

Uppsala Reports 29

UPPSALA REPORTS April 2005

For everyone concerned with the issues of pharmacovigilance

the Vioxx saga

WHO Drug Dictionary Enhanced

News from Ethiopia, Poland, Jordan

Consumer reporting

News from *the* UMC



DIRECTOR'S MESSAGE



Ralph Edwards
Director
the Uppsala Monitoring Centre

Läkemedelsvärlden, Sweden's main pharmaceutical journal, takes me to task in their 'Opinion'¹ for not mentioning the Vioxx situation in UR28. They seem to think that its impact on pharmacovigilance should lead to huge concern and change.

Leaving aside how one could cover fast-moving specific events in a quarterly magazine such as Uppsala Reports, Läkemedelsvärlden appear not to know that the first global signal of the problem came in 2000 in a presentation from the Netherlands at the WHO Programme annual meeting in Tunis – six months after the launch of the drug.² They may not know that changes in product information, and many bulletins and letters have been sent out since then by regulators in many countries (including Sweden³) about the cardiovascular risk. I agree there could have been more information concerning higher doses and risk, but that was mentioned in the very first signal.

So there's been considerable concern and follow-up among those working in pharmacovigilance – but perhaps they think that Vioxx should have been removed from the market earlier. In that case they under-estimate the need to look at overall effectiveness and risk in all indications, comparisons with other selective COX 2 inhibitors, comparisons with NSAIDs and other analgesics, as well as consideration of at-risk groups. Vast volumes of material have been produced by industry and assessed by regulators over years to try to avoid inappropriate action. Discontinuing the drug may even now be unnecessary, when it could be used at the lower dosage, and for short terms, with relative safety from a cardiovascular aspect and avoiding some GI bleeding.

The final irony for me is that co-proxamol (dextropropoxyphene plus paracetamol) has only just been discontinued in some countries after years of concern about its potential for lethal overdose, much greater than paracetamol alone, whilst only having the same analgesic efficacy. I tried to get the drug banned in the mid-1980s⁴, which effort also included discussions in Sweden. Perhaps those such as Läkemedelsvärlden should address why that decision took so long, for a less complex situation than Vioxx?

However, I am certainly not complacent about Vioxx, or those many people adversely affected by it. We should learn to do better all the time. My message is that Vioxx was a 'crisis' because parts of the media made it so, and that the issues are more complex than they appear.

In order to remedy the omission 'Läkemedelsvärlden' has pointed to I opened a Vigimed discussion (restricted e-mail distribution list for representatives of National Centres participating in the WHO Programme) to air the topic further. The result is presented in the centre pages of this Uppsala Reports.

1. Bergeå N. Vioxx glömdes bort. Läkemedelsvärlden, 2005, 3:14.
2. Report of the 23rd Annual Meeting of Representatives of the National Centres participating in the WHO International Drug Monitoring Programme, Tunis, Tunisia, 11–14 November 2000, p21–22.
3. Coxiber och biverkningsrapportering. Swedish Medical Products Agency website <http://www.mpa.se/biverkningar/biv00/coxiber.shtml> (published 21.12.2000, accessed 9.3.2005).
4. Edwards IR. Dextropropoxyphene. N Z Med J, 1985, 98(775): 201.

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2005 Annual meeting

A WHO-focussed meeting this year for the WHO Programme gathering in Geneva



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"Regulation of Vioxx: success or failure?"

The centre pages of this edition are given over to a major article by Ralph Edwards reviewing the recent withdrawal of Vioxx, "Regulation of Vioxx: success or failure?"



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Enhancing the WHO Drug Dictionary

A major advance in the WHO Drug Dictionary was launched at the DIA meeting in Lisbon



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UMC staff

New faces to put to new people



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Polish pharmacovigilance staff



Staff of the Polish pharmacovigilance unit: (seated, from left) Izabela Skibicka, Dr Agata Maciejczyk (Head); (standing from left) Anna Arcab, Monika Trojan, Iwona Gromek; (secretary, Justyna Bieczysko, not present).

The Polish experience

There is a long-standing friendship between the UMC and the Polish pharmacovigilance centre, which was reinforced when Anna Arcab and subsequently Monika Trojan came to Uppsala to attend the UMC training course. Dr Ronald Meyboom, Medical Advisor of the UMC, had the pleasure of visiting the Polish National Centre and its dynamic team in 2004 and was impressed by its achievements. This visit has prompted an update report from Anna Arcab, of the Pharmacovigilance Unit, Office for Medicinal Products, Medical Devices and Biocides.

Pharmacovigilance activities in Poland

The Polish national centre in Warsaw has been in co-operation with the Uppsala Monitoring Centre since 1972, having joined the WHO Programme soon after its foundation.

The activities of the National Centre naturally revolve around ADR monitoring, receiving individual reports, providing the information to marketing authorisation holders (MAHs), WHO and EMEA, management of follow-ups and assessment of periodic safety update reports (PSURs). The centre offers its opinion for the authorisation renewal process and concerning safety changes in the summary of products characteristics (SPC).

Poland has a 'Yellow card' form for reporting ADRs, which is downloadable from the website of the Office, sent to healthcare professionals on request, and provided to individual Polish medical journals from time to time. The Pharmacovigilance Unit collects reports from spontaneous monitoring (the yellow cards), post-marketing surveillance studies from MAHs and from the professional literature.

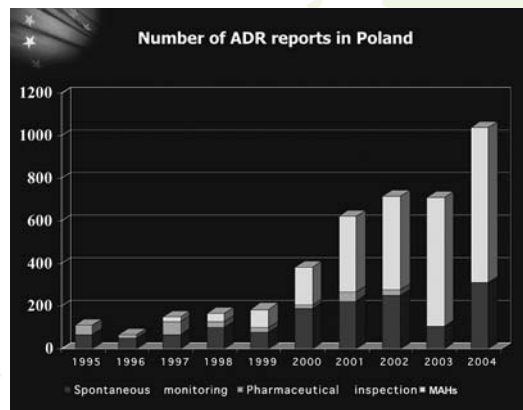
The legal basis of pharmacovigilance in Poland is based on a Pharmaceutical Act of 2001, updated in 2004. There is also 1996 legislation on the profession of the physician and an Order of the Minister of Health from 2003 concerning safety monitoring of authorised medicinal products.

Poland – recent results

Reports collected (CIOMS I forms, yellow cards, company forms) totalled:

- in 2003 – 106 spontaneous reports; 604 reports from MAHs
- in 2004 – 312 spontaneous reports; 726 reports from MAHs.

The national centre conducts analysis on these reports, examining any causal relationship between a drug and a reaction, and looking at ADRs according to groups of drugs, System Organ Classes affected, age of patients, sex etc (see graph).



An electronic database started to operate in autumn 2000, compatible with XML format. It enables direct transfer of data to the UMC database, and it is planned to enable direct transfer of the certain data to EMEA.

Promotion and Collaboration

Promotion of pharmacovigilance in Poland takes place in several forms. There are continuous educational activities in co-operation with the associations of MAHs. The national drug bulletin 'Biuletyn Leków' has been produced since 1991, and publications on ADRs have appeared in Polish and foreign medical journals.

The Polish National Centre has recently been involved in two twinning projects. One with Spanish experts included lectures concerning pharmacovigilance and clinical trials for physicians from medical academies in all the big cities in Poland, and discussion of a proposal to establish decentralised pharmacovigilance system in Poland. Another project with German experts is ongoing.

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1st Jordan Seminar on Pharmacovigilance

Jordan Pharmacovigilance Centre (JPC) conducted a two-day training course on 19th and 20th February 2005 entitled 'Assessment of Safety Information in a Pharmacovigilance System'. The audience consisted of the national pharmacovigilance team, staff working in drug registration, JPC officers, as well as specialist physicians and general practitioners. The opening ceremony marked the first JPC activity conducted in Amman, under the patronage of the director general.

Following contact with WHO, the JPC invited Jürgen Beckmann, former head of pharmacovigilance at the German Federal Institute for Drugs and Medical Devices (BfArM) and currently Professor at Rostock University, as principal lecturer, to share his wide experience.

The course aimed to:

- 1) develop the abilities of participants to analyze and evaluate all drug safety information – whether in the literature, studies, or spontaneous reports,
- 2) help health care providers to compare drug hazards and advantages in the light of new safety information, to be able to make the proper therapeutic decision for their patients, and
- 3) enable Jordan Food & Drug Administration (JFDA) staff to take regulatory decisions with regard to safety issues.

The Saturday, 19th February covered adverse drug reactions and such topics as:

- The scope and importance of pharmacovigilance
- Types of ADRs, risk factors, including interactions spontaneous single case reporting
- Technical handling of spontaneous ADR reports
- Assessment of single case reports: listedness, seriousness, causality, preventability
- Assessment of case series: signals, ADR profiles and trends, comparative frequency.

The Sunday session concentrated on drug-related risks and looked at:

- Pharmacoepidemiological cohort studies, case-control studies, prescription event monitoring
- Assessment and description of ADR frequencies
- Benefit/risk assessments for an individual drug, and in comparison with therapeutic alternatives
- Periodic safety update reports
- Options for improving the benefit/risk balance, criteria for withdrawals and suspensions of marketing authorisations
- Administrative handling of risk-lowering measures
- Pharmacovigilance plans, inspections
- Communication of pharmacovigilance issues.

Nidaa Bawaresh
Jordan Pharmacovigilance Centre

Mexico pharmacovigilance meeting

Leticia Rodríguez, School of Pharmacy, Universidad Autonoma del Estado de Morelos (UAEM), has written from Mexico following the '37 Congreso Nacional de Ciencias Farmaceuticas' (37th Annual National pharmaceutical sciences meeting) meeting held in Acapulco, Mexico last October.

Dr Ed Napke, one of the UMC's signal reviewers, attended on behalf of the UMC and gave a powerful overview, based on his long career in the field. He spoke of his 30 years experience, setting up the Canadian pharmacovigilance programme, 'do's and don'ts' in pharmacovigilance, definitions, and much else besides, illustrating his talk with colour slide examples of skin reactions, liver, eye, nervous system, as well as his innovatory 'pigeon-hole' system for ADR reports and user-friendly ADR forms.

Important Meeting

The audience of over 800 students, academics, health authority personnel, and industry professionals welcomed his knowledge and his lively personality. Ed Napke also listened in on other lectures (there were three concurrent sessions and simultaneous translation), posing probing questions. This meeting was an important event for stimulating interest in pharmacovigilance in Mexico.



The seminar in Amman (Jürgen Beckmann on left at table)

ISDB Declaration

European members of the International Society of Drug Bulletins have presented their 'Berlin Declaration on Pharmacovigilance', following an ISDB workshop which took place in Berlin on 31 October and 1 November 2003.

The aim of the workshop was "to discuss how to achieve more effective pharmacovigilance and so achieve the safer use of drugs" and the main proposals involved:

- greater openness should be the norm with regard to data from trials
- better co-operation and integration among national and international bodies in the form of a network for pharmacovigilance
- better reporting and information gathering – with early learning about pharmacovigilance in the training of healthcare students
- better information for patients and better collection of their feedback.

The declaration is available in pdf format in English and German from the ISDB (<http://www.isdbweb.dspace.it/pag/index.php>) and in French from 'Revue Prescrire' (<http://www.prescrire.org/aLaUne/dossierVigilanceBerlin.php>).

Bruce Hugman reports
from Addis Ababa



The participant journalists from twelve Ethiopian media organizations, along with members of the DACA team on the steps of the Desalegn Hotel, Addis Ababa, where the event took place.



Desalegn Assefa (Radio Fana), Tadesse G/mariam (Media Communications Centre/The Reporter) and Abraham Kassaye (Radio Fana) consider some thorny action-planning topics.



The DACA national ADR centre team: Dr Assegid Tassew, Getahun Gurmessa, Fitsum Tadios with (front) Dr Abraham Kahsay, Head of the Planning & Drug Information Department.

Medicines and the media in Ethiopia

DACA brings journalists together

With the aim of improving the knowledge and skills of journalists and the quality of health reporting in the country, the Drug Administration and Control Authority of Ethiopia (DACA) arranged a three-day workshop in the capital, Addis Ababa, from 14-16 March this year. 18 journalists from twelve media organizations took part in the training, sponsored by WHO Geneva, and led by Bruce Hugman, the UMC's communications consultant.

85% of Ethiopian's 70 million population live in rural areas of the country. Amharic is the national language, but eighty others are also spoken among the many ethnic groups. Radio is the principal means of mass communication, newspapers and TV being largely confined to urban areas. The majority of the population is served by government-owned media organizations, although there is a growing number of private newspapers.

The challenges of meeting the health-communications needs of the country are enormous. The Government, the UN, WHO and many NGOs are involved in projects to tackle the priority problems of malaria, TB, HIV/AIDS, maternal and infant mortality, access to health care, as well as the provision of clean water and sanitation. Traditional medicine and self-medication are widespread, and little is known about their safety and effectiveness. Smuggled drugs are readily available on the black market.

There were no trained, specialist health journalists in the country, and DACA felt that investment in raising the awareness, knowledge and skills of media professionals would improve health reporting and its influence on the health of the nation.

Major topics of the workshop were:

- The importance of health reporting for the health of the nation
- Health reporting ethics and practice
- Introduction to pharmacology
- Rational drug use and pharmacovigilance
- Making sense of medical research, risk statistics and drug information
- Priority health issues in Ethiopia
- What patients need to know
- Medical and scientific fraud, scandals and crises
- Interview technique and sources of drug information.

Participants were provided with 500 pages of material on all aspects of the workshop, along with copies of parts 1 and 2 of the UMC's 'Viewpoint'.

During the workshop, participants researched topics they regarded as being of prime importance to their audiences. Within days some of these had been completed and broadcast or printed. They also developed action plans for subjects which they wished to pursue and cover in the next six months.

"I was very pleased with the impact of the workshop," said Dr Abraham Kahsay, Director of the Planning & Drug Information Division of DACA. "Participants rated the experience very highly, took the event seriously and learnt a great deal. I'm confident the quality of health reporting will improve greatly and, I hope, influence the behaviour and health of the people of Ethiopia."

Addis ADR team sets the stage

The Ethiopian ADR team has all the elements of a good reporting system in place: guidelines, pre-paid reporting forms, training for healthcare personnel, promotional material, enthusiastic staff. Over the three years of their existence, they have held seven 3-day pharmacovigilance training events and contributed sessions on ADR reporting to other courses. In spite of such effective ground-work, so far they have received only a few dozen reports of less than ideal quality.

"Doctors already have a massive workload," says Dr Assegid Tassew, head of the three-man team. "The national target of treating around 70 patients a day means that they're under enormous pressure and don't see ADR reporting as a priority, even when they're aware of the system."

The ADR team is conscientious about acknowledging reports that do come in, but they don't have direct line telephones in their own office yet, so contact and follow-up with reporters is problematic. Few hospitals or physicians have access to computers and the internet, so electronic communication is not currently an option. (The team only has access to a (slow) internet connection for 2-3 hours a day.)

"We feel quite isolated," says Fitsum Tadios, one of the two pharmacists on the team. "There's a big job to be done and we'd like training in pharmacovigilance for ourselves, support on technical matters like causality assessment, and the chance to talk with other experts."

The three-man team has achieved much in laying the foundations, and is now set on the massive task of promoting the country's ADR reporting system, stimulating more quality reports, and submitting its qualifying batch of reports for full membership of the WHO Programme.

Kick-off training course in India

Sten Olsson reports

As described in earlier issues of Uppsala Reports (UR25 and UR28) a new nation-wide pharmacovigilance system is about to be established in India, headed by the central drugs regulatory authority CDSCO (Central Drugs Standard Control Organization). The national programme was formally launched in November 2004.

In addition to the Adverse Drug Reactions Advisory Committee connected to CDSCO there will be two zonal centres, five regional centres and at least 40 peripheral pharmacovigilance centres in the country. Running such a vast programme in a coherent and consistent way requires mobilization and training of many professionals on different levels, some with only limited prior knowledge and experience of drug safety monitoring.

The WHO regional office for South East Asia, SEARO, took the initiative to fund a training course for key persons in the new system in Mumbai (Bombay) from 17 – 21 January 2005. Dr Urmila Thatte and her team at the BYL Nair Charitable Hospital, Mumbai made an excellent job



The key personnel gathered at the Resort Hotel, Mudh Island, for the Indian programme meeting.

in organizing the course at a secluded beach hotel. Tutors were invited from the UMC (Sten Olsson), WHO HQ (Mary Couper), and John McEwen, TGA, Australia, participated in a telephone conference session.



Dr G Parthasarathi, Dr Renuka Kulkarni and Dr Urmila Thatte (standing) preparing for one of the interactive sessions.

Sessions were generally very interactive and participative since one of the aims was to establish good pharmacovigilance practice in an Indian context. It is very important that the key professionals charged with the task of training their peers, other health professionals, media and the general public about the principles of pharmacovigilance feel confident and have a shared ownership of the processes employed. Subjects discussed included:

- definitions of key concepts
- reporting forms and sources of ADR reports
- causality assessment of individual reports
- involvement of the pharmaceutical industry
- safety monitoring of non-allopathic medicines
- safety monitoring of vaccines
- ethics in pharmacovigilance
- benefit/harm assessment and regulatory decision making
- good communication practice in pharmacovigilance
- using media for educating professionals and the public.



Dr Urmila Thatte, Sten Olsson, and Mary Couper watch Dr M E Yeolekar, Dean, Lokmanya Tilak Municipal Medical College light the lamp to inaugurate the Mumbai meeting.

It was concluded that there is a need for continuous communication between the key professionals driving the new Indian pharmacovigilance programme ahead. Annual national meetings are being planned and regional meetings in between. There was a strong feeling of commitment to the new programme that is expected to make a major contribution towards safer and more rational use of medicines in India.

One year with ADR consumer reports

On 1st July 2003 patients and relatives were given the opportunity to report adverse drug reactions (ADRs) of medicinal products directly to the Danish Medicines Agency. This resulted in 149 reports, and the Danish Medicines Agency has made this analysis based on a year's experience.

7% of the Danish ADR reports derive from patients

Between 1st July 2003 and 30th June 2004 the Danish Medicines Agency received a total of 149 consumer reports on possible ADRs (see figure 1). The 149 reports mentioned 113 different medicinal products and 405 ADRs (see figure 2).

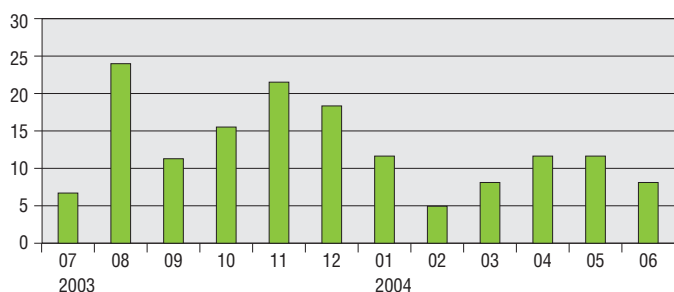


Figure 1:
Consumer reports received during the period:
1st July 2003 to 30th June 2004 - by month

During the same period the Danish Medicines Agency received 1,894 reports from health care professionals, i.e. a total of 2,043 ADRs from both patients and health care professionals. The 149 consumer reports amount to 7% of the total number of reports. In only two cases did the Agency receive a report on the same ADR from both the patient and the health care professional.

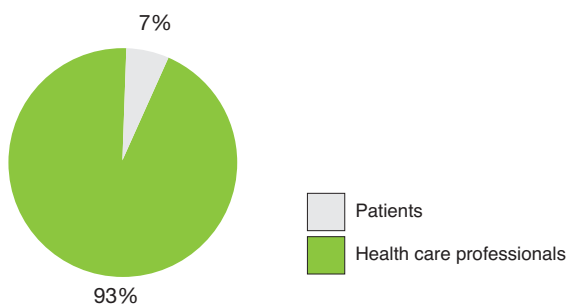


Figure 2:
Reports received during the period: 1st July 2003 to 30th June 2004 -
divided into reports from patients and health care professionals

Mostly reported ADRs are from women

105 consumer reports (71%) were sent in by women and 42 reports were sent by men (28%). The reporter's sex was not given in 1% of the reports. By comparison, 66% of the health care professional reports are on women, (see figure 3).

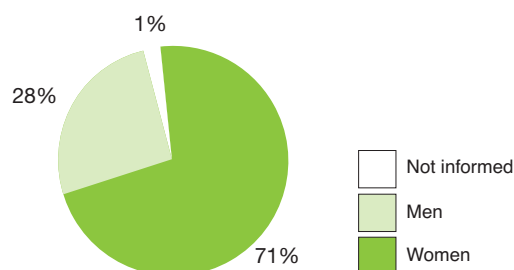


Figure 3:
Consumer reports received during the period: 1st July 2003 to 30th
June 2004 - divided into reports from women and men

Reporters divided according to sex and age

In table 1 and figure 4 consumer reports are divided on the basis of the patient's sex and age. Relatives are also permitted to report on behalf of a patient. The report in the column named 'Men', '0-9' years (1¹), is an example of a report from a relative.

Sex/Age	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	Not informed
Women	0	2	10	19	12	26	20	16	0	0
Men	1 ¹	3	4	5	5	4	5	11	3	1
not informed	0	0	0	1	0	0	1	0	0	0

Table 1: Consumer reports received between 1st July 2003 to
30th June 2004 - divided by sex and age

¹ Reported by a relative.

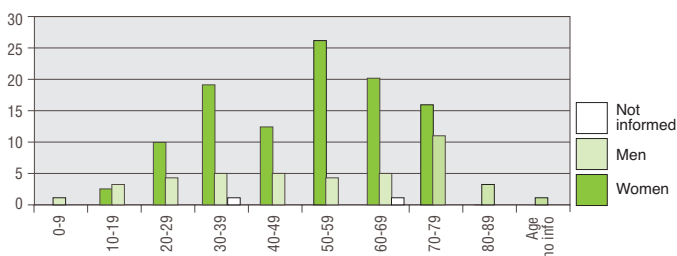


Figure 4:
Consumer reports received during the period: 1st July 2003 to 30th
June 2004 - divided by sex and age

Few medicinal products get many ADR reports

The consumer reports cover 113 different medicinal products. The Agency only received one or two reports on most of the products. ADRs on a small number of the medicinal products were reported 4 or more times (see table 4). This applied to:

Medicinal Product	No. of Consumer reports
Isotretinoin (Roaccutan® and Accutin®)	22
Citalopram (Cipramil®, Akarin® and Citaham®)	8
Rofecoxib (Vioxx®)	6
Simvastatin (Simvastatin®)	4
Glucosamine (Glucosamin®)	4

Table 2: Medicinal products with the largest number of consumer reports

The relatively large number of consumer reports on isotretinoin – used against severe acne – is connected with the fact that risk of severe psychiatric ADRs related to Roaccutan® were in great focus in the spring of 2003. The Danish Consumer Council encouraged patients to report ADRs associated with isotretinoin. This campaign was also covered by the media.

The reporting frequency on SSRIs (e.g. Cipramil® – used against depression) and Vioxx – used against arthritis – could also be related to media coverage.

The medicinal products Simvastatin® (lipid reducing) and Glucosamin® (against osteoarthritis and arthritis) are used by a large group of the population. In 2003 Glucosamin® was often mentioned in the media due to practical problems in connection with the registration of glucosamine as a medicinal product.

Diagnoses of ADRs

The ADRs most frequently reported are shown in table 3:

Adverse Drug Reaction	Number of reports
dizziness	11
depression	10
arthralgia	7
gastrointestinal pain	6
nausea	6
vision disturbances	6
dyspnoea	5
headache	5
myalgia	5

Table 3: ADRs most often reported

Long interval between the occurrence of the ADR and submission of the report

47 consumer reports out of 149 showed that the ADRs had occurred during the latest year. In 50% of the cases the ADRs had occurred more than one year before reports were submitted – in some cases more than 10 years before. The long intervals between the occurrences of the ADRs and the submission of the reports might reflect the need for patients and relatives to report before this was made possible in July 2003.

New information or already well-known ADRs?

It is very important to find out to which extent the consumer reports can contribute to the detection of ADRs not already known. At this time it is too early to reach any conclusion.

To get an impression the Agency checked whether the reported ADRs were already described in the SPCs* of the medicinal products concerned. The result was that approximately 2/3 of the ADRs (266 out of 405) were already described whereas the remaining 1/3 (139 ADRs) were not mentioned.

The quality of consumer reports

Consumer reports are handled in the same way as reports received from health care professionals (primarily doctors). The information given is registered in the Danish ADR database, and the ADRs are classified according to an international system for ADR diagnoses. All reports are forwarded to the Marketing Authorisation Holder and to the WHO. Reports classified as serious are also forwarded to the European Medicines Agency (EMA). Reports thus become part of the national and the international ADR-monitoring system.

The experience from the first year with consumer reports – received directly from patients and relatives – has shown that they require more time and resources compared with reports from health care professionals. The main obstacles appear to be less precise descriptions of the medical history. Furthermore it is often difficult to classify the ADRs, because it is more complicated to find appropriate diagnoses in the international coding system.

Continuous evaluation of consumer reports

The Danish Medicines Agency will continue to evaluate reports from patients and relatives to obtain more information about the reports. This will be done in co-operation with the Council for Adverse Drug Reactions and the other EU member states' authorities, currently gaining more experience with consumer reports.

The Danish Medicines Agency – www.laegemiddelstyrelsen.dk – 13th October 2004

*A Summary of Product Characteristics (SPC) is made for all marketed medicinal products. This document contains a wide range of information about the medicinal product – e.g. against which diseases the product can be used as a treatment, and which adverse drug reactions the product might cause.

The Netherlands Pharmacovigilance Centre Lareb has also recently published the results of its first year's experience with ADR reports directly originating from users of medicines.*

The aim was to determine the results of establishing a station at which patients can report the side effects of drugs. Since 1 April 2003, patients may submit reports of possible adverse drug reactions directly to the Lareb. The reports submitted during the period from 1 April 2003 to 31 March 2004 have been analysed and compared with the reports submitted by doctors and pharmacists. In the first year, 276 reports were submitted by patients and 3,131 by doctors and pharmacists. The reports from patients usually contained sufficient medical information and more frequently referred to serious adverse reactions than reports by health professionals. The reports from patients relatively often concerned psychotherapeutic agents, notably antidepressants. Based on the positive results during the first year, Lareb has decided to continue the reporting station for patients. Reports submitted by patients are currently part of the core responsibility of Lareb: the detection of signals of new adverse drug reactions.

Kees van Grootheest, Director, Lareb

*(Direct reporting of side effects by the patient: favourable experience in the first year. Ned Tijdschr Geneesj, 2005; 149:529-33)



Geneva and its lake

2005 Annual Meeting

Mary Couper, Quality Assurance and Safety: Medicines, Department of Essential Drugs and Medicines Policy, reports

As outlined in Uppsala Reports 28, the Annual Meeting of countries participating in the WHO Programme for International Drug Monitoring will be held this year in Geneva, Switzerland. As the meeting will take place at WHO Headquarters, the intention is to involve some other departments at WHO. The other WHO Programmes who are to be invited to be involved are the Malaria programme, HIV/AIDS, Vaccines and Poisons. We are delighted that Sir Liam Donaldson, UK's Chief Medical Officer, and now chairperson of the WHO World Alliance for Patient Safety (see UR27 for a report on this organisation) has agreed to be a guest speaker on the Monday, on the subject of patient safety.

There will be two interactive sessions on controversial subjects, a panel discussion on open access to the WHO database, as well as the usual working groups and three sessions for problems of current interest at which countries may present emerging drug problems. There will also be a session led by officers of Swissmedic (the Swiss national centre) demonstrating the reporting tool Vigibase Online.

The meeting will be held in the Executive Board Room of WHO. Nearby there is a cyberspace with free access to the internet on many computers. The meeting will start at 9.00 on Monday 26th September with registration from 8.30.

Outside the scientific side, there will be a reception on the Monday evening to give delegates the chance to socialize and meet old and new friends, and there will also be an official dinner – details to be confirmed. We hope to have some free time on Wednesday afternoon but how much will depend on how packed the programme is.

An official invitation was sent out to National Centres during the week of the 21st March; the agenda is still in the preparatory stage but a preliminary draft should be available as this Uppsala Reports is published.

A block booking of hotels in Geneva at a range of different prices has been made and details of these, will be available soon.

There is lots happening in the world of drug safety and we look forward to many National Centres delegates making the journey to Geneva to share their thoughts and expertise for the 2005 meeting.



Philippe Duclos, Medical Officer and Alison Delo, Administrative Officer, both of Vaccine Assessment and Monitoring, Immunization, Vaccines and Biologicals, World Health Organization

Safety Advisors for WHO

The Global Advisory Committee on Vaccine Safety met for the 11th time on 2-3 December 2004. Issues discussed were: the safety of adjuvants, hexavalent vaccines and yellow fever vaccines; the safety of residual cellular DNA in vaccines; the potential risk of vaccines produced in yeast; thiomersal; and transmissible spongiform encephalopathies.

The Global Advisory Committee on Vaccine Safety was established in 1999 to respond promptly, efficiently, and with scientific rigour to vaccine safety issues of potential global importance. The fourteen members of the Committee are acknowledged experts from around the world in the fields of epidemiology, statistics, paediatrics, internal medicine, pharmacology and toxicology, infectious diseases, public health, immunology and autoimmunity, drug regulation and safety. The Committee aims to provide a reliable and independent scientific assessment of vaccine safety issues through:

- rigorous review of the latest knowledge, in all fields ranging from basic science to epidemiology and clinical practice, concerning any aspect of vaccine safety of global or national interest, in close collaboration with all parties involved, including experts from national administrations, academia, and industry;

The Committee aims to provide a reliable and independent scientific assessment of vaccine safety issues

- assessment of the evidence for relationships between vaccines and/or their components and adverse events attributed to them; and
- creation, where necessary, of ad hoc task forces with a mandate to commission, monitor and evaluate appropriate methodological and empirical research on any purported association of specific vaccines/components and adverse event(s).

Topics reviewed since the establishment of the Committee include:

- hepatitis B vaccine and multiple sclerosis;
- hepatitis B vaccine and leukaemia;
- the Measles-Mumps-Rubella vaccine and autism;
- intranasal vaccination and the risk of Bell's palsy; and
- a potential adverse impact of routine vaccination on childhood survival.

The conclusions of the Committee, along with position statements and questions and answers on many of the topics discussed, can be found on the Committee's website (http://www.who.int/vaccine_safety/en/). Much of the material on the website is posted in Arabic, Chinese, French, Russian and Spanish, as well as English.

REGULATION OF VIOXX: SUCCESS OR FAILURE?

This paper is a result of a discussion via Vigimed, which is the WHO Programme for International Drug Monitoring e-mail forum.

I Ralph Edwards was the main editor of the discussion. Kees van Grootbeest provided many useful comments, and Chalbi Belkhabia and Roselie A Bright have also been most supportive. Many others have contributed major comments but have not indicated that they wished to be mentioned by name.

The Vioxx controversy

In major medical journals, as well as in the public media, it is said that regulators have not managed the risk issues of Vioxx well. The Canadian Medical Association is even calling for a new body to be set up there to monitor drug safety. They are reported as saying that North America's regulatory agencies have 'failed miserably'.¹ In another article, the authors say: 'Our findings indicate that rofecoxib should have been withdrawn several years earlier. The reasons why manufacturer and drug licensing authorities did not continuously monitor and summarise the accumulating evidence need to be clarified'.² These are but two examples of the criticism of pharmacovigilance as it relates to Vioxx, and reflects broader drug safety concerns.

Pharmacovigilance found the early signal

The rofecoxib (Vioxx) story is one of many successes of pharmacovigilance and the WHO Programme. At the Meeting of National Centres in Tunis (October, 2000) the Netherlands Monitoring Centre (Lareb) presented a new signal of cardiovascular disorders relating to rofecoxib, with a high reporting odds ratio for cardiovascular ADRs with some fatalities and which occurred early in treatment. The affected patients were elderly and in addition, the dosage is often high. This prompted a response from many countries that were seeing cases of myocardial infarction (MI).

Post-marketing studies confirmed the signal

A review of the discussions in the WHO e-mail conference system (Vigimed) and from discussions at subsequent Annual Meetings of the WHO Programme in 2001 and 2002 reveal continuous monitoring of the COX 2 situation, particularly of rofecoxib, by regulators. In several countries regulatory authorities did warn both health professionals and the public, on a regular basis via official newsletters and websites, about the latest developments reported in the literature. Even in February 2000, there was a recommendation to add information about cardiovascular events, in the USA³, and elsewhere.

More information came from the VIGOR study⁴, which received wide publicity. The main criticism was that the comparator, naproxen, may have reduced the myocardial infarction (MI) rate, and many further studies were done by industry with the MI rate in mind on a number of COX 2 selective drugs.

The Merck polyp trial (APPROVe) is but one study which included a good safety evaluation, and safety concerns led to the premature closure of the study at 34 months, when the MI rate at 18 months was found to be significantly higher than the control. Two odd features of this study were the relatively low MI rate in the controls and the non-linear increase in myocardial infarction in the rofecoxib group after chronic use. This study led to the withdrawal of the drug by Merck, and clearly could not have produced a result in less than 18 months.

For doses higher than 25mg, there was more than a signal before the withdrawal: in addition to the VIGOR trial, 3 observational studies had already been published pointing to an increased risk of MI, the first in 2002⁵. Other studies have confirmed the dose relationship, which has not been fully reflected in the package inserts/SPCs.

The main competitor to Vioxx, celecoxib, may not be any better than non-specific NSAIDs from a GI point of view⁶. Differences in the safety profiles of rofecoxib and celecoxib have also been reported^{7,8}, so there may be class differences. There is almost nothing in the current media debate on the overall effectiveness-to-risk balance of Vioxx and even less about its comparison with other COX 2 selective drugs, and other old or new analgesics, even though some such information is available.

There is little in the general media to guide either health professionals or patients as to what would be the best likely alternative to Vioxx. It is also worth noting that 80% of the prescribing of Vioxx in one country did not fulfil the requirements stipulated in the SPC.⁹

Insights and Challenges

Decision-making

Always in drug safety matters there is a need to link evidence to decision, and decision to action. This is true for the overall status of the drug as well as in a data-gathering sense. For example: the signal Vioxx/MI could be confounded by the age group or concomitant illnesses of patients, therefore there was a need for a study to determine this. But how important is the signal? What will the studies cost? As each study produces results, decisions must be taken about what to do with Vioxx, given its effectiveness and risk, both in terms of public health and in information to help patients and prescribers. Apart from overall decisions about what to do with the drug at each step, there are therefore judgements needed about communicating the decision, how to communicate, and to whom.

None of the decisions are straightforward, particularly when there is little information. It is very easy to see what to do with a safety signal after information is available; it is very difficult to decide which signals to follow up to get that additional information! This difficult decision is left to the regulators and their advisors largely, who decide on behalf of the public. Yet there is no real knowledge on what risks patients in particular, and the public in general, are prepared to take, given a certain benefit (even more difficult when one considers competing treatments). Quality of life tools are being developed and there are some very imaginative approaches to getting to understand risk perception and tolerance. These should

be pursued much more actively to try to find a set of baselines of acceptable risk for different situations. Patient groups in particular must play a role in decisions: an esoteric group making such decisions in secret is not tenable.

Acceptable risk-to-benefit balance is an individual judgement for each patient, and every effort should be made to obtain enough information on the issues of effectiveness versus risk to properly enable those singular judgements by doctors with their patients.

Comparisons in safety

There are older and newer drugs on the market which are much less well investigated than Vioxx. Many have more problematic effectiveness-to-risk profile than Vioxx. One is the analgesic co-proxamol, which has just been restricted in the UK in spite of concern over safety for many years (for example,¹⁰). Also, a new finding on one drug might apply to other drugs where information is lacking, as a class effect. Removing one drug on the basis of a highly publicised, single adverse reaction without considering the effectiveness-to-risk balance of competing products, also considering different indications, may lead to substituting another drug with the same problem, or worse. In the EU, complex comparisons with COX 2 drugs have been underway since 2002, but not publicised.

WHO has led the way for such comparison of drugs with its Model Lists of Essential Drugs. Comparisons between drugs for different indications, made by experts, result in clear guidance which can be appraised critically by all. It does not mean that drugs not on the Model List are ineffective or unsafe, but they must be considered carefully against the gold standard of the Model List.

Concern to evidence

In the Vioxx case concerns led quickly to further investigation. Due to regulations, an excessive amount of time is spent on making sure that every 'serious, unlabelled' report is sent by industry within the arbitrary time of 15 days⁽¹¹⁾. The '15-day rule' has no evidence basis. Undue delay in getting and analysing reports would be deleterious, but there is a greater need to understand the more difficult challenges of getting and analysing the useful extra evidence. It is frequent that regulatory responses occur years after the first signal is made known, and little is done to measure the impact of regulatory activity, or consequences of delays.

In the Vioxx situation, as in many others, it has largely been academia that has designed and conducted further studies. Many are done in collaboration with an industry that is naturally reticent to fund studies. Only some studies are agreed internationally between regulators. Almost all are undertaken without health professionals and the public knowing that a safety concern is being investigated. As with the APPROVe study, they may take years to produce a finding; as with the VIGOR study the results may produce more controversy. Regulators are taking more initiatives to conduct the studies they need, but since they have few resources they depend on others. Industry plays a key role in deciding when and how safety studies are done.

The WHO Programme for International Drug Monitoring publishes early concerns to all members of the Programme. There have been surveys of what is done about those early signals in different countries, and the responses are variable^(12,13). WHO has made requests to national centres to communicate to all about safety issues they are investigating. An internet discussion channel, Vigimed, was set up to facilitate this, but the input from developed countries about their on-going work on signals has been limited. Pressure from the industry to keep safety discussions confidential has been cited as a reason for this. Work may therefore be

duplicated in different countries unnecessarily, but more importantly, countries are often faced with a series of crises when regulatory decisions become public, and they may not even know that there was a problem under investigation. For example, when the third generation oral contraceptives were found to have a higher risk of venous thromboembolism, developing countries that were actually involved in the seminal study were excluded from the discussion of the results.

Evidence and decision

On receiving a first signal, the decision to take action should be based upon the level of certainty and seriousness. In the Vioxx situation a limited warning was quickly given, a reasonable one given the high background of cardiovascular disease in the treated population.

Repeated confirmation of a dose-response relationship both firmed-up the causative relationship and gave a reason to suggest limitation of dose. The final finding, before Vioxx withdrawal, of a relationship with long-term use (already disputed, and at variance with the early signal from spontaneous reports!) could also have led to a warning against such use. Why did this not happen, rather than withdrawal?

Many withdrawals of drugs over 'safety' problems are not necessarily warranted from a public health perspective. They may be strategic: the company has another drug for the same indication which they wish to launch, and the withdrawal of an old drug, out of patent, can remove some or all of the generic competition for the indication at the same time; a company may decide that a potential fall in sales following a warning renders the drug cost-ineffective; it may be the company does not wish to pay out for claims against them, which may sometimes be unjustified in a public health sense, though reasonable in strict liability in law.

The APPROVe study was sponsored by Merck; the independent ethics committee advised discontinuing the study because of the MI risk, and the numbers of possibly affected people was quite large, so it is easy to see why Merck pre-emptively discontinued the drug to avoid possible heavier litigation costs.

Almost all drug regulatory activity is part of a dialogue between the regulators and the industry. Safety issues are usually, but not always, raised by regulators. Large volumes of information are provided by industry to regulators, on request, for them to analyse. Suggested changes to the ADRs in the SPCs and warnings, are generally more easily accepted by the industry than restrictions or withdrawals. This may have been so with Vioxx. A question arises, given that early warnings on MI were in place, whether it was unnecessary to add the dose restriction. As the FDA Advisory Committee Document, 2001 states³, 'Rofecoxib (Vioxx) 50mg/day is the dose recommended for the treatment of acute pain, and twice the highest recommended dose for osteoarthritis (OA). Physicians should not have been prescribing doses greater than 25mg for more than very short periods.'

Given that some general warning about Vioxx was already extant, and that the broader, complex comparisons needed to be done, withdrawal of the drug was not necessarily the best public health action, but more communication of the unfolding situation would have helped.

Always in drug safety, evidence changes over time. Usually one has improving evidence of the nature and extent of the risk, but the judgement over what to do and when, is all too often a value judgement with little consistency between instances. Often a

publication in the academic or public media triggers action for one drug risk, when others go relatively unnoticed for years, like co-proxamol¹⁰.

Communication of decisions and information

The media are a major source of diversion from the broad consideration of drug safety issues as described above, to a very narrow focus on a newsworthy topic of their choice. Dealing with the consequences of this publicity takes a huge amount of professional time. This is partly due to the failure of regulators and industry in informing the public what they are doing in pharmacovigilance.

Regulators are very much involved in what information is given with a drug product, but it is the company which takes the legal responsibility and may face hugely expensive claims for damages. Consideration of possible litigation is the main consideration in the formulation of wording in drug information. It is not surprising that great pressure is put on regulators by industry (sometimes at a personal level) to have the drug information their way. Society needs to deal with the problem of acceptable risk, and whether or not, and how, those who are harmed should be compensated. The current situation of high levels of compensation after litigation leads to defensive wording in drug product information, which both over-warns and leaves out useful information.

Much useful information is available from pharmacovigilance that is dispersed around research papers in the literature. Ways must be found to provide this information so that it is useful to a prescriber. For example, there is little information on when to look for a particular adverse reaction: does it occur early in treatment only, or must one consider such an adverse reaction throughout the total time of use of the drug? The way to diagnose and manage a particular adverse reaction needs to be mentioned in the drug information unless they are truly a part of standard medical practice.

It is already known that warnings and letters to health professionals have little effect¹⁴, so it would seem that much more emphasis should be placed in better communication practices. This means new strategies, and not just blaming the health professions for not heeding occasional, and inconspicuous warnings: it means providing useful information that can be accessed at an appropriate place and time. This includes knowing about evolving risk situations, under investigation.

WHO has been involved in two major initiatives about communication^{15,16}, and the widely-quoted Erice Declaration (1997) contains the following:

- 1 *Drug safety information must serve the health of the public. Such information should be ethically and effectively communicated in terms of both content and method. Facts, hypotheses and conclusions should be distinguished, uncertainty acknowledged, and information provided in ways that meet both general and individual needs.*
- 2 *Education in the appropriate use of drugs, including interpretation of safety information, is essential for the public at large, as well as for patients and health-care providers. Such education requires special commitment and resources. Drug information directed to the public in whatever form should be balanced with respect to risks and benefits.*
- 3 *All the evidence needed to assess and understand risks and benefits must be openly available. Constraints on communication parties, which hinder their ability to meet this goal, must be recognised and overcome.*

4 *Every country needs a system with independent expertise to ensure that safety information on all available drugs is adequately collected, impartially evaluated, and made accessible to all. Adequate non-partisan financing must be available to support the system. Exchange of data and evaluations among countries must be encouraged and supported.*

5 *A strong basis for drug safety monitoring has been laid over a long period, although sometimes in response to disasters. Innovation in this field now needs to ensure that emergent problems are promptly recognised and efficiently dealt with, and that information and solutions are effectively communicated.*

Summary

The Vioxx situation is not a failure of regulation, neither an issue of data collection, nor of the quality of studies. It was and is a complex decision-making/communication challenge. Making wise drug safety decisions is not easy, and it is made worse by:

- Lacking clear goals of acceptable benefit and risk for those who are affected: the patients
- Regulatory structures being overly cumbersome, overwhelmed by data from industry, not being transparent, and not assessing impact of their actions
- Regulators needing to consult the pharmaceutical industry before decisions are made and information given, rather than patients
- Industry taking all the punishment (therefore being defensive), when decisions are shared with regulators
- Regulators lacking resources to perform studies quickly
- Safety departments in the pharmaceutical industry being over-ruled by marketing issues and concerns over litigation
- Industry strongly driven by market forces, leading to small safety budgets.

References

1. Kermode-Scott B. Agencies 'failed miserably' over COX inhibitor. *BMJ*, 2005, 330: 113.
2. Juni P et al. Risk of cardiovascular events and rofecoxib: cumulative meta-analysis. *Lancet*, 2004, 364(9450): 2021-9.
3. http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_03_med.doc
4. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. *N Engl J Med*, 2000, 343:1520-1528.
5. Ray WA et al. COX-2 selective non-steroidal anti-inflammatory drugs and risk of serious coronary heart disease. *Lancet*, 2002, 360(9339): 1071-3.
6. Bombardier C. An evidence-based evaluation of the gastrointestinal safety of coxibs. *Am J Cardiol*, 2002, 21; 89 (6A):3D-9D.
7. Wiholm BE. Identification of sulfonamide-like adverse drug reactions to celecoxib in the World Health Organization database. *Curr Med Res Opin*, 2001, 17(3): 210-6.
8. Zhao SZ, Reynolds MW et al. A comparison of renal-related adverse drug reactions between rofecoxib and celecoxib, based on the World Health Organization/Uppsala Monitoring Centre safety database. *Clin Ther*, 2001, 23(9): 1478-91.
9. van Grootheest AC, Edwards IR. Labelling and 'Dear Doctor' letters: are they noncommittal? *Drug Saf*, 2002, 25(15):1051-5.
10. Edwards IR. Dextropropoxyphene. *N Z Med J*, 1985, 98(775): 201.
11. European Commission- Enterprise and Industry- Pharmaceuticals Unit: Update of Volume 9, 'Pharmacovigilance of medicinal products for human use and of veterinary medicinal products'. http://pharmacos.eudra.org/F2/eudralex/vol-9/pdf/Vol9_07-2004.pdf
12. Fucik H, Edwards IR. Impact and credibility of the WHO adverse reaction signals. *Drug Inf J*, 1996, 30(2):461-4.
13. Ståhl M, Edwards IR et al. Assessing the Impact of Drug Safety Signals from the WHO Database Presented in 'SIGNAL': Results from a Questionnaire of National Pharmacovigilance Centres. *Drug Saf*, 2003, 26(10): 721-7.
14. Uhl K, Honig P. Risk management of marketed drugs: FDA and the interface with the practice of medicine. *Pharmacoepidemiology & Drug Safety*, 2001, 10(3):205-8.
15. Effective communications in pharmacovigilance: the Erice Report. Uppsala, Uppsala Monitoring Centre, 1997.
16. Dialogue in Pharmacovigilance – more effective communication. Uppsala, Uppsala Monitoring Centre, 2002.

Viewpoint Part 2 contents

1. The WHO Programme for International Drug Monitoring: primary activities and membership
2. The Heart of the Programme: ADR reporting systems and signal detection
3. Products and services: Vigibase Online, WHO Drug Dictionary, WHO-ART
4. Publications from *the UMC* and others
5. Collaborations
6. Communications
7. Audiences
8. Training from *the UMC* and elsewhere
9. Key terms and issues in pharmacovigilance
10. The current state of play in pharmacovigilance
11. The role of *the UMC* – a summary

Appendixes provide additional reference information:

1. The guardians of drug safety and the macro environment of drug regulation
2. A list of acronyms
3. Definitions and glossary of terms used in pharmacovigilance
4. Joining the WHO Programme for International Drug Monitoring
5. Current member and associate member countries of the WHO Programme
6. Caveat document accompanying data released by *the UMC*
7. Bibliography of key UMC publications in scientific journals and books
8. The Erice Declaration on communicating drug safety information
9. BCPNN: additional technical information
10. *the UMC's* signal detection process – Guidelines for reviewers

Viewpoint Part 2 – got yours yet?

Publication of Viewpoint Part 2 completes the picture

Viewpoint Part 2's 68 pages are packed with detailed information on drug safety, the WHO Programme, the activities of *the UMC*, and how international pharmacovigilance works. If you want a thorough – and accessible – description of the WHO Drug Dictionary or the meaning of neural networks; an outline of medical error or signal detection, causality assessment explained or background to risk management or herbals – then you should read Viewpoint Part 2!

Viewpoint 1 reprinted

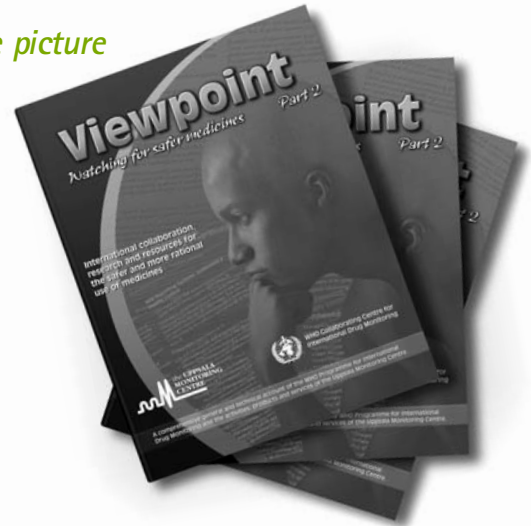
Viewpoint Part 1 'Watching for safer medicines' has just been reprinted in response to demand which exhausted the initial stocks. This introduction to issues, controversies and science in the search for safer and more rational use of medicines can also be obtained from *the UMC*.

Viewpoint Part 2 is attractive and accessible to an audience beyond professionals and specialists. It's in full colour, with photographs, diagrams and tables – designed to make the information as immediate as possible. Its audience includes patients, students, the media and many more. It could be a useful resource for medical, nursing or pharmacy training, and help staff in national ADR centres to see the international picture and *the UMC's* work.

Wanted: feedback

Among feedback so far received: "I am doing training for pharmacy employees, as well as nurses and medical personnel. They haven't been given correct information about pharmacovigilance, so Viewpoint will be excellent material. I will also hand this to my university professors – they will then have better information to teach about pharmacovigilance..." (Mexico). "We would like to send your publications to the centres who collaborate with us, especially regional centres in medical academies. We found both parts of Viewpoint comprehensive material on adverse reactions." (Poland).

Please let us know your views about Viewpoint 1 or 2 – you'll find a comment form at www.who-umc.org/publications, or contact us in the usual way (see page 3).



Some new publications from *the UMC*

Norén N, Orre R. Case based imprecision estimates for Bayes classifiers with the Bayesian bootstrap. *Machine Learning*, 2005. 58(2005): p79-94.

De Bruin ML, Pettersson M, Meyboom RHB, Hoes AW, Leufkens HGM. Anti-HERG activity and the risk of drug-induced arrhythmias and sudden death. *European Heart Journal*, 2005, 26: 590-597.

Sanz E J, De-las-Cuevas C, Kiuru A, Bate A, Edwards IR. Selective serotonin reuptake inhibitors in pregnant women and neonatal withdrawal syndrome: a database analysis. *Lancet*, 2005; 365:482-487.

de Boer HJ, Meyboom R, Ericsson, Farah M. Farmacovigilantie van fytotherapeutica door het Uppsala Monitoring Centre. *Nederlands Tijdschrift voor Fytotherapie*, 2004; 17:4, p2-4.

A new book on dermatology

Guide to Adverse Drug Reactions: Side Effects in Dermatology, 8th Edition (fully revised) 2004

This 132-page reference source is an invaluable aid in the everyday dermatology work. It is based on the editors' clinical experience, dermatological information available, but also on reports contributed. Published by Intermed Medical Publishers, ISBN 90 5884 003 4.

You can find more information at www.intermed.nl

New Challenges in Clinical Safety, Pharmacovigilance and Vaccine Vigilance

There can be few places more conducive to pursuing the collaborative work of pharmacovigilance than the Fundació Doctor Robert, at the Universitat Autònoma de Barcelona, designed by Luís Domènech i Montaner. In this stunning setting last February, the International Society of Pharmacovigilance (ISoP) held a successful training course with an international mix of 14 experts and 46 enthusiastic participants.

Professor Vladimir Lepakhin gave an overview of the role of WHO in the safety of patients and how international alliances may benefit public health. He described in detail WHO's policy on patient safety; including the WHO Programme for International Drug Monitoring.

The scene set, the meeting then confronted the new roles of drug safety officers at the headquarters of a pharmaceutical company and in an affiliate. Dr Irène Rebollo from Alcon Laboratories spoke on how an officer can interact with the whole organisation while satisfying the strict European and worldwide legislative pharmacovigilance framework. She felt that "paperwork and useless bureaucracy are giving way to a better understanding of the role of pharmacovigilance in public health protection". Dr Maria Astorga from Sanofi-Aventis emphasized the critical role of a subsidiary in looking after the quality of data included in databases: this is key to retrieving important and relevant information, and balancing the quality and speed for reporting.

A three-way session on ICH E2E guidelines was developed by Dr Ana Corrêa-Nunes from Informed (Portugal), Dr Conxita Barajas from Bayer Spain, and Dr Peter Schulz from Amgen HQ. Dr Schulz opened a discussion with the audience on the importance of giving the risk profile to the prescriber, emphasising that "drugs can safely stay in the market by targeting the right patient groups through a coordinated safety and marketing strategy where revenue expectations are consistent with what the safety profile supports".

Education and training in pharmacovigilance was introduced by Professor Jürgen Beckmann. He set out an ambitious but achievable ETP programme; he envisaged co-operation between WHO and ISoP, and public education on avoidable and unavoidable drug-risks.

Dr Tomás Moraleda (Medical Officer MSSO) spoke about data-mining and coding in MedDRA Universe. He pointed out the importance of the clinical meaning of adverse events and that the most important is once the data has been codified, retrieved, and sort to present it in the most understandable way that makes sense for prescribers and patients.

Pharmacovigilance of Orphan Medicine Products (OMP) was explained by Prof Josep Torrent. More than 6,000 identified rare diseases – mostly affecting children – are life-threatening, serious and/or chronically debilitating, impairing quality of life and causing long-lasting disabilities and dependency. Specific OMP regulation is needed because some conditions occur so infrequently that the development cost of medicines would not be recovered by expected revenue. He reviewed patients' and patients' associations role where partnering with all stakeholders is essential and concluded "when providing information about these drugs, transparency, objectivity, managing hopes and expectations, should be done on scientific and ethical grounds".



The practical group sessions in Barcelona.



Paula Marquez and Josep Torrent, two of the main speakers at the ISoP training course.

Another three-way session on 'The Marketing of Pharmacovigilance' was set out by Dr Paula Marquez, Professor Giampaolo Velo and Professor Lepakhin. Vaccines vigilance was examined by Elisabeth Loupi (Sanofi-Aventis Pasteur) who reviewed various aspects from vaccine composition to risk assessment including the definitions and classification of the Adverse Events Following Immunization (AEFI). She commented on the work of the Brighton Collaboration, VAERS system in USA, Canada PPHB and others. Professor Chalbi Belkahia (Tunisia) described the work of his national centre: the vaccines vigilance committee manages all the alerts emerging from a drug, while interacting and working together with the National Centre of Pharmacovigilance, primary health care (including paediatricians) and the Pasteur Institute.

The last topic was the pharmacovigilance of oncolytic drugs; Ronald Meyboom, Medical Advisor of the UMC, highlighted differences in pharmacovigilance for this class of drugs; the severity of the disease, the risk allowed for them, the speed to approve them when there is no other alternative. However, a thorough knowledge of the delayed adverse effects of such therapy, used chronically, in cycles, in combinations, with novel mechanism of actions, and possibly unidentified consequences is essential. These drugs are seriously underreported; new strategies: regulatory, scientific and financial, may be required to ensure rational and beneficial cancer chemotherapy. The lack of resources in healthcare systems for treating patients with the best – but expensive – oncolytics, is another growing concern.

Friday afternoon consisted of practical exercises: data-mining with MedDRA and using the Erice Declaration as a model for new communication strategies. Attendees and speakers went into four groups and discussed conclusions which will constitute a starting point to develop future working groups within ISoP.

Ron Meyboom comments "I congratulate the organisers on what probably was the most all-round successful ISoP training course held, both in the quality of presentations and interactions. It was a great achievement to tie together what, on paper, appeared diverse important topics. The enthusiasm of the younger colleagues gives me great confidence that the future of pharmacovigilance is in good hands."

International launch of the WHO Drug Dictionary Enhanced

UMC Products & Services is happy to announce the launch of the new WHO Drug Dictionary Enhanced. The WHO Drug Dictionary is the world's most comprehensive dictionary of medicinal products. It is used for identifying drug names, their active ingredients and therapeutic use, in the course of clinical research.

The on-going collaboration between *the* UMC Products and Services and IMS Health has made it possible to enhance the WHO Drug Dictionary with additional product data collected by IMS Health. The delivery date of the first version of WHO-DD Enhanced is scheduled for 1st June 2005.

Global

The inclusion of the IMS data will provide product data from more countries and more entries per country than ever before. This will improve daily activity in the coding of clinical data by minimising the need for manual investigations by users of the dictionary and reducing the risk of making incorrect assumptions. It will also more than double the number of entries per country and include products from the USA, Japan, the European Union – and 40 other countries.

Unique

The WHO-DD Enhanced contains the WHO's Anatomical Therapeutic Chemical (ATC) classification. The hierarchic classification helps users to aggregate statistics, find patterns in the co-medication and increase understanding of the properties of the drugs. The combination of the IMS data and the WHO Drug Dictionary structure and coding system will make the WHO Drug Dictionary Enhanced by far the most efficient solution for drug coding. *the* UMC has over thirty years' experience of classifying drugs; IMS Health has over fifty years' experience of collecting drug data. Subscribers to WHO-DD are regularly invited to attend the user group meetings, which prioritises the developments and suggests improvements for the dictionary.

WHO Drug Dictionary Enhanced –

combines the unique structure of the WHO Drug Dictionary with the strength of the IMS Health's comprehensive product data.

WHO Drug Dictionary Enhanced will provide:

- Data from more countries
- More data per country
- Fast and frequent updates

Which will:

- increase the number of direct hits
- minimise the need for manual fact finding
- reduce the risk of ambiguities.

Lisbon Launch

This major new advance in the WHO Drug Dictionary was launched at the DIA Euro meeting in Lisbon in March. At booth 113 UMC Products & Services staff Mats Persson, Annika Wallström and Hannah Ericson had a hectic time to take care of all the visitors that came to learn more about the WHO Drug Dictionary Enhanced and to 'refresh their memory'... cardboard 'cut-out' memory sticks were distributed to all delegates before the meeting in a promotional mailing; they could then exchange them for a real USP-memory stick (attached to a lanyard) at *the* UMC booth.

We also took the opportunity to ask the delegates to fill in a survey in return for the USP Memory stick (there is no such thing as a free lunch). The result of the survey will help UMC Products & Services respond to customers' needs in a better way.

Additionally, the DIA Euro meeting was the venue for a user group meeting for the WHO Drug Dictionary subscribers. At the meeting Annika Wallström, Daniel von Sydow and Mats Persson talked about the new WHO Drug Dictionary Enhanced for the first time. We also had a small 'pre-launch' about the next innovation from *the* UMC, the WHO Herbal Drug Dictionary, which will be released later this year.

Buying UMC services online

As reported in Uppsala Reports 28, *the* UMC's Products and Services website is not only up-and-running, but the majority of orders for our services and products can be made easily via the web shop. While placing an order in the web shop, you can also calculate the cost and, where appropriate, generate a standard licence agreement.

In addition, the website now has user group areas so that customers can always have easy access to the information they need on www.unc-products.com.

New price list

The new price list valid from 1st May 2005 – 2006 is available and will be distributed to customers at the end of April 2005. If you are interested in obtaining your own copy, please tap into our website and download.

Updates – 4th Quarter 2004

The new versions of the computerised WHO Drug Dictionary (WHO-DD) and WHO Adverse Reaction Terminology (WHO-ART), containing information for the 4th quarter of 2004 are now available. These were sent to subscribers during March 2005. The WHO-DD pack contained the updated version of WHO-DD, as well as a wide range of background material.

Need help?

If you have any queries about WHO-DD, or need further information about your current subscription or how to upgrade it, do contact *the UMC Products & Services*.

You can e-mail:

- drugdictionary@umc-products.com for comments about the WHO-DD, corrections and 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, please contact Katarina Hansson.

Data files for the 1st quarter of 2005 should be available for web customers to download around the beginning of June 2005.

Introducing new staff

We are pleased to present new staff who have joined us to strengthen our team and improve product capacity, to enable us to provide a more comprehensive service to users of WHO Drug Dictionary and other UMC products. Björn Moberg, Nike Meder, Kristina Johansson, Åsa Lindeberg, Johanna Eriksson and Anna Mattsson join Erica Walette and Malin Nord as the main contacts for technical questions on UMC services. See page 18 for more information on them all.



Meet us there!

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

- 41st DIA Annual Meeting, 26-30 June 2005, Washington DC, USA
- 21st International Conference on Pharmacoepidemiology and Therapeutic Risk Management, 21-24 August 2005, Gaylord Opryland Resort and Convention Center Nashville, TN, USA.

We look forward to seeing many customers at one of these; if you wish to arrange a meeting with us, please contact Mats Persson, e-mail mats.persson@umc-products.com



Lars Magnusson cutting the tape to open the new Products and Services office

A new home

To accommodate the increased staff working on WHO Drug Dictionary and Vigisearch the Products and Services team moved into a new office in January. Located a few hundred metres from the main offices of *the UMC* in Stora Torget the opening was celebrated in the traditional way with singing, dancing and a little alcohol.

Our direct phone number is now: +46 18 65 63 30, fax +46 18 65 60 80

World Champion?

He may not be very widely known in international pharmacovigilance circles. Still he might be the most experienced assessor of individual ADR case reports around. He is not a happy traveller which explains why we do not see him very often at international pharmacovigilance meetings. As an amateur astronomer, he prefers to sit under the stars and travel to distant galaxies through one of the telescopes he has built.

His name is Patrick Purcell. He joined the Adverse Drug Reaction Section at the Australian Therapeutic Goods Administration (TGA) in 1987, while Alain Rohan was still in charge of the unit. This was his background when joining: after having graduated from medical school at Sydney University in 1971 he served as a resident at Newcastle, Australia, for a couple of years before working in general practice for some nine years. He then joined the Australian Health Department as a Commonwealth Medical Officer. (Duties included formal medical examinations on behalf of the government – superannuation, fitness for employment in the Public Service, invalidity retirements, sickness benefits, handicapped children, etc.) He moved to Canberra in 1985 where he first served in the Secretariat of the Standing Committee on Child Health, then a subcommittee of the National Health and Medical Research Council.



Patrick at the TGA

Patrick is now one of two medical officers who evaluate incoming reports, especially the more serious ones. The TGA internal quality requirement is that every report should be assessed within two working days. If details are missing the reporter is contacted, but a personal acknowledgement is sent in any case. Duties shared with other Medical Officers in the Adverse Drug Reactions Unit include providing information from the database to enquirers (including health professionals, pharmaceutical companies, consumers, etc.) and drafting items for publication e.g. in the TGA Adverse Reactions Bulletin. There's also preparation of agenda items for ADRAC, taking

part in videoconferences with New Zealand, USA and Singapore, participating in the work of the local hospital's ADR committee, and assisting three PhD projects on drug safety at the University of Ballarat.

According to Patrick the most stimulating aspect of his job is the challenge of finding new signals. He particularly mentions the quality related problems detected by the unit in recent years e.g. hypotension related to the plasma expander Haemaccel (polygeline) and several cases of hyoscine poisoning resulting from quality control problems in the manufacture of an 'over the counter' travel sickness preventive medication. This prompted detailed follow-up investigation by the TGA's GMP inspectors ultimately resulting in the major recall of over 1,500 products produced by Pan Pharmaceuticals and the withdrawal of that company's manufacturing licence. Interestingly, this episode also prompted extensive revision of the relevant legislation, the Therapeutic Goods Act.

Patrick expresses concerns about how data from spontaneous reporting sometimes are being misused in media and political circles

He became interested in data-mining of spontaneous reports in 1996 when the Adverse Drug Reactions Committee asked the Secretariat to investigate quantitative methods of signalling. Over the ensuing years he developed a method called PROFILE which involved probability filtering. He presented this work at the symposium at the Drug Safety Research Unit's symposium in Southampton, UK in mid 2001. He has less interest in this area now since he claims that it has become much more difficult with the introduction of MedDRA.

Patrick expresses concerns about how data from spontaneous reporting sometimes are being misused in media and political circles and he would wish them to be better educated about issues of effectiveness and risks of medicines. Also the activities of anti-vaccination lobbyists worry him at times.

At the moment there are four Medical Officers at the Adverse Reactions Unit of TGA but many years ago there was somewhat of a staffing crisis and he alone had to scrutinize all 14,000 case reports received in a year. In all, he believes he has assessed well over 100,000 case reports!

Is this a world record? Uppsala Reports expects those who have scrutinized a higher number of individual case reports to come forward.

More functions in Vigibase Online

The latest version (2.5) of Vigibase Online came into effect in March. Vigibase Online is the web based case management system developed by *the UMC* for national centre use.

The changes since October are:

1. Reports can now be exported in E2B - XML format from the Vigibase Online interface, eg. downloaded to a local work station. One export option allows 'secret' information to be concealed for external use, and the other shows all this information plus extra non-E2B information for internal use.
2. The search function is fully installed which makes it possible for users to create report listings such as a CIOMS line listing and a PSUR listing directly from the interface.
3. WHO-ART is now searchable in multiple languages (English, French, German, Spanish, Italian, Portuguese).

4. The laboratory values entry page as well as the product page are enhanced to allow for easier entry.
5. The working list (the first list that the logged-in user is confronted with) is now searchable and it is also possible to sort the reports on different criteria.
6. The audit trail of a report can be seen in the interface.
7. It is now possible to edit, add to or delete the notes that follow the report in the main report list.

Over 1,500 reports have been submitted direct to the WHO database via Vigibase Online. Most are from Switzerland, but Brazil, Ghana and Morocco are now also sending reports regularly. DR Congo, India, Ireland, Jordan, Mozambique, Serbia & Montenegro and Sweden are currently trying it out.

For more information or additional questions do contact Magnus Wallberg or Sten Olsson at the UMC.

Suspicious reporting (or is someone trying to fool us?)

In July last year *the UMC* received a regular batch of ADR reports from one of our European national centres. What was particular about this submission was the covering letter that stated "Please note that several of the attached reports refer to DRUG X, which is a generic product containing SUBSTANCE Y. We suppose that the reports may originate from the marketing strategy of the main competitor, the marketing authorization holder of the original product DRUG Z. We do not have any proof of our suspicions, but there are several hints for this".

For us this was a serious issue since we do not want to keep fraudulent case reports in our database. On the other hand we cannot dismiss reported cases submitted to us unless we know for sure that they are invalid. We looked at the suspicious case reports and noted that they described many serious conditions. Some contained free text statements such as "The patient was treated with the original product without problems before being switched to the generic". Since we could not confirm that the reported cases were invalid we chose to process them and to advise *the UMC* signal review team that they should be particularly alert to any potential signals relating to SUBSTANCE Y.

Five months after the batch of suspected fraudulent reports had been received at *the UMC*, the national subsidiary of the multinational company that is the marketing authorization holder of DRUG Z approached the custom services department of *the UMC* asking for a list of ADR reports of SUBSTANCE Y from this particular country. The printout of the search result should clearly distinguish between ADRs reported in association with DRUG X and DRUG Z. Since the staff of *the UMC* custom searches department were already sensitized to the suspicions about fraudulent reports regarding SUBSTANCE Y from this country they reacted to the inquiry and advised the national centre accordingly.

One month later we received a new batch of ADR reports from the same national centre. Again the covering letter mentioned the same suspicion as with the previous batch but also made the observation that the reporting rate had declined. With next submission it had decreased even further.

We still do not have any proof of reporting manipulation by the marketing authorization holder but we want to use this example to demonstrate that

- spontaneous reporting programmes are vulnerable to manipulation of reporting
- there is a need to be able to trace back the identity of each patient in order to rule out or verify cases of alleged fake reporting
- the example gives the impression that certain manufacturers may be prepared to manipulate spontaneous ADR reporting systems to create an impression of a safety advantage of their product
- pharmacovigilance centres at all levels, regionally, nationally or internationally, must be alert to signs of invalid reporting and to communicate suspicions of such cases to colleagues.

the UMC encouraged the national centre in this case to investigate the matter fully, as there seemed to be a potential of either a serious risk with a generic product or a serious problem of fake reporting. Further investigation proved difficult, however. The national centre tried to contact every doctor who sent a report but they were unwilling to provide the centre with any further information. Letters which were sent remained unanswered.

On checking the quality of DRUG X and DRUG Z they were both found to be of good quality. In the country in question there is no provision in the pharmaceutical law to allow a pharmacovigilance inspection to be performed, and in any case this would only reveal the situation inside the company. The national pharmacovigilance centre has no control over physicians' practice.

the UMC, responsible for the quality of the WHO database, does not wish to store invalid information. This case also makes us wonder if individuals or groups have tried to fool us in the past, and whether they succeeded. Other sponsors might have used more cunning and less transparent methods. Pharmacovigilance is about being alert!

VISITORS TO STORA TORGET

Our visitors from France



Julian Alescu and Cédric Bousquet

Terminology researchers from France

In March 2005, Cédric Bousquet and Julian Alecu visited *the* UMC. Cédric Bousquet is a pharmacist working part-time in the regional pharmacovigilance centre of Georges Pompidou European Hospital, Paris and he spends the rest of his working time doing research. "In December 2004 I presented my PhD thesis on integration of the adverse reaction terminologies in automated signal generation with Marie-Christine Jaulent, of the 'Institut national de la santé et de la recherche médicale' (INSERM) U729. Our group has a special interest in knowledge-based systems and medical terminologies."

Julian Alecu is a physician also working with Marie-Christine Jaulent, as a PhD student. "My main research interest is knowledge extraction from the UMLS (Unified Medical Language System). Developed by the National Library of Medicine, UMLS is a huge methathesaurus that links terms from over 100 controlled vocabularies including WHO Adverse Reaction Terminology and also provides semantic definitions of terms."

"We are working with *the* UMC in order to improve the WHO Adverse Reaction Terminology".

"We are working with *the* UMC in order to improve the WHO Adverse Reaction Terminology. WHO-ART can benefit from advanced features developed using artificial intelligence techniques to improve information retrieval, case selection for review and signal detection. The objectives are to provide formal definitions of WHO-ART terms in order to facilitate the addition of new terms, checking for possible inconsistencies and grouping of preferred terms.

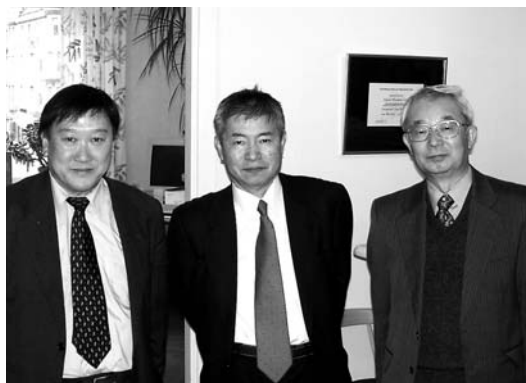
We were privileged to meet Cecilia Biriell and Andrew Bate to discuss the WHO-ART terminology; Jessica Nilsson for the handling of incoming case reports; Malin Nord for the WHO Drug Dictionary; Niklas Norén for Bayesian statistics; Malin Ståhl for triage logic; and Johanna Strandell for case selection and signal review. It was interesting and useful to see how a case report is processed, from its arrival at *the* UMC to the signal detection procedure. From these meetings we learned much about the specific terminological issues related to pharmacovigilance data.

We were happy to be invited by Sven Purbe to his house and enjoyed his impressive classical music collection digitally stored on his server. We also played a typically Swedish game 'inne bandy' ('floor-ball') with UMC staff."

Post-marketing surveillance in Japan

We were pleased to welcome three visitors from Japan in February. Masayuki Yokota, Yukio Kasahara (Manager, Accounting Section) and Akira Hamanaka (Chief, Technical Affairs) of the Japan Health Sciences Foundation came to *the* UMC to talk about the latest updates of the post-marketing surveillance system in Japan.

In 2003, 29,000 ADR reports had been submitted by health care professionals and manufacturers in Japan. Following legislation in 1997 (Post-marketing surveillance for re-examination of applications of new drugs) and 2002 (Revised Pharmaceutical Affairs Law), post-marketing safety measures 'Good Vigilance Practice' (GVP) will be enforced in April 2005. The GVP will allow for a responsible person for post-marketing surveillance management in every manufacturer, who will be accountable for collection, evaluation and analysis of ADR information, taking measures such as revision of precautions for use, as well as managing medical and pharmacy staff working in the front line of surveillance. Although independent of government, the Foundation, funded by member companies in Japan, undertakes research alongside universities and the Ministry of Health, Labour and Welfare.



Visitors from the Japan Health Sciences Foundation (left to right): Mr Akira Hamanaka, Dr Masayuki Yokota and Mr Yukio Kasahara

Accepted Scientific Names and Synonyms of Plants in Therapeutic Use

Mohamed Farah

The latest addition to the Uppsala Monitoring Centre's catalogue of publications to assist in promoting the safety of herbal medicines, contains a checklist of cross-referenced botanical accepted names, botanical synonyms, and vernacular names. These accepted botanical names have been assigned in collaboration with the Herbarium of the Royal Botanic Gardens at Kew in London. The reference lists of botanical synonyms and vernacular names for the accepted botanical names have been assigned in collaboration with the Department of Systematic Botany at Uppsala University.

Quality assurance in herbal medicine

An important aspect of quality assurance and signal detection in the field of herbal medicine is the use of a correct and accepted scientific name of the plants in question. Scientific plant names are an international language used by botanists worldwide for naming and describing plants. A scientific plant name has three parts: a genus name, a species epithet and an author's name (usually abbreviated). The genus name and the species epithet are in Latin.

The problem of nomenclature

A crude drug should be designated by the complete scientific plant name of the plant (including the author name) from which the crude drug is derived, followed by the English name (in singular form) of the plant part constituting the crude drug or preparation. The plant name should be written in italics (except the author name). However, in practice several different names are used for a crude drug.

Scientific names

Although plants don't change their habits, taxonomists occasionally change the scientific names of plants, causing confusion among non-professional plant people. Pharmacopoeias and herbal monographs often use different scientific names of the same plant and treat them differently.

Here is an example of seven names, all denoting the plant from which the crude drug 'squill' is obtained:

Drimia maritima (L.) Stearn
Scilla lanceolata Viviani
Scilla maritima L.
Squilla maritima (L.) Steinh.
Stellaris scilla Moench
Urginea maritima (L.) Baker
Urginea scilla Steinh.

The currently accepted name is *Drimia maritima* (L.) Stearn, but the other names are found in pharmacopoeias and handbooks and should therefore be regarded as synonyms. As herbal substance synonyms are used extensively, both in the form of other botanical names in Latin and as vernacular (common) names, the UMC produced a checklist linking synonyms to the accepted scientific plant names entered in the WHO Drug Dictionary.

Vernacular names

Herbal products often mention only the common names for the ingredients. For example, the common names True aloe (English) is found in *Lexicum Plantarum Medicinalium* and in Agriculture & Agri-Food Canada, and Echte aloe (German) is found in *Lexicum Plantarum Medicinalium* and in Pharmaceutical substance 14th edition; both these common names refer to *Aloe ferox* Mill. and *Aloe vera* (L.) Burm. f. Inconsistent orthography of vernacular names is another difficulty – the dictionary attempts to present correct or recognisable spelling for common names.

Herbal synonyms

The book is in three sections:

The dictionary of herbal synonyms – an alphabetical classification of plants by accepted botanical names, offering corresponding given botanical names and common or vernacular names.

Plus two reference lists:

botanical synonyms with the appropriate accepted scientific name, common or vernacular names (names used in commerce or by local consumers, including names of crude drugs derived from the plant in question), with the accepted scientific name.

Place of herbals in the WHO database

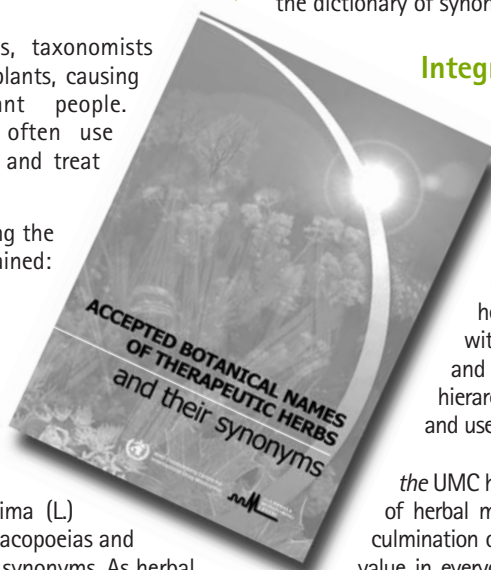
The WHO database of ADR reports from member countries of the WHO Programme for International Drug Monitoring uses the accepted botanical name for the plant in question, followed by the plant part (root, bark, leaf, etc) and type of preparation (water extract, tincture, etc). Only plant names occurring in the WHO database are included in the dictionary of synonyms.

Integration with the Herbal ATC Classification

Identifying synonyms is even more important given that the WHO uses the ATC (Anatomical Therapeutic Chemical) classification for classifying drugs and coding adverse reaction reports. The Herbal ATC Guidelines, which provide classification of many herbal medicines is updated regularly. It is used with the WHO Drug Dictionary to link to products and can be used in a pragmatic, transparent, hierarchical way in a computerised system to capture and use information of various degrees of precision.

the UMC has been working on the classification and safety of herbal medicines for many years, and this book is the culmination of that effort. We hope it will be of interest and value in everyday work and research and welcome reactions, comments and suggestions from professionals in the field.

Enquiries should be addressed to the UMC – see contacts on page 3.



NEW FACES AT *the* UMC

The process of strengthening of the support team for the UMC's Products and Services has been covered in recent editions of Uppsala Reports. Here we introduce six of our newest recruits to the Centre's work.

Björn Moberg Systems Developer, Production

Björn is a native of Uppsala and started working in IT in 1979 at *the* Uppsala Data Centre – while still studying at Uppsala University – and has been working with programming, system development and relational databases ever since. His main role at *the* UMC is to secure and improve the quality of WHO-DD production. Björn has two (sometimes) grown-up children. He says "I like to spend free time with my family and friends. In the winter mostly skiing and skating, and in summer outdoor activities like golf, swimming and fishing."

Anna Mattsson Drug Dictionary Services, Customer Support Services

Anna, 36 years old, is a BSc trained pharmacist and works with coding, and internal and external support of the WHO Drug Dictionary. "I graduated from Uppsala University last year, so this is my first 'real' job." However, she worked as a receptionist in an Uppsala hotel for ten years, as a waitress in a hotel in Switzerland, and as a nature guide in the Swedish archipelago. She has two children aged 5 and 6.

*From top:
Björn, Åsa, Nike, Kristina,
Johanna, Anna*



Kristina Johansson Database Services, Customer Support Services

Kristina is 24, and graduated from Uppsala University with an MSc Pharm in 2004. "I did my Master's thesis at *the* UMC on the e-mail discussion group Vigimed. Now I work with database services, mainly with searches in Vigibase for external customers." Her main hobby is Brazilian Jiu-jitsu, which she practice and competes in.

Johanna Eriksson Manager, Production and Customer Support Services

Johanna's work tasks include project management and quality assurance. In my previous employment she worked with drug dictionaries and related databases for the WHO, the Swedish Association of the Pharmaceutical Industry and the Swedish national drug compendia, both as system developer but foremost as project manager. "I'm married and have three children. When I'm not working or taking care of my family, I spend most of my spare time in the stable and horse riding."

Åsa Lindeberg Web Editor, Products & Services, Sales & Marketing

Åsa is Web coordinator for *the* UMC, a job that allows her to combine three of her main interests: "humans, technical things and information". She is currently working a lot on new layouts for the Product & Services website in combination with a more developed web shop and order handling processes. "In my spare time I like to photograph and to read, especially crime novels..."

Nike Meder Drug Dictionary Services, Customer Support Services

Nike is a pharmacist at *the* UMC, dealing with coding, and internal and external support of the WHO Drug Dictionary. Before joining *the* UMC she worked at pharmacy for two and a half years.

"I was born in May 1976 in Germany where I spent my childhood until my family moved to Uppsala seventeen years ago. As a child I liked to experiment in the kitchen baking and making desserts so before becoming a pharmacist I have an education as a pastry chef. Hopefully my parents and friends enjoy my biscuits more these days..."

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
12-13 May 2005	Compliance in Pharmacovigilance	London, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dstru.org
16-20 May 2005	Pharmacovigilance – principles and practice	Stockholm, Sweden	Karolinska Institute / EACPT / EMEA Fax: +46 8 585 810 50 E-mail: sissi.myllyniemi@karolinska.se
24 May 2005	Pharmacovigilance for support staff	London, UK	Management Forum Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 E-mail: info@management-forum.co.uk www.management-forum.co.uk
26 May 2005	Role of the Qualified Person in Pharmacovigilance	London, UK	Management Forum Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 E-mail: info@management-forum.co.uk www.management-forum.co.uk
27-28 May 2005	Current Controversies in Pharmacoepidemiology (60 year anniversary symposium)	Kolding, Denmark	Basic & Clinical Pharmacology & Toxicology E-mail: ghoppemouret@health.sdu.dk www.bcpt.dk
15-17 June 2005	Basic course in Pharmacovigilance	London, UK	Management Forum Tel: +44 (0)1483 570099 Fax: +44 (0)1483 536424 E-mail: info@management-forum.co.uk www.management-forum.co.uk
25-29 June 2005	EACPT 7th Congress – sessions on 'Clinical pharmacology and herbal medicine' and 'Pharmacovigilance' (in association with ISO-P)	Poznań, Poland	EACPT Tel: + 48 61 852 40 03 ext. 31, +48 61 852 73 10 Fax: + 48 61 852 74 72 or 63 E-mail: info@eacpt.pl www.eacpt.pl
26-29 June 2005	21st International Symposium on Drug Safety & Pharmacoepidemiology	Nice, France	Boston Collaborative Drug Surveillance Program Tel: +1 (781) 862 6660 Fax: +1 (781) 862 1680 E-mail: info@bcdsp.org www.bcdsp.org/symposium.html
26-30 June 2005	DIA 41st Annual Meeting	Washington DC, USA	DIA Fax: +1 215 442 6199 www.diahome.org
6-7 July 2005	Risk Benefit Assessment in Pharmacovigilance	Southampton, UK	DSRU Tel: +44 (0)23 8040 8621 Fax: +44 (0)23 8040 8605 E-mail: jan.phillips@dstru.org
21-24 August 2005	The 21st International Conference on Pharmacoepidemiology & Therapeutic Risk Management ISPE	Nashville Tennessee, USA	International Society for Pharmacoepidemiology Tel: +1 (301) 718 6500 Fax: +1 (301) 656 0989 E-mail: ispe@paimgmt.com
24-26 August 2005	Herbal medicine - analysis and identification	Canberra, Australia	TGA Training Co-ordinator PO Box 100, Woden, ACT 2606, Australia Fax: +61 2 6232 8469 E-mail: TGA.international@health.gov.au
2-3 September 2005	Pre-meeting on 'Information, Pharmacovigilance and Patient Safety' at <i>International Pharmaceutical Federation Congress</i>	Cairo, Egypt	FIP Congresses & Conferences Tel: +31-(0)70-302 1982/1981 Fax: +31-(0)70-302 1998/1999 E-mail: congress@fip.org www.fip.org
20-21 September 2005	Pharmacovigilance and Risk Management: 2006 and beyond	Brussels, Belgium	DIA Tel: +41 61 225 51 54 Fax: +41 61 225 51 52 E-mail: phyllis.suter@diaeurope.org
10-12 October 2005	Drug Safety Surveillance and Epidemiology Training Course	Washington DC, USA	DIA Fax: +1 215 442 6199 www.diahome.org
17-19 October 2005	ISO-P Annual Scientific Meeting	Manila, the Philippines	ISO-P Administration Tel/Fax: +44 (0)20 8286 1888 www.vasia.com/psecp/



the Uppsala Team

Director

Ralph Edwards, MB, ChB, FRCP (Lond), FRACP **Professor in Medicine, Director**

Science and Technology

Administration

Ali Bahceci **Network technician**

Cecilia Biriell, MSc Pharm **Senior Specialist, Head of Internal Affairs**

Anneli Lennartsson **Economy Assistant**

Marjatta Leván, BA **Manager**

Data Management & Systems Development

Bill Dagérus **Senior Systems Developer**

Stefan Lewenfalk **Systems Developer**

Annica Lundström, BSc Pharm **Data Management**

Jessica Nilsson, BSc Pharm **Programme Leader, Data Management**

Helena Sjöström **Pharmacist, Data Management (maternity leave)**

Magnus Wallberg, MSc Eng Phys **Manager**

Bo Östling **Senior Systems Developer**

External Affairs

Geoffrey Bowring, BA **External Affairs Co-ordinator**

Jenny Ericsson, BSc Pharm **Programme Leader, Traditional Medicines**

Mohamed Farah, Pharm D **Senior Specialist, Traditional Medicines**

Helena Fucik, BSc Pharm **Senior Specialist, External Affairs**

Anna Lindquist **Web Editor, External Affairs (on study leave)**

Sten Olsson, MSc Pharm **Manager, Head of External Affairs**

Research & Development

Andrew Bate, MA (Oxon), PhD (Umeå) **Manager**

Jonathan Edwards **Programme Leader, Data Mining Development**

Niklas Norén, MSc Eng Phys **Data Mining Research Engineer**

Sven Purbe, BA **Senior Specialist**

Malin Ståhl, MMedSc **Research & Development**

Erik Swahn, MA **Data Mining Developer**

Signal Detection & Analysis

William Frempong, BSc Pharm **Signal Detection & Analysis**

Anne Kiuru, MSc Pharm **Signal Detection & Analysis**

Monica Plöen, BSc Pharm **Manager (maternity leave)**

Kristina Star, Registered Nurse **Signal Detection & Analysis**

Johanna Strandell, MSc Pharm **Signal Detection & Analysis**

Marie Lindquist, Dr Med Sc **Deputy Director, General Manager**

Products and Services

Administration

Linda Wallin **Team Support**

Business & Product Development

Daniel von Sydow, MSc Pharm **Project Co-ordinator**

Annika Wallström **Product Manager**

Customer Support Services

Anna Blomquist, BSc Pharm **Drug Dictionary Services (on external placement)**

Kristina Johansson, MSc Pharm **Database Services**

Anna Mattsson, BSc Pharm **Drug Dictionary Services**

Nike Meder, Pharmacist **Drug Dictionary Services**

Malin Zaar Nord **Pharmacist, Programme Leader, Drug Dictionary Services**

Erica Walette, BSc Pharm **Programme Leader, Database Services**

Production

Johanna Eriksson **Manager**

Björn Moberg **Systems Developer**

Lars Magnusson **General Manager, Products & Services**

Sales & Marketing

Hannah Ericson **Sales and Marketing Assistant**

Inger Forsell **Sales and Customer Relations Executive**

Katarina Hansson **Sales and Marketing Assistant**

Åsa Lindeberg **Web Editor, Products & Services**

Mats Persson, BA **Manager, Business Development**



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