For everyone concerned with the issues of pharmacovigilance | UPPSALA REPORTS | April 2014

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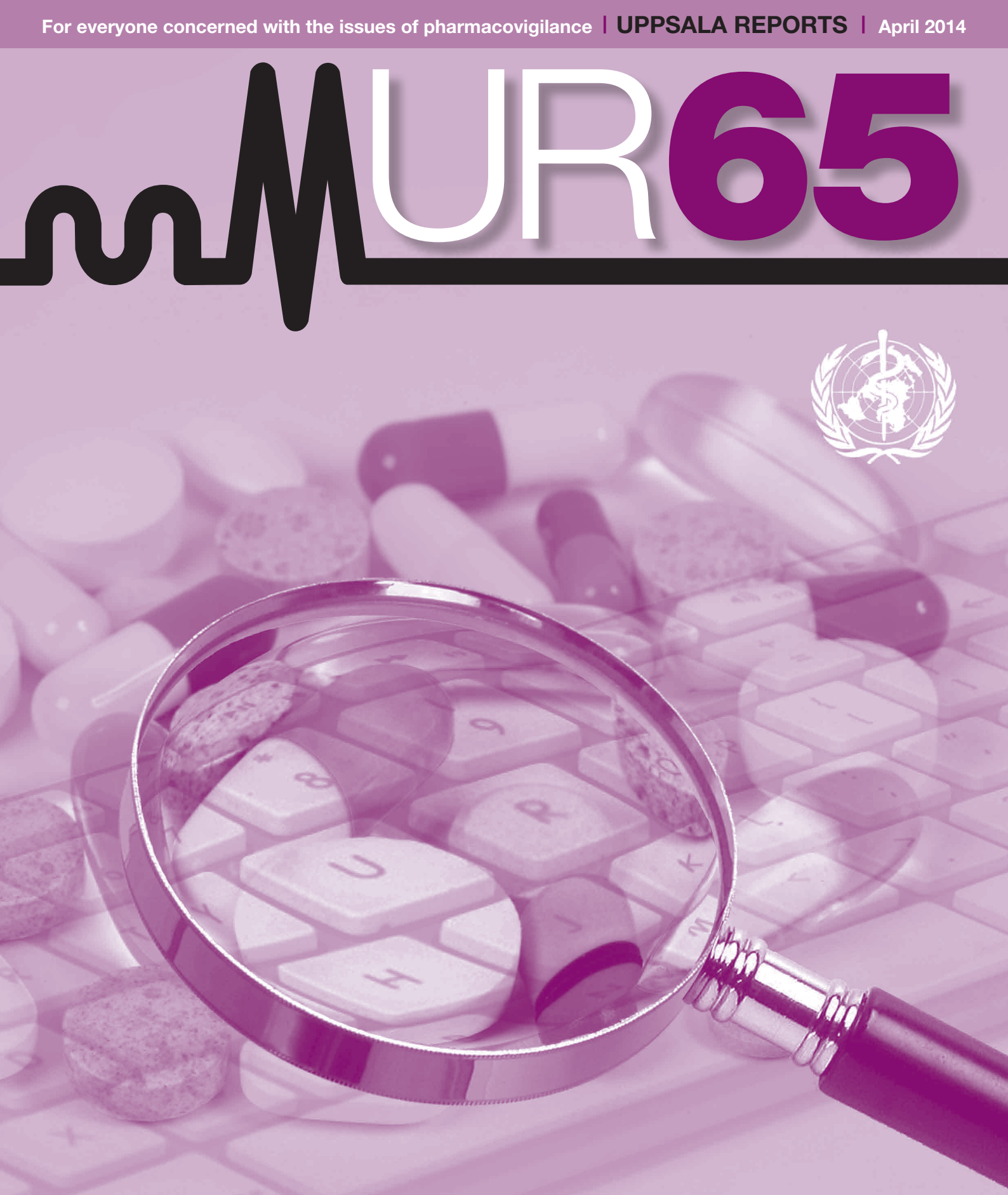


A view from Geneva | New PhD at UMC

Thalidomide | Arab guidelines | Monitoring in MDR-TB

Marie Lindquist
Director
Uppsala Monitoring Centre

My sister, born in the spring of 1961, could have been one of the Swedish 'thalidomide babies'. Having read in the newspaper about what seemed to be a 'wonder drug', my father suggested my pregnant mother would benefit from its tranquillizing effect. She went to see her doctor, who did not agree. He said there was no need for her to take any drug, and that she should go home and tell her husband that if anyone needed calming it was probably him. A brisk walk was proposed as a suitable remedy. Both my parents are exceptionally grateful for this advice. I can only imagine the feelings of shock, and grief, and self-blame other parents experienced when they realised that their children had been so horribly harmed by what they had thought was a perfectly safe drug.

"It all started with thalidomide". How many times have we not heard, or ourselves used this phrase as an introduction to the history of pharmacovigilance. Indeed, the thalidomide catastrophe was the catalyst that brought about new science and regulation; and it was the rationale for countries to join forces under the WHO umbrella and create a programme with the aim of preventing future patient harm from medicines.

In this issue of Uppsala Reports, Ralph Edwards gives an account of a recent meeting at WHO headquarters in Geneva, with the aim of discussing and defining diagnostic criteria for thalidomide malformations. After 50 years, there is still no internationally-agreed case definition for a 'thalidomide syndrome' that will allow the distinction, beyond reasonable doubt, between malformations caused by thalidomide, and those that have other causes. How can that be? The horror of the thalidomide deformities led to public outcry and calls for governments (particularly in Europe) to organise lifelong support for victims. Physicians were called upon to assess those thought to be damaged by the drug. There was little epidemiological data to help them in those decisions, so the diagnostic criteria were a developing set, at the same time as uncertainty about exposure at the critical time in pregnancy was common.

What happened then belongs to the past - but the use of thalidomide is not history. The first victims of thalidomide teratogenicity, now in their fifties, are not the only ones. Since it was found that thalidomide has positive effects in the treatment of erythema nodosum leprosum, myeloma and some autoimmune disease, it has been used in many seriously-ill patients with good results. Tragically however, in spite of rigorous safety measures in countries where thalidomide is registered for use, there are new cases of babies being born with phocomelia and other malformations connected to maternal thalidomide use. That's why it is imperative that renewed efforts are put into the development of evidence-based guidance for causality assessment of possible thalidomide foetal malformations.

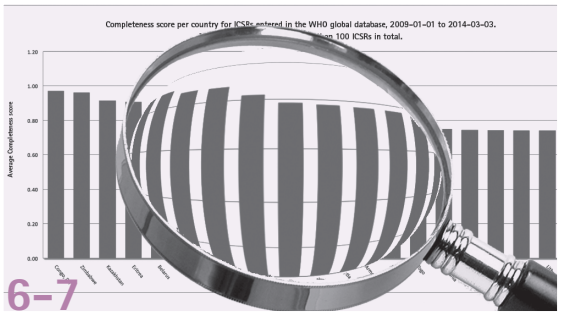
The meeting in Geneva also served as a stark reminder of the dilemmas facing anyone making decisions about the benefits and harms of medical treatment. In the case of thalidomide, and other teratogens, where the difference between the best and worst possible outcomes is so great, these decisions are even more difficult. Do regulatory measures and patient information provide adequate protection for vulnerable patients, such as those with leprosy, many of whom are living in impoverished, rural areas, where illiteracy is rife, and where the natural behaviour is to share medicines among the extended family? Is one child born without arms and legs one too many? If I were that child, or its parent, I know what I would think. One the other hand, is it reasonable that we should deprive patients who suffer from debilitating, perhaps fatal, disease, of a treatment that can save their life, or provide relief from what otherwise would be intolerable suffering?

How can we make the right decisions? I believe in good use of epidemiological and healthcare data to inform regulatory and clinical decision-making, and find the development of computerised clinical decision support systems both important and exciting. But they will not replace sound clinical judgment! The need for competent and caring doctors to provide support and advice when making tough treatment decisions is as great today as it was in 1961.

FEATURES

REGULARS

the UPPSALA MONITORING CENTRE



Statistics

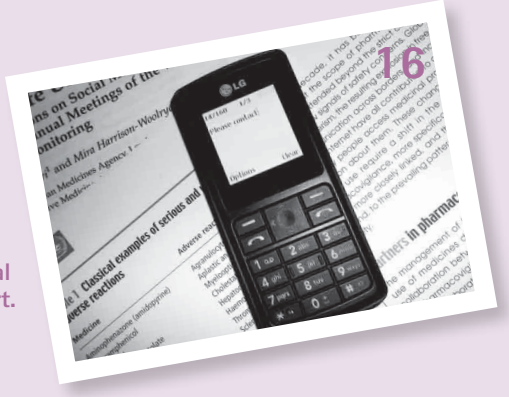
Quantity is not the only consideration for the WHO database.

Collaboration reviewed

Looking back on the successful Monitoring Medicines project.

Research to the fore

Highlights of recent activities in UMC research, including Ola Caster's doctorate.



Innovation around the world

Nigeria and India introduce additional ways to report.

An integrated, global approach

Dr Clive Ondari is Coordinator of the WHO-SAV (Safety and Vigilance) team in Geneva, managing medicine safety, vaccine safety and SSFFCs. Previously he served in WHO as the coordinator for Access to Essential Medicines as well as the focal point for antimalarials. At the same time, he was Chair of the Ethics Review Committee at WHO/HQ.

Prior to joining WHO, he was Associate Professor of Pharmaceutics at the University of Nairobi and also served as the Vice-Chair of the Pharmacy Board (Kenya's medicine regulatory agency). *Uppsala Reports* invited him to share his thoughts on a wide range of medicines safety topics.

A vital restructure

Dr Ondari sees immediate benefits of now having medicine safety, vaccine safety and SSFFCs under one roof at WHO. "By moving away from a product-based approach to one of function / service (safety in this case), we now have the opportunity to put the patient at the centre of our attention. Bringing these functions within one team, we give out a strong message that it is not just about the medicine or the vaccine, but vigilance is valid only when we look at it all together, across various medicinal products, in the

Medicine safety, vaccine safety and SSFFCs together
WHO can now lead by example
The patient at the core

context of the patient who will receive these products in his / her lifetime." Historically, vaccines and medicines programmes have developed in parallel, often operating in isolation. "WHO can now lead by example and demonstrate how we should share infrastructure, resources, knowledge and information, across the product streams, for the benefit of the patient."

Reaching out to PHPs

However, many public health intervention programmes (PHPs) continue to run vertically in countries. "As we roll out this unified approach to safety monitoring of medicinal products we will support the strengthening of the links between these programmes and safety monitoring in countries. We are mindful that without exchanges between immunization, treatment programmes and safety monitoring, the use of resources is wasteful, and leads to partial/incoherent strategies to contain the harmful effects of pharmaceutical products in patients."

Strengthening links between PHPs and safety monitoring

Expanding and broadening pharmacovigilance

Since the 2002 WHO definition of the term pharmacovigilance, its scope has expanded into three broad categories:

- Harm caused by the inherent properties of the active substance
- Harm caused by products of inferior quality
- Harm caused by inappropriate use e.g. medication errors.

WHO encourages and supports all Member States participating in the WHO Programme for International Drug Monitoring to collate and communicate all adverse reactions due to medicinal products, including those due to inferior quality and inappropriate use, to the WHO global adverse drug reactions (ADR) database.

"The database is managed and maintained by the Uppsala Monitoring Centre on behalf of WHO and the Member States. Bringing all the information to one global repository allows the data to be managed in a coherent and efficient manner. Of course this global database is a harms database. When a poor quality product or an inappropriate use of the product does not lead to a discernible harm in the patient the problem might not be reported to the ADR database. In those instances, we would rely on information from other networks, such as the WHO SSFFC rapid reporting system, to complete our knowledge. This allows us to access, manage and learn from the information efficiently across the two networks."

All information at one global repository
Other networks complete our knowledge
Access, manage and learn from the information across networks

Collaborating centres

The WHO Programme for International Drug Monitoring is managed by WHO-SAV but its operational aspects are taken care of by four WHO Collaborating Centres with more manpower, capacity and direct exposure to national pharmacovigilance centres.

WHO-SAV global coordination
Strong WHO-SAV and effective network of Collaborating Centres
SAV coordinates CCs, driving WHO Programme

"As part of the WHO secretariat, WHO-SAV's role includes providing relevant support to countries. This means being 'there', in the countries, working with them, for them, hands-on – that is the principle that governs WHO-SAV in its leadership role: global coordination through local support. A strong WHO-SAV thus requires an effective network of Collaborating Centres (CCs) to serve as the SAV field-force, in the countries and the regions, supporting WHO-SAV in its mandate. A strong WHO CC network will help SAV deliver its pharmacovigilance strategy without undermining the SAV leadership. And by providing clear, well-defined roles with terms of reference for each of those CCs, SAV will make sure that all aspects of safety and vigilance are addressed by them, from training to tool kits, from pharmacovigilance in public health to patient reporting. SAV has the important role of coordinating these CCs, driving the Programme forward. There is a lot to be done and we all have our distinct roles, it's all about collaboration, not competition."

Vigilance in PHPs

Introducing pharmacovigilance in PHPs is a particular challenge because of their focused and vertical nature in countries. WHO-SAV is leading the efforts to bring together PHPs and pharmacovigilance centres. "We are emphasizing the gains achievable by joining forces, how PHPs benefit from pharmaco-vigilance data and how pharmacovigilance centres benefit from working closely with the PHP including the sharing of resources

WHO-SAV leads efforts to bring together PHPs and pharmacovigilance centres, working with Global Fund

– that are often very limited. We also have an unique opportunity with some of the new medicines such as bedaquiline where pharmacovigilance will need to accompany the introduction of the medicine in MDR-TB treatment. Working with partners such as the Global Fund has also paved the way for integrating pharmacovigilance into PHPs; countries are being encouraged to introduce at least the minimum pharmacovigilance requirements when accessing Global Fund grants for medicines. We need to invest in similar collaborations and work with all relevant partners to ensure that PHPs and PV centres work together, towards evidence-based treatment policies that pose minimum risk to patients."

Central role of patients

There is then the role of patients/consumers in the learning process for the safe use of medicines. "If we keep patients out of the picture, we will never get the full story about medicines safety. We could learn about the ADRs a lot quicker, and we could learn about those aspects of information that only a

Who but the patient can describe an ADR?

patient can provide, such as the effect of ADRs on quality of life, for example. The patient is the one experiencing the ADRs. Who else could describe the ADR better? How could we possibly exclude them in this learning process?"

Monitoring prequalified medicines

Pharmacovigilance requirements apply for all medicines, and WHO Prequalified medicines are no exception. As part of the pre-qualification process the WHO PQP (medicines programme) reviews safety data in the product dossiers submitted by manufacturers.

"The WHO PQP does not have a regulatory mandate nor authority to ensure the post-marketing surveillance of these products. This aspect remains the responsibility of national regulatory authorities; of course WHO-SAV will work with national authorities to build the necessary competence for this post-marketing surveillance in the country.

WHO PQP and SAV programmes working with relevant manufacturers

However, whenever post-marketing safety data would prompt risk minimization activities and / or risk management plans for prequalified products, then, in those instances, the WHO PQP and SAV programmes would work with the manufacturer in question, to make sure that the relevant RMP are in place for the product in question. A good example of this is the case of the prequalified Amodiaquine-Artesunate (AS-AQ) combination product; based on key post-marketing safety data and a signal from the WHO-UMC data on extra-pyramidal symptoms with AS-AQ, the WHO PQP and SAV programmes worked with the manufacturer to update the AS-AQ Summary of Product Characteristic (SPC) with the relevant information."

The next threats?

Dr Ondari also has in mind medicine-related threats, (e.g. antimicrobial resistance, health impacts of SSFFC, adverse reactions) that will have the greatest impact on public health over the next ten years.

"They are all interconnected, have a 'cause and effect relationship', if you will. For example, an SSFFC antimicrobial product could lead to a loss in therapeutic effect (an adverse outcome), which in turn could (arguably), lead to antimicrobial resistance. So it's not about what will have the greatest impact over the next ten years, but to understand the root cause and to have a strategy in place to address and resolve the root cause.

Our current efforts in maintaining a database on SSFFC medical products will give us the solid evidence to inform policy and ensure appropriate interventions at the global, regional and country level."

Innovations for the WHO Programme

"We would like to see a strategic and concerted effort to be more supportive to

More support to Member States in LMIC and public health programmes

Member States in low- and middle-income countries (LMIC) and to public health programmes. For example, we would like to

Methods that can better characterize safety issues within PHPs

How to detect signals relevant to quality patient care in LMIC

push for pharmacovigilance methods that can better characterize safety issues within PHPs, towards better evidence for treatment polices within these programmes. We would also like to explore how we could detect signals that are relevant to the provision of quality of care of patients in these countries."

Clive Ondari was born in Kenya, educated in the USA up to PhD level. He was an intern at the US FDA which sparked his interest in regulatory affairs. He worked briefly in the pharmaceutical industry before returning to Kenya to work in academia and the medicines agency.

"Outside the pressures of international vigilance I enjoy walks in the many lovely paths in the Geneva area. I listen to African and Latino music; and my last non-work reading was *Buddha* by Deepak Chopra – recommended by my 17-year old son."

VigiBase: Quality in focus

Therese Lundin and Sara-Lisa Fors

In the past few years UMC focus has shifted from mainly recognizing the total number of collected Individual Case Safety Reports (ICSRs) to also emphasizing the importance of ICSR quality, if the collected data is to be useful for its purpose. Efficient ICSR analysis and signal detection work demands ICSRs of sufficient quality.

Quality versus quantity

For measuring ICSR quality the UMC uses the Completeness score, a measure of the amount of essential information available in a structured format, as it appears in VigiBase. The Completeness score is calculated from certain fields of information, selected for their importance for medical assessment. Each report receives a score from 0 to 1, and a high score corresponds to a well documented case. It is important to remember that the score does not take into account the relevance of the reported information, i.e. the evidence for a causal relation between medicine and reaction.

Figure 2

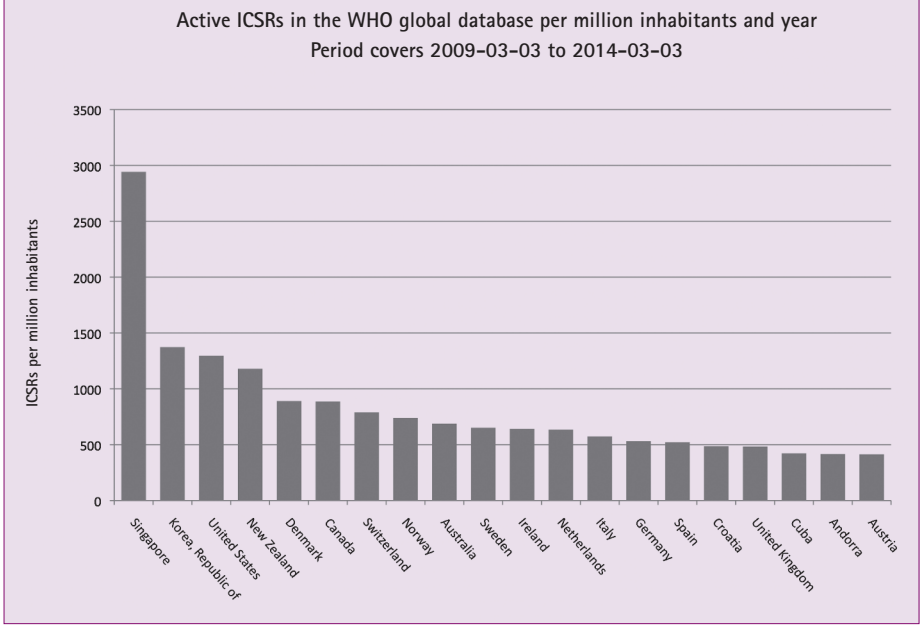


Figure 1 shows the top 20 countries with regard to average Completeness score on ICSRs submitted to VigiBase during the past five years. Several African countries are represented in this graph, including DR Congo and Zimbabwe at the very top. Many pharmacovigilance systems in the African region are relatively young, and creating a robust reporting system to establish a steady high flow of ICSRs takes time. It is not surprising therefore that countries with more mature systems appear in the quantitative graphs more often than most African countries. ICSR quality, on the other hand, is possible to invest in right from the start.

It is also worth noting that Italy, Croatia and Spain all show up among the top 20 countries both in terms of their Completeness scores and the number of ICSRs submitted per year and population (Figure 2), i.e. they achieve good results in both the quality and quantity parameters.

Different measures of quality

It is useful to keep in mind that apart from the completeness, several other parameters also affect the quality of the ICSR data, as outlined in Table 1. Ideally, all these listed parameters should be considered for a complete picture of the quality of any dataset such as an ICSR database.

Hence, the Completeness score alone does not give a comprehensive picture of a dataset's quality, and its potential usefulness

Figure 1

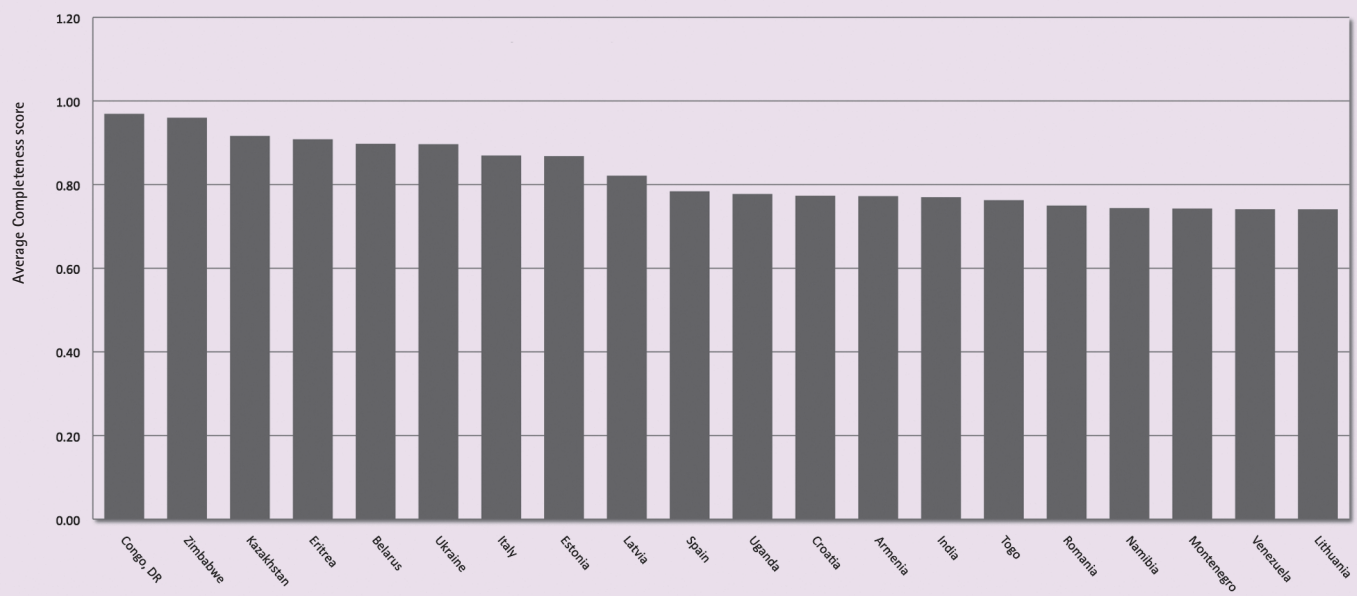
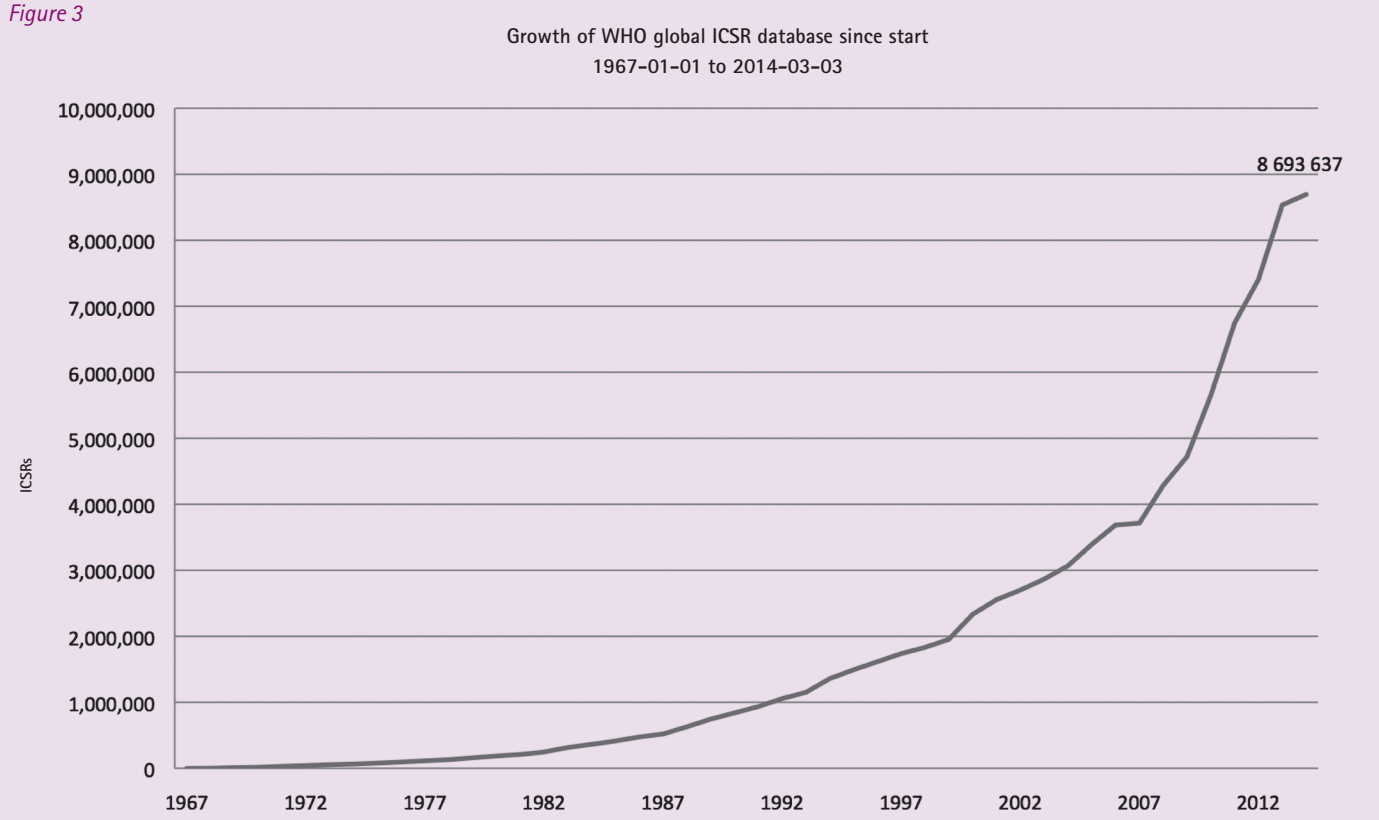


Figure 3



for efficient signal detection. The Completeness score is, however, a good indicator of (for example) essential data that is not being collected at all, or of available data that is lost in ICSR extraction for external submission. The Completeness score on single ICSRs (on report level) can also be used to identify ICSRs which are likely to contain the most valuable information, for example if you need to review a large dataset in a short time.

Steady growth

The growth rate of VigiBase continues to be stable, and the total number of ICSRs is now close to 8.7 million (Figure 3). Since our last statistics update in *Uppsala Reports 63*, two new official member countries (United Arab Emirates and Angola) are now contributing to this growth.

The top 10 contributors to VigiBase since the start of the WHO Programme remain the same (Figure 4), although in a slightly different order.

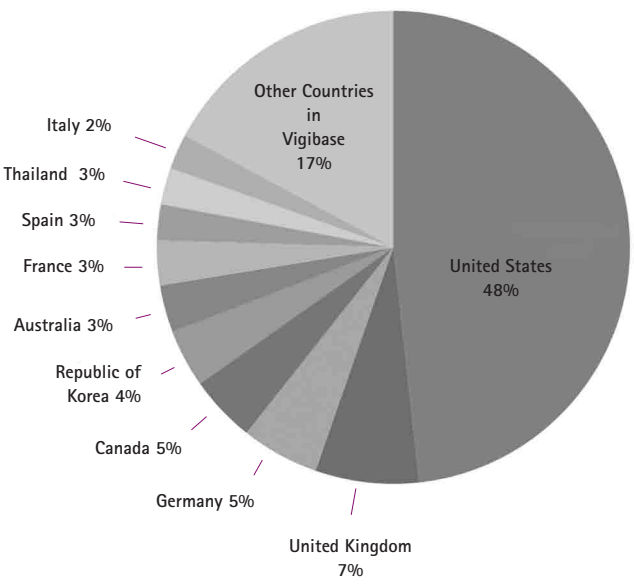
Table 1. Quality parameters that should be considered in a complete quality management system.

Parameter	Description
Accuracy	Does the information represent the "real-world" values correctly?
Completeness	Are all critical items included? Are they recorded in a usable way?
Conformity	Do the data values conform to specified formats and controlled vocabularies?
Consistency	Do interdependent data items provide conflicting information?
Currency	Is the information up to date?
Duplication	Does the data set contain multiple representations of the same case?
Integrity	Can related records be linked together?
Precision	Is the output level of detail supported by input data?
Relevance	Is the data fit for purpose?
Understandability	Can the data be interpreted correctly? No ambiguities?

Sources: Lindquist M. Data quality management in pharmacovigilance. Drug Safety 2004;27(12):857–70

Bergvall et al. vigiGrade - a tool to identify well-documented individual case reports and highlight systematic data quality issues. Drug Safety 2014;37(1): 65-77

Figure 4 Country distribution in WHO global ICSR database
1 January 1967 to 3 March 2014



Thalidomide: a tough topic

Thoughts from Ralph Edwards on a meeting held in Geneva, February 2014

Why have a meeting?

It is over 50 years since McBride published the first article on thalidomide and congenital abnormalities[1]. Much has changed since then, and this meeting was concerned with four major topics:

- the diagnosis of thalidomide-induced limb reduction in humans and the frequent absence of clear evidence of exposure to the drug
- experimental work concerning the mechanism of action of thalidomide in the human fetus, and whether any of that work helps with diagnosis in humans
- current understanding of genetic causes of limb reduction deformities as alternate diagnostic possibilities
- increasing use of thalidomide for new indications, particularly in serious erythema nodosum leprosum reactions, and the current clinical situation regarding foetal damage around the world.

The UK Thalidomide Trust proposed that an independent, expert, international clinical and scientific group meet and discuss the situation regarding thalidomide, and generously paid for it. They asked the UMC and WHO to ensure the meeting's scientific independence. How far did the meeting go in answering the questions?

The diagnosis

Whilst it is clear that clinicians, both in the early days and now, generally agree on the main features of the syndrome, genetic abnormalities may provide alternative diagnoses. Physicians in the early years, on humanitarian grounds, gave the benefit of the doubt to possible thalidomide victims with clinical features other than phocomelia, even when exposure was in doubt. At the meeting a set of data, derived from a thorough search of world literature, was tested with a few examples, which produced a group of core clinical features that were agreed by the clinical experts.

German cases

Even better was an un-translated and unpublished set of old cases from Germany with known exposures to thalidomide. These were compared to the contemporary background of all unexposed cases of foetal limb deformities. It was agreed that this data should be translated and reviewed by clinical experts. Following this, a probabilistic decision tree would be developed using the old data, current data from known exposures in Brazil, and compared with up-to-date data on known unexposed cases (mainly genetic causes).

Problems of causation

It was not solid logic to assume drug exposure from the clinical syndrome. It is essential to have an agreed set of core clinical findings that have been associated with known exposure to thalidomide, and excluding alternative causes. It was also agreed that it would be currently wrong to assume that the many foetal abnormalities found in animal experiments should be considered part of an accepted core syndrome in humans.

Possible mechanisms

There was an introductory talk on the known basic genetics, biochemistry and physiology of limb development. Three major possible mechanisms for thalidomide damage are:

1. Binding to a cereblon (CRBN) which is a protein encoded by a gene on chromosome three. Normally, CRBN via ubiquin ligase forms a complex with damaged DNA, but if its activity is altered by thalidomide it might possibly cause damage to normal DNA during limb development.
2. There has been extensive investigation of possible damage to the neural crest. Thalidomide is certainly neural toxic in animals and humans. For many years it has been postulated that human foetal limb defects might be related to neural crest damage.
3. There is clear evidence that thalidomide reduces angiogenesis in adult humans as well as in experimental animals. It is postulated that reduced angiogenesis may result in limb reduction in humans.

Scientists look forward

There was a separate discussion amongst the scientists, who knew each other by name but had never met. They thought the meeting extremely useful, and although they were rightly reticent about guessing the future, it appeared that some increased, basic understanding of pharmacological and physiological importance might come from this work. There was also speculation that the mechanisms proposed above may result from a single fundamental process induced by thalidomide.

Genetic defects confused with thalidomide damage

Since the 1960s there has been a steady growth in clinical genetics. In the last decade there has been a rapid expansion of databases of foetal abnormalities associated with genomic data. We were given an overview of Poland's database on foetal limb reduction and genetic causes. There were several syndromes that might be confused with thalidomide damage. Ideally, genetic testing should now be done routinely to confirm diagnoses, though this may not be possible in some emerging economies.

The current clinical challenge

Thalidomide is a useful drug during leprosy treatment. It is also an effective night sedative, anti-emetic and tranquilliser. It has found a useful place in treating myeloma and is explored for its use in other cancers and in vasculitic autoimmune diseases. Thalidomide is becoming more available through new manufacturers, and not just the originating company. It is sold by one company as a drug 'with no side effects'!

In the current cases some people had been exposed to thalidomide that had been handed on to their mothers. In many countries where leprosy is prevalent there may be little or no effective control or information about the devastating foetal effects of thalidomide.

There was a clear proposal at the meeting that more should be found out about the global availability and use of thalidomide, perhaps first concentrating on its safe use in leprosy.

1. McBride WG. Thalidomide and congenital abnormalities. *Lancet.* 1961;2:1358.

Your contribution matters!

Anna Hegerius

Last September, a large group of excited pharmacovigilance professionals from over 50 countries arrived in Rome for the annual National Centres meeting. As always, the outcome was a couple of intense but very rewarding days with shared experiences and new knowledge. During the meeting, a questionnaire was handed out by UMC representatives. Except for a few people who might enjoy filling in forms, the majority probably thought: 'Oh no, not another form!' In spite of this, the response rate was high and we would like to thank everyone who took the time to fill it in, particularly those who also provided very valuable additional comments.

Some outcomes of the survey are presented here. The numbers represent the National Centres that participated in the survey, not all those in the WHO Programme.

Sending ICSRs to UMC

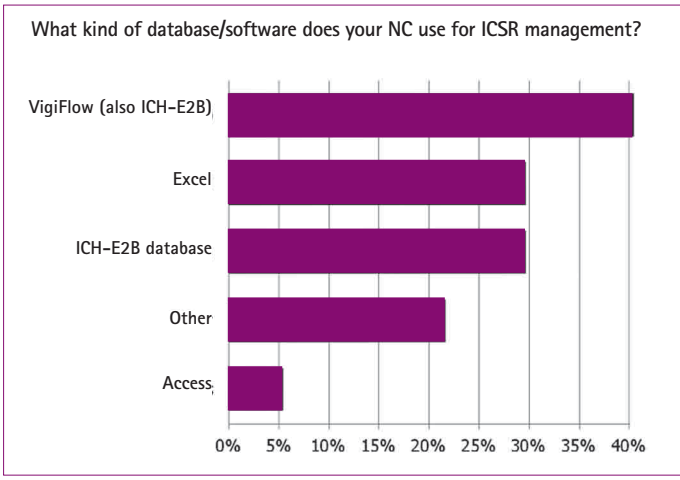
- Almost all National Centres (NCs) are aware of the requirement to send ICSRs to UMC at least every quarter.
- Over 80% also submit non-serious ICSRs to UMC.
- The majority of NCs are satisfied with UMC feedback on ICSRs and their quality.

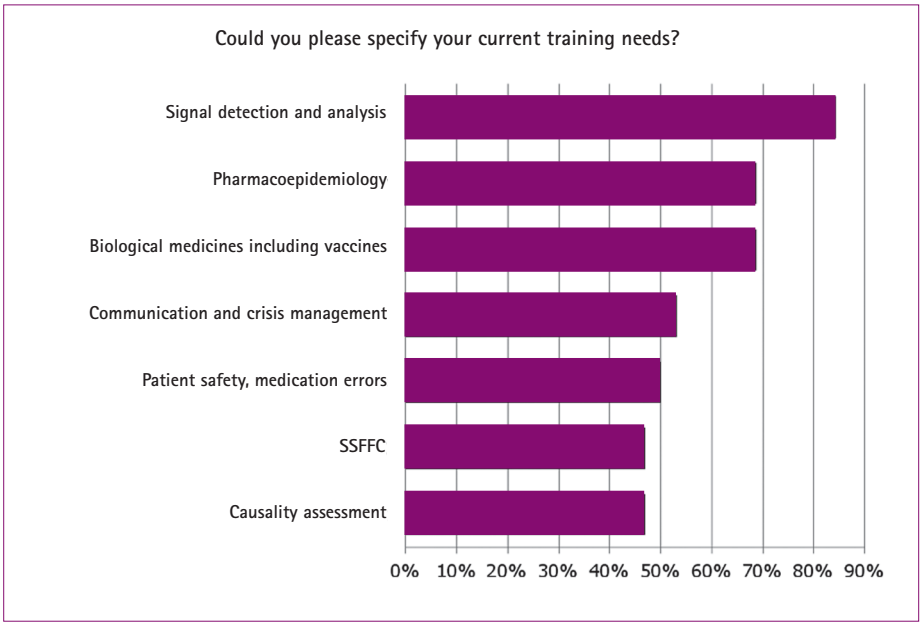
Data management

- 70% of NCs use an E2B compatible database, including VigiFlow (see graph).
- UMC tools such as VigiFlow and VigiLyze are well known and appreciated.
- The majority of NCs are aware that VigiBase search requests can be sent to UMC; about half have used this service.
- Of NCs using WHO-ART, almost 90% are satisfied, a few countries need WHO-ART in their local language. (WHO-ART is currently available in English, French, Spanish, Portuguese, German and Italian, and will be soon in Chinese.)

Training

- 80% of NCs are in need of training. The most requested topic is signal detection and analysis (over 80%), followed by biologicals including vaccines and pharmacoepidemiology (both over 70%), crisis management, medication error (around 50%), SSFFC and causality assessment (over 40%).
- 70% of NCs have had staff on the UMC Pharmacovigilance Course and 10% plan to attend.
- Most prefer interactive workshops but many have also indicated that they prefer distance training such as e-learning and webinars. Half also use the UMC web lectures (http://media.medfarm.uu.se/play/kanal/4). UMC aims to extend distance training.





Communications

- Almost all NCs read both Uppsala Reports and SIGNAL. 75% also follow-up on the signals.
- The majority of NCs are aware of the online information channel and discussion forum Vigimed, but unfortunately not many are actively using it. Many are unfamiliar with the guidelines.
- The UMC website is frequently visited by NCs. Most information available is considered relevant and much appreciated.

This feedback is highly relevant in order to ensure that UMC serves National Centres in line with their current needs and expectations. Please do not hesitate to contact us anytime if you have feedback or suggestions regarding our services. And the next time you are asked to fill in a form, please remember that your contribution really matters. Thank you for helping us to support you!

Global Services

As of January 1, 2014 the Pharmacovigilance Services Department at UMC is named Global Services. Global Services supports the WHO Programme for International Drug Monitoring by providing education, training and pharmacovigilance consulting services. Global Services also works with key stakeholders adjacent to the Programme supporting strategic initiatives, regional coordination, and effective communication.

The re-organization is another step to building an effective team, led by Anki Hagström – Head of Global Services, to support the WHO Programme. In addition, to Anki key leadership and support is provided by Sten Olsson – WHO Programme Expert, Pia Caduff – Chief Medical Officer, Paula Alvarado – Head of Global Communications and Antonio Mastroianni – Chief Operations Officer.

Monitoring Medicines 2009–2013

Ennita Nilsson

On the 5th March 2014, Uppsala Monitoring Centre staff joined the project team to commemorate the end of the Monitoring Medicines project. Ghazaleh Karimi, Monica Plöen and Ola Caster, the sub-project leaders, together with the project coordinator Sten Olsson, the Chief Finance Officer Birgitta Toreheim formed a panel to share the project results, hosted by Ennita Nilsson, the project manager. Although the project has officially ended, the team was proud to announce several project spin-offs that are being rolled-out or being prepared to be launched.

The final Monitoring Medicine presentation at the UMC.

From plan to reality

The idea of this international project came from Shanthi Pal, group lead for medicine safety at WHO headquarters who wrote the project plan and application to the Seventh Framework Programme (FP-7) of the Research Directorate of the European Commission in 2007. The project was granted nearly 2 million euros in 2009.

The Uppsala Monitoring Centre coordinated the project with WHO as lead partner, working together with selected partners in a project consortium. These were: Medical Products Agency (Sweden), Lareb foundation (Netherlands), National Patient Safety Agency (UK), Centre Antipoison et de Pharmacovigilance du Maroc (Morocco), Copenhagen HIV Programme (Denmark), Elliot Brown Consulting Ltd (UK), Zuellig Foundation (Philippines), University of Ghana Medical School, Accra, and Pharmacy & Poisons Board (Kenya).

Ambitious objectives

- Support and strengthen direct consumer reporting
- Expand the role and scope of pharmacovigilance centres to also consider medication errors
- Promote better and broader use of existing pharmacovigilance data focusing on indicators of dependence and substandard quality
- Develop additional pharmacovigilance methods to complement spontaneous reporting systems particularly Targeted Spontaneous Reporting (TSR) and Cohort Event Monitoring (CEM)
- Develop a learning tool for prediction and management of adverse reactions associated with HIV/AIDS treatment.

A catalogue of achievement

- Guidelines and web-based tools for direct patient reporting of drug-related problems
- A guidance document on learning from medication error reports, and methods for detection and analysis of medication errors in pharmacovigilance centres
- Methods to improve identification of early indicators of dependence liability in VigiBase
- Methods highlighting clusters of suspected substandard medicines from ICSR reports
- Methods with guidelines to complement spontaneous reporting adapted to public health programmes CEM and TSR
- Training for application of developed methods in HIV/AIDS and malaria (Africa and Europe)
- Web-based tools for data management
- Pilot safety studies in three countries
- Database of validated information of adverse reactions to HIV medicines, and tools to easily search, retrieve and evaluate information from this database, via www.hivpv.org.

Some key publications

- Safety Monitoring of Medicinal Products: Reporting system for general public
- Experiences with Adverse Reaction Reporting by patients – an eleven-country survey
- Practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis
- WHO Strategy for collecting safety data in public health programmes: Complementing spontaneous reporting systems
- Reporting and Learning systems for medication errors: detecting, analysing and preventing within Pharmacovigilance centres
- The contribution of direct patient reporting to pharmacovigilance: Florence van Hunsel, PhD Thesis.

Other highlights

- EU-funded patient safety project to share best practice (accessible on www.paneuropeannetworks.com - search for 'safety project wric')
- World Research Innovation Congress (WRIC) in Brussels https://www.timetag.tv/wric/play/19537 (video of talk by Shanthi Pal)
- Reinforcing global patient safety, EU-funded project share best practice at the WRIC: go to the 16 May 2013 news item at www.who-umc.org/
- Special feature : Health Inequalities: Drugs and data via www.paneuropeannetworks.com/ST8/files/assets/basic-html/page164.html (Science and Technology, September 2013 Issue 8, p164-167)

To follow the project lifespan, please refer to *Uppsala Reports* 47-64, accessible via the *Uppsala Reports* Archive at www.who-umc.org/ or www.monitoringmedicines.org

Thanks to many people

On behalf of the project management team, we would like to extend our appreciation to all the partners mentioned above and to the UMC staff who devoted their time and commitment during almost four years of the project. Invaluable contributions were made by representatives of patient organisations and national centres. Finally, we extend our gratitude to the European Commission for supporting the project.

Excellent performance for vigiMatch™ duplicate detection

Niklas Norén

A recent study finds excellent performance for UMC's award-winning algorithm vigiMatch™ at detecting duplicated individual case reports[1]. The study was led by the Medicines and Healthcare Products Regulatory Agency (MHRA) in the United Kingdom, within the European public-private partnership PROTECT. It engaged researchers at the Danish Health and Medicines Authority (DHMA), at Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) in Spain, and at the Uppsala Monitoring Centre (UMC).

Matching information

Duplicate reports represent an important impediment to effective pharmacovigilance; they distort statistical screening and may mislead expert assessment of suspected safety signals. vigiMatch™ was invented by the UMC in 2005 and named Best Paper at the world's most prestigious data mining conference the same year[2]. It identifies suspected duplicates based on patterns of matching information on seemingly distinct records[2,3]. One of its strengths is that it accounts for the likelihood of each matching piece of information: matches on rare events such as a specific date of onset are highly rewarded whereas matches on common events such as female gender receive modest rewards. Another strength is that vigiMatch™ allows for mismatches in any database field so long as there is sufficient matching information elsewhere on the report. These features set it apart from rule-based duplicate detection methods employed elsewhere.

Assessed by national experts

In the study at hand, suspected duplicates identified by vigiMatch™ in VigiBase® were assessed by national experts from the three participating countries. Most of the highlighted reports were assessed to be true or likely duplicates, in particular for the MHRA (86%) and the DHMA (64%). For AEMPS, the proportion of confirmed duplicates was lower (33%) and most of the highlighted reports were related in other ways (53%) – examples include reports of different reactions in the same patient and multiple reports on a particular drug and adverse event from the same health professional. Altogether unrelated reports were very rarely flagged as suspected duplicates by vigiMatch™ across all three countries.

From theory to practice

Since the completion of this study, vigiMatch™ has been adapted for use on any data set and evaluated on the MHRA Sentinel database, which includes more detailed information such as patient initials, length, and weight; the outcome is even better and will be published separately. Implementation of vigiMatch™ in VigiBase® for routine use is planned for 2014, and the results will eventually be propagated into VigiLyze™

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1 Tregunno PM, Fink DB, Fernandez-Fernandez C, Lázaro-Bengoa E, Norén GN. Performance of Probabilistic Method to Detect Duplicate Individual Case Safety Reports, *Drug Safety*. 2014 Mar 14. [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/24627310

2 Norén GN, Orre R, Bate A. A hit-miss model for duplicate detection in the WHO drug safety database. *Proceedings of the Eleventh International Conference on Knowledge Discovery and Data Mining* SIGKDD 2005, Chicago IL, 2005. KDD'05 Best applications paper award. http://doi.acm.org/10.1145/1081870.1081923

3 Norén GN, Orre R, Bate A, Edwards IR. Duplicate detection in adverse drug reaction surveillance. *Data Mining and Knowledge Discovery*, 2007. 14(3):305-328. http://link.springer.com/article/10.1007/s10618-006-0052-8

UMC celebrates further academic success

Ralph Edwards

During the last couple of years, UMC's research horizon has broadened further to include also the important and challenging task of assessing the benefit-risk balance of medicinal drugs. This work has partly been conducted as a joint endeavour with Professor Love Ekenberg and his research group within the Department of Computer and Systems Sciences at Stockholm University. Ola Caster's successful defence of his PhD thesis 'Quantitative methods to support drug benefit-risk assessment' on 21st March marks a significant milestone, and further adds to the impressive pile of UMC-based doctoral theses.

Theory meets reality

This thesis builds on Ola's licentiate thesis that was defended in May 2011 and covered in Uppsala Reports 54. As the title of the freshly-brewed PhD thesis suggests, the focus is on method development. However, a major step forward from the licentiate lies in the inclusion of a real-world case study that emerged during the thesis work. Aided by the statistical screening technique devised in paper I and the considerations on causality evaluation in paper II, a prospective signal of methylprednisolone-induced hepatotoxicity was discovered in VigiBase. This signal was communicated in paper III and followed up with a complete benefit-risk assessment of methylprednisolone in multiple sclerosis relapses in paper VII. Although the assessment makes use of quite involved methods - presented in papers V and VI - it has a clear clinical message: short-term methylprednisolone treatment at cumulative doses of below 1,000 mg is not recommendable in multiple sclerosis relapse management.

The thesis at large attempts to bridge the instrumental pharmacovigilance activities of risk identification and benefit-risk assessment, and this case study provides a means to explain and demonstrate the usefulness of the devised methods in a real clinical context.

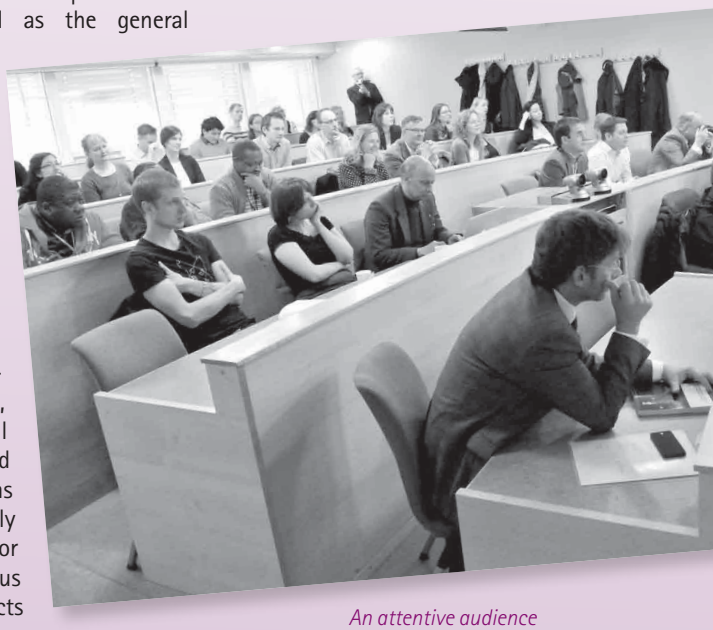
Processing diverse and uncertain information

A general challenge in benefit-risk assessment is that the information at hand is typically both diverse and fraught with deficiencies and uncertainties of many kinds. Just consider the multitude of ways in which medicines are studied, e.g. clinical trials, observational studies, spontaneous reporting, and preference elicitations, and that each comes with important limitations. In this thesis, so-called probabilistic decision analysis is used as the general framework to meet this challenge: each benefit-risk assessment is posed as a problem of deciding between available therapeutic alternatives, and the information considered in this decision is allowed to be uncertain.

For example, in the assessment of methyl-prednisolone in paper VII, data from several clinical trials is aggregated and used together with distributions that indicate quantitatively the desirability or undesirability of the various beneficial and adverse effects pertinent to the assessment. These distributions are in turn driven by clinically or logically implied qualitative statements, using methods devised in papers IV and V.

A role for spontaneous reports

It is known from real benefit-risk assessments within the regulatory setting that the evidence provided by spontaneous reports often has great impact. However, in methods proposed for formal benefit-risk assessment this data source is rarely acknowledged at all. This thesis deviates in this respect and instead puts considerable emphasis on spontaneous reports. Most significantly it is proposed in paper VI that collections of individual case reports under certain circumstances can serve as a basis to



An attentive audience

Identifying SSFFC patterns

Ghazaleh Karimi

Medicinal products of poor quality – whether being caused by bad practices in manufacturing, storage and distribution, or representing fraudulent counterfeits – pose a significant danger to public health. The potential harm to patients by poor quality products ranges from therapeutic failure and/or unexpected adverse drug reactions to life-threatening toxicity. WHO has introduced the acronym SSFFC, summarizing this category of medicinal product as 'Substandard/Spurious/Falsely-Labelled/Falsified/Counterfeit'.

Pilot of an algorithm

In 2011, the UMC led a pilot project under the Monitoring Medicines initiative, funded by the European Commission, which aimed to construct an algorithm for the identification of reporting patterns suggestive of SSFFCs in databases of individual case safety reports. The resulting algorithm is based on geographic and temporal patterns for specific products within VigiBase®. During initial evaluation of this new approach, the algorithm allowed detection of several historical clusters on medicinal products, confirmed by the relevant national centres to be associated with quality issues.

Further study

There is a growing interest in the potential of using compiled individual case safety reports for detection of SSFFC medicinal products, an activity included in the scope of pharmacovigilance as defined by WHO.

Currently, the UMC is undertaking a pilot project, partly funded by WHO, with the objective of evaluating the potential of the novel algorithm for identification of suspected SSFFC clusters within the WHO Programme for International Drug Monitoring. The evaluation is being conducted in collaboration with selected national centres which have agreed to analyze a list of suspected SSFFC clusters generated by the algorithm. As of 10th March 2014 the participating countries are Australia, Malaysia, Peru, Singapore,

Ola Caster, defending his thesis

The opponent, Sir Michael Rawlins

derive upper and lower limits on the risk of rare adverse effects. This is a novel approach with interesting prospects for UMC, as VigiBase is the world's largest such report collection. However, more empirical testing is required to appraise the real usefulness of this approach.

Battling a knight to get into the night

The defence act itself took place in the Stockholm suburb of Kista, which is the hub of information technology research and development in Sweden. There was attendance from a mixed audience of UMC employees, other pharmacovigilance professionals, faculty staff, family, and friends.

Professor Sir Michael Rawlins, former chairman of the National Institute for Health and Clinical Excellence (NICE) and currently president of the Royal Society of Medicine in the United Kingdom, kindly agreed to serve as opponent. Professor Rawlins' status as a foundational figure in pharmacovigilance as well as his courteous manner brought an aura of distinctiveness and dignity to the event. Even though the defence involved an intellectual battle with a proper knight, it all went smoothly and only lasted about two hours.

Following the evaluation committee's positive decision, everyone, including the new UMC doctor could enjoy a drink and some food, and start to prepare for the proper celebrations during the evening and night to follow.

Papers

I. Caster O, Norén GN, Madigan D, Bate A. Large-Scale Regression-Based Pattern Discovery: The Example of Screening the WHO Global Drug Safety Database. *Statistical Analysis and Data Mining*, 2010. 3(4):197-208.

II. Caster O, Edwards IR. Reflections on Attribution and Decisions in Pharmacovigilance. *Drug Safety*, 2010. 33(10):805-809.

III. Caster O, Conforti A, Viola E, Edwards IR. Methylprednisolone-induced hepatotoxicity: experiences from global adverse drug reaction surveillance. *European Journal of Clinical Pharmacology*, 2014. 70(4):501-503.

IV. Caster O, Ekenberg L. Combining Second-Order Belief Distributions with Qualitative Statements in Decision Analysis. *Lecture Notes in Mathematics and Economical Systems*, 2012. 658:67-87.

V. Caster O, Norén GN, Ekenberg L, Edwards IR. Quantitative Benefit-Risk Assessment Using Only Qualitative Information on Utilities. *Medical Decision Making*, 2012. 32(6):E1-E15.

VI. Caster O, Norén GN, Edwards, IR. Computing limits on medicine risks based on collections of individual case reports. *Theoretical Biology and Medical Modelling*, 2014. 11:15.

VII. Caster O, Edwards IR. Quantitative benefit-risk assessment of methylprednisolone in multiple sclerosis relapses. [In manuscript.]

Paper VI is openly accessible. The thesis summary is freely available from http://su.diva-portal.org/smash/record.jsf?pid=diva2:692438&trvn=1

Analysis and research

Niklas Norén

South Africa, the United Kingdom and the United States.

Evaluation for future use

This pilot project will shed light on the performance of the algorithm and provide the basis for decisions on the feasibility of putting this method to use.

The mission of Uppsala Monitoring Centre Research is to:

Explore the risks and benefits of medicines, advancing the science of pharmacovigilance

As of January 2014, the former Pharmacovigilance analysis team and Research department have merged into a broader Research section responsible for routine signal detection and methodological research. These are core UMC activities, and a key strategy to reinforce their value is to shorten the lead times from methodological research to routine use. Employing novel methodology and data sources in routine signal detection will enable us to better identify and describe relevant safety signals. It will guide methodological research and guarantee that it does not stray from our fundamental ambition of providing real value to the pharmacovigilance community.

The new Research section is divided into two teams that bring together staff from the two former organisational units, led by team managers Dr Kristina Star and Dr Johan Ellenius. Chief Science Officer Dr Niklas Norén remains Head of Research and will work closely with Chief Medical Officer Dr Pia Caduff to oversee the transformation of UMC's signal detection process.

WHO Programme to China

Geoffrey Bowring

In 2014 the representatives of national centres participating in the WHO Programme for International Drug Monitoring will meet in Tianjin, China. At the 2013 WHO Programme meeting in Rome, a message was conveyed from Yuan Lin, Deputy Director General, Department of International Cooperation, inviting members of the WHO Programme to come to China in 2014 for their annual discussions. This will be the first time the WHO Programme has met in China.

ISoP too

The annual scientific meeting of ISoP, the International Society of Pharmacovigilance, with its mix of lectures, posters and group training, will take place from 18-22 October just after the WHO meeting, also in Tianjin.

Chinese expansion

Naturally for such a large country the pharmacovigilance system in China is particularly extensive, and the China Food and Drug Administration has reported substantial growth: by March 2011 all 406 prefectures in the country had an ADR centre. As of 2013 there were over 6.5 million ADRs in the national Chinese database.

The WHO meeting will take place on 14-17 October at the Holiday Inn Tianjin Riverside hotel in the centre of Tianjin. Tianjin is an important regional city half an hour by high-speed rail from Beijing, also with direct connections from Beijing International Airport. Tianjin was once a major marine trading port. It is also famous for the goubuli, a delicious savoury steamed dumpling.

A night view of Tianjin

Central venue

Further information about the programme and other arrangements will be circulated to national centres in due course, and we look forward to meeting many centre staff in China this October.

Building pharmacovigilance capacity for multidrug-resistant tuberculosis

Geraldine Hill

A workshop in Copenhagen brought together 22 national staff from eight countries in Eastern Europe (Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Republic of Moldova, Russian Federation, Ukraine) - the part of the world where tuberculosis patients have the highest risk of multidrug-resistance (MDR-TB) - as well as Viet Nam. The participants included personnel from national TB programmes, national drug safety and regulatory authorities, USAID, Global Fund and the regional Green Light Committee (which supports countries to manage MDR-TB).

Lively discussions on implementing pharmacovigilance in the monitoring framework of MDR-TB.

The meeting, on 3-7 March 2014, was organised and facilitated by the WHO Regional Office for Europe (which hosted the workshop), WHO-Headquarters (Global TB Programme and Safety and Vigilance), Global Drug Facility and the WHO Collaborating Centre for International Drug Monitoring (Uppsala Monitoring Centre).

Anticipating new anti-TB drugs

This was the first ever workshop on pharmacovigilance specific for the TB treatment programmes. Mindful of the complexity of treatment for MDR-TB, and the additional challenges that will be faced by TB programmes with the use of new anti-TB drugs that are entering the market ahead of the completion of Phase 3 trials, the strengthening of pharmacovigilance components within the monitoring framework of TB treatment programmes was considered timely.

This workshop was particularly relevant for countries that have some of the highest burdens of MDR-TB in the world. Effective pharmacovigilance at national level will require a close collaboration between the government structures concerned, as well as other stakeholders, for technical assistance and funding.

Preparing plans for action

During the workshop participants had the opportunity to use information from the latest methodologies in pharmacovigilance and lessons learnt from experiences of countries to discuss how they could adapt these techniques to their respective country contexts. The country personnel also had time to start drafting plans for the introduction of pharmacovigilance components - spontaneous, targeted or cohort event monitoring - into their national strategies, with a budget and a timeline for implementation, including a plan to adapt the existing recording and reporting systems for the monitoring of patients.

The participants will, in the weeks following the workshop, finalise their plans, identify how to incorporate them into existing strategic documents (e.g. national strategic plans, concept notes for Global Fund support), organise national training within the country, and start to advocate for resources and for actions that will better safeguard patient safety.

Arab pharmacovigilance guidelines

Amr Saad, Head of the Egyptian Pharmaceutical vigilance Center and the Head of the Arabic higher technical committee for medicines

With the increasing and ever- more stringent regulations in pharmacovigilance, the regulatory authorities face greater demands for patient welfare and safety. These in turn necessitate standard levels of monitoring and data analysis that ensure safe drug delivery. This can be only attained by well-structured pharmacovigilance centres backed-up with a robust legal framework and clear guidelines.

Amr Saad

Situation in the Arab region

In the context of the Arab world, Egypt, Saudi Arabia and Jordan already have strong regulations in pharmacovigilance based in their drug regulatory authorities which are addressed to marketing authorization holders (MAHs). These regulations require important documents to be present in registration dossiers and follow-up procedures to be done post-marketing; this can be described collectively as 'regulatory pharmacovigilance'. These three countries also have activities directed towards health care practitioners (HCPs). Morocco and Tunisia have pharmacovigilance centres located outside drug regulatory authorities and which do not assess registration dossiers and marketing authorization holders' obligations. United Arab Emirates, Oman, Kuwait, Iraq, Sudan and Syria are at early stages in this sphere.

Adapting the EU models

The robust regulations that are present in Egypt, Saudi Arabia and Jordan were mainly adopted from the volume 9A of the EMA. The routine activities covered by old regulations included the monitoring and assessment of:

1. Marketing Authorization Holders' infrastructure, described in a document 'Detailed Description of Pharmacovigilance System' (DDPS)
2. Qualified Person for Pharmacovigilance (QPPV)
3. Periodic Safety Update Reports (PSURs)
4. Individual Safety Case report (ICSRs)
5. Reported new signals.

Additional pharmacovigilance activities included:

1. Risk Management Plans (RMPs)
2. Dear Healthcare Professional Communication (DHCPC)
3. Post-Authorization Safety Studies (PASS).

Recent developments

However, new advances in the world of regulatory pharmacovigilance include:

- Moving from assessment of whether MAHs have infrastructures or not (described in Detailed Description of Pharmacovigilance System (DDPS)), to the concept of assessing the intelligence of such infrastructures (described now in Pharmacovigilance system master file (PSMF)).
- Moving from assessing only Periodic Safety (described in PSURs), to assessing Benefit/Risk ratio (described in Periodic Benefit Risk Evaluation reports (PBRER)).
- From assessing only submitted documents, to performing pharmacovigilance audits and inspections.
- From relying on Standard Operating Procedure (SOPs) of performance, to assessing quality systems as a whole.

Moves by the Arab League

In order to cope with these changes and to unify guidelines and performance across the Arab world, Arab ministers of health came to a common decree (number 9) in their 37th regular meeting in March 2012. Under the umbrella of the Arab League 'The Higher Technical Committee for Medicines' was established with representatives from all Arab countries, to create common Arab guidelines in pharmacovigilance, and in bioequivalence.

This committee elected Dr. Amr Saad, head of the Egyptian centre, to lead the committee across all its rounds. The committee has finished the final drafts of the two common guidelines which were submitted to the 41st regular ministers meeting, and which has been approved by them.

Guidelines adopted

The new guidelines are mainly adapted from the newly-established international Good Pharmacovigilance Practice, composed of 16 different modules together with some product/population specific considerations, as well as annexes and templates of submission. The Guidelines were published in March 2014 and the effective date will be 1st July 2015.

It is expected that these guidelines will significantly influence pharmacovigilance practice in general in the whole Arab world, and will enhance such activities including reporting rates and signal detection in that part of the world. It will also help some Arab countries to develop in the area of 'Regulatory Pharmacovigilance'.

Mauritius

Alex Dodoo and Haggar Hilda Ampadu

A pharmacovigilance mission by Uppsala Monitoring Centre Africa (UMC-A) to the Mauritius National Pharmacovigilance Centre to provide training in VigiFlow and to assist in individual case safety report (ICSR) management was undertaken from 9th to 16th February 2014, in Port Louis.

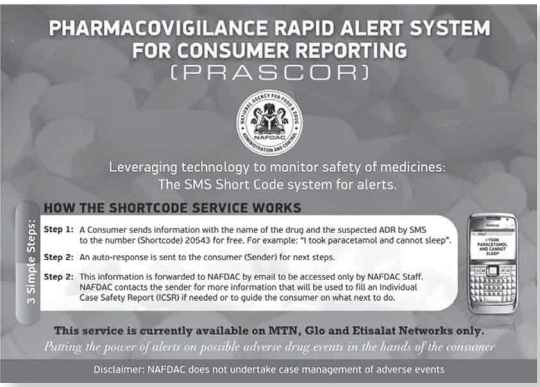
Mauritius is currently an Associate Member of the WHO Programme for International Drug Monitoring. The country has a national ADR reporting form, which is in English. There is a National Pharmacovigilance Centre located within the Pharmacy Department of the Ministry of Health and Quality of Life, and one full-time and one temporary officer undertake pharmacovigilance activities. A National Pharmacovigilance Committee exists, to collect and analyze data on any ADR, and to monitor the quality of medicines.

During their visit the UMC-A team updated pharmacovigilance centre staff on available and upcoming tools for ICSR management and elaborated on the purpose and utility of key UMC/WHO tools – VigiFlow and VigiLyze. They also trained two staff on the use of VigiFlow and took the opportunity to discuss opportunities and challenges for pharmacovigilance in Mauritius. By the end of the mission, 30 ICSRs were submitted to Vigibase (the World Health Organization database for ICSR) by the Mauritius staff.

Rapid consumer reports

Fatimah Jajere

The current need in pharmacovigilance systems in developing countries has gone beyond reporting by healthcare providers and marketing authorization holders to a more organized system where consumers may report directly to the national pharmacovigilance centre (NPC).



In 2012 this increasing need led the NPC in Nigeria, in collaboration with the National Malaria Control Programme, to create a means for consumers to directly report adverse drug reactions (ADRs) to the relevant authority. This system is termed 'Pharmacovigilance Rapid Alert System for Consumer Reporting' – (PRASCOR).

Accessible technology

PRASCOR takes advantage of a readily accessible, cheap and widely used technology available to 64% of consumers; that is the mobile phone. Consumers who take a medicine and experience an ADR send a text message to a prepaid short code 20543 using one of three major national networks. The service providers convert the text message into an e-mail and send it to NPC. Trained staff phone the sender to advise, reassure and get details to complete an Individual Case Safety Report (ICSR) form. Other reports of safety and quality are channelled appropriately for follow up, investigations and regulatory actions.

Results so far

From its inception in July 2012, 7,622 alerts were received, classified as (see table):

1. Reportable: alerts having at least a suspected medicine, suspected ADR, other drug details (batch number, NAFDAC registration number, expiration date, name and address of manufacturer)
2. Non-reportable: alerts containing quality and safety issues of all regulated products (sales of suspected counterfeit drugs, fake product manufacturing outlets, sales of expired medicines). These reports have led to several regulatory actions
3. Unclassified: alerts not meeting criteria for reportable and non-reportable (seeking medical consultation, request of reward).

Gains of PRASCOR

- It allows consumers to report other quality and safety issues (counterfeit and substandard) with no fear of identification
- It is affordable and easily accessible
- Consumers become active partners in decisions that affect themselves
- Follow-up by NPC is easy.

Drawbacks of PRASCOR

- Lack of awareness of its existence
- Inadequate drug information provided by consumers
- Consumers expect NPC to bear the cost of managing ADRs
- Sender denies sending the text message.

Cumulative alerts received	1. Number of Reportable alerts	Total converted to ICSR	2. Alerts concerning NAFDAC feedback/ safety alerts	3. Unclassified alerts
7,622	277	99	400	6,945

Helpline in India

V. Kalaiselvan

The Indian Pharmacopoeia Commission (IPC), National Coordination Centre (NCC) for the Pharmacovigilance Programme of India (PvPI) has created a toll-free helpline facility to provide assistance in reporting ADRs.

Open system

The helpline is open to healthcare professionals, as well as non-healthcare professionals including patients, who can report any adverse reaction related to any medicinal product: drug, vaccine, medical device, blood product, nutritional/dietary supplement or herbal product.

Comprehensive recording

The system encourages the reporting of ADRs, either serious or non-serious. The reporter has to give his information: reporter type (healthcare professional, non-healthcare professional, patient), name, address and contact details. All the usual details about the patient, reaction, other medication and whether the patient recovered are requested.

Built-in feedback

The NCC will help reporters by advising on how to report an ADR in future, explain the available ADR forms and offer details of their nearest ADR monitoring centre (AMC). Once validated by the respective AMC the submitted ADR report is fed into VigiFlow and thence to the WHO database.

SMS acknowledgement

To further boost pharmacovigilance activities PvPI recently upgraded its helpline facility by providing acknowledgment and feedback. This is done via an SMS acknowledgement service, to build the support and trust of ADR reporters across the country. With this upgrade NCC will be able to send an SMS acknowledgment and feedback to all reporters. This is essential, since proper feedback and acknowledgment for the stakeholders of PvPI builds confidence.

The Helpline launched by Sten Olsson on 11 October, with (from left) V. Kalaiselvan and Dr G.N. Singh, Drugs Controller General of India, head of the PvPI.

A Collaborating year in Rabat

Souad Skalli, Raja Benkirane and Rachida Soulaymani

Many activities were undertaken at the Centre Anti Poison et de Pharmacovigilance du Maroc (CAPM) during 2013 in our role as a WHO Collaborating Centre (WHOCC). We would like to share our activities related to CAPM/WHOCC Rabat involvement in the improvement of pharmacovigilance in Africa.

Pharmacovigilance training

The francophone pharmacovigilance training course took place in Rabat, Morocco during two weeks from 17 to 28 June 2013. The course aims to support African francophone countries by providing participants with basic knowledge, tools, and practical skills to develop or strengthen pharmacovigilance in their countries. Twenty-eight participants from nine countries attended: Burkina Faso, Burundi, Brazzaville Congo, Côte d'Ivoire, Guinea Conakry, Haiti, Mali, the Democratic Republic of Congo and Morocco.

New topics

In 2013, new items have been added to the programme: anti-malarial drugs, substandard/spurious/falsely-labelled/falsified/counterfeit medical products, and pharmacovigilance in children. Training combines oral presentations, working groups and exercises with small groups for specific items: VigiFlow, causality assessment, pharmacovigilance of herbal medicines, vaccinovigilance, patient safety and medication error, to help put learning into practice. Exchange of experiences from participants concerning their pharmacovigilance system (where it exists), adverse drug reaction cases, and notification also enriches the course.

Study aids

Pedagogical material has been developed: PowerPoint slides of oral presentations; specialized supplementary literature; WHO documents related to the training, and CDs including all data in relation with the training. The course was partly financed by WHO HQ.

Assessments

The CAPM/WHOCC Rabat has finalized the pharmacovigilance assessments in African countries under the title of "Pharmacovigilance in Africa and contributing factors of its development". The objectives were to describe the current systems in African countries, to evaluate their performance, and to identify the contributing factors to its development through a descriptive and analytical study.

Performance classified

Data has been gathered from a survey of African countries. Scores have been assigned to structural, process and impact indicators and countries have been classified depending on a final performance score. This performance has been correlated to selected contributing factors including demographic, socio-economic, human, health and pharmaceutical development factors in each country. The outcome of this study will be shared.

Herbals survey

The CAPM/WHOCC has also conducted a study to describe and evaluate herbal medicine pharmacovigilance in African countries which are members of the WHO Programme for International Drug Monitoring. The results of this study will be published during 2014.

Missions

The CAPM/WHOCC Rabat team has been involved in many activities in African countries for the development of pharmacovigilance:

- Meetings for development of pharmacovigilance in Africa in collaboration with UMC Africa through the *Pharmacovigilance Sans Frontières African* consultants in pharmacovigilance. This group was initiated by the WHO in 2007 in order to develop experts from Africa, for Africa.
- Ghana 26 to 28 June, 2013, on improving pharmacovigilance systems in developing countries.
- Durban, South Africa, October, 2013. We provided a Chair and Moderator for 'Malaria, an entry point for Pharmacovigilance in Africa' sessions during the 6th MIM Pan-African Malaria conference.
- Nouakchott, 19 and 20 December, 2013, during the First Medical and Paramedical Scientific Meeting. Our aim was to advocate for the decision-makers to set up a Mauritanian national pharmacovigilance centre. CAPM/WHOCC technical support was agreed with the medical chief of the national hospital centre of Nouakchott, Pr Abdelali ould Sidi Aly.

Partnership congress

Attended by 340 participants from 34 African countries, the First African Congress of Pharmacovigilance on 12 and 13 December was hosted by the CAPM and jointly organized by the Moroccan Society of Pharmacovigilance and the African Society of Pharmacovigilance in Rabat. Graced by experts from Africa, North America, Europe and Asia, its theme was: 'An efficient partnership for an efficient pharmacovigilance in Africa', it covered many current topics of concern for pharmacovigilance in Africa (see UR64 p13).

Reporting from Rabat

ISoP and UMC collaborate

Antonio Mastroianni and Anna Hegerius

The International Society of Pharmacovigilance (ISoP) and the Uppsala Monitoring Centre (UMC) have a common interest to promote scientific research and practice through mutual exchange of information on adverse events and risks related to medicinal products.

Training collaboration

In January 2014, a Memorandum of Understanding (MOU) was signed which establishes a strategic framework for training collaboration. A primary focus will be on Asia, a continent with 60% of the world's population. Harmonisation of safety reporting requirements and pharmacovigilance systems will benefit public health on a global, regional and national level. There is a need to increase education and training efforts in the region and UMC and ISoP foresee an added benefit in joining forces.

The Memorandum of Understanding signed by Hervé le Louet (left, on behalf of ISoP) and Antonio Mastroianni (UMC)

International harmonization

The first pharmacovigilance training course jointly organized by ISoP and UMC is on 5-7 June 2014 in Manila, Philippines. The three-day course, 'Ensuring Safe Medicines: How harmonisation underpins international pharmacovigilance', aims to engage pharmacovigilance professionals in a regulatory, industry, hospital, university or community setting, with Asian and international expert speakers. The course will include lectures, hands-on sessions and panel discussions, with ample opportunity to exchange views and ideas.

Book now

Please visit the ISoP website for information, draft programme and registration forms: http://www.isoponline.org/index.php?page=isop-umc-training or contact ISoP Administration: administration@isoponline.org

Why Asia, why now?

Pharmacovigilance activity is increasing in Asia, and many organizations are promoting more effective pharmacovigilance:

- In 2012 UMC and WHO conducted causality training with the Singapore Health Sciences Authority.
- In 2013 ISoP and UMC ran a pharmacovigilance harmonisation symposium in Asia.
- In late 2013, the Asia-Pacific Economic Cooperation (APEC) hosted a Pharmacovigilance Workshop in Seoul, the first step to regulatory convergence within APEC economies.
- In 2013, the Chinese Food and Drug Administration (CFDA) began sending ADR reports to the WHO global database, VigiBase; a multi-year collaboration aims also to improve the WHO Drug Dictionary and signal monitoring and data mining; and to establish a platform for technical exchange and cooperation between China's ADR data and the UMC.
- In 2013, four of the top 10 reporting countries in the WHO Programme were in Asia – India, Thailand, Japan, and Republic of Korea.
- In 2014 annual meetings of the WHO Programme and ISoP take place in Tianjin, China.

Due to this increase in activity the importance of structured data through the use of dictionaries, terminologies, classifications, and adherence to international standards, is more important than ever. UMC and ISoP aim to promote effective communication and training and education in pharmacovigilance throughout Asia.

Eritrean progress

Mulugeta Russom

The National Medicine & Food Administration, Ministry of Health (NMFA) conducted its first annual national pharmacovigilance conference from 31 January – 2 February 2014 in the sea port Massawa. Over 140 representatives (nearly 90% physicians and pharmacists) participated, including members of medicine and therapeutics committees, government departments, Zonal Medical Officers, the WHO Country Office, pharmaceutical industry, academia, and public health programmes.

The WHO representative in Eritrea, Dr. Usman Abdulmumini, and Dr. Ghirmay Tesfasllassie, on behalf of the Hon. Minister of Health, emphasized the significance of pharmacovigilance across health care systems including public health programmes, and urged health-care professionals to play their role to keep patients safe. 'Pharmacovigilante Awards' were awarded to the highest reporters of ADRs from different disciplines and to the best coordinators of hospital medicine and therapeutic committees.

Lessons from Accra

The National Pharmacovigilance Center has received technical assistance on Cohort Event Monitoring (CEM), clinical trials and risk management planning from the WHO Collaborating Centre for Advocacy and Training in Pharmacovigilance, Accra, Ghana. In October 2013 Mr. Abdul Malik Sulley and Mrs. Adwoa Anima Ohene led semester-level training for representatives of the School of Pharmacy, Pharmacy Services Division, public health managers and NMFA staff. The consultants delivered guidelines on clinical trials, CEM, risk management as well as standard operating procedures for the NMFA.

Development of policy

The NMFA has drafted a National Pharmacovigilance Policy with technical assistance from the WHO Collaborating Center for Advocacy & Training in Ghana. The NMFA has been working closely with Prof. Alex Dodoo and Mrs. Haggar Hilda Ampadu for about four months to develop a national pharmacovigilance policy. A consultation meeting with stakeholders took place on 10–21 December 2013.

Pharmacovigilante award winners in Massawa

Pharmacovigilance Fellowship

As part of the capacity-building to strengthen the Eritrean Pharmacovigilance System, the Ministry of Health, NMFA sent five Eritreans to attend a one-month 'Pharmacovigilance Fellowship' offered by the WHO-CC in Accra. The participants returned with much knowledge on pharmacovigilance methods and their application in hospital settings and are now playing a major role in strengthening the pharmacovigilance system in Eritrea.

Visitors

WHO Headquarters in Sweden

Sten Olsson

Recent organizational changes in the Essential Medicines and Health Products department at WHO-HQ, and restructuring also at the UMC, made a joint high-level meeting to streamline working relationships, strategic planning and communication channels a timely event. The meeting took place in Uppsala on 17 – 18 March, 2014. The WHO delegation consisted of Lembit Rägo, Head, Regulation of Medicines and other Health Technologies, Clive Ondari, Coordinator, Safety and Vigilance (SAV), Shanthi Pal, Group lead, Medicines Safety, Patrick Zuber, Group lead, Vaccine Safety and Michael Deats, Group lead, SSFFC. On the second day Rachida Soulaymani-Bencheikh, from the WHO Collaborating Centre in Rabat, Morocco, and Haggar Hilda Ampadu from the WHO Collaborating Centre in Accra, Ghana, joined the meeting. Discussions covered how best to combine the strengths of the different

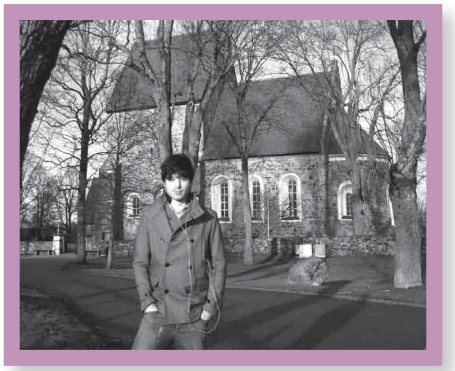
WHO-HQ, UMC and Collaborating Centre staff meeting in March

components of the WHO Programme for International Drug Monitoring, to optimize pharmacovigilance services to, and capacity-building in countries.

Italian intern

Daniele Sartori is a PharmD who has made pharmacovigilance the focus of his professional career. He writes "the most fascinating elements of drug safety are the enormous benefits patients and public health gain from it, but also the diversity and internationality of it all".

Daniele joined a post-graduate programme in pharmacovigilance and regulatory affairs run by the University of Verona, which allowed him to undertake an internship for half a year with the UMC analysis team and learn signal detection techniques. His signal detection activity involved the analysis of individual case safety reports of suspected



Daniele beside the church at Gamla Uppsala

adverse events highlighted in VigiBase; "I supported my work with extensive literature reviews in order to exclude any known reaction. Finally, all potential unexpected events were discussed in the team with the help of UMC's medical officers".

"The most rewarding aspect was finally witnessing how my motivation and knowledge could be helpful to many more people than at the small community pharmacy where I worked. I would like to thank the UMC staff for all the support, encouragement and mentoring, as well as the University of Verona for making this opportunity available to young graduates."

Daniele was a most welcome visitor and we wish him all the best for the future.

Dictionary researcher

Carolina Pulido Moreno, a MSc student in Pharmacy at Uppsala University, was welcomed to the UMC during the autumn of 2013 to conduct her Master's thesis.

"Ever since attending a conference with pharmacovigilance as the main theme in 2011, I have been interested on how to improve drug safety through international collaboration. Since then I have dedicated my time to international students' organizations and also undertook a pharmacovigilance course offered by Uppsala University and the UMC – my first contact with them. When it was time for me to decide on the subject for my degree project, it was evident which subject I wanted to immerse myself in."

"I got involved in a study related to combining information available in WHO Drug Dictionary Enhanced (DDE) and VigiBase; the study was based on how VigiBase data can contribute with drug safety information as an integrated part of the DDE. It is intended to act as a hands-on tool for the safe and effective use of medicines and a pilot version of the results will be carried out in the first half of 2014."

"I am very grateful to my supervisor Torun Bromée for her guidance and expertise, as well as to everyone else who made this project possible. My thanks to all UMC staff for the warm, welcoming atmosphere and for being part of this valuable experience."

Carolina Pulido Moreno

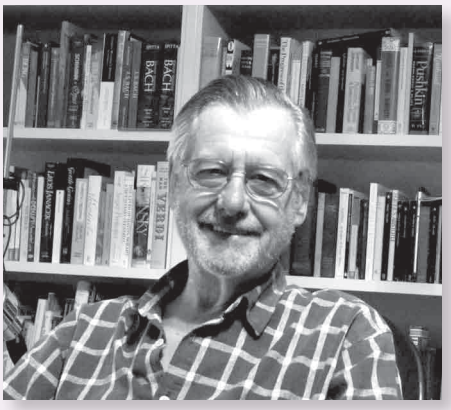
Children in Norway

Kristina Star had the pleasure to host Jenny Bergman from the Norwegian Regional medicines information and pharmaco-vigilance centre in Bergen in February. Jenny is very involved as a safety expert in the Norwegian Medicines for children network, and shared the challenges they've come across. Jenny joined in the UMC's research section's weekly discussion group 'Clinical innovation coffee', where we had the chance to discuss how best information about adverse drug reactions in children may be communicated. The day ended with a consultation about report narrative writing with Pia Caduff.

Jenny Bergman from Bergen

Laurie Mashford

Maurice Laurence 'Laurie' Mashford – a pioneer of pharmacovigilance in Australia - died in December 2013 aged 83 after a long illness. Laurie graduated with Honours in medicine from the University of Sydney in 1952, Master of Science (Melbourne) in 1970 and was a Fellow of the Royal Australasian College of Physicians. Clinical training at Royal Prince Alfred Hospital, Sydney and the Royal Melbourne Hospital was followed by research at Harvard Medical School and Tufts School of Medicine, as well as Australian universities.



Laurie Mashford

In 1974 he was appointed as Reader in Clinical Pharmacology at the University of Melbourne and established the Department of Clinical Pharmacology at St Vincent's Hospital. From his retirement from St Vincent's in 1996 until shortly before his death, he was an active member of the staff in Clinical Pharmacology and Therapeutics at the Austin Hospital, chairing that hospital's Drug Trial Advisory Committee.

In late 1971 Laurie was invited to join the Australian Drug Evaluation Committee (ADEC) and served as a member for 25 years. He was a founder member of the Adverse Drug Reactions Advisory Committee (ADRAC), and was Chair of ADRAC for ten years. He carried a major responsibility for the content of the *Australian Adverse Drug Reactions Bulletin* and was central to the genesis of the unique teaching film *The New Epidemic*.

In addition to promoting voluntary reporting, he was from the early 1970s a strong advocate of intensive monitoring programmes in hospitals and the community.

Laurie was a wholehearted supporter of the WHO Programme. He spent a sabbatical as an adviser at the UMC (1994) and attended annual meetings of the national centres.

Laurie's other professional interests were broad: drug metabolism in liver disease, therapeutic drug monitoring and quality use of medicines with a special emphasis on antibiotics. Over many years he devoted great energy to Therapeutic Guidelines Ltd – an independent, not-for-profit self-funding organisation producing independent and expert advice for Australian prescribers on the best use of prescription medicines.

Laurie contributed internationally as an adviser and teacher in China (Beijing; Shanghai), Vietnam, Philippines, to WHO, and on advisory panels of the US Pharmacopoeial Convention. He hosted visitors from those countries at St Vincent's.

Laurie had many other interests, including eclectic reading, music of all ages and genres and poetry. Ralph Edwards has commented that no tribute can capture what fun Laurie was and how interesting it was to talk with him over a huge range of topics. He was a consummate and model clinician, educator and researcher who was remarkably caring and unassuming despite his many achievements and gave readily of his time and advice.

Laurie bore his illness including the unwanted effects of treatment with humour and great fortitude. He is survived by his partner Enid Meldrum, four children and their families.

John McEwen

Peter Jacobs

I sadly note the passing of my friend and colleague Peter Jacobs who died in Cape Town on 18th November 2013. He was eighty. Whilst born in South Africa, his early life was in Rhodesia (Zimbabwe) where he trained and worked as a lab assistant and technician in Bulawayo. He was proud of that training, and those skills were important to him: he would joke about my lack of them.

Peter Jacobs

He studied medicine at the University of Witwatersrand and became a specialist haematologist. In 1972, he became the founding Professor of the Haematology Department, University of Cape Town. He was later Foundation Professor and Head, Division of Clinical Haematology, Stellenbosch University and Tygerberg Academic Hospital. He did not forget Zimbabwe, and helped out academically and clinically when he could.

Peter was involved in all aspects of haematology though his main interests were in oncology, bone marrow transplantation and stem cell research. Very few people had his breadth and depth of experience.

It was natural that when the UMC needed expert haematological views on drugs used in his field, or affecting the bone marrow, we would contact him. Peter was a strong supporter of the UMC's work and would produce excellent and lengthy analyses of drug problems, and visit Uppsala when he could. He was a chapter author in *Risk and Safety in Medicine*, used as a reference around the world.

Peter was incredibly hard working, but his main attributes were his apparent solidity and humanity which clothed his humour and intelligence. Although in many ways he was low-key and modest, one was always clear that one was in the presence of a great man.

One could always trust him.

He will be missed by many.

Ralph Edwards

Ronald Mann

Ron Mann (1928-2013) had a long career as a pharmacoepidemiologist and pharmaco-vigilance expert, for several years as a medical assessor to the UK Committee on the Safety of Medicines, and from 1994 to 1999 as Director of the Drug Safety Research Unit. He was very active in the European/ International Society of Pharmacovigilance, editor of the *Pharmacoepidemiology and Drug Safety* journal and author of key books in the field.

New publications

e-Reactions

The pharmacovigilance newsletter *Reactions Weekly*, published by Adis since 1980, has moved to an e-only format in 2014. In line with industry trends the publisher has discontinued print production to concentrate on the evaluation, synthesis and rapid online publication of pharmacovigilance information. *Reactions Weekly* content is also available in the format of a proprietary database - Pharmacovigilance Insight, also offered for subscription by Adis. This database offers superior search functionality, data analysis and sharing with automatic alerts and data exports in many formats, and also hosts a tool enabling easy visualization of search results.

For any queries contact pharmacovigilance@adis.com.
Reactions Weekly Online Newsletter - http://link.springer.com/journal/40278
Pharmacovigilance Insight Database - http://www.springer.com/adis/databases/pharmacovigilance+insight

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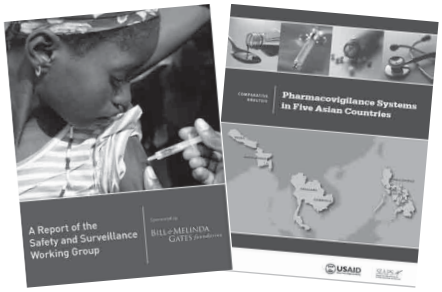
Five Asian systems

A team from the Systems for Improved Access to Pharmaceuticals and Services (SIAPS) programme, funded by the US Agency for International Development, has carried out an in-depth assessment of the pharmacovigilance systems in Bangladesh, Cambodia, Nepal, the Philippines and Thailand. The assessment benchmarked each national system's performance, and identified replicable and successful experiences. It also mapped donor agencies' contributions and gave options for enhancing pharmacovigilance and post-market surveillance systems' capacity and performance. Site visits and indicator-based assessments were carried out in the five countries at various levels, including national, public health programmes, health facilities, pharmacies, consumer groups, pharmaceutical industries and academia.

In the assessment by Jude Nwokike, Elisabeth Ludeman and Melissa Thum, the five systems are characterized and compared. The report is very rich in information and includes 40 tables and 11 figures. Country profiles are provided. Recommendations are made for enhancing systems at all levels. National level recommendations refer to:

- Strengthening regulatory policies and framework
- Ensuring convergent regional and international regulations
- Improving information-sharing, and participation in regional harmonization
- Reforming organizational structure to achieve integrated safety surveillance
- Improving funding
- Strengthening spontaneous reporting
- Confronting falsified and substandard medicines.

The full report and executive summary is accessible from: http://siapsprogram.org/publication/comparative-analysis-of-pharmacovigilance-systems-in-five-asian-countries/



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Global health report

The Safety Surveillance Working Group has reported on a year-long initiative to develop a practical, scalable strategy for improving drug and vaccine safety in low- and middle-income countries.

The report includes a risk-based, data-driven assessment of the global health product pipeline and its demands on the regulatory systems in low- and middle-income countries. Multiple new drug and vaccine launches occur in the same countries over a relatively short period and many of those countries are clustered together regionally. Based on analysis of that data, the report outlines strategies for strengthening post-market safety surveillance in these countries.

The authors note "the coming decade will be vital for improving drug and vaccine safety surveillance. The only way we can make progress is through a coordinated international effort of policymakers, regulators, industry, and health professionals".

This new report on drug and vaccine safety in global health is available at: https://docs.gatesfoundation.org/documents/SSWG%20Final%20Report%2011%2019%2013_designed.pdf

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Dear Doctor...

The US FDA recently issued a valuable guide entitled *'Guidance for Industry and FDA Staff : Dear Health Care Provider Letters: Improving Communication of Important Safety Information'.* This is interesting guidance on pharmacovigilance communication.

The document is accessible via this link: http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm233769.pdf

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Drug allergy book

Springer has published a book by Brian Baldo and Nghia Pham entitled *'Drug Allergy – Clinical aspects, diagnosis, mechanisms, structure-activity relationships'.* The book is a comprehensive overview of the subject covering the history and definition of drug allergy, classification of allergic reactions and mechanisms, before moving on to diagnosis and clinical considerations.

More information via: http://link.springer.com/book/10.1007%2F978-1-4614-7261-2

Conflicts of Interest Advisory Group

The nature of the Uppsala Monitoring Centre's (UMC) work requires close interaction with numerous other organizations and different stakeholders, some of whom may have, or be perceived to have competing interests, i.e. public health versus individual benefit and risk, competing commercial interests and others.

It has been decided to establish an advisory group to consider potential areas of conflict of interest, to advise the UMC Board and the Director of the UMC in this important area.

Further details are on the UMC website under 'About UMC'

Staff news

Paula Alvarado

Paula was born in Lima, Peru but has spent most of her life outside her home country, working and studying in the UK, Argentina, USA and India. Paula has extensive experience with large international organizations, including the International Federation of Red Cross and Red Crescent Societies, WHO, Conservation International, Peru's Office of the President and Peru's Human Rights Office. She has worked in challenging environments, from those unjustly imprisoned under terrorism laws and child soldiers in Peru to indigenous land rights in Brazil, Pakistan's floods, security scares in Afghanistan, internally displaced people in Sri Lanka, health risks in India and volunteering and gender challenges in Sudan. Most recently she ran her own consultancy, Seeds for Change International.

Paula moved to Stockholm two years ago and has embraced the culture of fika, endless summer nights and long winters. A good Latina, she loves music and dancing, and has a passion for reading, exploring, discovering and going on long hikes with her family. She lives in Sollentuna with her husband and three boys, by Edsviken lake - equally popular among skiers in winter and sailing lovers in summer.

"We moved to Sweden after living in different places – across four continents - and experiencing many different cultures. We have learned from all those countries we called 'home', and feel grateful for every encounter and challenge – 'culture fusion' defines who we are, and yes, we are the kind of people who hesitate when asked where we are from... and it is always hard to choose a team to support during the World Cup. Our mantra is that home is where the heart is – where we gather every evening and make new friends and take on new challenges.

At UMC I will focus on developing and implementing a world-class communications strategy to promote, enhance, and protect our reputation as a centre of excellence in pharmacovigilance. I will build relationships with the media and key stakeholders, including member countries of the WHO Programme for International Drug Monitoring, pharmaceutical industry, and adjacent stakeholders to drive broader awareness and support for the organization and our mission."

Maria Näsström

Born and raised in Uppsala, Maria worked at the Swedish Post Office as a developer and from 2003 was as a software tester within the IT sector (she is an ISTQB certified tester). "At the UMC I am a Senior Test Manager. This means that I have strategic responsibility for all software testing at the UMC, also working as a software tester in different projects (VigiLyze, VigiFlow, etc)."

Paula, Cecylia, Alem (from left, standing); Maria, Damon (seated)

"I am married and have two sons; with my husband we spend our spare time supporting our sons' sports activities: football, ice hockey, bandy and running. It's a way of life for us and we love it!"

Damon Wallin Fahimi

Damon was born in Uppsala and studied at the Uppsala University. He graduated with a Master of Science in Pharmacy in 2012. He worked as a UMC consultant since he graduated and has now become a full-time employee. Damon will maintain and develop the WHO Drug Dictionaries as well as support Drug Dictionaries customers worldwide. He will also work with the Standardised Drug Groupings (SDGs).

"I live in Uppsala with my fiancée. In my spare time I enjoy playing and performing music with my reggae and ska band. I am also into running and hope to set a personal record on my fourth marathon later this year. I am truly proud to become a permanent member of the UMC organisation."

Cecylia Wojcik

Cecylia was born in Poland, but has lived most of her life in Sweden. "I live with my husband and two children in Denmark, Uppsala. Denmark is like a small village, though situated near town, which suits me fine because I enjoy being in the outdoors with my family".

She started as a sales assistant at UMC in August 2013. Before that she worked at the Border Police Department for almost 13 years, latterly within human resource planning for staff at the Border Police at Arlanda and Stockholm.

Alem Zekarias

A pharmacist with a Master's in Bioscience and Drug Safety, Alem started at the UMC a year ago with signal detection within Research. "I always wanted to work with pharmacovigilance in a multicultural environment such as the UMC. Since March I am the new Team Manager for Global Services (previously Consulting, Training and Education). My responsibilities include leading and managing the operations of the team, ensuring that we support the WHO Programme via country support, education and training, as well as achieving the planned objectives and deliverables."

"I'm originally from Asmara in Eritrea. My family moved to southern Sweden when I was three; I've lived and worked in Uppsala for nine years. Previously I was a pharmacy manager and have also worked with drug preparation within phase I-III trials for a CRO. When I am not working I enjoy spending time with friends and family, exercise and travel."

...and farewell to

Hanna Pedersen, Jeanette Johansson, Ennita Nilsson and Hanna Lindroos, who have left the UMC in the last few months. We wish them the best for the future.

DATES	TITLE	PLACE	ORGANISER/CONTACT
19 May 2014	Signal detection and regulatory expectations	London, UK	Management Forum Ltd Tel: +44 (0)1483 730008 E-mail: registrations@management-forum.co.uk www.management-forum.co.uk
21 May 2014	Pharmacovigilance for support staff - a basic course	London, UK	Management Forum Ltd (see above for contact details)
21-22 May 2014	Signal Management in Pharmacovigilance	Prague, Czech Republic	DIA Europe www.diahome.org/en-GB/Meetings-and-Training/
22-23 May 2014	Uppsala Monitoring Centre Research Conference 2014 - Risk: What risk? Whose risk?	Uppsala, Sweden	UMC E-mail: conference2014@who-umc.org www.who-umc.org
4-5 June 2014	Constantly changing global regulatory pharmacovigilance environment	London, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org/trainingcourses
5-6 June 2014	Annual course in ATC/DDD Methodology	Oslo, Norway	WHO Collaborating Centre www.whocc.no/courses *Please note the deadline for registrations is 20 May 2014*
5-7 June 2014	Ensuring Safe Medicines: How harmonisation underpins international pharmacovigilance	Manila, Philippines	International Society of Pharmacovigilance/UMC E-mail: administration@isoponline.org www.isoponline.org
9-11 June 2014	Pharmacovigilance - basic training course for those working in drug safety monitoring in the EU, USA and Japan	London, UK	Management Forum Ltd (see above for contact details)
11-12 June 2014	New Guidelines on Periodic Safety Reports: PSURs and PBRERs	Southampton, UK	Drug Safety Research Unit (see above for contact details)
16-27 June 2014	8ème Cours Francophone de Pharmacovigilance	Rabat, Morocco	Centre Anti Poison et de Pharmacovigilance du Maroc www.capm.ma/
25-27 June 2014	Medical Aspects of Adverse Drug Reactions	Southampton, UK	Drug Safety Research Unit (see above for contact details)
24-25 July 2014	Introduction to Pharmacovigilance	Accra, Ghana	UMC-Africa Tel: +233-302-268-746 / +233-289-014-000 E-mail: info@umcafrica.org www.umcafrica.org/index.php/training-alerts
10-11 September 2014	Back to Basics in Pharmacovigilance	Southampton, UK	Drug Safety Research Unit (see above for contact details)
8-9 October 2014	Pharmacovigilance Planning and Risk Management	Fareham, UK	Drug Safety Research Unit (see above for contact details)
13-17 October 2014	Excellence in Pharmacovigilance: Clinical trials and post-marketing	London, UK	DIA Europe www.diahome.org/en-GB/Meetings-and-Training/
18-22 October 2014	2014 ISoP Annual Meeting	Tianjin, China	International Society of Pharmacovigilance E-mail: administration@isoponline.org www.isoponline.org
24-27 October 2014	30th Anniversary ICPE	Taipei, Taiwan	ISPE E-mail: ISPE@paimgmt.com www.pharmacoepi.org/meetings
5-7 November 2014	Latin American PV Congress	Lima, Peru	E-mail: salvarez@digemid.minsa.gob.pe
3-5 December 2014	2nd African Society of Pharmacovigilance (ASoP) conference 'Pharmacovigilance In Africa : New Methods, New Opportunities, New Challenges'	Accra, Ghana	ASOP 2014 www.asop2014.com

14–17 October 2014	**37th Annual Meeting of representatives of national centres participating in the WHO Programme for International Drug Monitoring**	**Tianjin, China**

the UPPSALA MONITORING CENTRE

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

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

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