFER (Semantic integrAtion and reasoning Framework for pharmacovigilancE signals Research) project, has as its goal the construction of an integrated, semantic framework that aims to enable the

combinatorial exploitation of diverse computational signal detection methods and relevant data sources.

The ultimate goal of SAFER is to contribute in timely and accurate signal detection by establishing the means for the concurrent exploitation of multiple data sources and analysis methods in a systematic way. Further information: <http://safer-project.eu/>

*Institut national de la santé et de la recherche médicale (French Institute of Health and Medical Research)



US visitors

Keaton Smetana and Bryan Cartmell, advanced pharmacy graduates from the University of Tennessee College of Pharmacy paid a short visit to the UMC offices last June. They were on an international rotation in Sweden to gain understanding of the pharmacist's role outside the United States. They also traveled to Stockholm, Umeå, and Luleå during their rotation as well as two different pharmacy schools.



DATES	TITLE	PLACE	ORGANISER/CONTACT
5–6 November 2014	Case Narrative Writing for Reporting Adverse Events	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 www.dsru.org/courses E-mail: jan.phillips@dsru.org
5–7 November 2014	Latin American PV Congress	Lima, Peru	E-mail: salvarez@digemid.minsa.gob.pe
11–12 November 2014	Monitoring the Effectiveness of Risk Minimisation	London, UK	Drug Safety Research Unit (See above for contact details)
19–20 November 2014	Pharmacovigilance in Products Subject to Licensing Agreements	London, UK	Drug Safety Research Unit (See above for contact details)
1–3 December 2014	14 th Annual Conference of Society of Pharmacovigilance, India	Aligarh, India	SoPI http://sopicon-2014.blogspot.in/ E-mail: pharma.jnmc@gmail.com
1–3 December 2014	Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 E-mail: registrations@management-forum.co.uk www.management-forum.co.uk
21–23 January 2015	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (See above for contact details)
25–26 February 2015	Back to Basics in Pharmacovigilance	Southampton, UK	Drug Safety Research Unit (See above for contact details)
11–12 March 2015	EU Regulations and Guidelines for Pharmacovigilance	Southampton, UK	Drug Safety Research Unit (See above for contact details)
20–22 April 2015	International Meyler course in Pharmacovigilance	's-Hertogenbosch, the Netherlands	Lareb www.lareb.nl/WHOCC
23–24 April 2015	Lareb conference on patient reporting: Current perspectives and future possibilities	Leiden, the Netherlands	Lareb www.lareb.nl/WHOCC
18–29 May 2015	UMC Pharmacovigilance Training Course	Uppsala, Sweden	www.who-umc.org > Pharmacovigilance > Education & Training
11–14 April 2015	ISPE Mid-Year Meeting	Bordeaux, France	International Society for Pharmacoepidemiology (ISPE) www.pharmacoepi.org
9–11 June 2015	Signal Detection Conference	London, UK	Drug Safety Research Unit (See above for contact details)
22–26 August 2015	31 st Annual Conference ICPE	Boston MA, USA	International Society for Pharmacoepidemiology (ISPE) www.pharmacoepi.org
27–30 October 2015	ISoP 2015 Annual Meeting	Prague, Czech Republic	International Society of Pharmacovigilance www.isoonline.org E-mail: administration@isoonline.org

The 2nd African Society of Pharmacovigilance Meeting scheduled for Accra, Ghana from 3–5 December 2014 has been postponed. The new dates for the 2nd ASoP Conference will be 25th to 27th November 2015, in Accra, Ghana.



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.

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

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

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

Internet: www.who-umc.org

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