

Uppsala Reports 42

UPPSALA REPORTS July 2008

For everyone concerned with the issues of pharmacovigilance

Four million reports landmark

VigiFlow version 4.0

Conference reports

News from around the world



DIRECTOR'S MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring
Centre

I have just returned from a drug safety satellite meeting to the latest, main OMERACT meeting in Calgary, Canada. OMERACT stands for Outcome Measures in Rheumatology Clinical Trials, but the work since 1992 has become generalized to the broader area of rheumatology.

The following are extracts from their website www.omeract.org :

'... the OMERACT initiative has turned into an international informal network, working groups and gatherings interested in outcome measurement across the spectrum of rheumatology intervention studies.

OMERACT strives to improve outcome measurement through a data-driven, iterative consensus process. OMERACT has a 5 member Organizing Committee with members from 3 continents; it has a 15 member Scientific Advisory Committee composed of international opinion leaders from 9 countries.

What does it do?

To improve outcome measurement, OMERACT organizes conferences that take place every two years and rotate around the globe.

For these conferences, topics of interest are prepared by self-appointed groups of experts. These topics are then prepared for the conference by literature review and specification of the points for discussion. Most topics are discussed in workshop format, where the aim is to make explicit the areas of agreement and disagreement, and to prioritize the research agenda. In several areas, the group has taken the lead in actually performing the necessary research to bring back to the conference. Recently, small group workshops have emerged alongside OMERACT conferences to speed up the work. When enough data is available, a full module is organized with the intention to come to a consensus on guidelines.

How does it work?

The process is data-driven. Literature reviews and validation studies are usually performed by small groups. The formulation and selection of the domains are made by larger committees, and the presentation of evidence (both from literature and from targeted studies) and final selection occurs at the conference. Here, plenary presentations alternate with small group sessions where participants express their views and preferences. These views are brought back to the plenary session, where a final consensus is formulated, often with the help of interactive voting. Consensus does not always imply agreement on measures or domains; it can also mean the formulation of a research agenda in areas where data-driven decisions cannot be made. The process is iterative, in that guidelines are forever "preliminary" based on the assumption that future data (sometimes a direct result of the research agenda) will serve to refine or modify them.

When is a measure "applicable"

A measure is applicable when it passes the OMERACT Filter in its intended setting. The OMERACT Filter can easily be summarized in only three words: Truth, Discrimination, and Feasibility.

Each word represents a question to be answered of the measure, in each of its intended settings:

1. Truth: is the measure truthful, does it measure what it intends to measure? Is the result unbiased and relevant? The word captures the issues of face, content, construct and criterion validity.
2. Discrimination: does the measure discriminate between situations that are of interest? The situations can be states at one time (for classification or prognosis) or states at different times (to measure change). The word captures the issues of reliability and sensitivity to change.
3. Feasibility: can the measure be applied easily, given constraints of time, money, and interpretability? The word captures an essential element in the selection of measures, one that in the end may be decisive in determining a measure's success....!

The drug safety meeting was a one-day workshop, bringing in a variety of drug experts, in addition to eminent rheumatologists. It was an absolute delight to belong to such a group for a short time. The debates on methods and measures which could be useful in drug safety were forthright, sharp and good-humoured. Views were made explicit and there was time for healthy debate, along the lines above. Confidential, interactive voting was carried out by an automated system and was a major part of the exercise. Interactive voting is used mainly to quantify views on a particular statement which is then revised to see if closer consensus can be achieved.

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The Uppsala Monitoring Centre (*the UMC*) is the field-name of the WHO Collaborating Centre for International Drug Monitoring, responsible for the management of the WHO Programme for International Drug Monitoring.

An independent centre of scientific excellence, *the UMC* offers products and services, derived from the WHO database of Adverse Drug Reactions (ADRs) reported from member countries of the WHO Programme.

With an independent and global perspective on drug safety, *the UMC* provides resources for regulatory agencies, health professionals, researchers and the pharmaceutical industry.

The UMC's important worldwide work is financed solely by the organisation itself, without support from WHO, the Swedish Government, member countries of the WHO Programme or any grant-making body.



4 Uppsala 2008

Aspects of the week-long scientific gathering in Uppsala, including the WHO Annual Meeting



8 Summer celebration

Four million ADR reports in the WHO Global Individual Case Safety Report (ICSR) database, Vigibase



10 VigiFlow version 4.0

Released in June, with E2B import and address book functions and available in Spanish for the first time, VigiFlow also now comes in a free version for sending reports to *the UMC*



22 UMC staff news

New arrivals at the office, a post to be created in vaccines safety and the staff out and about

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Uppsala in 2008

The 31st meeting of countries participating in the WHO Programme for International Drug Monitoring is the centrepiece of a week of activity in the sphere of drug safety in Uppsala this October.

The WHO Programme's meeting from 20-23 October will coincide with related meetings about vaccines and terminologies along with one for members of *the UMC's* signal review panel.

The agenda for the WHO meeting will not only look back over the past 40 years of the Programme but also forward to challenges in medicines safety over the next few years. The formal invitations to national centres heads were sent from WHO Headquarters in Geneva in early June. As well as the usual 'Problems of Current Interest' where country representatives present and discuss early case hypotheses, plenaries will include patient safety, the European Network of Centres of Pharmacovigilance and Pharmacoepidemiology (ENCePP), counterfeit medicines and biotechnologically-produced medicines and vaccines. Different workshops will focus on definitions, measuring impact of pharmacovigilance, training to support patient reporting and better use of pharmacovigilance data.



*The Museum of Uppland in central Uppsala viewed from the river bank
(Photo credit: Ulf Eriksson)*

We do hope that representatives will take the opportunity while they are at the conference to explore a little both of the beautiful university city of Uppsala as well as the nearby Swedish capital Stockholm or other places around Sweden.



The old university library in Uppsala, Carolina Rediviva ('Carolina risen from the dead')

Uppsala is a very pleasant city to explore on foot, with restricted motor traffic in and around the centre. The river Fyris runs through the centre, which abounds with cafés – and if the weather changes for the worst there are indoor shopping centres.

A few kilometres north is Gamla Uppsala ('Old Uppsala'), where you can see the ancient burial mounds of Viking princes. The royal castle on a hill overlooking the city will be the venue for the Annual Meeting's formal dinner on the Tuesday. Unique sights such as the house where Linné lived, his garden and the Gustavianum can all be seen. Biotopia, an interactive modern audio-visual exhibition of the natural history of *the Uppsala* region, the Botanical Gardens near the castle, the Carolina Rediviva with its remarkable collection of manuscripts, the university's Gustavianum museum and the cathedral and its exhibition will all be open to visitors in October.

Stockholm is only 45 minutes by train from Uppsala and has often been described as one of the most attractive capital cities in the world with its harbour setting, characterful quarters and parks. Again, it is an easy place to explore on foot or two wheels.

Welcome to Uppsala!

Impacting patient safety: Adverse drug reaction signal detection

There are already many bookings for *the UMC* research conference on the Friday following the Annual Meeting – 24th October. The meeting details can be downloaded from the conference pages of *the UMC* website which are regularly updated.

Key speakers include

Dr Jeffrey Aronson, University of Oxford
Professor Stephen Evans, London School of Hygiene and Tropical Medicine
Dr Manfred Hauben, Pfizer, New York
Dr Gunilla Sjölin-Forsberg, Swedish Medical Products Agency
Professor Hugh Tilson, UNC School of Public Health

Hotels in Uppsala tend to get busy so we recommend early booking if you are intending to come to any of events during the week.

Moves afoot in Costa Rica

Elki Sollenbring

Earlier this year I was in Costa Rica on vacation and took the opportunity to visit the National Centre there, and get a general view of the Centre's work. I made two visits. During the first one I met the head of the Centre, Dr Adolfo Ortiz and his colleague the pharmacist Xiomara Vega. They received me with open arms and invited me to a delicious Costa Rican dinner, after which they showed me the routines of daily work.



Xiomara Vega, Elki Sollenbring and Adolfo Ortiz at the Costa Rica national centre

At the moment the Centre is situated in the Dirección de Vigilancia de la Salud del Ministerio de Salud (Direction of health vigilance of the Ministry of Health). The centre has to cope with various problems that hinder their desire for better work. One of the problems is their work environment: the offices are very small, the bibliographical library is too small and the computers don't have enough capacity. Another problem is the quality of received ADR reports: sadly, many of them are worthless, Adolfo told me.

Despite all these difficulties I saw that the Centre's work was of a high standard. Xiomara is a very ambitious and meticulous person who works very hard to get the best results. She is responsible for the data input and analyzing of the ADR reports received. Adolfo is the co-ordinator of the programme and is dedicated to improving the work quality and conditions.

The good news is that the Centre will probably move to the Dirección de Registros y Controles del Ministerio de Salud (Directorate of Registration and Control at the Ministry of Health). There they will have more facilities and better equipment.

During my second visit I met Dr María de los Angeles Morales Vega (Marielos), Director of the Dirección de Registros y Controles del Ministerio de Salud who was very enthusiastic about my visit. She will probably become the new overall head for the group and will work hard to give them the facilities they need.

She also mentioned a sub regional technical commission of drugs who will work on a programme to improve the use of medicines. The group has already met once in the Dominican Republic to discuss the

different points they will take up during a conference later this year. One of the items on the agenda is pharmacovigilance and the UMC is therefore invited to participate. Among the participating countries are Belize, Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama and the Dominican Republic.

During this visit I also made a presentation for Adolfo and Xiomara about the UMC, and gave a brief demonstration of the use of VigiFlow. They were happy when I told them that VigiFlow will be released in a Spanish version soon.

Ambitious initiative in Namibia

A new Therapeutics Information and Pharmacovigilance Centre (TIPC) was established by the Namibian Ministry of Health and Social Services earlier this year. The inaugural ceremony was held at Safari Court Hotel in Windhoek on 13 May in the presence of prominent representatives of the Namibian healthcare service, local media and international guests. The keynote address was given by Deputy Permanent Secretary Dr Nobert Foster. The UMC was represented by Ralph Edwards and Sten Olsson.



A new slogan in Namibia

The TIPC has been provided premises in a major hospital in Windhoek with access to good communication facilities and literature resources. Support for the establishment of the centre has been given by USAID through Management Sciences for Health (MSH) and Spanish aid organizations including Médicos del Mundo. The operation of the



The TIPC launch in Windhoek

centre follows closely a model that is advocated by WHO in that drug information, poison information and pharmacovigilance is brought together in one joint service with common resources. This set-up is ideal for achieving a good two-way communication with health care providers.

The objectives of the centre are to provide both proactive and query response therapeutics information to health professionals and the general public in Namibia and to become a reference unit on pharmacovigilance by collecting and monitoring medicine related problems. TIPC has chosen 'Know Your Medicines' as its slogan and logo which is prominent on its printed material (fig.) TIPC is initially manned by a pharmacist, Mr Augustine Odo, and a physician, Dr Assegid Tassew. Dr Tassew attended the UMC pharmacovigilance training course in 2007. Since TIPC is also subscribing to VigiFlow, the UMC software for individual case management, it is expected that Namibia will soon join the WHO pharmacovigilance network. This process ought to be facilitated also by the fact that Mr Johannes Ghaseb, Drug Registrar of Namibia, and Mr Ewans Sagwa serving at the MSH country office in Namibia, also attended the Uppsala pharmacovigilance training last year. We look forward to following the achievements of this model centre and hope to have it as an active partner in the international pharmacovigilance network soon.

Community Pharmacist reporting

A novel initiative towards community pharmacovigilance in Nepal

In Nepal, qualified doctors are often reluctant to set up practice in the villages and as a result rural patients often rely upon traditional healthcare practitioners. In addition, due to remoteness, poor socioeconomic status, high cost of modern medicines and non-availability of doctors in rural areas, it has been difficult to access modern healthcare facilities in Nepal. This leaves people dependent on self-medication which is known to cause Adverse Drug Reactions (ADRs). Retail pharmacies frequently serve as people's first point of contact with the healthcare system in the rural areas.

In Nepal presently, two regional pharmacovigilance centres are in operation. These two centres are located at teaching hospitals, Tribhuvan University Teaching Hospital, Kathmandu and Manipal Teaching Hospital (MTH), Pokhara. The current system of ADR monitoring in Nepal covers only the ADRs that occur in hospital settings. ADRs following self-medication occurring outside the hospital remain unreported. The Pharmacovigilance centre of Western Nepal located at MTH has recently started a community-based pharmacovigilance project in which the community pharmacists report the ADRs.

Baseline Knowledge, Attitude and Practice (KAP) towards drug safety of 116 community pharmacists from Pokhara valley was evaluated using a

validated KAP questionnaire. The questionnaire comprised 20 questions [(knowledge 11, attitude 5 and practice 4) with a total maximum score of 40].

Altogether, the KAP questionnaire of 116 community pharmacists [21.6% (n=25) males, 78.4% (n=91) females] was evaluated. The respondents mean \pm SD age was 33.11 ± 10.70 years and mean \pm SD length of experience was 10.31 ± 8.41 years. The overall KAP scores was 31.25 ± 2.37 [knowledge 14.08 ± 10.00 , attitude 9.77 ± 0.60 and practice 7.39 ± 0.89].

Six community pharmacists with higher scores were trained by the regional pharmacovigilance centre staff in three sessions spread over two months, covering the basic information and expertise needed to identify and report ADRs. The trained community pharmacists were asked to report the ADRs by filling out the ADR reporting form. The pharmacists from the regional pharmacovigilance centre visited these community pharmacists every alternate day and collected the filled ADR reporting forms. The filled ADR forms were analyzed.

During the initial two months, 21 ADR reports from 21 patients (10 males and 11 females) were reported to the pharmacovigilance centre by the six community pharmacists. Antibiotics/ antibacterials accounted 35.29% (n=12) of the total ADRs, followed by NSAIDs [26.47% (n=9)]. Ibuprofen/paracetamol combination was on the top of the ADR list. The top ten ADRs are listed in Table 1.

Table 1. Top ten suspected drugs causing the ADRs

Drugs	No. of reports
Tab. Ibuprofen/paracetamol combination	7
Cap. Amoxicillin	3
Cap. Ampicillin/cloxacillin combination	3
Tab. Metronidazole	3
Tab. Diclofenac	2
Inj. Gentamicin	2
Inj. Ceftriaxone	2
Tab. Folic acid	2
Cap. Omeprazole	1
Tab. Norgesterol+ Ethynylestradiol	1

The most common type of ADR reported was itching [22.22% (n=10)] followed by generalized edema [13.33% (n=6)]. Thirteen patients (61.9%) needed medical treatment for managing their ADRs. Most [90.5% (n=19)] of the ADRs were mild [level (2)] type as per Hartwig scale¹ and 47.6% (n=10) of the ADRs were definitely preventable as per Schumock and Thornton scale.²

The study was conducted for a short period of time (2 months) and included only a few (six) community pharmacists. Similar studies covering more retail pharmacists for a longer period of time are needed to validate our finding. Similar training programmes are needed for other community pharmacists in order to strengthen the programme.

Acknowledgements:

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Staff at the Drug Information and Pharmacovigilance Center at Manipal Teaching Hospital in Pokhara, Nepal

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Caribbean islands knock on the door

The Organisation of Eastern Caribbean States (OECS) was founded in June 1981, when seven Eastern Caribbean countries signed a treaty agreeing to co-operate with each other and promote unity and solidarity. As the islands gained their independence from Britain it became evident that there was need for a more formal arrangement to assist with their development efforts.

The OECS is now a nine member grouping comprising Antigua and Barbuda, Commonwealth of Dominica, Grenada, Montserrat, Saint Kitts and Nevis, Saint Lucia and Saint Vincent and the Grenadines. Anguilla and the British Virgin Islands are associate members of the OECS. Since 2000, with support from the French Government a Health Sector Reform Plan has been undertaken.

In May 2008, The WHO-QSM Department in Geneva received an application from these nine island states to participate in the WHO Programme for International Drug Monitoring so we have nine new associate member countries in the WHO programme. This has come about through a coordinated effort within the OECS which has set up a regional pharmacovigilance centre in Saint Lucia with Nicole Burkett-Felix as the pharmacovigilance coordinator. The following countries have now all applied for membership in the WHO Programme with reference to the regional centre:

Anguilla
Antigua and Barbuda
British Virgin Islands
Dominica
Grenada
Montserrat
Saint Kitts and Nevis
Saint Lucia
Saint Vincent and the Grenadines

Another initiative was recently taken by Naomi Jessurun in Surinam who, using a platform provided by UMC, set up a Vigimed-like e-mail network for pharmacovigilance centres in the Caribbean.

The 4 million milestone is reached!

Helena Wilmar

The new import process, as described in UR40, for Individual Case Safety Reports (ICSRs) to be inserted in the WHO international database 'Vigibase' is now up and running and we have managed to hit the 4 million milestone! (Figure 1 shows the cumulative growth in the WHO database.) A high quality and up-to-date database is essential in all our work for global patient safety and we are grateful for the work of colleagues around the world and for their collaboration in achieving this important target.

In parallel, a migration to a more suitable database platform has been on-going, since the present database engine is no longer suitable for the amount of information currently held by Vigibase (see p11). The result of the migration will speed up many processes connected to Vigibase, for example the search tool VigiSearch, where users perform searches in Vigibase.

Not all members of the WHO Programme are sending their ICSRs in the international E2B-format (xml-files). Approximately 50% of the members are instead sending their cases in the format INTDIS (text files). Since Vigibase contains ICSRs from many different sources (84 National Centres globally), harmonization of the submitted data is needed before the results are recorded in Vigibase.

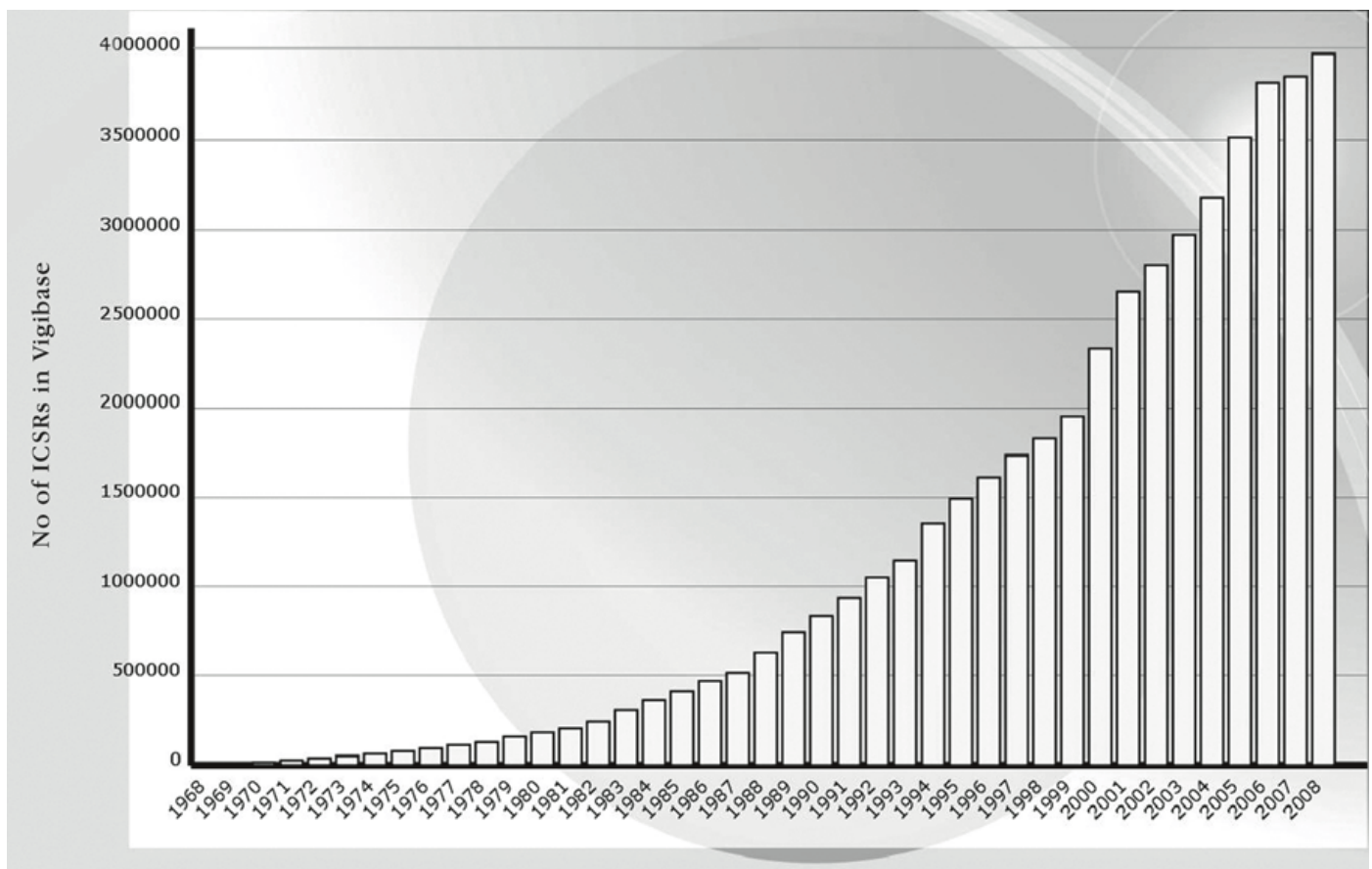
Due to the development and implementation of this new process (described in UR 40) there was a pause in the insertion of ICSRs into Vigibase from April to October 2007. This resulted in a backlog of ICSRs, and when the insertion of reports was renewed, import of E2B-cases was prioritized. The remaining backlog will be entered into Vigibase during the autumn. In the new process INTDIS cases will be converted into the E2B-format prior to import into Vigibase, which will facilitate the validation of the cases.

The process of inserting ICSRs into Vigibase is as follows: A first check of the format of the file is performed by a member of the Safety Reporting Team. If a file contains errors, we either correct manually ourselves, or ask the reporting country to correct this and resend the batch.

If the format is correct, the file will be uploaded and processed into Vigibase. Depending on the coded information on the ICSRs, a case will be

- Active in Vigibase, or
- Non-active (for example if ADR-terms or/and medicinal products don't have a match in the terminologies MedDRA and WHO-ART or WHO Drug Dictionary Enhanced), or
- Rejected (for example incomplete cases or duplicate reports).

Figure 1. Cumulative growth of ICSRs in Vigibase.



UMC validates VigiFlow data entry

Sten Olsson

In Uppsala Reports 38, July 2007, we wrote that *the* UMC has agreed to provide pharmacovigilance training and VigiFlow services in collaboration with the RaPID (Rapid Pharmacovigilance Implementation in Developing countries) initiative. The RaPID project office in India wishes to offer countries assistance with data entry of individual case safety reports (ICSRs) using quality assured processes. It was agreed that UMC VigiFlow experts would assess the accuracy by which operators at the RaPID office record case details from original case reports in the VigiFlow ICSR management system.

A set of scanned original reports were submitted to *the* UMC VigiFlow team. The UMC team then checked the accuracy by which the case details were recorded by the individual operators, using the VigiFlow user guide as a standard. A review template was designed and feedback was provided to the operators. Once they had reached a level of high proficiency the operators was given an examination. Each operator was provided with 5 test cases, some with rather complex sets of data. Once the operator had passed the test he/she was presented with a diploma as a certified VigiFlow data entry operator. Seven persons associated with RaPID have been certified so far.

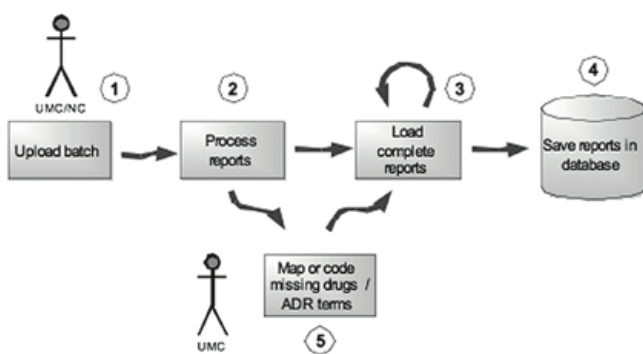
The quality assured entry of ICSRs in VigiFlow is offered by the RaPID team as a resource to national pharmacovigilance centres. The centre in Nigeria has already chosen to benefit from it since the internet service available locally is inadequate for conveniently operating VigiFlow. Instead original ICSRs are scanned and sent to the RaPID office by e-mail for entry into VigiFlow. Nigerian ICSRs are now again being updated in the national database and in the WHO database after this function having been interrupted for some time.

The time from receipt of a file until the ICSRs are active in VigiBase varies greatly, depending on the quality. Countries that send ICSR files in correct format and according to reporting guidelines are directly uploaded and processed into VigiBase without delay.

For ICSRs that don't have an exact match in the mentioned terminologies and dictionary, manual mapping/coding need to be done before the ICSRs will be active in VigiBase. This manual process depends on available sources for identification of product information and resources at *the* UMC. This applies also for ICSRs sent in incorrect format and/or not according to reporting guidelines. Figure 2 shows the new inputting process.

Later in the year when the whole backlog is entered into VigiBase, we aim to resume presentation of updated ICSR reporting statistics from WHO member countries.

Figure 2. The new report import process.



The new process has the following steps:

- 1. Upload batch**
The submitted file containing ICSRs is uploaded via a web-based interface.
To begin with the upload will be performed by UMC staff; in the future the upload interface will also be available for National Centres.
- 2. Process reports**
All individual reports in the batch are extracted and stored separately before loading into VigiBase.
- 3. Load complete reports**
All complete reports, that is reports that do not need any mapping or coding of drug information in the WHO Drug Dictionary and/or ADR terms in WHO-ART/ MedDRA, are loaded directly into VigiBase.
- 4. Save reports in database**
The reports are saved in VigiBase.
- 5. Map or code missing drugs/ADR terms**
Drugs that have been identified as missing in the WHO-DD are mapped to existing drugs (if possible), or coded into the WHO-DD.

VigiFlow – release of version 4.0

Ulrika Rydberg

VigiFlow is the Individual Case Safety Report (ICSR) management system maintained at *the* UMC. It is a system used by National Centres and other organisations to manage their own reports. National Centres can also use VigiFlow for sending reports to *the* UMC and the WHO Global ICSR database, VigiBase.

VigiFlow is developed in collaboration with its users, especially the Swiss national medicines agency, Swissmedic. The new version of VigiFlow contains major improvements for all users. The full system is now an even more complete tool for managing the ICSRs being handled by national pharmacovigilance authorities.

Multilingual

With the help of the National Centres in Argentina and Morocco, the entire VigiFlow interface has now been translated into both Spanish and French. The user can easily switch languages by clicking on the flags in the lower left corner in the interface. The help pop-up windows in the interface have also been translated for the convenience of the users.

Free version for reporting to *the* UMC

Several National Centres have requested a free version of VigiFlow to primarily use for sending ICSRs to *the* UMC. One reason for this is the problem of paying a yearly licence fee with an unstable economic situation in the country. A free-of-charge version of VigiFlow has now been realised, and those members of the WHO Programme that are interested in this can contact *the* UMC to find out more. The free version of VigiFlow has limited functionality and is meant to be used as a complement to another system for managing the national reports. The functionalities still available are primarily those for entering reports, making follow-ups (reassessment/amendment) of reports and sending the reports to *the* UMC. The possibility of having Regional Centres has also been kept in the free version, since this functionality is crucial for sharing the work-load of report entry between the National and Regional Centres in a country.

VigiFlow 4.0 at a glance

- Released on June 12, 2008.
- E2B import functionality.
- Submission manager to handle report exports (in both E2B and PDF format).
- Address book to keep contact details.
- Administrative information chapter for each report.
- Available in Spanish and French as well as English.
- Free version with limited functionality for sending reports to *the* UMC.

For more information about VigiFlow contact the Reporting team at *the* UMC by e-mail: vigibase@who-umc.org

Handling of E2B reports

The main advance in VigiFlow 4.0, compared to earlier versions, is the E2B report handling capability. Now it is possible to both import and export reports in E2B format. Many new input fields have been added to improve the E2B compatibility of VigiFlow and to ensure that all information on an imported report will be available in the interface. Several new modules have also been developed to keep track of imported and exported reports and their senders and receivers.

The screenshot shows the VigiFlow 4.0 interface for entering a report. The top navigation bar includes 'report handling', 'search and statistics', 'tools', and 'exit'. Below this, there are buttons for 'new report', 'send report', and 'list reports'. The main content area is titled '2008-0000 - rash + allergic reaction'. A callout points to the 'tools' menu, stating: 'The tools menu contains the E2B handling functionality, including the Submission manager and the Address book.' The form has a 'reporter's comments' section. Below that, a 'Rash' section is highlighted with a callout: 'New layout in lists.' The 'Reaction / event (Rash)' section contains various input fields: 'reaction term' (set to 'Rash'), 'reaction/event as reported by primary source', 'treatment of reaction', 'outcome of reaction' (with radio buttons for 'recovered/resolved', 'recovered/resolved with sequelae', 'not recovered/not resolved', 'fatal - unrelated to reaction', 'fatal - reaction may be contributory', 'fatal - due to reaction', and 'unknown'), and 'highlighted'. A callout points to the date fields: 'Fields are grouped together to make the interface layout more logical.' Below the main form is a 'Relatedness of drug(s) to reaction(s)' section with an 'expand' button. A callout points to this section: 'Some rarely used fields are hidden behind an "expand"-button.' In the bottom left corner, there is a 'version 4.0' label and a callout: 'Change the language here.'

Example from the new VigiFlow interface.

When an E2B file is imported, an acknowledgement file will be created automatically for the user to return to the sender of the file. If there was an error in the file that prevented the upload of one or more reports in the E2B file the user will be notified. Statistics of all uploads are kept and can be viewed at any time.

Export of reports in both E2B and PDF format is handled by a submission manager. This module tracks both planned and performed submissions in one comprehensive interface. All contact details of senders and receivers of ICSRs are kept in an address book that is also integrated in the system.

Administrative information page

A new page has been introduced for information regarding the status of the report and the sender and receivers of the individual report. On

this page, it is also possible to link the report to other reports in the database of the VigiFlow organisation, and see if other reports have been linked to the report. If there is any duplicate information, this can also be viewed. The administrative information page is kept separate from the rest of the report and is accessed from the report lists.

The user experience

The layout of the system has been improved to make room for the new added fields and still keep the system as user-friendly as possible. On some pages, fields that are rarely used are hidden until an 'expand' button is clicked. Also, fields that cover the same area are grouped together and the 'look-and-feel' of the system has been updated.

New look-up functions help the user to, for example, select the correct report when a duplicate should be removed. The user enters the report Id and the system will show the title of the relevant report for the user to verify and select.

In conclusion, the full version of VigiFlow is now a complete ICSR management system for National Centres. All entered ICSRs are safely stored and easily retrieved, both as single reports and as part of advanced searches or statistical analyses. From version 4.0 the system allows electronic communication of reports in E2B format, with for example pharmaceutical companies, and keeps a record of which reports have been sent or received from whom. At the same time VigiFlow 4.0 can function as a streamlined, free-of-charge, reporting tool to *the* UMC for countries that do not want the full version or cannot pay the licence fee.

More information

Contact *the* UMC for more information about VigiFlow and the new release. Release Notes are available on request. The new functionality is also described in the User Guide (available from the VigiFlow interface after log in).

WHO database migration

WHO global ICSR database, Vigibase, grows beyond current database platform capacity

Johanna Eriksson reports

A high quality and up-to-date database is essential in all our work for global patient safety. This includes suitable and effective tools but also stable database platforms.

Amount and use of data increased

The recent implementation of MedDRA (Medical Dictionary for Drug Regulatory Affairs) terminology in Vigibase, as well as in VigiSearch, as described in UR41, has made the search tool useful for more users, and as a result the number of VigiSearch queries submitted per month has doubled since the implementation. Passing the 4 million milestone of ICSRs in Vigibase and having the new import process up and running increases the amount of ICSR data rapidly. The WHO Drug Dictionary Enhanced has also grown to contain information on 193,755 unique names, 1,462,205 different medicinal products, plus trade names with for example form and strength information added, there are 9,995 different ingredients mentioned in these products (release June 1, 2008).

Platform upgrade needed

This increase in data is of course very good news, but it also challenges the technical environments used by *the* UMC. It has become clear that the existing database platform is no longer suitable for the amount of information currently held by the database, nor the search capacity. It is the contributing factor of lowered performance that has been a problem within the VigiSearch query tool during the past month or so.

Migration plans underway

A migration to a more suitable database platform has started. Vigibase will be split into different databases depending on functionality: a scalable, high-performance search and statistics database, a process database for importing and validation of received ICSRs and a production database for the production of the WHO Drug Dictionary Enhanced data.

The timeline for the migration project is divided into several stages. The search and statistic database will be in production by the end of July 2008, the production environment for the WHO Drug Dictionary Enhanced. The WHO Herbal Dictionary and WHO-ART will also be migrated and put into production by August 2008. We expect to complete the migration project by the end of October 2008.

New muscle in African PV

9 countries meet in Accra to review progress

Bruce Hugman reports from Ghana

'Building capacity' can sometimes sound like a management platitude, but evidence from a recent meeting in Accra suggests that it can also represent real achievement.

In 2007, WHO held a week-long course in Ghana to train regional pharmacovigilance (PV) professionals in acting as consultants for neighbouring countries. The advanced PV training, and the introduction of cohort event monitoring (CEM) to some of the participants, seem to have had a considerable energising effect with solid, practical results.

This year's follow-up training, held in Accra in June, brought representatives from nine countries together to review progress and to tackle new skills and topics.

The programme

Among the main topics and activities were:

- Problems and solutions in spontaneous reporting and CEM
- ICSR reporting and database management – intensive exploration and practice in VigiFlow, the UMC's ICSR reporting and data-management software
- Review of country achievements in PV development and CEM (where projects were in hand)
- Extending the concerns of PV: review of the Patient Safety pilot project carried out by the Moroccan PV Centre
- The challenges of fund-raising
- Developing check-lists and standard operating procedures (SOPs) for consultancy and support in other countries
- The challenges of anticipating, preventing or managing scares and crises
- Advanced communication skills

Countries represented on the course:

- ◆ Cameroon
- ◆ Ghana
- ◆ Kenya
- ◆ Mozambique
- ◆ Nigeria
- ◆ Sierra Leone
- ◆ Togo
- ◆ United Republic of Tanzania
- ◆ Zambia

New member of the WHO Programme

Shortly before the course, Togo had qualified as a full member of the WHO Programme, and an immense amount had been achieved since last year:

- Legislation drafted and implemented
- National commission and PV Centre established

- Focal points nominated for some disease programmes
- Training and promotion of PV initiated
- Pharmacology added as examined subject in medical and public health education
- ICSR reporting guidelines produced
- Active monitoring of adverse events following immunisation (AEFI) during yellow fever immunisation campaign
- ICSR surveillance in hospitalised patients
- Preparing of CEM for artemisinin combination therapy ACTs (10,000 subjects)
- First batch of ADR reports submitted to WHO/UMC

Progress in many locations

Following last year's meeting, Kenya had become an associate member of the WHO Programme. Much had been done: national ICSR reporting and AEFI guidelines, active surveillance of drugs in several fields, development of clinical trials protocols, sensitisation and training in the use of ACTs, and preparing for CEM of ACTs and antiretrovirals (ARVs).

Similarly in Mozambique: 201 ICSR reports received in the past year, PV training across a broad range of audiences, a bulletin produced, medicine legislation being reviewed, and a PV chapter introduced into the National Formulary. Two serious crises were negotiated, one in response to serious ADRs and a death after use of albendazole and praziquantel for pediatric parasitosis, and another resulting from ineffective anaesthesia because of confusing labelling of magnesium sulphate and lidocaine. A study of drug exposure in pregnancy was carried out with more than 3,000 patients, and intensive monitoring of anti-malarials and ARVs in pregnant women was started in one province.



The group photo of the participants at the Accra training meeting

Progress was also reported in the other countries. There was one astonishing story of the impounding of container-loads of contaminated and counterfeit toothpaste in Sierra Leone, as part of the regulatory authority's duties. Counterfeit and sub-standard drugs were a major problem for many of the countries, with officials often working with few resources in unsupported, even hostile environments.

Building capacity

On this course, the capacity in question was primarily equipping participants with the knowledge, skills and confidence to take part in missions to other countries to help set up and develop PV systems and to support research and development in the field. It was evidently a challenge relished by course members, while acknowledging the

great sensitivities and problems of such work. A draft guidance document for this was one of the important outcomes of the meeting.

Participants have a dedicated email network for exchange of ideas, the posting of documents and research results, and for requests for help. A further follow-up is planned for 2009 when the prediction is that even more substantial progress will have been made.

Both courses were organised by WHO-QSM (Geneva), with the support of WHO AFRO, the WHO Country Office in Ghana and UMC. The meetings were hosted by the University of Ghana Medical School with the collaboration of the Ghana Food and Drugs Board.

PhRMA discusses data mining

Andrew Bate reports

An invitation-only 'think tank' meeting, on pharmacovigilance and data mining, was organized by the Center for Drugs and Public Policy at the University of Maryland School of Pharmacy, and funded in part by the Pharmaceutical Research and Manufacturers Association (PhRMA). The one-day workshop, 'Best Practices in Pharmacovigilance: Developing Standards for Data Mining' took place on 5 June 2008 at the Universities at Shady Grove in Rockville, Maryland, near Washington DC, USA.

Two years ago PhRMA funded two major projects to critically evaluate data mining. The Center for Drugs and Public Policy at the University of Maryland School of Pharmacy (in collaboration with the company DrugLogic), and the company ProSanos received funding to conduct studies on pharmacovigilance practices and data mining. At this workshop the results of their studies were presented, and speakers attempted to address several questions, such as:

- What is the clinical value of a statistical alert across various data mining algorithms?
- Can data mining be used to rank signals?
- How does the increased reporting by consumers impact the validity of data mining?

A survey from the University of Maryland group on Industry Practices shows that two-thirds of companies (69%) use some form of data mining; but only 31% have standard operating procedures (SOPs), while 35% are developing SOPs. Furthermore, survey responses indicate that there is great variation in how data mining is implemented and why it is being used, and this led to much discussion at the workshop.

The workshop generated debate on best practices in the use of data mining in the pharmaceutical industry. The 'think tank' forum allowed around 80 experts and key stakeholders from industry, government and academia to examine data mining in the context of evolving scientific, regulatory, and legal issues. It focussed on the use data mining from the industry perspective, in order to develop an expert consensus on how the study results can be used to inform the development of SOPs and potentially, regulatory guidance.

The workshop was designed to address several aims:

1. To disseminate the most current research findings within the programme topics;
2. To critically assess the impact of new findings on future directions for research;
3. To provide a forum for discussion of current and emerging issues; and
4. To establish best practices to serve as guidance to regulatory agencies.



Drs Goldhammer and Palumbo leading a discussion at the PhRMA meeting.

The structure of the day was a welcome from hosts Dr Manfred Hauben of Pfizer on behalf of PhRMA, and from Dr Sheila Weiss Smith of the University of Maryland. Then Dr Alan Hochberg presented the ProSanos results, and Dr Vic Gogolak and Sheila Weiss Smith the University of Maryland and DrugLogic work. Dr Andrew Bate of the UMC then gave the invited keynote address 'Spontaneous report mining – state of the art and future prospects'. He was asked to give an overview presentation linking the morning presentations from the two study groups to the workshops scheduled for the afternoon. Andrew commented on the results of the two funded projects, presented on issues within spontaneous report quantitative screening that had been well addressed, those that hadn't and

finished by presenting a view on the role of spontaneous reporting in a future where large-scale analysis of other types of healthcare data, such as electronic patient records, is routine. (The analysis of patient records being an area of pioneering focus of research at the UMC over the last 5 years, already leading to high-profile publications.) Andrew concluded by saying there was a need for both.



Judith Jones addresses a group at the Maryland meeting.

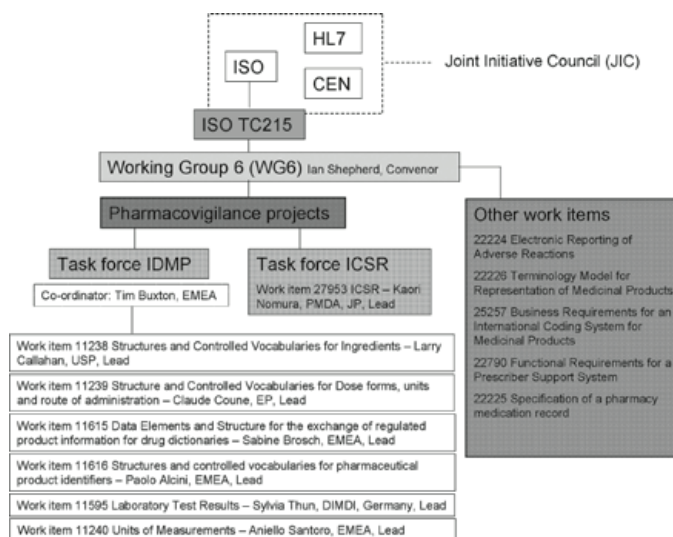
In the afternoon the meeting participants split into four groups to discuss different aspects of data mining in pharmacovigilance. Two workshops focused on methodological aspects (led by Dr Judith Jones of the Degge group, and Dr David Goldsmith, of Goldsmith Pharmacovigilance & Systems). Dr Steve Goldman, Stephen A. Goldman Consulting Services led a workshop on the integration of Data Mining into Company Processes and Procedures, while Frank Palumbo, Professor and Executive Director, University of Maryland School of Pharmacy Center on Drugs and Public Policy and Dr Alan Goldhammer of PhRMA jointly led a workshop on legal and policy issues. Professor Hugh Tilson of the UNC School of Public Health led a general discussion summarising the discussions of the workshops and looking for consensus from the meeting delegates. Although there was much consensus that in some scenarios data mining was useful, it was clear that delegates felt there was a need for more work on 'good data mining practices', and particularly around the need for recommendations and policies on the use of data mining for spontaneous report screening.

We would like to thank Sheila Curry of the University of Maryland for kindly providing the photos included in this article.

ISO ploughs on

Marie Lindquist attended the latest ISO (International Organization for Standardization) Working Group 6 meeting in Göteborg, Sweden, in May 2008 on behalf of the WHO Programme. (Figure shows extent and structure of current work in the drug safety area.)

There were intense discussions in the task force meeting on Identification of Medicinal Products (IDMP) and in the following WG6 meeting, which will potentially affect the WHO Drug Dictionaries. An ICSR task force was also meeting concurrently with the other pharmacovigilance-related sessions.



ISO working group structure

Work on various items which will impact on the WHO Programme continues, with a further meeting in October, but with lots of work on-going during the intervening months.

VigiGravida

ARVs and ACTs monitoring among pregnant women in rural Mozambique

Esperanca Júlia Pires Sevene and Alda do Rosário Elias Mariano

First there was Vigibase, the database of the WHO Programme for International Drug Monitoring, then Vigibase on-line (now VigiFlow) came along as a reporting tool to help national centres in reporting ADRs to the UMC in Sweden. Now there is VigiGravida, an exciting scientific project of immense public health importance being carried out by the Mozambican National Pharmacovigilance Centre to monitor the safety of anti-malarial and anti-retroviral drugs during pregnancy. VigiGravida is the commonly-used name for a European and Developing Countries Clinical Trials Platform (EDCTP) funded 2-year study entitled 'Intensive safety monitoring of anti-malarial and anti-retroviral drugs used during pregnancy in Manhica'. It was initiated in 2006 under the leadership of Drs Esperanca Júlia Pires Sevene and Alda do Rosário Elias Mariano of CIMed, the Mozambican National Pharmacovigilance Centre, together with collaborators from Spain, Mozambique and Ghana.

VigiGravida was designed at a time of rapid change in public health programmes in Mozambique, including the introduction of sulfadoxine-pyrimethamine (SP) for intermittent treatment of malaria in pregnancy; the switch of national first line treatment for uncomplicated malaria to a combination of artesunate+SP as well as a national roll-out of anti-retroviral drugs for patients living with HIV/AIDS including the use of zidovudine and nevirapine to prevent mother-to-child transmission of HIV.

In order to monitor the safety of the recommended anti-malarial and antiretroviral drugs as well as other medicines used during pregnancy in Mozambique, CIMed designed a protocol on intensive safety monitoring of these drugs in Manhica district. The pregnant women are recruited at the first ante-natal visit and closely monitored throughout pregnancy until they give birth, after which both mother and baby are followed up until the child is 12 months old.

The objectives of this study are

- To describe potential adverse drug reactions to anti-malarial and anti-retroviral drugs in pregnant women including adverse pregnancy outcomes
- To measure the incidence of these adverse drug reactions, and
- To determine risk factors that may contribute to the development of adverse drug reactions to anti-retroviral and anti-malarial drugs in these pregnant women.

The study is being implemented by researchers from the Faculty of Medicine of the Eduardo Mondlane University (UEM) in Maputo, Mozambique and the Manhica Health Research Centre (CISM), which include the Manhica Health Centre and the Maragra Health Centre.

Patient recruitment started in September 2007. By May 2008, about 1,224 pregnant women had been recruited at the antenatal clinic of the Manhica and Maragra Health Centres. These women have been reporting for follow-up visits and 624 of them have delivered their

babies. Safety information is collected at each visit and double-entered into the database at CISM. Interim analysis will soon be carried out to determine the presence of any safety signals.

As part of the project proposal, which included a component to permit collaboration with other scientists and pharmacovigilance experts, Dr Clara Menendez from University of Barcelona is regularly visiting the site and closely monitoring the implementation. Dr Alex Doodoo from the University of Ghana Medical School visited the site in April 2008 to assess the progress being made in the project and to interact with key project staff. During his visit Dr Doodoo trained the co-investigators on causality assessment and presented a lecture on Pharmacovigilance in Africa to increase South-South cooperation in this area. He also participated on the health professionals training in Manhica. Dr Xavier Carné is reviewing the reported adverse drug reactions and provides support in causality assessment. Other collaborators include Drs Sónia Machevo, Sureia Hassamo, Ana Sofia Roberto, Lidia Laço and Joaquina do Rosário of Mozambique.



The VigiGravida Study Team posing for a picture at Manhica

VigiGravida is clearly an important project, which will have its own challenges, particularly the analysis of risks and benefits of the several medicines being administered during pregnancy, sometimes to healthy women in a bid to prevent disease or adverse pregnancy outcomes. The study team however believes that the multi-country group of experts and the on-going participation in the WHO Programme for International Drug Monitoring as well as the strong technical links to the Uppsala Monitoring Centre are keys to success. They will help to provide the needed technical and technological expertise and resources required to extract useful safety data from the minefield of multiple medicine administration to women in Mozambique during pregnancy.

My journey in *the UMC*...thinking globally

Completing an Argentina – UMC exchange

Maximiliano Bergman

At the National Centres Meeting in Buenos Aires last year the idea was born. Anna Celén from *the UMC* wished to spend a month in Buenos Aires to learn Spanish and work at the national pharmacovigilance centre (ANMAT), and the exchange between junior staff members soon became a reality.

The first part took place in February with Anna Celén's visit (see UR41 p16). Two months later I was arriving at Arlanda Airport with a lot of expectations and questions: Would I cope with Swedish culture? Would I find the work interesting and relevant? Would I miss my home too much?

Planning my Uppsala work schedule

Everything began with a meeting with Sten Olsson and Anna Celén and right away I knew that it would be a lot of work, but I also discovered a lot of good will from them, because we discussed my goals and wishes. My schedule included presentations from the different teams, VigiFlow translation into Spanish and daily work with the Signals team.

I started by looking at the Combinations Database and trying to filter out some signals. I would describe this as being a fisherman, trying to catch a big fish (signal), and eventually with a lot of patience and practice I managed to get some! I was really happy when we met with Ralph Edwards and analyzed the possible signals and sent them to review. It was a great surprise when I was asked to be part of *the UMC* review panel and I felt really honoured.

The VigiFlow translation was a lot of fun actually, because it was a good chance for Anna Celén to practice her Spanish, and for me to make fun of her mistakes! Anyway, we made a great team working together and I'm proud of the work we have done.

Every group at *the UMC* gave a presentation for me. It was really interesting to discover how the Drug Dictionary was created and evolved, to learn from the Marketing team how *the UMC* generates the money needed to survive, and witness how the Reporting team deals with the incoming reports. Learning about herbals was a good opportunity for me, as we don't have a herbal database at ANMAT.

With a global outlook

If I have to describe the work of *the UMC* in one word, that word would be Global and the presentations emphasised that perspective. It was fascinating to learn about all on-going and future projects, interactions, quality assessment and patient safety. I have to admit that I started to think globally too; hearing about all the projects was so mind-blowing that a lot of ideas were rushing in my head, ideas to put in practice in Argentina.

I also visited the national centre of Sweden, a big building in a green area of Uppsala where they work globally too, towards EMEA. I gained a lot that afternoon thanks to Anne Kiuru and all the kind people working there.

Looking to the future

Discussing the future of pharmacovigilance in the world and particularly in South America, Sten Olsson opened my mind and told me that my visit to *the UMC* was just the beginning of this journey. At first I wasn't able to see it clearly but when I left I could, and there is a whole world of opportunities in this global affair.

So, what did I bring home? I'm trying to put the patient safety project into practice here. We have also started on the quality assessment pilot programme that Marie Lindquist proposed. Another idea is putting VigiFlow in every corner of my country and making it the official database. I will also begin my reviewer's work and continue with my translation duties when needed.

Memories and Friendships

What about Uppsala? It's such a beautiful city with a river, little bridges, a cathedral, a castle and lots of bicycles. Every time I look at the pictures of my stay there I can't help but miss the 'April weather', the early closing of shops and restaurants and the extraordinary Walpurgis celebration.



Tova, Maria, Maxi, Jeanette, Monica on a bridge over the River Fyris in Uppsala

Yes, it was a month to remember, an experience of a lifetime and I have no words to describe how thankful I am to all UMC staff, especially Maria Tengstrand, Jeanette Johansson and Helena Sköld in the Signal team for introducing me to the field of signal detection. I also want to thank Ralph Edwards, Marie Lindquist and Sten Olsson for letting me spend a month at *the UMC* and for all the interesting conversations and ideas. Last but not least I want to thank Anna Celén, for being there all the time, caring about my needs and well-being, for showing me the city and Stockholm.

I really hope that my collaboration with *the UMC* will continue in the same manner in the future!

WHO Policy Briefing

The Quality Assurance and Safety: Medicines team (in the Department of Medicines Policy and Standards), WHO is organizing its second Technical Briefing Seminar entitled **Quality Assurance and Safety of Medicines: Promoting Global Collaboration**. This will take place at WHO Headquarters, Geneva, from 22-26 September 2008.

Programme

The objective of the Seminar is to advance collaboration between WHO and other stakeholders from governmental and non-governmental organizations engaged in promoting the quality and safety of medicines in the global community.

The programme aims to increase awareness and knowledge of quality assurance and safety of medicines, blood products and related biologicals with a special focus on WHO standard-setting processes.

Audience

The technical briefing will be of interest to technical officers, WHO Representatives, regional advisers and country office staff of WHO and other UN agencies, drug regulators, and government and non-government officials working in related areas.

Seminar format

An interactive seminar with presentations on individual topics is followed by working group exercises on specific tools and techniques (e.g. databases, adverse drug reaction reporting forms, case studies etc). Technical officers from WHO and Collaborating Centres, senior consultants and WHO experts will lead and facilitate the programme.

The programme and application details are available at:
http://www.who.int/medicines/areas/quality_safety/qsm_tbs/en/index.html

Attendance is limited to 35 places. Participation is free although each participant is responsible for their own travel and accommodation costs. **The closing date is 10 August 2008.**

Completed application forms should be sent to:
Ms Ana Garcia-Miguel
Quality Assurance and Safety: Medicines, World Health Organization,
Geneva 1211, Switzerland
Fax: 00 41 22 791 4730
E-mail: garciamiguela@who.int

WHO targets Western Pacific

WHO will conduct a training course for introducing pharmacovigilance for Western Pacific countries, from 2 to 11 September 2008 in Manila. Officials in charge of medicines safety monitoring at the health authorities, and/or representatives of national pharmacovigilance centres of selected countries will be invited. The main objectives of the course are to demonstrate the importance of pharmacovigilance activities, to provide the latest tools on basic ADR reporting mechanisms, and to build or reinforce capacity of national pharmacovigilance centres. The participants are expected to learn basic principles of pharmacovigilance and to grasp the roles and responsibilities of stakeholders and be able to communicate effectively with them.

Patient Safety Research Grants – Better Knowledge for Safer Care

The WHO World Alliance for Patient Safety is offering grants for small research projects dealing with issues of patient safety, including developing or testing local interventions to improve patient safety and cost effectiveness of risk-reducing strategies. The call for proposals opened on 1 July and will close on 30 September. Studies should start in 2009. Sums ranging from \$10,000 to \$25,000 will be available, and proposals from developing countries and those with economies in transition are being particularly encouraged. The Programme concentrates its efforts in four specific areas:

- Global research priorities
- Methods and measures
- Strengthening capacity
- Country research studies

To find out more please go to: <http://www.who.int/patientsafety/research/en/>

National newsletters and web sites

Many national pharmacovigilance centres and academic departments around the world produce newsletters, in print and digital format on patient safety. These vary over frequency and content and the group to which they are aimed. Some regulatory authorities and pharmacovigilance centres maintain internet web sites at which you can subscribe to updates.

the UMC is pleased to receive many examples of pharmacovigilance centre newsletters* and we circulate and store recent issues for reference and for educational purposes.

ADR newsletters and bulletins are a good way of sharing important information. We would like to make a list of available newsletters and patient safety web sites from pharmacovigilance centres around the world. Anna Celén at *the UMC* would be grateful to receive information about the following:

1. The Internet address to the website of your centre (if not already present on our website). Go to www.who-umc.org, click on 'Links' and 'Regulatory authorities' to check.
2. Information about your newsletter (if available). Is it printed, distributed by e-mail and/or downloadable from your website? Is there a subscription service where you can subscribe to newsletters and/or updates on your website?

National Centres can also invite members via Vigimed to join their mailing list.

We hope to return to the subject and information-sharing at a future date.

**but please ensure that when sending copies to us you amend your posting address to the new UMC address – see back cover – as items are no longer being forwarded from the old address.*

And the winner is...

In March this year *the UMC* distributed a questionnaire to a great number of countries around the world with the intention of documenting pharmacovigilance practices in resource-limited settings. The investigation was part of a so-called landscape assessment providing a background to the elaboration of a global pharmacovigilance strategy. The UMC offered everyone who had responded by 31 March entry in a lottery in which a free return flight ticket in economy class to Uppsala in connection with the National Centres meeting from 20–23 October was the first prize. Other prizes were copies of the books 'Drug Benefits and Risks' and 'Pharmacovigilance in Focus'. We were happy that these prizes had attracted contributors from 47 countries to submit their filled-in questionnaires.

The draw was organized in front of all UMC staff and David Coulter, undertaking a consultancy at *the UMC*, was asked to make the draw. As documented in the picture David first picked South Africa from the bowl. The South African questionnaire was completed by Mukesh Dheda and he is consequently being offered an economy class return flight ticket South Africa – Stockholm in October. We look forward to welcoming Mukesh to the national centres meeting.

A further reminder to those countries that have still not responded to the questionnaire was sent in June 2008. The questionnaire is available in French, Spanish and English. The English version can be completed on line from www.who-umc.org > WHO Programme > 2008 Pharmacovigilance Survey.



David Coulter draws the winner of the questionnaire prize

Case report journal launch

A new open access journal is being launched entitled *Cases Journal*, which aims to publish tens of thousands of case reports from right across healthcare.

Cases Journal will publish any case report that is authentic, understandable and ethical, in the belief that "every case, no matter how 'everyday', teaches us something". By aggregating all published case reports in a database, it is hoped to enhance the value of each case report. As an online journal, *Cases Journal* has none of the space constraints of traditional medical journals.

The aim is to create a valuable new clinical resource by compiling thousands of case reports and incorporating them into an easily searchable free-to-access database. Users will be able to search for a wide variety of symptoms, drugs and disorders, among many different patient groups.

Cases Journal also aims to include patients' perspectives in the published case reports - in the hope that increasing patients' involvement will add important detail to each case that clinicians and other patients can learn from.

Visit <http://casesjournal.com/> for instructions on how to submit.

Two new theses

We note two recent theses of interest to those working in pharmacovigilance:

Knowledge Creation about Adverse Drug Reactions – Analyses of Data from Pre- and Post-marketing Files by Lise Aagaard, PhD thesis in the Faculty of Pharmaceutical Sciences at the University of Copenhagen.

The thesis sought to discover how knowledge about ADRs is created and used in drug surveillance. This was done with reference to the possibility of foreseeing serious ADRs based on information reported in the clinical trials before marketing, analysis of the characteristics of ADRs reported by consumers compared to those reported by health professionals, and exploring the structure and processes of the Danish and Australian spontaneous reporting systems. (See also Danish delegation on p20.)

Drug-related morbidity and mortality: pharmacoepidemiological aspects by Anna Jönsson at the University of Linköping was published last year and describes the pattern of pharmaceutical use related to morbidity and mortality and in particular observational studies from Sweden and Denmark.

ISoP in Argentina

The International Society of Pharmacovigilance is offering two parallel courses prior to its Annual Meeting in Buenos Aires this October.

On Sunday 5th October there will be

- **Pharmacovigilance, from fundamental basis to practice** (Language: English / Spanish with simultaneous translation) with Luis Alesso (chair), Marie Lindquist, Nicholas Moore, Ronald Meyboom, Paula Márquez, Jan-Willem van der Velden.
- **Drug-related Risk Management** (English only) with Xavier Kurz (chair), Miles Braun, Gerald Dal Pan, Aparna Mohan, Analía Pérez.

The main conference will cover a wide range of topics through plenaries, including 'Pharmacovigilance in Hospitals', 'Counterfeit Medicines', 'Pharmacogenetics and Drug Interactions in Pharmacovigilance', 'Education and Training', 'Results of Intensive Pharmacovigilance Programmes', 'Lack of Effectiveness', 'Vaccines Pharmacovigilance', 'Estimating AE/ADR seriousness, causality and frequency as the basis of risk assessment', as well as a round table discussion: 'Customising Risk Management: Global or Local?' led by Joan-Ramon Laporte and key note lectures from Gerald Dal Pan, Mike Rawlins and Ralph Edwards, who will give the Beje Wiholm Lecture.

Full details are available from http://www.isop2008.org/en/scientific_programme.php

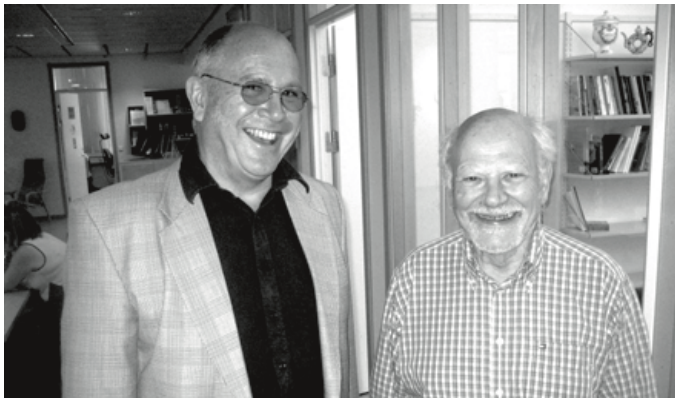
Uppsala Reports printing

We apologise for the various printing mistakes on the last edition of Uppsala Reports which regretfully occurred after a satisfactory proof had been approved by the UMC to go to print. Thankfully the text was only minimally affected and we trust this did not affect your appreciation of the issue.

Visitors

A challenge to national centres

Prof Andrew Herxheimer honoured *the UMC* and myself by a brief visit *writes Ralph Edwards*. He is a well-known figure in Health Action International and an ardent supporter of important specialist journals in drug regulation science, such as '*La Revue Prescrire*'. He is also a splendid academic clinical pharmacologist.



Ralph and Andrew Herxheimer "a wonderful raconteur"

As always, he both amused (he is a wonderful raconteur) and challenged me. His challenge to me was to help him fill in a short questionnaire concerning global pharmacovigilance activities as part of a 'Delphi project'. The statements/questions he wished me to comment upon are reproduced below *with some explanatory text of mine in italics where I think it may be needed*:

- ◆ Preclinical animal toxicology (*What access does the PV centre have to such data*)
- ◆ Human toxicology, including AE monitoring during clinical trials (*What access does the PV centre have to such data*)
- ◆ Gather & analyse spontaneous reports of suspected ADRs
- ◆ Monitor adverse effects in clinical practice (*this includes patient safety and observational and cohort studies, and also it means that the PV centre would either do the studies or control them*)
- ◆ Describe characteristics & natural history of particular effects (*this means having detailed patient information on such issues as severity and outcomes*)
- ◆ Investigate/ discover the pharmacological/ biological mechanisms involved (*this, and the following questions, imply active involvement of the PV centre in initiating such activities, or doing it themselves*)
- ◆ Investigate the epidemiology of adverse effects, eg frequency, seriousness, risk factors
- ◆ Research ways of preventing or attenuating the effect, & testing them
- ◆ Develop treatments for people who have suffered damage
- ◆ Design and test a framework for compensating people avoidably harmed
- ◆ Review balance of benefits and harmful effects of the drug in different clinical situations

- ◆ Communicate the knowledge gained to health professionals and public
- ◆ Revise the Summary of Product Characteristics, the leaflet for patients, and the licensing status
- ◆ Develop means of checking that the new knowledge is used in practice
- ◆ Investigate & assess the social impact of medicines: on communities; the development of dependencies; quality of life.

Some of you will recognise that I have expressed similar thoughts, but I was astonished to be confronted with the contrast of these key questions on scientific and public health performance against our usual concentration on bureaucratic parameters of success, such as numbers of reports, timeliness of transfer, terminologies, etc. I must straight away stress that neither Andrew nor I think that these latter factors are unimportant, only that it was a strong reminder that we really must ensure that we keep a strong focus all matters which will contribute to the better, safer use of medicines.

It is also clear that the pharmacovigilance centre may not need to undertake all activities themselves, but to ensure that they have the access to facilities that will help them.

Thank you, Andrew!

From Sudan

At the beginning of April, Nageeb Sulaiman Saeed from Sudan made a short visit to *the UMC* to learn about our activities. He is the Director of the National Health Laboratory as well as the Chairman of the National Poison Control Council in Sudan, which is why he also visited the Swedish Poison Information Centre.



Nageeb Sulaiman Saeed

Karolinska course calls in

The course 'Pharmacovigilance – Principles and Practice' was arranged by the Karolinska Institute in Stockholm from 7–11 April. The programme included a day in Uppsala with visits to both *the UMC* and the Swedish Medical Products Agency. 28 participants



Karolinska Institute course participants at the UMC

from drug authorities, companies, universities and hospitals all over Europe were given an overview of UMC activities as well as presentations about Signal detection and the latest research in ADR surveillance. The group seemed very interested and asked a lot of questions; WHO and UMC publications were also very popular.

Visitors from Finnish National Centre

In late April, visitors from the Safety and Drug information department at the Finnish National Agency for Medicines (NAM) spent a day at *the* UMC. The NAM delegation consisted of Dr Kirsti Villikka, Dr Tiina Karonen, Dr Radhakrisnan Rajaratnan, Marja Forsell, Suvi Loikkanen, and Kari Salmela.

The Finnish National Centre is in the process of developing their tools for ADR management and wanted some input from *the* UMC in order to proceed. We discussed options for how to upgrade their present system, for example to switch reporting format to the E2B international standard.



Helena Wilmar with the visitors from Finland.

A short status report on the MedDRA implementation was introduced. In addition, presentations on signal detection, duplicate detection, data mining in Vigibase as well as other research projects were provided by UMC staff. All topics opened up fruitful discussion throughout the day.

Continued from page 2

But notice the website descriptions given, the general aims are quite clear and so is the thrust towards turning disagreement into a positive move towards clarity.

Over the years that I have been in pharmacovigilance I have attended too many meetings where conservative, partisan, ill-informed and deceitful agendas have been pursued in meetings which should have had critical appraisal of science and its development as their goals. The statements that, 'Case reports are the poorest form of epidemiology'; that, 'Observational studies are so subject to confounding to be worthless', or that, 'Controlled clinical trials are the only evidence to base decisions upon', are all



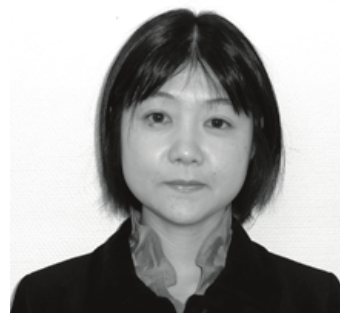
Cecilia Biriell, Camilla Bilcher, Lise Aagaard and Anna Celén.

Danish delegation

In May, Lise Aagaard and Camilla Bilcher from the National Centre of Denmark visited *the* UMC. The usual UMC programme was presented with a focus on database structure and signal detection. The E2B reporting from Denmark was also discussed to improve quality and communication.

Japan

In June *the* UMC was visited by Mitsuko Imai from Japan. She is a pharmacist who recently started a two-year secondment in the WHO. She has been working in different departments within the Ministry of Health, Labour and Welfare in Japan for 13 years. One of her tasks was the coordination and planning of the Official Development Assistance activities in health and social welfare sectors for ASEAN countries. She was also seconded to EMEA during 2002. In *the* UMC, she attended a series of presentations to obtain a full overview of our work and activities.



Mitsuko Imai

Cedric Bousquet

Our French collaborator Cedric Bousquet revisited *the* Uppsala Monitoring Centre on 29-30 May in relation to the on-going project to develop new techniques of using vocabularies for adverse reaction terminologies, and applying this to WHO-ART.

retrogressive. They fuel distrust and public speculation, anger politicians and promote bureaucracy and legislation over science.

A day in OMERACT was worth a decade of the meetings I usually attend. I hope that working in retirement I can, 'Make the day count', more than hitherto.

New faces at the office



Introducing Britt

Britt Gustavsson McCurdy joined *the UMC* in May as the Corporate Secretary where she works closely with the Director and Chief Financial Officer.

"Uppsala became my city when I came here from Dalarna to study. It is also the place where I met my American husband John. How did I end up at UMC? Well, as often in life, contacts

are the key. I knew Birgitta (Toreheim) from working with her at a Swedish pharmaceutical company and she talked highly about her new workplace, so I got curious and when a job opportunity came my way I grabbed it. I find the atmosphere very positive and energetic and the work performed by all is very important.

Free-time is often spent at our summerhouse in Dalarna or on a trip to sunny California where part of the family lives. There are also visits to the 'spinning class' at the gym. With two grown-up sons now living their own lives there is time over again to be involved in Amnesty International which I was very devoted to many years prior to bringing up the boys."

Medical Assessor appointed

The UMC is delighted to announce that Dr Richard Hill has been appointed to a new post of Medical Assessor at *the Uppsala Monitoring Centre*.

A full profile of Richard with background to the scope of this post will appear in the October issue of Uppsala Reports.

Vaccine Safety

The UMC is advertising for a Vaccine Safety Specialist to be the focal point for a major step forward in global monitoring of adverse events following immunisation (AEFI).

WHO has identified a need for a vaccine safety focal point at *the UMC* in order to support global monitoring of vaccine safety. This includes improving the reporting and analysis of vaccine-related adverse events through the WHO Programme for International Drug Monitoring; and related work by the Global Advisory Committee on Vaccine Safety Subgroup on Global AEFI Monitoring.

The deadline for applications is 18.00 on 1 September 2008 and the full job advertisement is accessible via the What's New page of *the UMC* website: www.who-umc.org.

Running for blood



Monica, Ulrika, Jeanette and Elki on the Blodomloppet run.

Staff from *the UMC* took part in a nationwide event held in twelve cities around Sweden on the 3rd of June called 'Blodomloppet'. The aim was to raise awareness, in a fun way, of the importance of donating blood and was co-ordinated by organizations which run those services in Sweden. On payment of an entrance fee 4,700 participants walked or ran around a 5km route through the parks and leafier areas of Uppsala – 21 of them representing *the UMC*. Six of our fitter colleagues took the advanced option and ran a longer 10km route. Fortunately it was a fine evening and afterwards everyone met up for the picnic that was also provided.



Carl, Anders, Thomas, Bjorn and Ola – the 10km runners relax after completing the circuit.

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
4-8 August 2008	Curso de Farmacovigilancia: análisis y gestión de riesgos (Pharmacovigilance training course: Analysis and Risk Management)	La Antigua, Guatemala	Spanish Medicines Agency in collaboration with the Spanish Agency for International Cooperation for Development E-mail: fvigilancia@aged.es www.aecid-cf.org.gt/
17-20 August 2008	24th International Conference on Pharmacoepidemiology & Therapeutic Risk Management	Copenhagen, Denmark	International Society for Pharmacoepidemiology Tel: +1 (301) 718 6500 Fax: +1 (301) 656 0989 E-mail: ispe@paimgmt.com www.pharmacoepi.org/
1-2 September 2008	Adverse Event Reporting and Pharmacovigilance	London, UK	Customer Services - PTI Tel: +44 (0)20 7017 7481 E-mail: registration@pti-europe.co.uk www.iir-events.com/
10-11 September 2008	Back to Basics in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
22-23 September 2008	Medical Approach in Diagnosis and Management of ADRs	Paris, France	DIA European Branch Office Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
24-25 September 2008	Critical Appraisal of Medical and Scientific Papers: How to read between the lines	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
24-26 September 2008	Advanced Pharmacovigilance	London, UK	Management Forum Ltd Tel: +44 (0)1483 730071 Fax: +44 (0)1483 730008 www.management-forum.co.uk
5 October 2008	Pre-conference meetings on 'Pharmacovigilance from fundamental basis to practice' and 'Drug-related Risk Management'	Buenos Aires, Argentina	International Society of Pharmacovigilance Tel/fax: +44 (0)20 3256 0027 E-mail: administration@isoponline.org www.isop2008.org
6-8 October 2008	8th Annual Meeting of ISoP	Buenos Aires, Argentina	International Society of Pharmacovigilance Tel/fax: +44 (0)20 3256 0027 E-mail: administration@isoponline.org www.isop2008.org
15-16 October 2008	Risk Benefit Assessment in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
20-24 October 2008	Excellence in Pharmacovigilance: Clinical Trials and Post Marketing	Barcelona, Spain	DIA European Branch Office Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org
24 October 2008	Impacting patient safety: Adverse drug reaction signal detection - Quantitative and qualitative approaches in screening healthcare data	Uppsala, Sweden	The Uppsala Monitoring Centre E-mail: info@who-umc.org Fax: +46 18 65 60 80
November 2008 - April 2009	Certificate in Pharmacoepidemiology & Pharmacovigilance	London, UK (and self-directed study)	London School of Hygiene and Tropical Medicine Tel: +44 (0)20 7299 4646 E-mail: ann.arscott@lshtm.ac.uk www.lshtm.ac.uk/prospectus/short/scpp.html
7 November	Irish Medicines Board Pharmacovigilance/Safety-based conference	Dublin, Ireland	IMB E-mail: Karen.Dooley@imb.ie
12-13 November 2008	Case Narrative Writing For Reporting Adverse Events	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
17-18 November 2008	Adverse Event Reporting and Pharmacovigilance	London, UK	Customer Services - PTI Tel: +44 (0)20 7017 7481 E-mail: registration@pti-europe.co.uk www.iir-events.com/
23-25 March 2009	DIA 21 st Annual Euro Meeting	Berlin, Germany	DIA European Branch Office Tel: +41 61 225 51 51 Fax: +41 61 225 51 52 E-mail: diaeurope@diaeurope.org

the Uppsala Team

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