

MUR 26

UPPSALA REPORTS July 2004

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

Immunization safety training

UMC Products and Services launched

New member country - Colombia

Data-mining news



DIRECTOR'S MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring Centre

After the long, dark winter in Sweden, spring brings the dramatic flush of new growth, increasing hours of daylight, followed by the hope of warm summer days, lifting the spirits, and encouraging optimism.

Sadly, optimism is not what we can feel about the closure of the Intensive Medicines Monitoring Programme in New Zealand, which I referred to in my last message to you: that is a dark cloud in the pharmacovigilance skies, and the source of deepest sadness to many of us.

However, the year also brings positive news: there is evidence of increasing interest in and commitment to pharmacovigilance in other parts of the world, from new activity in countries such as Eritrea, Nigeria and Georgia. Vigimed, *the UMC's* exclusive e-mail forum for member countries, is busy with enquiries and information exchange.

Pharmacovigilance has achieved recognition as a core partner in WHO public health programmes, currently in the concluding debates about Lapdap, and in the availability, later this year, of a major WHO publication on the role of drug safety in public health.

At *the UMC* we have created a new division to offer more focused and effective service to our commercial customers, and to concentrate on the generation of the income which represents the only funding for every aspect of *the UMC's* work (see page 4).

As the demand for UMC services expands, among member countries of the WHO Programme and beyond, the organisation is growing too: we are now a team of forty people. At a recent social gathering of the team one spring afternoon, we were astonished to discover that not only were there forty people working here, but that, between them they had fifty children! We can hope only that some of those will provide a new generation of enthusiasts for drug safety and continue the work into the future.

While the science is thirty or more years old now, it still has a long way to go, and a long way before we can feel confident that it is beyond political and economic expediency.

My good wishes to all our readers. As always, I hope you will let us know what you think of Uppsala Reports, and how we can make it more useful and attractive for you.

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Copyright WHO P Viroit

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Employment at WHO

During discussions at the WHO Executive Board, some Member States have raised the need to be more pro-active in identifying possible sources of candidates for employment opportunities within the WHO.

In late 2002 WHO created a web-based e-recruitment system which has proved very successful. However, in order to reach out even further and target specific areas of expertise, WHO invites you to use the WHO Employment site www.who.int/employment/en/ with its daily updated list of vacancies. If you need further information, the focal point in WHO to contact is:

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Department of Human Resources Services,
World Health Organization - 20 Ave. Appia - CH-1211 Geneva 27
Switzerland

Direct tel. +41 22 791 1294 E-mail andersent@who.int

Going where the customer leads...

Bruce Hugman takes a look at *the UMC's* new organisational baby, the Products and Services Division, and talks to its boss, Lars Magnusson, about what he and his team are up to.



Recognising that a scientific team is not always best qualified to promote itself and market its products, *the UMC* and its Director, Ralph Edwards, have decided to upgrade the former Sales and Marketing team into a fully fledged, customer-focused division. The vision and principles underlying this new operation remain exactly as those which have driven *the UMC* for more than 25 years.

the UMC has always had two principal groups of client customers:

- member countries of the WHO Programme for International Drug Monitoring, and
- commercial companies involved in the manufacture of medicines, in clinical trials, the biotech industry and a wide variety of medicine-related operations.

The tools and resources developed on the basis of the WHO Programme - the WHO Drug Dictionary, WHO-ART, and the promising BCPNN technology, for example - have achieved a currency and reputation far beyond the boundaries of the WHO Programme, and are used extensively around the world. They are also the sole sources of income for the funding of the entire UMC operation.

Currently branded UMC Products and Services (somewhat unambitiously, at this stage, everyone admits) it will evolve into a new organisation with a new identity in the next year. More importantly, it will evolve into an operation with customers' interests at its heart, and the delivery of first class service as its number one priority.

So says Lars Magnusson, newly appointed boss of the fledgling enterprise. "*the UMC* has a great record in the field of international pharmacovigilance," he says, "but the demands of the science do not always leave time and resources for the kind of attention and service our commercial customers need within drug safety and beyond. We're now putting significant resources into this important work."

A new team

Some familiar UMC names appear on the organisation's roll-call of staff as well as two newcomers who bring a wealth of relevant experience to the enterprise: Lars Magnusson himself, and Product Manager, Annika Wallström. There is now a team of nine devoted exclusively to product delivery and customer service. More will join them in the months ahead.

"Service to member countries of the WHO Programme has always been the core commitment of *the UMC*," says Lars. "Based on Vigibase and its more than 3,000,000 adverse reaction reports, a range of unique tools and resources has emerged. If these are to be refined and tailored to what our commercial customers require for their work, and if they are to evolve at the speed of modern developments, then we have to be in close contact with our customers and able to respond to their changing needs."

"The team is designed to achieve this: our first activity, already in progress, is a market survey of 1200 customers and potential customers. This is



Mats Persson and Daniel von Sydow (behind), Hannah Ericson, Malin Nord, Anna Blomquist, Annika Wallström, Lars Magnusson and Katarina Hansson (front row) with a new angle on UMC Products and Services

designed to refine our knowledge of what customers want and of what we can do to improve the quality of products and of service delivery. We'll be paying very close attention to the results."

As well as improving existing products and services, Lars says that they will be looking for new opportunities and openings for diversification, led by customers' wishes. The development of Vigibase Online and a new pilot project with IMS Health are the first fruits of these efforts.

Continued service to member countries

Ralph Edwards, the UMC's Director, is keen to emphasise that the new developments, far from diminishing service to member countries, should provide more resources and a clearer focus for the rest of the organisation (the large majority of the forty staff).

"Since we receive no funding of any kind from anywhere, and are responsible for funding the

international work from our own efforts," he says, "we have often been preoccupied with issues of simple financial survival. Now we plan to extend our commercial activity and entrust it to a capable and dedicated team. Our scientific activities and support for member countries of the WHO Programme now have a much clearer field, and I hope we shall be able to focus even greater energy on these priorities."

Find out more...

To meet the new team and get an overview of their activities - and of what they may be able to do for you - please do visit the new website at www.umc-products.com, make contact through the website, or e-mail Lars or Annika (lars.magnusson@umc-products.com; annika.wallstrom@umc-products.com). "We'll be pleased to hear from you," says Lars Magnusson: "Our business is to listen, learn and deliver. Tell us how we can help you, and we'll be doing our very best to meet your needs."



Annika Wallström

In the critical role of Product Manager for the new team, Annika took her Master's in Pharmacy Science and began her professional life as a pharmacist with the Medical Products Agency (Sweden). In her twenty-two year career since, she has taken increasingly senior research, marketing and management roles in several of the world's leading pharmaceutical companies. In 2001 she founded her own company, developing IT solutions for clinical trials and for biotech companies. Annika is married, with two children.

Lars Magnusson

Heading up the new UMC Products and Services team, Lars was a student of maths, physics and computer science. Starting his career as a research engineer and instructor in computer technology, he has since held senior posts in a number of hi-tech and communications companies. In the last decade he has broadened his scope to include responsibilities in business leadership development, marketing and management consultancy, including a period running his own company. Lars is married, with three adult children. His interests include music-making, singing and some physically more strenuous activities like jogging and skiing.

PRODUCT NEWS

Updates – 2nd Quarter 2004

The new versions of the computerised WHO Drug Dictionary (WHO-DD) and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 2nd quarter of 2004 will be available from the beginning of September 2004 and will be sent to subscribers during that month. The WHO-DD pack sent out contains the updated version of WHO-DD.

Need help?

If you have any queries about the content of this pack, or any detail of the DD itself, or need further information about your current subscription or how to upgrade it, do get in contact.

You can e-mail: drugdictionary@umc-products.com for comments about the DD, corrections, additions, and katarina.hansson@umc-products.com for queries about your subscription. If you are a subscriber to either WHO-DD or WHO-ART and have not yet received the update for the previous quarter, please contact Katarina Hansson

Meet us there!

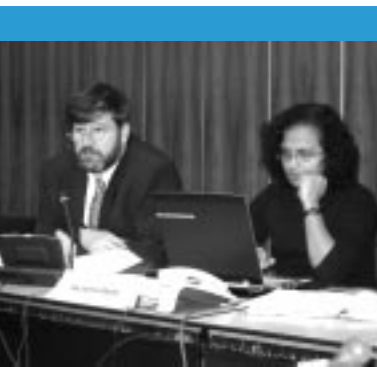
UMC staff are planning to attend the following conferences in the coming months:

- 20th International Conference on Pharmacoepidemiology & Therapeutic Risk Management - Bordeaux, France, 22-25 August
- Society of Clinical Data Management 2004 Conference - Toronto, Canada, 3-6 October

We look forward to seeing many of you at one of these events; if you wish to arrange a meeting with us, please contact Mats Persson.

Mats reports on the UMC in Washington

"the UMC attended the 40th Annual DIA Meeting in Washington DC, USA, where we had an exhibition booth where new potential customers of UMC's services could meet UMC personnel. The meeting was an opportunity to talk to old and new customers, collaboration partners and other contacts. The meeting was attended by delegates from the pharmaceutical industry, CROs and regulators not only from the USA but from all over the world."



Mr Michel Zaffran, Co-ordinator, Access to Technologies, Immunization - Vaccines and Biologicals, WHO, and Ushma Mehta at the Geneva meeting on vaccines vigilance

AEFI and the WHO Global Training Network on Vaccine Quality

Surveillance for Adverse Events Following Immunization (AEFI) is part of the activities of the WHO Global Training Network on vaccine quality (GTN). This network was established in 1996 as a means of providing educational resources to vaccine regulatory and production staff throughout the world.

The Network consists of 13 training centres which offer instruction in priority areas using approved syllabi and standardized documentation materials. An Advisory Committee on Training meets annually. *the UMC* was invited as observers to its latest meeting in Geneva, 6 – 8 April 2004, chaired by Ushma Mehta, South Africa. Sten Olsson, representing *the UMC*, briefly presented the basic concepts of the WHO International Drug Monitoring Programme and gave some overall data on vaccine related adverse reactions reported to the database. He suggested a closer collaboration be developed between the AEFI activities and those of the WHO International Drug Monitoring Programme.

WHO's Training on Immunization Safety

In recent years there has been growing recognition of the importance of integrating pharmacovigilance into public health programmes. In many countries national pharmacovigilance centres have served a primarily regulatory function, while public health programmes have focused on ensuring that their programmes are effective in controlling or eradicating infectious diseases. More recently, however, there has been a growing recognition of the need for public health programmes and national pharmacovigilance programmes to support each other in their shared goal of protecting the public, with a recognition that safer medicines translate to more effective disease control programmes.

The Expanded Programme on Immunization (EPI) is probably one of the largest and arguably, most successful public health programmes. As vaccine-preventable diseases such as polio, measles and pertussis become less frequent as a result of effective immunization programmes, more attention is focussed on adverse events following immunization (AEFIs). In addition to unforeseen crises, a fairly constant level of adverse events can be expected to occur in all immunization programmes. These events may be vaccine-related, programme related or coincidental. If these events, regardless of the cause, are not handled well, hard-earned public health gains can be lost or compromised. Appropriate handling of AEFIs involves the rapid and appropriate detection, assessment, management and prevention of such events, including a sound communications plan.

WHO Global Training Network's AEFI training programme

WHO has recognised the importance of national monitoring and reporting systems for immunization safety to be efficient and adequately coordinated to deal with such adverse events and public concerns. In response to this need, the WHO Vaccines and Biologicals (V&B) section commissioned the University of Cape Town's Division of Pharmacology (UCT) (which houses the South African National Adverse Drug Reactions Monitoring Centre) to develop a 6-day training programme on adverse events following immunization in 1998. This training would be co-ordinated by the V&B's Global Training Network (GTN) (a network of 13 training centres that offer instruction in various areas of vaccine

regulation using approved syllabi and standardized documentation materials).

Employing problem-based teaching methods including discussions, workshops, assignments, role-playing activities and individual presentations a 6-day training course was developed for regulators, immunization programme staff and other relevant ministry of health officials on adverse events following immunization. The training material was peer-reviewed by an international expert panel to ensure that the content is accurate, relevant and up-to-date. The curriculum was designed to encourage discussion and collaboration between the immunization programme participant/s and the regulatory authority participant/s from each country to ensure that a working relationship is established between these two individuals during the course of the training, if one doesn't already exist.

Selection of individuals who are likely to effect constructive change after their training is considered essential. To achieve this GTN uses a multi-level screening process to ensure that the appropriate participants from priority countries are selected. The training institution and WHO Global Training Network offices are also involved in the screening process.

The training materials have been adapted and translated from English into Spanish, Russian and French. Due to the increasing need for this training, especially in these other languages an additional three AEFI training centres have been established, making a total of four immunization safety training centres now in place:

- **South Africa:** managed by Dr Ushma Mehta, Division of Pharmacology, University of Cape Town.
- **Tunisia:** managed by Professor Chalbi Belkahlia and Professor Mohammed Lakhel of the Tunisian national pharmacovigilance centre.
- **Sri Lanka:** managed by Dr Sudath Peiris from the Sri Lankan epidemiology unit, and
- **Russia:** managed by Professor Tagir Bektimirov of the Tarasevich Institute.

A mobile training team approach has been employed by the Pan American Health Organization (PAHO) for rapid and tailor-made training across southern and central America.

Since November 1999, 12 training courses have been conducted in English, French and Russian using the standardized training material developed by UCT. The graph below provides an overview of the number of trainees that have been trained per annum. In the PAHO region more than 300 additional participants have received training in various elements of AEFI (e.g. case investigation, crisis communication, vaccine licensing and testing). Observers from USAID, Roll Back Malaria, and UNICEF have also attended the AEFI training courses in order to determine how the training can be adapted to their particular public health programmes.

Impact of the training

While the rollout of this training across all WHO regions has been quite successful, the impact of such a training programme on public health is very difficult to measure. In some countries, there is anecdotal evidence of better collaboration between regulators and programme staff. Adverse events suspected to be vaccine-related, which were previously not reported to regulatory authorities are now being forwarded to the national pharmacovigilance centres for evaluation. Pharmacovigilance programmes receiving reports of AEFI through their spontaneous reporting systems have called upon programme staff to assist with field investigations. Clusters of serious adverse events related to programmatic errors (e.g. septic shock from contaminated measles vaccine vials) have been rapidly investigated and managed by the immunization programme staff. Participants have also stated that they felt better equipped to communicate with the media during times of crisis.

Challenges for the future

Trainees have also had to face several problems on return to their countries after the training. Limited resources, lack of political support, limited regulatory capacity and conflicting priorities within the ministry of health have prohibited many of the trainees from putting their plans into action.

Therefore, in a meeting held in Cape Town in November 2003, a comprehensive plan of action for supporting alumni of the training programme was developed by the 4 training centres and WHO, to include:

- A post-training mentorship programme facilitated by the training centres and regional offices.
- Development of key indicators to allow programme managers and regulators to measure the function and efficiency of their immunization safety monitoring programmes.
- Development of assessment tools for measuring the impact of the training on the trainees themselves
- Assistance from training centre staff to provide support to priority countries during the early planning and implementation phase of their immunization safety programmes.

In addition to these initiatives, the training materials are being updated and translations into Arabic and Chinese are being planned for 2005. Three more courses are being planned in 2004.

For further information about the AEFI training course offered by GTN, visit the GTN website: <http://www.who.int/vaccines-access/quality/gtn/>

Ushma Mehta,
Global Training Centre: Immunization Safety
University of Cape Town, South Africa

Dublin Meeting of the WHO Programme

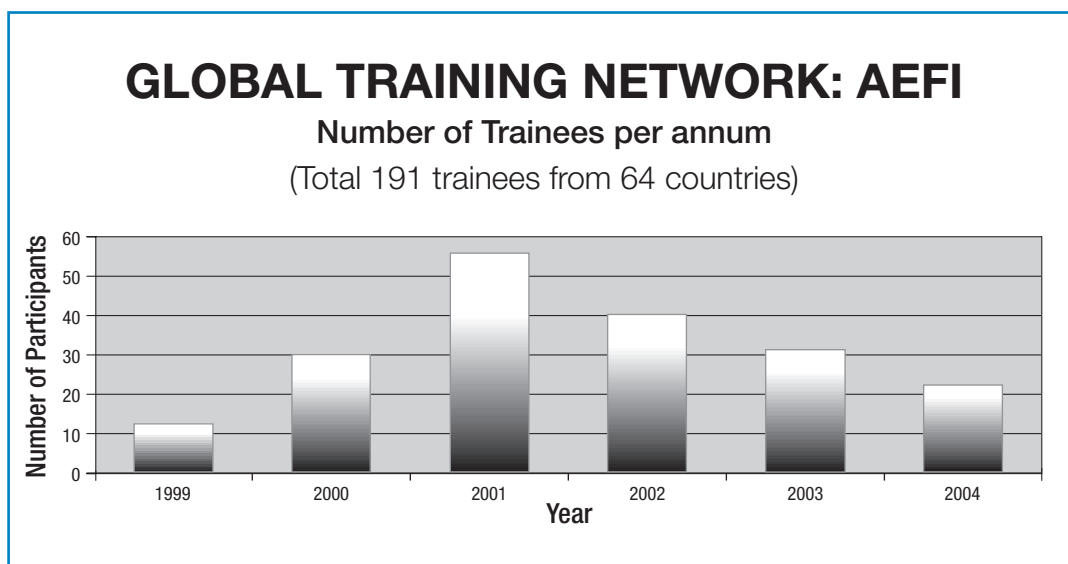
National Centres have now been sent the draft programme, some early information on other activities and the list of Dublin hotels suggested by the organisers. Delegates are also advised to check their visa requirements in good time. In August, further information for the National Centres meeting in this historic and welcoming capital city will be sent out.



Malahide Castle, just north of Dublin

Internet information on both the WHO Programme meeting and the Annual Scientific Meeting of the International Society of Pharmacovigilance (which follows immediately after that of the WHO Programme) is available via the Irish Medicines Board website (www.imb.ie); documents mailed to member countries are automatically placed in the password-protected area of the UMC website under 'Meetings'.

If you wish to present a poster at the WHO meeting please notify Geoffrey Bowring at the UMC



Strengthening pharmacovigilance through collaboration: Singapore's experience

Ms Chan Cheng Leng, Head (Pharmacovigilance) Centre for Drug Administration Health Sciences Authority Singapore

The Health Sciences Authority's Centre for Drug Administration (CDA) is entrusted with the mission of protecting public health by ensuring the safety, efficacy and quality of medicinal products in Singapore. CDA administers a comprehensive regulatory framework that comprises critical regulatory components of pre-marketing assessment of products to ensure that they meet appropriate standards of safety, efficacy and quality as well as post-marketing surveillance activities for which pharmacovigilance is one of the major programmes. Over the last 3 years, CDA has strengthened its various regulatory frameworks including pharmacovigilance to meet the challenges faced by all regulatory agencies in this time of rapid advancement in biomedical sciences and trade globalization.

Development of pharmacovigilance in Singapore

The Adverse Drug Reaction Monitoring Programme was first established in 1993 as an extension of Singapore's Drug Registration system. With the increased emphasis on post-marketing surveillance in recent years, a Pharmacovigilance Unit (PV) was formally established in 2001 to develop CDA's capabilities in the management of risks associated with medicinal products. The PV Unit is the national centre for the monitoring of ADRs. The unit conducts causality assessments of local ADR reports and performs risk assessment of emerging drug safety concerns reported in scientific literature and by other regulatory authorities. The unit also provides expert inputs in the evaluation of safety before a product is approved for marketing in Singapore.

Singapore is a city state with a population of 4.2 million and a land area of 700 sq. km (about 3 times the size of Washington, DC). It has a modern healthcare system and well-developed infrastructures. Because of this operating environment, the PV Unit (PV) has been able to establish close networking with our doctors and pharmacists. Our rapport with these key partners is maintained through regular updates in the form of talks and lectures as well as our ADR Bulletin. The PV Unit also proactively engages opinion leaders in the medical and pharmaceutical arena to assist in influencing their peers in the reporting of ADRs. As a result, the rate of reporting of ADRs by doctors and pharmacists has increased by an average of 20% yearly. We have now achieved a reporting rate of 260 reports per million inhabitants.

All major signals detected from local ADRs and overseas safety reports are reviewed and, when necessary, are communicated in a timely manner to our healthcare professionals through e-mails or conventional mails.

Therapeutic Good Administration, Australia

We recognize that while being a city state has many advantages, it is important for us to collaborate with other larger agencies to overcome our limitation of having a small population base which does not allow us to detect adverse events with very low incidences. The collaboration also allows us to lever in overseas expertise that might not be available locally.

In this respect, we can highlight our co-operation and collaboration with the Australian Therapeutics Goods Administration (TGA) which is forged under the Memorandum of Intention (MOI) of Cooperation signed by TGA and the Health Sciences Authority (HSA). The scope of the MOI covers professional training, scientific collaborations and the exchange of information which includes confidential safety information and reports between the two agencies.

Through HSA's MOI, the PV Unit was invited to participate in the bi-monthly Trans-Tasmanian tele-conference that has been established between TGA, the New Zealand Medsafe and the NZ Centre for Adverse Drug Monitoring. Since May 2002, a total of 11 such tele-conferences have been held and numerous current drug safety issues of concern shared and discussed. The forum also allows the participating agencies to share the assessments of ADR reports and update each other on the intended regulatory measures to minimize risks of certain products.

From HSA's perspective, we have benefited from this international collaboration as we are able to tap into the larger ADR database of these two countries. In addition, the opportunity to share and learn from other agencies has enhanced our staff's technical expertise and confidence in dealing with safety issues.

Further international collaboration

Since the signing of the MOI with TGA, HSA has signed a Memorandum of Understanding (MOU) with State Food and Drug Administration, People's Republic of China. HSA and the US FDA have also established a medical products working group under the US-Singapore Free Trade Agreement to advance scientific exchanges and co-operation between HSA and US FDA. Collaboration in pharmacovigilance will be one of the key areas that HSA would like to pursue with the two agencies.



CDA staff outside the National University of Singapore, from left: P S Ang, K N Ting, L Tan, C L Chan, M Goh, B H Tan, C Y Wong and M F Tan

Data-mining team join up

Andrew Bate reports

Three new staff members – who are not entirely new to *the* UMC – recently joined the Centre's staff. In April, Niklas Norén, Erik Swahn and Jonathan Edwards transferred from NeuroLogic to work full-time for *the* UMC. They form a data-mining cluster in the research and development team, with Jon as Programme Leader. NeuroLogic has provided consultancy services for *the* UMC for over four years (and, through Dr Roland Orre, will continue to do so). However, while still based in Stockholm and engaged in the same type of data-mining work as before, by working directly in UMC projects Jonathan, Erik and Niklas will provide distinct advantages for *the* UMC:

- better focus on drug safety
- integration of data-mining researchers in the overall UMC IT strategy
- an enhanced capability to undertake more research, particularly in the key area of pattern-recognition
- an improved ability to develop useful data-mining tools for both the analysis of the WHO database and for others working with large amounts of data.

Niklas brings his considerable statistical ability in-house; Erik is a neural network programmer with a Masters degree in computer linguistics – which proved extremely valuable in the analysis of free text in the NPSA (National Patient Safety Agency – UK) project in 2003 (see UR23 p8). Jonathan has a broad experience in project management and diverse IT solutions with nearly 15 years programming and database systems experience.

At present I manage the research and development department here in Uppsala which, together with the data-mining group includes Sven Purbe (a specialist in database systems) and Malin Ståhl (applied research on BCPNN and development tools for routine signalling use). In close collaboration with the staff in *the* UMC IT department, we are working to produce improved tools for signal detection in the WHO database.

The data-mining projects we currently have are mainly aimed at providing software tools for users outside *the* UMC to make searches in the WHO database. Future ideas include:

- more work from the BCPNN in other diverse applications
- improving research techniques for the analysis of the WHO database
- applying our data-mining techniques to other safety-based datasets – potentially an exciting development

the UMC is always interested in the possibility of new data-mining applications, so we are interested in hearing from those working with large databases. If you are enthusiastic to collaborate and have data which might benefit from our approach, do let us know.

The employment of three highly-competent data-mining specialists is an important step forward for *the* UMC. Watch this space!

The new staff



Jon, Niklas and Erik – now officially in UMC's back yard

Jonathan Edwards was born in Sheffield, England but grew up in New Zealand. "My computer science education is from the University of Otago in Dunedin, New Zealand. I have worked as a computer programmer / project manager at the teachers college in Uppsala, as a consultant to UMC (and employed by *the* UMC) and at various IT companies - Logic Systems, Dimea, Aeroplane." Prior to NeuroLogic Jonathan was manager of Aeroplane AB, an IT company specialising in web based applications. "I live with my girlfriend Malin and my daughter Milly in Stockholm. Outside work I enjoy climbing (indoors mostly), squash and inline skating. I will be skating to work quite a bit this summer instead of using my bike."

Niklas Norén is originally from Järbo, Sweden. "I hold a MSc degree in Engineering Physics from Chalmers University of Technology in Gothenburg. I did my MSc thesis project as part of a joint NeuroLogic/UMC project on refined quantitative signal detection, and after that, I continued at NeuroLogic as a research engineer. While at the university, I ran my own small technical consultancy business." Now preparing his PhD at the Mathematical Statistics Department at the University of Stockholm, Niklas is a keen amateur photographer (but recently abandoned digital media for traditional film-based photography).

Erik Swahn is from Gothenburg, but moved to Stockholm a few years ago. Immediately before joining NeuroLogic he undertook his studies in computational linguistics and psychology. He is an occasional jogger and a prolific, though unpublished, poet.

Report by Oscar O Simooya
Pharmacovigilance Resource
Person, WHO Roll Back
Malaria Programme,
Copperbelt University, Kitwe,
Zambia

Burundi is a sub-Saharan African country where malaria Programme continues to cause great morbidity and mortality.

Over 60 percent of the population are continuously at risk of malaria while more than half of hospital beds are occupied by patients with malaria. Because of the growing problem of resistance by *Plasmodium falciparum* to chloroquine and sulfadoxine/pyrimethamine, the Ministry of Public Health has decided to change the policy for the treatment of malaria. Since November 2003 amodiaquine in combination with artesunate is the first line treatment.

Pharmacovigilance in the malaria sentinel sites of Burundi

Artemisinin based combination therapies (ACTs), have been recommended for the treatment of malaria in countries where there is widespread resistance to commonly-used anti-malarial drugs. However, there is limited information about the safety of ACTs outside South East Asia where their use has been well documented.

Burundi has 6 sentinel sites for malaria:

Buhiga (Buhiga Province),
Cankuzo (Cankuzo),
Kigobe (Bujumbura),
Muhanga (Kayanza),
Mutoyi (Gitega)
Ninga (Bubanza).

Languages in Burundi are Kirundi (official), French (official), and some Swahili.



As with all new medicinal compounds, monitoring a drug's safety is important, especially where co-morbid conditions such as malnutrition, HIV/AIDS and tuberculosis are common; also, genetically distinct populations may respond differently to any given drug. As WHO Roll Back Malaria's resource person for the introduction of pharmacovigilance in the region, I undertook a mission to Burundi to support and promote the development of a functional pharmacovigilance system in that country. I specifically wanted to facilitate the monitoring of the amodiaquine and artesunate combination therapy in the malaria sentinel sites.

Burundi pharmacovigilance system

Arriving in the Burundian capital Bujumbura on 29th February, I was received by the WHO Consultant, Dr Gninoussa Akadiri. To collect data and information on the preparedness of Burundi for pharmacovigilance, I interviewed health and government leaders, and international partner organisations; and visited sentinel sites to observe practice. I scrutinised official Burundian documents, including protocols for pharmacovigilance, the draft of the pharmacovigilance structure, draft ADR report form, operational budget for pharmacovigilance and Technical Report on the new malaria treatment policy.

I was keen to learn about:

- Availability of new medications
- Pharmacy stock records
- Treatment protocols for new policy
- Patient records
- Laboratory records
- Public messages about amodiaquine and artesunate

Status of pharmacovigilance in Burundi

I noted the great interest in the establishment of pharmacovigilance in Burundi. The Minister of Health expressed his desire for the rapid development of the drug monitoring system and pledged his personal support for pharmacovigilance. Without this backing it is difficult to involve health personnel who are a critical component in drug safety monitoring. Additionally, there was overwhelming desire by local offices of both the WHO and UNICEF to support the development of pharmacovigilance.

Dr Liévin Mizero, Director of Pharmacies, Medicines and Laboratories has been appointed by the government to be the Focal Point Person for pharmacovigilance. Dr Mizero was trained in pharmacovigilance at the WHO workshop organised by Roll Back Malaria in Lusaka, Zambia last year (see UR22). The functions of the pharmacovigilance system are currently operated from the offices of Dr Mizero with basic equipment, computers and telephone lines.

Pharmacovigilance structure/system

In the new structure, most case reports will be sent via provincial offices to the national centre. The national centre will be responsible for coordinating pharmacovigilance activities, including training workshops, preparing report forms, receiving case report forms and processing them, collaborating with

the WHO International Drug Monitoring Programme and liaising with the National Therapeutic Committee.

Overall responsibility for pharmacovigilance in terms of policy decisions and communication with government rests with the National Therapeutic Committee. The University of Burundi School of Medicine is expected to play a crucial role in this committee and drug safety monitoring should be added to the medical curriculum.

ADR report form

In discussing the proposed ADR reporting form, forms from Mozambique, South Africa, Zambia and Zanzibar were compared before finally adopting a form for Burundi. It was later presented to participants at the training workshop for their comments. The form has four components; patient information, description of adverse event, details of medication/s received, and name, job title and institution of the reporter.

Observations from field visits

Both Muhanga and Buhiga sites had adequate stocks of amodiaquine and artesunate. Most health professionals were familiar with the new drugs and had experienced no major problems. It is well-known that patients who are knowledgeable about their drugs are better able to adhere to treatment and more likely to report adverse effects, so a concerted effort to educate the public about drug safety is vital for all pharmacovigilance programmes.



Oscar Simooya

Training Workshop

The highlight of my visit was at the National Institute of Public Health on 9th and 10th March. A workshop attended by health practitioners from all six sentinel sites was officially opened by the Director General of Public Health, Dr Pascal Ntziyimana who reiterated the government's commitment to drug safety monitoring in the country and requested the full and active

participation of all delegates. Participatory training methods were employed including case studies of some adverse drug reactions. Participants were divided into five groups – each assigned to practice how to investigate and report adverse drug reactions.

Drs Mizero and Akadiri led the discussion on how to report ADRs. Participants were informed that for the new malaria treatment regime, all adverse effects would need to be reported, whilst for established drugs only serious events should be reported. This session was much appreciated, as participants were able to get hands-on experience with drug safety monitoring. Delegates agreed that on return to their stations, they would brief other health professionals and start recording adverse events. It was also the consensus that a person responsible for drug safety monitoring be appointed at each sentinel site. All teams returned with the ADR report forms.

The future

The Government in Burundi is keen to begin monitoring the safety of medicinal compounds; a structure and system to report adverse drug events has been elaborated and a team leader for the system identified. The new treatment policy and pharmacovigilance is to be monitored through sentinel site field visits – where operational funding, diagnostic and communication equipment is needed. Case report forms have been finalised and distributed; health workers from the sentinel sites have been trained on how to recognise and report adverse drug reactions. Reports from staff in the field must be acknowledged and backed by regular visits to the sites by both the malaria programme staff and the WHO Consultant responsible for the implementation of the new policy.

Patient safety theme of Paris pharmacy congress

The joint congress of the European Society of Clinical Pharmacy (ESCP) and the American College of Clinical Pharmacy (ACCP) in Paris 28 – 30 April, 2004, focused attention on how to assure optimal safety for the patient. In the opening session, devoted to systems for surveillance of drug safety, Sten Olsson of the UMC provided a brief account of the WHO International Drug Monitoring Programme and the systems used for early detection of new drug-related risks. Steven Goldman, former head of the US MedWatch programme, provided a US perspective on the need for continuous safety surveillance. The final speaker of the session, Fernand Sauer, representing the European Commission, told the congress delegates of the systems and institutions that are being constructed within the European Union to strengthen patient safety.

Subsequent sessions of the congress considered processes for development of therapeutic guidelines and how to improve adherence to them. Validation of the drug supply chain in order to minimize medical errors was also covered. Working group sessions included two on pharmacovigilance. They were well attended by pharmacists from many parts of the world, not only Europe and America.



A lively session at the Paris congress

WHO Programme News

The drug regulatory authority in Colombia has correctly submitted a batch of 75 ADR reports to the UMC. Since Colombia was already an associate member country of the WHO Programme for International Drug Monitoring, we were only waiting for these cases to arrive. Colombia is now member country number 73 in the Programme. The National Centre is located at the drug regulatory authority INVIMA. There is a three member pharmacovigilance team with Dr Carlos Arbeláez as the lead person. Colombia has the country code CO or COL in the WHO database.

The Ministry of Labour, Health and Social Affairs of Georgia has submitted an application to WHO for Georgia to be admitted as a member of the WHO Programme for International Drug Monitoring. The UMC has not had much contact with professionals in Georgia since the early 1990s. The nominated centre is The Pharmacological Committee in Tbilisi. Georgia is now our thirteenth associate member.

Professional and consumer reporting

The safety of medicines is a hot topic among physicians, pharmacists, nurses and economists from non-governmental organisations and governments in the Newly Independent States (NIS) of the former Soviet Union. This is the conclusion of the organisers of a three-day conference which took place on May 26-28, 'Quality and Safety of Medicines - Patient Safety', DrugInfo Moldova and KILEN Sweden. The participants came from 6 NIS countries - Kazakhstan, Kyrgyzstan, Moldova including Transnistria, Tajikistan, Ukraine and Uzbekistan.

The venue for the conference was a small city in the northern part of Moldova, Bricheni, where the chief of the hospital, Claudia Veltman, was the local host. The host and the organisers had also involved the local administration, the Mayor of Bricheni and the representative of the President of Moldova for the North to the conference, which was very successful. During the opening ceremony, the City Mayor, the collaborating parties and the international guests were talking about safety of medicines as a topic of paramount importance to us all.

Working in small groups, the participants explored the problems around safety of medicines and pharmacovigilance and the needs and possibilities for establishing systems for a medicine safety programme. The participants also made a personal plan for their own safety of medicine programmes - how to establish reporting facilities for professionals and consumers and how to collaborate with each other. The huge interest among the participants and the great delight of exchanging experiences about working conditions and medicine problems was striking.

At the end of the conference a statement 'the Bricheni Declaration' was adopted. It is in Russian and will also be translated into English. The Bricheni Declaration will work as a platform for future engagement and work in the region. Hopefully this is a start of a three years project which has as its aim to involve professionals and consumers in 'safety thinking' when it comes to medicines and to encourage organisations to start working in the field of pharmacovigilance.

Some of these NIS-countries are not yet members of the WHO Programme, while others are members. Conferences like this one are very good preparatory venues for a future membership of the WHO Programme, but most of all, good for safety thinking of medicines.



The City Mayor and the organisers of the conference, Dr Natalia Cebotarenco, DrugInfo Moldova; Lena Westin and Jan Albinson KILEN Sweden, outside the conference hall in Bricheni, Moldova.

The conference was made possible by support from the Swedish aid agency, Sida. For more information, please contact Dr Natalia Cebotarenco, DrugInfo Moldova, druginfo@mtc.md or Jan Albinson, Lena Westin, KILEN, kilen@kilen.org

Old and new friends visiting *the* UMC

Norwegian regional staff

In May and June we were happy to receive several international visitors at *the* UMC. First a delegation from the newly-formed regional pharmacovigilance centres in Norway visited us on 5 May. (A full feature on the regional system in Norway is on page 9 of Uppsala Reports 22). The group consisted of Kirsten Myhr, Odd Brørs, Hege Grefslie Ugland and Sofia Frost. In late 1980s Kirsten Myhr was the head of the Norwegian National Centre. We gave the group an overview of current UMC activities and we specifically looked into the process for analysis of new safety signals and how to search the WHO database using the Vigisearch tool.

CIOMS participants visit

In May, CIOMS (Council for International Organizations of Medical Sciences) and the MedDRA Maintenance and Support Services Organization held a meeting at the Medical Products Agency in Uppsala on MedDRA search categories, and some of the distinguished participants took the opportunity of popping into *the* UMC.



Andrew Bate and Judith Jones

The new acting head of the Australian National Centre, Kerri Mackay, spent a day with us to discuss reporting issues and how to work together more efficiently. We are very happy to welcome her to the family of the WHO Programme and with her ambitious approach we are sure Australia will continue to play a very active and important role in our collaboration.

One of the early pioneers of international pharmacovigilance, Jan Venulet, visited us on May 26

(see our story about his pharmacovigilance career in Uppsala Reports 22). This was his first visit to our present offices and he was very pleased to note the expansion of the WHO Programme over the last decade. He primarily held discussions with Ronald Meyboom and Sten Olsson on how the definitions of adverse reaction terms that CIOMS has published may best be employed and promoted.

On May 28, Judith Jones, Director of the Degge Group, USA, visited us. In early 1980s she was head of the National Centre at FDA, USA. Mainly due to her strong support of the International Drug Monitoring Programme during a WHO investigation in 1981 the advice of the reviewer was to sustain the Programme, which we are happy about today! We are pleased that Judith Jones has maintained her contacts with us over the years. She spent some time discussing data-mining methodology with Andrew Bate.

Doctoral student from Nepal

On June 11 Prenaya Mishra from Pokara, Nepal visited *the* UMC. He had come for a day from Copenhagen where he is finalising his PhD studies in epidemiology. We discussed his plans for setting up a combined drug information/pharmacovigilance service at his hospital in Nepal and the training and technical support that may be provided by *the* UMC. There are plans to set up a national pharmacovigilance programme in Nepal and Dr Mishra's hospital would be a regional centre in the national network. He specifically studied UMC's Vigibase Online software that provides case management support for regionalized pharmacovigilance programmes.



Ron Meyboom demonstrating the latest UMC signal work to Jan Venulet

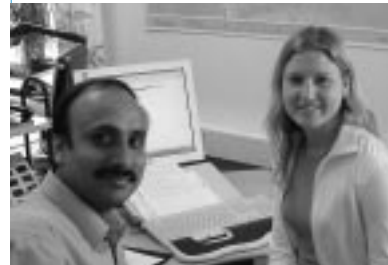
Meeting our visitors



From left: Kirsten Myhr, Odd Brørs, Hege Grefslie Ugland and Sofia Frost from Norway, with Erica Walette



Kerri Mackay (left) in conversation with Kristina Star



Prenaya Mishra from Nepal with Annica Lundström, demonstrating ADR report submission

Staff updates

We are sad to say goodbye to **Anna-Karin Flygare**, who is retiring from work at *the* UMC. Anna-Karin started here in 1993 working first with input of ADRs and later being closely involved in medical terminologies. After several years of poor health, she leaves with our best wishes for her retirement. The current lead person for WHO-ART and terminologies is Cecilia Biriell.

Anna Blomquist has decided to move in a northerly direction, Örnsköldsvik, and will be on leave of absence from August 1. Anna will be employed full time by Umeå University, working as a supervisor for students of pharmacy, and we wish her all the best.

Annika Wallström has recently joined *the* UMC as Product Manager. She started on a half-time basis from 10 May, and will work full-time from September. (See page 4, Products and Services)

Bill Dagerus has joined *the* UMC to work on tools for importing drugs into DD and to help National Centres in maintaining their computer based systems.

Bill has been working in the systems development area for over thirty years – in Europe, Africa and Asia, as well as such diverse settings as the Sema Group and the Swedish pensions office, Uppsala University and PharmaSoft. He worked in Bahrain for three years for their Ministry of Housing. He brings a lot of experience in a wide range of programs and systems. Together with Bo Östling, who became a UMC staff member two years ago, he wrote a major part of the original program code for the INTDIS database which served the WHO Programme from 1978 to 2002. Bill's interests outside work are his summerhouse and four grandchildren.

Malin Ståhl is now happily settled in the Clinical Pharmacology Department at Linköping's University Hospital where she works alternately with her visits to *the* UMC offices in Uppsala.

Uppsala Reports 25 (April 2004)

We would like to apologise to our readers who receive a copy of Uppsala Reports through the mail for the late delivery of Uppsala Reports 25. We understand that many of you did not get your copy until at least six weeks after despatch from Uppsala. Needless to say, we are changing our postal provider, but would still like to hear from anyone whose Uppsala Reports takes a long time to arrive. If you would like a copy of UR25 and the supplement that came with it, please ring or e-mail *the* UMC and we will send another copy to you.

New downloads available

Various documents have recently been put on *the* UMC website for download by users. Background to the WHO Adverse Reaction Database 'Basic Facts', a 9-page document, covers :

- The WHO database system
- Format and data exchange
- Medical terminology
- Drug classification
- Lexicon tables
- Quality management
- Documentation grading
- Signal detection and analysis
- Advantages and disadvantages of the WHO database system.

We have also made available a three-page explanation of how to join the WHO Programme. 'Joining the WHO Programme' leads through the process for becoming a member of the WHO Programme for International Drug Monitoring. The requirements are general acquaintance with the methodology of spontaneous monitoring; a National Centre for Drug Monitoring must be designated and recognized by the Ministry of Health, and technical competence to fulfil reporting requirements to WHO. The practical procedure for joining the WHO Drug Monitoring Programme and additional measures to be taken to facilitate collaboration are also described.

The password protected area for National Centres now contains the Official Report from the last Annual Meeting of the WHO Programme in Delhi in 2003. If you have forgotten the password please contact Geoffrey Bowring or Sten Olsson at *the* UMC.

Korean translations

Korean translations of 'The Importance of Pharmacovigilance' and 'Guide for setting up and running a pharmacovigilance centre' have recently been issued by the Pharmaceutical Safety Bureau of the Korea Food and Drug Administration. Enquiries about translations of UMC publications should be addressed to Sten Olsson.



COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
1-6 August 2004	8th World Congress on Clinical Pharmacology and Therapeutics	Brisbane, Australia	CPT 2004 Congress Secretariat Tel: + (61 2) 9241 1478 Fax: + (61 2) 9251 3552 E-mail: cpt2004@icmsaust.com.au
22-25 August 2004	20th International Conference on Pharmacoepidemiology & Therapeutic Risk Management (ISPE)	Bordeaux, France	International Society for Pharmacoepidemiology Tel: +1 (301) 718 6500 Fax: +1 (301) 656 0989 E-mail: ispe@paimgmt.com
6-8 September 2004	Drug Safety in the Enlarged EU	Warsaw, Poland	IQPC Tel: +44 (0)20 7368 9300 E-mail: enquire@iqpc.co.uk
29-30 September 2004	Advanced Adverse Event Reporting and Pharmacovigilance	London, UK	IIR Conferences Tel: +44 (0)20 7915 5055 E-mail: registration@iir-conferences.com www.iir-conferences.com/
6-8 October 2004	ISoP Annual Scientific Meeting	Dublin, Ireland	ISoP Administration Tel/Fax: +44 (0)20 8286 1888 www.isoponline.org
12-15 October 2004	II Congreso Internacional de Farmacología y Terapéutica	Havana, Cuba	Cubatour SA Fax: +53 7-336471 E-mail: opc_eventos@cbtevent.cbt.tur.cu http://cencomed.sld.cu/farmacologia
13-14 October 2004	Risk Benefit Assessment in Pharmacovigilance	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
20-23 October 2004	Risk Management in Pharmacotherapy (33rd European Symposium on Clinical Pharmacy)	Prague, Czech Republic	European Society of Clinical Pharmacy Tel : +32 2 743 1540 Fax : +32 2 743 1584 E-mail : geraldine@associationhq.com www.escpweb.org
8-19 November 2004	UMC pharmacovigilance training course at the TGA	Canberra, Australia	UMC at TGA Training Course Tel: +61 2 6232 8180 Fax: +61 2 6232 8392 E-mail: pharmacovigilance.course@health.gov.au
11-12 November 2004	Workshop on Case Narrative Writing for Reporting Adverse Events	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
12-13 November 2004	V Jornadas de Farmacovigilancia	Barcelona, Spain	Fundació Institut Català de Farmacologia Tel: +34-93 428 3029/3176 Fax: +34-93 489 4109 E-mail: hag@icf.uab.es www.icf.uab.es; www.agemed.es > Actividades > Congress
24 November 2004	Data Safety Monitoring Boards & Data Review Committees	London, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
29-30 November 2004	Hot Topics in Pharmacovigilance	Paris, France	Drug Information Association (DIA) Tel: +41 61 225 5151 E-mail: diaeurope@diaeurope.org www.diahome.org
8-9 December 2004	Introduction to Pharmacoepidemiology	Southampton, UK	Drug Safety Research Unit Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dsru.org
10-11 February 2005	New Challenges in Clinical Safety, Pharmacovigilance and Vaccine vigilance	Barcelona, Spain	ISoP Administration Tel/Fax: +44 (0)20 8286 1888 www.isoponline.org
7-9 March 2005	Drug Information Association (DIA) Euro meeting	Lisbon, Portugal	Drug Information Association (DIA) Tel: +41 61 225 5151 E-mail: diaeurope@diaeurope.org www.diahome.org
23 May - 3 June 2005	UMC pharmacovigilance training course	Uppsala, Sweden	the UMC Tel : +46 18 65 60 60 E-mail : info@who-umc.org www.who-umc.org



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