

Uppsala Reports 22

UPPSALA REPORTS APRIL 2003

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

*the UMC to work with Roll
Back Malaria Programme*

The Thai regional
pharmacovigilance system

News from Norway, Canada,
Jordan, Serbia, Ukraine

Herbals projects in the UK

Vigilance of women's health

Profile of Jan Venulet



DIRECTOR'S MESSAGE



Shortly after writing this message, I shall be setting off for my first visit to the Indian Society of Pharmacovigilance for its annual meeting, in Delhi at the beginning of March. A small and dedicated band of committed doctors and academics are working hard to raise the profile of drug safety in that vast country, and I am very happy to offer what support I can and to learn how we may help.

We're a very small group here at *the* UMC – even though we are still growing – and I feel we often cannot give the time and resources to member countries that they want and is due to them. That's true also of our external communications – not least finding out what members want from us – which sometimes suffer through pressure of internal priorities, particularly the development of new projects.

But our preoccupation does deliver results: I hope you will all be aware of the new database (Vigibase) which brings us up to the very best scientific and regulatory standards in drug safety reporting and analysis; and of the Vigibase-online software, (described in Uppsala Reports 21), which offers National Centres a new and streamlined reporting system for their countries and their communications with us. Both of these have occupied the team here for many months.

A further important potential concerns the WHO Drug Dictionary: it has been suggested that it could possibly be adopted for international use as part of the International Conference on Harmonization (ICH) package. This would bring the Dictionary the status which its long-established authority and utility surely deserve. This is something about which we need your comments and advice: how can we make the WHO Drug Dictionary even more useful to you?

We have started an active campaign of contact with users of the Dictionary to learn what they want: market research, user groups and an already active email discussion group, are among our plans (see page 19 for the contacts you can use). Do please let us know your views!

I'm being asked to travel to more and more meetings and events, and while I do love the stimulation and pleasure of meeting colleagues all over the world, I have to remember my responsibilities here in Sweden too! We're setting up teleconferencing facilities to try a bridge the gap a little and I have just bought my first tablet PC which I hope will improve the efficiency of my mobile communications. Do complain if you're not getting what you want from us: we'll do our very best to respond positively.

A handwritten signature in black ink that reads "Ralph Edwards". The signature is written in a cursive style and is positioned above a horizontal line.

Ralph Edwards

Director
the Uppsala Monitoring Centre

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Looking forward to Delhi

The 26th Annual Meeting of Representatives of National Centres taking part in the WHO International Drug Monitoring Programme will be held at the Grand Hyatt Hotel in New Delhi, 8 - 10 December, 2003. National Centres can expect to receive an official invitation very soon from WHO, Geneva. *the UMC* will be

canvassing views on National Centre preferences regarding the meeting agenda. Professor S.K Gupta at All Indian Institute for Medical Sciences will provide suggestions for accommodation at various budget levels.

References

¹ Mishell DR. Intrauterine devices: mechanisms of action, safety and efficacy. *Contraception* 1998; 58: 45S-53S

² Harrison-Woolrych ML, Ashton J and Coulter D. Insertion of the Multiload Cu375 intrauterine device; experience in over 16,000 New Zealand women. *Contraception* 2002; 66: 387-391

³ Harrison-Woolrych ML, Ashton J and Coulter D. Uterine perforation on intrauterine device insertion: is the incidence higher than previously reported? *Contraception* 2003; 67: 53-56

⁴ Harrison-Woolrych ML, and Woolley J. Progestogen-only emergency contraception and ectopic pregnancy. *Journal of Family Planning and Reproductive Health Care* 2003; 29 (1): 5-6

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Safety of Medicines for Women

Report from the New Zealand Pharmacovigilance Centre

Dr Mira Harrison-Woolrych BM DM MRCOG DFFP

During the last year the New Zealand Pharmacovigilance Centre has developed a special interest in studying the safety of medicines used by women. Recent work has focussed on contraceptive products, in particular intrauterine devices (IUDs) and emergency contraception.

Studies of Intrauterine Devices

IUDs are reported to be the most widely used reversible method of contraception in the world⁽¹⁾. The New Zealand Intensive Medicines Monitoring Programme (IMMP) has collected post-marketing data on two IUDs since 1991. For the copper IUD Multiload Cu375, the IMMP cohort includes 17,469 insertions in over 16,000 women - which is thought to be the largest cohort for any one IUD in the world. Using these data we have completed two studies which have recently been published in an international journal^(2,3).

The first study was a detailed analysis of the insertion procedure for Multiload Cu375⁽¹⁾. Problems fitting the device (for example failed or difficult insertion) occurred at a low rate - about 2% of all insertions. More difficulties were reported for insertions in nulliparous (never had children) women (3.9%) compared to parous women (1.95%) and when the inserting doctor performed few insertions. Adverse reactions occurring at the time of insertion (for example pain, bleeding or vaso-vagal episode) were reported in 1.2% of all insertions. Again, nulliparous women had a greater risk of adverse reactions - 3.5% compared with 1.1% in parous women, but the overall incidence of problems was considered to be acceptably low.

The second study was performed to determine the rate of uterine perforation on IUD insertion in 'real-life' clinical use⁽²⁾. Analysis of the IMMP database identified 28 reports suggesting uterine perforation in 17,469 insertions (1.6 per 1000 insertions). This rate is higher than previously reported (less than 1 per 1000 insertions) which might be due to the longer follow-up period, larger cohort and/or the inclusion of both complete and partial uterine perforations in this study.

Progestogen-only emergency contraception and ectopic pregnancy

At the time of licensing the progestogen-only emergency contraceptive pill in NZ, the UK and the

USA, there were no reports of ectopic pregnancy associated with this product in the clinical trials nor in the WHO database. However, within two years of marketing, three cases of ectopic pregnancy following use of the progestogen-only emergency pill were reported to the New Zealand Centre for Adverse Reactions Monitoring (CARM). We collaborated with the UK Medicines Control Agency, which had received 12 spontaneous reports of this adverse event and assessments were presented to advisory committees in both countries⁽⁴⁾. As a result, product information was checked (and strengthened where appropriate) for both the prescription-only and pharmacy emergency contraceptive pills. An editorial summarising our assessment was published in January this year⁽⁴⁾.

Further Work Planned

Following on from the work described here, we intend to broaden our scope to study other aspects of medicines used by women. We have several projects for which we are currently trying to raise funding, including gender differences in adverse reactions to medicines and the safety of medicines taken in pregnancy. Ultimately, if appropriate resources can be found, we would like to appoint a specialist position in the safety of medicines in women. International collaboration is important and we would welcome hearing from other centres that have a special interest in this area of pharmacovigilance.

Roll Back Malaria and WHO Programme link up!

Transforming the anti-malarial regime

Because of the wide-spread and increasing resistance in Africa to the commonly used drugs chloroquine and sulfadoxine-pyrimethamine (S/P), many African countries are in the process of revising their anti-malaria policy. The revisions are supported by the WHO Roll Back Malaria (RBM) programme. They include introducing artemisinin derivatives (artemether or artesunate) in combination with either halofantrine, S/P or amodiaquine as first or second line treatment of uncomplicated malaria. However, since artemisinin derivatives have not been used in public health programmes in an African setting before, there is a need to study the safety of the new medicines as they are introduced in large populations. Many donors, including the 'Global Fund' supporting the introduction of the new, effective but more expensive new medicines, require that their safety be studied in the exposed populations. However, many African countries do not have national pharmacovigilance systems in place.

Collaborators in attendance

The WHO Roll-Back Malaria Programme, the Quality and Safety; Medicines department and *the* UMC organized a first pharmacovigilance training course in Lusaka, Zambia, 23 March - 2 April for Burundi, Democratic Republic of Congo, Mozambique, Zanzibar and Zambia. Each country was represented by a manager of the malaria control programme and of the drug regulatory authority (see group photo). The main tutors were Sten Olsson (*the* UMC), David Coulter (New Zealand) and Ushma Mehta (South Africa). Alex Doodoo (Ghana), Mary Couper (QSM/WHO) and Andrea Bosman (Medical Officer, RBM) served as very important facilitators.

Planning for event monitoring

The course covered basic pharmacovigilance concepts and methods. The feasibility of carrying out cohort event reporting in addition to spontaneous reporting was discussed. Methods of involving health workers at all levels of the health care system were considered. Course participants were trained in working with media in communicating important messages and educating the public. Each participating country developed a guide and an action plan for implementation of the pharmacovigilance system. The first priority is to establish a system for the monitoring of anti-malaria drugs but once the structures and reporting lines are

established, other drug-related events associated with other medicines may also be studied. It is envisaged that other public health programmes e.g. those for the treatment of HIV/Aids and tuberculosis, also in the process of introducing new medicines in the public sector, will use the same system for drug safety monitoring.

Dr Oscar Simooya, a Zambian clinical pharmacologist, has been attached to WHO as a temporary consultant to support and document progress made in the early phases of the establishment of pharmacovigilance in the countries involved.

the UMC will be collecting adverse reaction case reports from the new centres which will be using the Vigibase on-line case management system (see Uppsala Reports 21) for recording of case information. *the* UMC will also provide other kinds of technical support, as to all other emerging pharmacovigilance centres.

Resources

For more information on the Global Fund and Roll Back Malaria, see the following sections of the WHO website:

www.who.int/global_fund/en/

www.who.int/health_topics/malaria/en/



From left to right - Salhiya Muhsin (Zanzibar), Christine Manyando (Zambia), Celestin Nsibu (DR Congo), Oscar Simooya (Zambia), Abdullah Ali (Zanzibar), Mary Couper (WHO), Alex Doodoo (Ghana), Esperança Sevene (Mozambique), Caesar Mudondo (Zambia), Alda Mariano (Mozambique), Andrea Bosman (WHO), Dorothy Shamatutu (Zambia), Lidia Mendes (Mozambique), Kwame Atuah (UK), Jérôme Ndaruhutse (Burundi), Frank Kanumpepa (DR Congo), Fred Masaninga (Zambia), Sten Olsson (UMC), David Coulter (New Zealand), Liévin Mizero (Burundi).

Report from

O. Stefanov,
M. Sharayeva,
V. Jajtchenja.

First results in Ukraine

Founded in 1996

The National Pharmacological Centre of Ukraine started to create a pharmacovigilance system in 1996, and has been operating on a regular basis since 2000. Our system aims to establish and develop a national drug safety and efficacy control system that covers all medicines, either submitted for official registration (pre-marketing control) or already on the market and widely used in medical practice (post-marketing surveillance).

A sound legal basis

The focus of the National Pharmacological Centre's activity is ensuring the quality of medicinal products in Ukraine and reaching conformity of national legal documents with WHO recommendations and directives of the European Union.

Our pharmacovigilance legislation is based on:

- Ukrainian Law 'On Medicinal Products' (1996)
- ICH Guidelines
- EEC Directives 75/318, 85/870, 93/39
- Orders of Ministry of Health of Ukraine (N375, N51, N292, N497)

Roles and responsibilities

The Pharmacovigilance Department provides regulatory services (in collaboration with the Inspection of Drugs Quality) that include data collection and analysis, database management, publication and dissemination of educational materials, and international contacts, issuing recommendations for physicians, investigators, manufacturers, as well as proposals to the Ministry of Health of Ukraine for taking appropriate measures and decisions (figure 1).

Physicians are requested to submit to the Pharmacovigilance Centre information about any ADR, using special forms: for any suspected serious or unexpected ADR within 48 hours, and for spontaneous cases of ADRs within 15 days. The responsibilities of ADR reporting by health care settings are placed on regional principal medical specialists. The Region Health Administration provide information about collection of cases of ADRs in health care settings, as well as requiring physicians to register ADRs as concurrent diseases or complications to be included in primary documentation, hospital records, case history, and the patient's discharge card.

The Medical Statistics Centre of Ukraine collates branch statistical reports from annual submissions by all health care settings.

After much preparation, we accepted the framework, definitions and methodology of spontaneous ADR reporting, set up our database, and obtained about 1,500 ADRs occurring in medicinal use and more than one hundred ADRs from clinical trials.

Joining the WHO Programme

In June 2002, Ukraine fulfilled the requirements of the WHO Programme for International Drug Monitoring, and became its 68th member country. The number of case reports of suspected ADR are shown in figure 2. The increases in reporting for 2000 and 2002 were due to the setting-up of the legislative and administrative system, conferences being organised, and staff being given responsibility for pharmacovigilance in different regions. Of 1,489 case reports of patients with suspected ADRs, almost all the reports concern hospital patients (figure 3). Almost half of all ADR case reports concerned domestic medicinal products, such as hyperpyrexia, and local reactions were more frequently reported with domestic drugs. This presumably reflects widespread use of generic drugs with substandard pharmaceutical quality. Generics should meet the requirements of quality, efficacy and safety, but few domestic producers in Ukraine have GMP certificates.

Involving people

We are involving physicians in a more active way to stimulate the reporting of ADR. Reasons for our current level of reporting include:

- Lack of awareness by physicians of the pharmacovigilance centre and the need to report
- Lack of commitment and motivation
- Lack of information regarding ADRs
- Absence of clinical pharmacists
- Lack of commitment of pharmaceutical companies to pharmacovigilance.

We envisage increasing the reporting of ADRs by the further development of a network of regional pharmacovigilance centres, more active involvement of medical practitioners, improving drug regulation, and the feedback of information, through setting up an appropriate legislative, administrative and educational system. The ultimate goal is to foster rational and safe drug use and to improve the quality of pharmacotherapy in Ukraine.

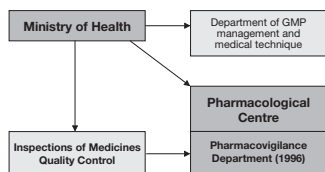


Figure 1

Regulatory bodies for medicinal products

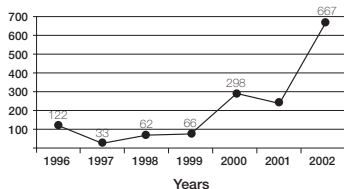


Figure 2

Annual numbers of case reports in Ukraine (1996-2002)

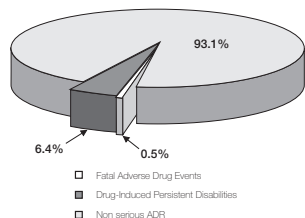


Figure 3

ADRs reports in hospitalised patients (1996-2002)



Marina Sharayeva

JPC takes off

Three Centre Structure

The Jordanian Pharmacovigilance Centre (JPC) was established at the beginning of 2001 and consists of three offices. The main central office is part of the information and follow-up department, in turn part of the Drug Directorate at the Ministry of Health (MOH). The other two subsidiary offices are at Jordan University Hospital (JUH) in Amman, and King Abdalla University Hospital in Irbid.

JPC's offices are equipped with hardware and software which serve the handling and analysing of ADR data. The three offices are connected via an on-line network. 'Wisperlite' program is used as software to enter data of ADR spontaneous reports.

Our seven member team at JPC consists of five pharmacists and two physicians. One of the pharmacists (the writer of this text) holds a MSc in Pharmaceutical Technology and the other a MSc in Clinical Pharmacy.

Training and Reporting

Our team has been trained in pharmacovigilance by participating in local and international training courses, workshops, meetings and conferences. We have participated in WHO meetings in Dunedin and Amsterdam and the TGA/UMC training course in Canberra. One of our team has been admitted to participate in the 8th UMC pharmacovigilance training course in Uppsala in May 2003.

The responsibility of the Members of JPC team working in the two subsidiary offices is to review spontaneous reports sent to them. They contact reporters to ask for missed information, then send these reports to the main office by using the case management system Wisperlite on-line. In the main office reports are reviewed again by our team, by comparing them with hard copies provided by the companies. These reports are e-mailed to the UMC every 3 months. Following that our team in the main office prepare collective reports as a result of these data, which are raised in the committee for the evaluation of drug safety.

Communications

From JPC we have prepared and distributed ADR report forms and promotional posters directed at physicians and patients. In addition we have established a library containing essential books and references relevant to ADRs. We are also promoting the concept of pharmacovigilance to the public and to health professionals by giving lectures in hospitals and health

centres. We are also going to present lectures to school children, and are planning to publish brochures to promote pharmacovigilance principles.

We have already established ADRs monitoring guidelines, to be approved by the Minister of Health this year. After that, it will be a matter of time for local drug manufacturers and drug distributors to commit to implement these guidelines in order to jointly achieve our mission in drug safety.

Two months ago the Drug Directorate launched its web site (www.Drugdirect.gov.jo) through which the JPC publishes important alert letters, recalls and safety information that can be easily accessed by anybody (Arabic and English).

Our enrolment in the WHO Programme for International Drug Monitoring (as its 70th member) is considered the greatest achievement of MOH.

The MOH is in the process of reorganizing its organizational structure including the Drug Directorate through which the JPC will be a separate department. This will be a very promising step for pharmacovigilance in Jordan.

Report from Nancy Ghaboun,
Head of Jordanian
Pharmacovigilance Centre



More information

To receive the Canadian Adverse Reaction Newsletter and health product Advisories free by email, join Health Canada's Health_Prod_Info electronic mailing list. Go to www.hc-sc.gc.ca/hpb-dgps/therapeut/htmleng/adr.html and click Asubscribe@.

In addition you can explore adverse reaction information on the site, including:

- Advisories for health professionals and consumers;
- Guidelines for the voluntary reporting of adverse drug reactions by health professionals and mandatory reporting guidelines for industry;
- The Canadian Adverse Reaction Newsletter;
- Forms for reporting suspected adverse reactions;
- Fact Sheets, including 'How Adverse Reaction Information on Health Products is Used'.

Contact information for MHPD is:

Marketed Health Products Directorate
Health Products and Food Branch
Health Canada
Room D-162, 1st Floor,
Finance Building
Tunney's Pasture, A.L. 0201C1
Ottawa, Ontario K1A 1B9

Telephone: +1 613-954-6522
Fax: +1 613-952-7738

E-mail: MHPD_DPSC@hc-sc.gc.ca



Dr. Christopher Turner, Acting Director General, Marketed Health Products Directorate

Post-marketing surveillance at Health Canada – Santé Canada

Health Canada created the Marketed Health Products Directorate (MHPD) on April 1, 2002. The creation of MHPD established an organization with responsibilities focussed entirely on post-market surveillance. MHPD assures the consistent coordination of safety surveillance, assessment and risk communication activities of all marketed health products in Canada.

Aims

- Monitoring marketed health product safety data, such as adverse reaction reports, evaluating product effectiveness, conducting risk/benefit assessments and recommending appropriate regulatory action when problems are identified.
- Having greater access to Canadian and foreign adverse reaction information through national and international collaborations, and increased use of expert scientific advice and consumer input.
- Partnering with others to promote adverse reaction reporting, study product effectiveness, and communicate to health professionals and the public. Providing policies to effectively regulate marketed health products and advertising.
- Disseminating risk related information to health professionals and the public through the Canadian Adverse Reaction Newsletter, health product Advisories, the Health_Prod_Info electronic mailing list, Health Canada's website, and other means.

Activities

The MHPD is expanding its range of activities for post-approval surveillance and assessment of all marketed health products (pharmaceuticals, biologicals, vaccines, medical devices natural health products, radiopharmaceuticals, veterinary drug products).

The MHPD coordinates the response to marketed health product safety matters by conducting a range of activities to:

- Increase the quantity and improve the quality and timeliness of post-approval information collected and assessed, placing greater emphasis on health outcomes research and product effectiveness. Included is an expansion of regulation of health product advertising.
- Enhance the current passive data collection by making it easier for the public and health care

professionals to report drug safety and effectiveness information and by initiating more active surveillance activities in clinics and hospitals. Increased use of Regional Adverse Reaction Centres located across Canada is planned as part of this activity.

- Strengthen methods to assess risks and benefits of marketed products and take appropriate actions in a timely manner.
- Promote informed use of products and communicate product related risks to consumers, health care professionals and others.
- Improve access to information on the safety and effectiveness of marketed regulated health products to facilitate Health Canada regulatory decisions and Federal Provincial Territorial decisions through the common drug review for drug benefit plan formulary listings.

Workforce and structure

The current workforce of MHPD is approximately 55 scientific staff and 17 support staff, with Dr Christopher Turner as Director General.

The MHPD consists of the following Divisions:

- Marketed Health Products Safety and Effectiveness Information (Monitoring of adverse reactions and medication incidents, detection of health product safety signals)
- Active Surveillance, Research and Development, Product Utilization and Effectiveness
- Operations and Policy (Policy and Regulatory Affairs, Advertising and Risk Communication, Planning and Quality, Management Services)
- Product Assessment Divisions (Assessment of risks and benefits, Appropriate actions)
- Marketed Pharmaceuticals
- Marketed Biologicals and Biotechnology Products
- Marketed Natural Health Products
- Marketed Medical Devices.



Promotion of the MHPD at Family Medicine Forum, Montreal. From left: Ann Sztuke-Fournier, Susie Dallaire, (Advertising and Risk Communications), Dr Mano Murty, Medical Evaluator, Marketed Pharmaceuticals Division, Geneviève Létourneau, Quebec Regional Centre

Establishing regional centres in Norway

Harald Lislevand
Scientist, Norwegian National Pharmacovigilance Centre

History – appraisal

For more than 30 years, the spontaneous reporting system in Norway has been based on reporting of ADRs from physicians and dentists directly to the Norwegian Medicines Agency (NOMA) in Oslo. The organisation of this reporting system is not considered optimal, as the distance from the reporters to the NOMA is too far. Additionally, the data handling and assessment of the individual reports at the agency has been time consuming, taking resources needed for signal generation.

We also believe that reporting an ADR should be of value not only for the receiver, but also for the reporter. Our policy is therefore to provide the reporter with feedback so that, if possible, similar ADRs can be prevented in the future. Feedback is also considered useful in order to increase the awareness of the importance of spontaneous reporting of ADRs. Establishing local contact points in the reporter's own regions and clinical settings is considered to reduce the threshold to report ADRs.

Regionalisation

We therefore decided to establish five regional pharmacovigilance centres. Each centre is located at a regional drug information centre (RELIS), which is situated in the major hospital in the five health regions in Norway. The employees at these centres are experienced in working with questions from health professionals regarding ADRs.

Since January 1st 2003, the physicians and dentists are to report ADRs directly to the regional centre in the health region where they reside. The regional pharmacovigilance centres enter all the data from the reports in a local database, assess the cases individually and give feedback to the reporters. This also includes requests for additional information regarding the cases. The reports are transmitted electronically to the NOMA, where they are automatically loaded into the national ADR database. All papers and electronically data relating to an ADR case are transferred to the NOMA, so that there exist no local files. If necessary, the regional centres can easily retrieve the ADR reports electronically from the NOMA for further assessment and entry of follow up information. The reports generated in their local data entry tools comply with the ICH E2B/M1/M2 standards for the electronic transfer of individual

case safety reports. Reports from the pharmaceutical industry are still handled at the national agency.

Better communication, research

We anticipate that decentralisation of the spontaneous reporting system will improve feedback to the reporters. This and local education of health professionals and pharmacovigilance projects, will most likely contribute to better reporting, both in terms of quantity and quality. On a longer perspective, it is anticipated that decentralisation will also initiate research within the pharmacovigilance area.

The transfer of responsibility to the regional centres will release resources at the NOMA to perform pharmacovigilance activities on a higher level, both nationally and internationally. This includes improved signal generation, signal evaluation and risk communication. Additionally, when the initial phase of the decentralisation of the pharmacovigilance reporting system is over, a project of establishing reporting of ADRs from pharmacists will be initiated.

New translations

New Chinese translation of WHO Adverse Reaction Terminology

WHO-ART has been translated into Chinese. The publication will be available after April 2003. The first print-run of is 2,000 copies, and a CD-ROM is included with each book. The retail price is RMB 92.00.

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A Portuguese edition of 'The Importance of Pharmacovigilance' is being planned by WHO. The original English version is still available on application to either the Essential Drugs and Medicines Division, WHO, Geneva or the UMC.

Feature by Bruce Hugman

In the 20 years since it was set up by the Ministry of Health, the Thai national pharmacovigilance programme has become one of the most active and productive in the WHO Programme and has the potential to achieve even more in years to come.

Thailand has seen a remarkable growth in the number of reports received annually. From 170 reports in 1983, the launch year of the National ADR Monitoring Centre (NADRM), the annual total has risen to nearly 13,000 in 2002 (see Figure 1).

In 1997 the responsibilities of the NADRM were broadened to include all health products, and it was renamed the Adverse Product Reaction Monitoring Centre (APRMC). As well as drugs, the brief now included narcotics, psychotropic substances, foods, cosmetics, medical devices and toxic substances. These products generated 927 reports 1997–2002.

The year after starting its national programme, Thailand became the 26th member of the WHO Programme for International Drug Monitoring. It has maintained a high position in the table of numbers of reports per country submitted to WHO.



Traditional Medicines on sale in northern Thailand

Two Decades of Development in Thailand

Out to the Regions

From the beginning, an effective national reporting network has been a priority. In 1992 nineteen ADR reporting centres were established in regional tertiary hospitals, and the figure is currently twenty-three. Thailand is one of twelve countries in the WHO Programme with a de-centralised system, firmly believing that only pro-active local management will stimulate and develop a successful reporting culture.

The national programme is managed by the Technical and Policy Administration Division of the Food and Drug Administration (FDA) where all reports are sent, though many may be subject to local action in the meantime. Reports of serious events are sent to the FDA immediately.

New Drugs

While the main national scheme depends on spontaneous reporting for its data, the Safety Monitoring Programme (SMP) is a separate, more systematic scheme for monitoring newly-registered drugs for their two-year conditional-approval period. Other priorities of SMP are serious, non-labelled and unexpected ADRs.

Communications

- A quarterly publication, The Medical and Health Product Bulletin, is issued to circulate the latest information about product knowledge and hazards, including a case-study column and regulatory information
- APR Newsletter distributed to all healthcare personnel, especially dealing with serious or emergency ADR issues
- Alerts communicated to doctors and pharmacists and professional associations

- A manual describing the work of the APRMC
 - A variety of leaflets and a training video
 - Annual report of the previous year's reporting.
- Reporters receive a postcard acknowledgement from the national or regional centre.

Outcomes

The APRMC manual reports that:

The adverse events reported are mostly known, not serious and self-limiting after stopping the medication or receiving the treatment.

The challenges for Thailand – as for many other countries – are:

- to increase clinical awareness and diagnosis of ADRs of system-organ classes other than skin
- to encourage reporting of all suspected associations, where causality is by no means certain
- to focus greater attention on reactions which are serious and/or unexpected
- to establish a culture in which recognition and reporting of ADRs is an essential element in all clinical practice, in which doctors understand the contribution they make to patient welfare in general.

Thailand appears to have been very successful in using the data available to limit or prevent the occurrence of repetitive known and minor adverse reactions from particular medicines. But doctors do not all understand the objectives of the ADR monitoring programme and many do not believe there is any benefit to their reporting new ADRs. Many are afraid that acknowledging ADRs will lead to criticism or even litigation and notification of pharmacists (the recommended route for reporting) rarely happens. Many clinicians are probably mainly focused on disease and much less on pharmacology, leading to a lower likelihood of recognition of drug-related problems. An account of some of the action taken on the basis of reports appears in Table 1.

Pharmacists, however, are beginning to see that there is an important role for them, and that in taking some responsibility for ADR monitoring and management they can move towards greater involvement in clinical and pharmaceutical care.

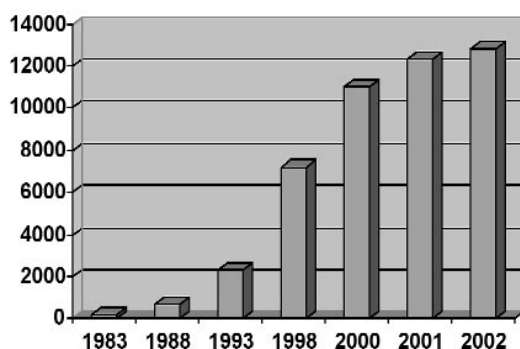


Figure 1: Reports received by Thai APRMC 1983–2002

International hospitality

As well as being an active contributing member of the WHO Programme, Thailand hosted the annual meeting of member countries in Bangkok in 1995 and made a lasting impression on the participants of the generosity and elegance of Thai people and the professionalism of Thai ADR Monitoring.

While preparing this article, the annual meeting of APRMC was taking place in Bangkok (5–6 February). Many more than the 350 attendees were present. National experts and international guests contributed to a wide-ranging and lively programme.

For the Future

Thailand has shown a very strong commitment to pharmacovigilance in the last twenty years, and clearly has the basis of a highly successful programme in place. Many new developments are planned, including internet ADR reporting, already in its pilot stage. Further development in signal detection skills is high on the team's agenda.

Khun Pornpit Silkavute, Director of the Centre at the

time this article was prepared, told Uppsala Reports, that the Thai vision was to achieve "world class best practice in pharmacovigilance and toxicovigilance for health-related products." You really can't aim higher than that!

Adverse Reactions in the North

The ADR Monitoring Centre for the provinces of Chiang Rai and Phayao, in the northernmost part of Thailand, is located in the Chiang Rai Regional Hospital.

Primary healthcare in Thailand is largely delivered through the outpatient departments of hospitals. Patients pay 30 Thai baht (about 75 cents US) for whatever treatment or drugs they require. In this 800-bed hospital, between 800 and 1000 outpatients are seen every day. There is a total staff of 1500, including 25 pharmacists. As in many centres in many countries, ADR staff here face the challenge of convincing busy doctors and pharmacists that ADR reporting is important and should be given some priority.

Last year, the centre received 633 reports from the 28 hospitals in the two provinces (a population of 1.95m). The majority of these were relatively minor, such as allergic skin reactions. There were no reports of drug-related deaths, and only two or three a month of more serious reactions, such as Stevens-Johnson syndrome, associated with use of the antiretrovirals cotrimoxazole or nevirapine in HIV patients.

ADR staff in Thailand



Pornpit Sikavute, now Director, Hazardous Substance Control Group, Bureau of Cosmetic and Hazardous Substance Control, Thai Food and Drug Administration,



Many readers may remember Suboonya Hutangkabadee (third from left) from National Centres annual meetings; now she is one of the three Deputy General Secretaries of the FDA. Here she is with colleagues (left to right), APRMC Chief Wimon Suwankesawong, Nipaporn Jaiyawat (Director of Public and Consumer Affairs Division) and APRMC pharmacist Yaowares Oppamayun.

Risk Management

Withdrawal of manufacturing of sample rabies vaccine of the Thai Red Cross due to serious adverse effects

Withdrawal of the single active formulation of Keelek (Cassia siamea L.)

Reclassification of cisapride from pharmacy-only to controlled drug (prescription) to be used in hospitals only and restricting indications for the treatment of gastroesophageal reflux disease (GERD) after ADR monitoring indicated inappropriate use of drug, especially in high-risk patients or in combination with other interacting drugs

Label warnings about propylthiouracil (PTU) induced agranulocytosis and visual problems after ethambutol administration

Epidemiological Investigations

Superficial punctate keratitis (SPK) induced by ophthalmic agents (3 reports from one hospital)

Phlebitis and adverse reaction associated with injection site adaptor (10 reports from one hospital relating to one company's product)

Adverse reactions to rabies vaccine; 10 reports from one hospital

Research

Post-registration surveillance of the artemesin derivatives used operationally in Thailand

Study of drug-induced Stevens-Johnson syndrome

Incidence of ADRs in hospitalised patients: a prospective observational study in 21 selected Thai hospitals



The team running the national Adverse Product Reaction Monitoring Centre in Bangkok: (back row) pharmacists: Yaowares Oppamayun, Pakawadee Sripirom, Wimon Suwankesawong (APRMC Chief), Chonladee Puthasuwan, Wanida Kaewpankrungsri, Uma Chaiyapa; (front) support role, data-input team: Amnuay Suwannachai, Withaya Prachachalerm

Table 1: Sample outcomes and activities within the Thai APR Monitoring Programme

NEWS FROM AROUND THE WORLD

Chiang Rai Regional Centre



Khun Nipaporn Boonsaruxapong, Chief Pharmacist (front row left), with ADR manager Premjit Jariyapongpaiboon (behind) and pharmacist colleagues from one of the satellite dispensaries, Waraporn Sookpromsan and Prajuab Wongmaneerodin. (At the back is a fax machine on which doctors' prescriptions arrive). Responsible for the Province's ADR monitoring, Premjit Jariyapongpaiboon has first and master's degrees in pharmacy. ADR monitoring is her primary job, but, like all pharmacists, she has other duties, particularly in managing the hospital pharmacy service.



The healthcare team on the medical ward is said to have good inter-disciplinary communications and good measures for prevention of drug-related problems.



Satellite dispensing - the pharmacy team responsible for paediatric and gynaecological dispensing. Utaiwan Kanta, Parinya Suwanprapa, Chittima Buranont

Under control or under-reported?

Chief Pharmacist Khun Nipaporn Boonsaruxapong runs a very tight ship, with exemplary management, preventive and quality control processes evident in all departments. The Pharmacy Department, for example, has a standard of 15 minutes maximum waiting time for patients to receive their drugs.

All infusions for paediatric use are prepared in the pharmacy, as are all cytotoxic drugs, rather than on the ward. ADRs are logged on patient records available on the hospital LAN/intranet to all medical personnel. Patients experiencing ADRs are screened for allergies and are given an ADR alert card which they can show should they seek treatment elsewhere. Pharmacists are instructed to ask all patients if they have any history of ADRs. New drugs to the hospital are intensively monitored, along with those specified in the national Safety Monitoring Programme.

In 2002, the Pharmacy Department undertook a project to test whether there was under-reporting of ADRs in the hospital. For thirty-five days, they monitored every patient in one medical ward, recording all suspected ADRs. 1021 patients came within the scope of the project, and 41 ADRs were identified, including 12 skin reactions and 29

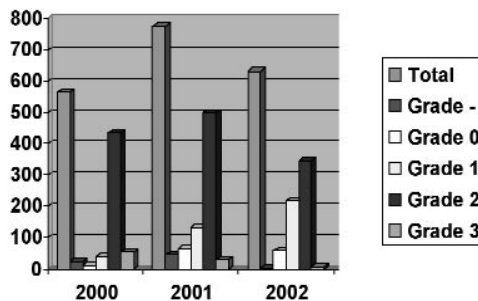


Figure 2:

Numbers of ADR reports in the Chiang Rai and Phayao Provinces 2000-2003, graded by quality. (Grade - fails the WHO criteria for submission to the international database; Grade 3 represents the most complete data, including information about rechallenge. There is a reduction of reports assessed as Grade -, an increase in those assessed as Grade 1 and 2; Grade 3s have fallen, as have overall numbers. But does this result from fewer actual ADRs (possibly because of successful preventive measures), or just lower reporting?

systemic reactions. This compared with 10 spontaneous reports from the medical team for the same group of patients, with a number of further ADRs recorded on patient notes but not reported.

So, are these provinces fine examples of the rational use of drugs and the effective prevention of ADRs through multi-disciplinary team work and allergy-screening, or are ADRs slipping through the net?

Future challenges

The pharmacist responsible for ADR monitoring at the regional centre, Khun Premjit Jariyapongpaiboon, believes that both are true. For her, the next challenge is to raise awareness of systemic ADRs and the importance of diagnosing and reporting them.

However, doctors and pharmacists are at the limits of capacity in such busy hospitals; pharmacists in the ADR network change jobs quite frequently, so there is difficulty in building a core of ADR expertise; and there is not yet a widespread understanding, among doctors particularly, of the importance and benefits of diagnosing and reporting ADRs.

In these two provinces, everything seems to be set for the regional centre to manage a highly successful ADR monitoring programme: the systems are clearly excellent; the pharmacists are committed and knowledgeable; already there is evidence of success in the prevention and management of ADRs.

For the future, the demands – as in so many other places – are for more time and for more thorough and effective communication, printed, electronic and face-to-face, to raise awareness of the importance of reporting and to fulfil the vision of the national policy for Thailand.



Hazardous medicines are prepared in secure conditions in Chiang Rai Regional Hospital Pharmacy Department. Surin Sriworrarat (front), and Pattanapong Wongyod

Acknowledgements to:

Pornpit Silkavute, former Director, Technical and Policy Administration Division, and Director of APRMC Wimon Suwankesawong, Chief of APRMC and her team.

APRMC (Adverse Product Reaction Monitoring Centre, 2001), and the FDA (FDA Thailand, 2001, ISBN 974 244 044 1) for much of the background information.

Serbia: Vitalization of pharmacovigilance

The European Agency for Restoration has initiated a project for reforming the pharmaceutical sector in Serbia. The consultancy company Euro Health Group was selected to manage and provide support for the project. One of the components of the reform process was to re-establish and vitalise the Serbian pharmacovigilance programme. The UMC was invited to provide methodological training for key Serbian professionals in Belgrade from 10-14 February; this was carried out by Ronald Meyboom and Sten Olsson.

The Euro Health Group selected 15 participants for the course, which included lectures, working groups, discussions and study visits at the Clinical Centre of Serbia and the Institute of Pharmacy. Course participants worked out an action plan for the



Members of the group in Belgrade discussing with Ronald Meyboom (back to camera)



From right: Slobodan Jankovic, Branislava Miljkovic and Biljana Novakovic in one of the training sessions.

upgrading of pharmacovigilance in Serbia against the background of proposed new drug legislation being considered by the Serbian parliament. According to the proposed law a new Drug Regulatory Agency, including a department for pharmacovigilance, will be established. The action plan suggests regional pharmacovigilance centres being established at major hospitals or departments of clinical pharmacology. The plan also includes training and promotional activities for health professionals, interaction with media and a pilot project directed towards consumers (see report on right).

A core team of professionals involved in the further development of Serbian pharmacovigilance will visit the Uppsala Monitoring Centre and the Swedish national centre during the first week of May.

Co-ordination meeting in Peru

News from Susana Vasquez, Peru National Centre

On 23 and 24 of January 2003 a Technical Meeting took place in Lima, Peru with the objective to motivate and to offer the technical bases for the implementation of Centros de Referencia de Farmacovigilancia y Informacio'n de Medicamentos in the different regions of Peru.

This meeting included representatives from the 34 Regions of the country, 18 hospitals in Lima, 8 specialized institutes of the Ministry of Health and 4 hospitals of the armed forces and police officers. We

felt that universities have a key role in the development of pharmacovigilance in our country, so representatives of the Faculties of Pharmacy of all Peruvian universities were invited. This event had the support of the Pan-American Organization, Health Action International and professionals from the main Directorate of Medicines, and many Peruvian universities and health programmes.

We discussed many issues and drew attention to our objectives, and hope that new centres will become attached to the Peruvian system of pharmacovigilance.

Patient ADR reporting

Slobodan Jankovic describes an interesting outreach initiative in Serbia. "I have printed 10,000 leaflets (flyers) with following content:

Dear fellow citizens,

Taking drugs sometimes may have a bad impact on health, since drugs have adverse effects on the human body, too. In the majority of countries up to 10% of all patients actually became sick due to the drugs they were taking. Sometimes the adverse effects were insidious, and could be discovered only after health was seriously and irreversibly affected (e.g. prolonged intake of the drugs against rheumatic diseases could decrease the functioning of the kidneys).

Therefore, if you are taking drugs, and you have any new symptom, please report it to the physicians of the Regional centre for adverse effects in Clinical Hospital Centre, Kragujevac, by phone (370060, ext. 224) or in person (the office is located at the entrance of the Clinical Hospital Centre), every working day from 8 am. to 2 pm. The physicians will give you proper advice, of course, free of charge. Be informed on time!

With the help of my students, we put these 10,000 leaflets in the post boxes of 10,000 families, and I am now waiting for responses. After the first day we had received 20 calls, of which one was a real adverse effect report. I expect that reactions will keep arriving for a month, and then I will be able to summarise the results. Local media spotted the leaflet, and all of them came to me for an interview, so the information is spreading further! It will be interesting for me to see what finally happens."

Professor Jan Venulet

Professor Jan Venulet is considered by many to be the father of the WHO Programme for International Drug Monitoring.

He now lives near Geneva and was pleased to offer Sten Olsson some reflections on pharmacovigilance and his legacy.

WHO Programme Founder

Jan Venulet was born in Poland in 1921 and grew up in Warsaw. His medical studies were partly in the underground (illegal) university during the German occupation, then completed at the Jagiellonian University in Kraków. He later became Reader in Pharmacology at the University in Lublin, Head of pharmacology in the Institute of Tuberculosis, and in the Drug Research Institute in Warsaw. There followed longer scientific sojourns in Budapest, London, Basel and three years as pharmacology professor in Damascus, Syria.

He joined WHO as professor of pharmacology in Rabat, Morocco and Bangkok, Thailand. "While in Bangkok as part of the WHO programme for strengthening of medical education, at Siriraj University, I was approached by WHO in Geneva, and asked whether I would be interested in organising the WHO programme for drug monitoring. My answer was YES."



The 'pilot research phase' in Alexandria, Virginia, USA consisted of a unique group, 12 people from 10 countries, not knowing much about computers, planning and developing practically nearly from scratch the ADR terminology and the Drug Reference List, both, to a large extent in concept still unchanged. "I was extremely lucky to have such excellent collaborators. Being 'parachuted' in from so many places we were lucky to develop an esprit de corps, and to become friends." After three years of the pilot phase, the project was positively evaluated by the World Health Assembly, and became an ongoing WHO activity, transferred to Geneva.

"From 1968 I was Senior Project Officer and thus responsible for the development of all aspects of the project. Lloyd Christopher, and later, Edmund de Maar were the medical officers responsible for development of ADR Terminology and for overlooking the coding. Margaretha Helling was responsible for the Drug Reference List and Alvaro Aldama was most helpful in developing signals. The development of the computer system was in the hands of Sam Molander."

Signals

Signalling 'reports' with the intention of automatically drawing attention to the occurrence of certain predetermined conditions were developed. Reports included increasing reporting on a drug, drug-adverse reaction combinations, signals 'new to the system' (drug, ADR or drug/ADR combination); signals on most reported drugs; and signals on drugs suspected of being responsible for death. Signals were analysed/commented upon by the group or by National Centres and circulated as 'Drug comments' to participating National Centres. Regulatory action (warning, Dear Doctor letter, withdrawal) was taken on several occasions and in different member countries.

After WHO

"I left WHO in 1975 because of the withdrawal of the agreement by the Polish government, and immediately became Visiting Professor of Clinical Pharmacology at Geneva University. Afterwards I spent 10 years with Ciba-Geigy as head of intensive surveillance. After retiring I continued with different consulting activities, mainly with CIOMS as senior adviser."

Some thoughts on case assessment

The assessment of whether a given drug is the cause of an adverse event remains for Venulet the most controversial issue in all considerations of drug safety. Epidemiological studies are much less controversial as causal relationship is postulated on statistical grounds. Nothing is said about any individual case. Causality assessment of individual cases is radically different, as it can easily turn into an endless argument of pros and cons for a causal relationship with known scientific and commercial consequences. But it is done all the time in the privacy of pharmaceutical companies. It is done mostly in an unstructured way, ie the evaluator takes into account and develops his assessment on whatever is in the case report, using his knowledge and experience (which may vary enormously from person to person). The structured approach, 'standardized assessment' considers every case nearly in the same way, ie following the specific requirements of the method.

According to Professor Venulet "An unstructured assessment means: I have taken everything into account, applied my fullest knowledge and this is my final judgement (and the experts frequently disagree). Standardized assessment means: this case meets certain criteria build into the method what suggests a certain level of causal relationship - period. It is an objective tool, and in a way safer from the point of view of responsibility than the result of individual assessment."

"During my Ciba years both assessments were done for every case and recorded. If the difference between them was more than one step, (for example probable/unrelated) the evaluator was required to go through the case again and either confirm or change his judgement. Standardized assessment improves communication between users, indicates how judgement was reached and the assessment itself is less equivocal. The reproducibility of results is far greater. Everything depends on the method, and the one I developed with my colleagues was among the most widely used. Now the interests have changed but I still believe in the usefulness of an independent yardstick."

Thoughts on Terminology

He is overwhelmed by the 70,000 terms in MedDRA: "I never heard about a drug safety problem misrecognised because of shortcomings in the WHO-ART terminology. What is needed in MedDRA and WHO-ART are definitions of terms and criteria for their use built into the terminology - we were doing exactly that at CIOMS. But the idea about agreed upon Standard Search Queries is a valid one."

Pharmacology and epidemiology

In his professional life Jan Venulet went full circle from research and teaching, regulatory work, WHO, and pharmaceutical industry. He also went from experimental pharmacology to clinical pharmacology and the application of epidemiological methods. This experience led him to realise that application of an epidemiological approach to drug treatment is a distinct and new branch of science deserving closer attention. He wrote the first Polish book on adverse drug reactions in 1964 "I already knew it was important!". While still with WHO, in 1974 he published an article¹ in which the two words 'epidemiological pharmacology' (pharmacoepidemiology) were used together for the first time. "I defined this new branch of science (though practiced for many years - the name was new) as dealing with biological effects of pharmacologically active substances in populations exposed, regardless of the reasons for such an exposure, which could be therapeutic or accidental or experimental or related to drug dependence." Two more papers on the topic were published by him in subsequent years. "Epidemiological pharmacology, I suggested, was a

stage in the evolution of pharmacology from materia medica through experimental, clinical and epidemiological pharmacology to social pharmacology."

Impact of Pharmacovigilance

Jan Venulet never dreamt that his project would develop into the 'Uppsala' undertaking. He still sees problems with under-reporting, the quality of reports and lack of tools for validation of reported data by the evaluator. For the impact on public safety, he feels this has been, unfortunately, quite limited. There is the psychological difficulty for a physician to accept that his efforts misfired or caused additional health problems. On the other hand, doctors are in general not trained in looking for ADRs; drug interactions attract even less attention. "In the past I did a study about doctors asking their patients about taking drugs prescribed by other doctors or OTCs - with very discouraging results."

Professor Venulet sees possibilities in future consideration of the genetic background of ADRs, as well as monitoring in developing countries - in particular in relation to pathologies prevailing in these countries.

Reference

- ¹ From experimental to social pharmacology - Natural history of pharmacology. *International Journal of Clinical Pharmacology* 1974; 10: 203-205.

HERBALS EXPEDITION TO UK

Report from Jenny Ericsson

If you are interested to know more about Kew Gardens, the Eden Project or what Professor Ernst and his team are doing please visit their web pages:

www.rbgkew.org.uk

www.edenproject.com

www.ex.ac.uk/sshs/compmed/



Photos, from top:

The Eden Project; Helena Fucik, Mohamed Farah and Ralph Edwards inside one of the biomes;

Christine Leon shows the UMC team part of the vast Kew herbs resource;

Helena, Ralph, Mohamed and Debbie Shaw in the snow at Kew Gardens

Cultivating Collaborations

Complementary medicines in Exeter

At the end of January, a small delegation from *the UMC* set out from a wintry cold Uppsala to the south of England. The purpose was to create new, and strengthen already established collaborations in the herbals area – and possibly to get a glimpse of the spring. With Director Ralph Edwards at the wheel, *the UMC* herbal group, consisting of Mohamed Farah, Helena Fucik and myself, headed for our first stop – the Peninsula Medical School in Exeter, to meet UMC herbal reviewer Professor Edzard Ernst and his team. The Herbal review team (see below) was set up last year to support *the UMC* with expertise and consultation in herbal pharmacovigilance. Professor Ernst and his colleagues perform clinical research on complementary medicine, and have years of experience in the area of herbal drug safety. The meeting with the Exeter group resulted in many new useful ideas for herbal signal detection work.

The Eden Project

We continued through the beautiful landscapes of south-west England to what has been called the Eight Wonder of the World: the Eden Project. A disused china clay pit – an open wound in the Cornwall landscape – is now a living celebration of nature. As you walk down the pathway in the outdoor garden it is difficult to take your eyes from two gigantic biomes at the bottom of the pit. The Eden Project differs from traditional botanical gardens not only in appearance but also in its purpose. The main aim of the Project is to raise awareness of human dependence on plants in everything from clothes and medicine to the very air that we breathe, and the importance to protect natural resources for the future. We met with the Director of Living Collections, Sue Minter, to discuss collaborations. Our hope is that sometime in the near future our message on safety of herbal medicines will reach the 2 million people who visit the Eden Project every year.

Collaboration with Kew

After having enjoyed a couple of days of (mostly) sunshine and what a Swede at least would call springtime, we headed off to London where winter caught us up again. Our final stop was the Royal Botanical Gardens, Kew where we spent the day with Christine Leon, Head of the Chinese Medicinal Plants Authentication Centre, and Debbie Shaw from the Medical Toxicology Unit at Guy's & St Thomas' Hospital. Our collaboration with Kew has been going on for some time now, mainly in the area of classification of plant names. Most people think of Kew Gardens as a magnificent botanical garden, but

ever since it opened its gates in 1841 it has also worked as a scientific institution. Mrs Leon took us to the Herbarium, which holds a reference collection of over 6 million specimens of dried plants and fungi, and the library with over 120,000 books, as well as journals, papers and illustrations, and an extensive archive. If you are interested in studying plants and their properties, Kew is definitely the place to be.

Herbals reviewers

For over 20 years *the UMC* has received adverse reaction reports on herbal medicines. Growing public interest in herbal remedies in recent years has increased the number of herbal reports in the WHO database from 8,986 cases in 1997 to 11,716 cases last year.

One of the biggest challenges with herbal ADRs is how to handle the often incomplete information on identity and composition of the active herbal ingredients. Development of the Herbal ATC classification and extensive work in the area of classification of herbal substances has been done by the Centre. *the UMC* has also taken action on the output side, and we are very pleased to present the three members of *the UMC* Herbal Signal Review panel; Dr Jan G Bruhn, Professor Edzard Ernst and Professor Kiichiro Tsutani. The Herbal review panel is not a separate team, but part of *the UMC* review panel. However, since it is concerned with herbal drugs, and because the number of herbal ADR reports is far less than ADR reports on conventional medicine, the work of finding herbal signals has to be dealt with a bit differently.



Herbal Signal Reviewers and UMC staff: Helena Fucik, Malin Stahl, Dr Jan Bruhn, Ralph Edwards, Mohamed Farah, Professor Kiichiro Tsutani, Professor Edzard Ernst and Jenny Ericsson

Changes at the Signal group

We have recently recruited for a new post in the Signal group. Kristina Star started working at *the UMC* on 17th of March. In addition, during Malin Ståhl's maternity leave Anne Kiuru is the main contact for Signal reviewers. Johanna Strandell joined us in February as temporary replacement for Malin.



Kristina Star

Kristina's first professional work was as a registered nurse, working particularly in hospital departments of infectious diseases, in her home town of Borås in west Sweden, and then in New Haven, Connecticut, USA. Her current role in the Signals group at *the UMC* is checking the progress of signals from the WHO database and following-up on those investigations which signal reviewers have marked as 'potential'. Kristina also has seven years' experience working in ADRs in clinical trials and some post-marketing experience, as well as product information leaflets at the Swedish national pharmacovigilance centre.

Niklas New at Neurologic

The Neurologic team, which works closely with *the UMC* on its data-mining project (see Uppsala Reports 19), has a new member. Niklas Norén, who recently completed his Masters Degree in Engineering Physics at Chalmers University of Technology, Göteborg University, Sweden, is now working with Roland Orre, Andrew Bate and colleagues. Based partly at *the UMC* and partly at the Neurologic office at the University of Stockholm, Niklas is initially engaged in following up some research from his thesis 'A Monte Carlo Method for Bayesian Dependency Derivation', before he moves on to work on the pattern recognition element of the BCPNN project.

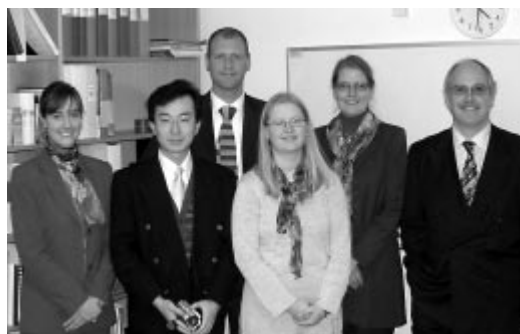
Visitors to *the UMC*

On Friday 28 February we welcomed Dr Vera Vlahovic-Palcevski from Croatia to *the UMC*. She is a clinical pharmacologist who will be running a new regional pharmacovigilance centre in Rijeka.



Vera Vlahovic-Palcevski, Monica, Mike Ufer

She had a 6 month attachment at the Karolinska Institute in Huddinge and wanted to take the opportunity of learning something of what *the UMC* is doing. Also visiting the same day was Mike Ufer, a PhD student from Tübingen, Germany, a guest researcher also at the Karolinska, working on the metabolism of the oral anticoagulant Phenprocoumon.



Another important visitor: Helena, Dr Daisuke Koide (International University of Health and Welfare in Tochigi, Japan), Daniel, Monica, Marie, Ralph

Recent published papers

Fucik H, Backlund A, Farah M. Building a computerized herbal substance register for implementation and use in the World Health Organisation International Drug Monitoring Programme. *Drug Information Journal*, Vol 36, pp839-854, 2002.

Edwards IR. Withdrawing drugs: nefazodone, the start of the latest saga. *Lancet* 2003; 361: 1240.

Spijset O, Hägg S, Bate A. Hepatic injury and pancreatitis during treatment with serotonin reuptake inhibitors: data from the WHO database of adverse drug reactions. *Int Clin Psychopharmacol* 2003 May; 18(3): 157-161.

New Book examines data protection and drug safety

Learning from Experience – Privacy, Data and Health Research
by Dr William Lowrance

This report is available from the Nuffield Trust (price 10 pounds) +44 (0)20 7631 8450 or www.nuffieldtrust.org.uk

Dr Lowrance states "We are in a fast-moving age of data banking, data brokering, data mining, biobanks and genetic trusts. In pharmaceutical and other research, data are routinely transferred around the world electronically. Health research is avidly feeding into and analysing these collections and streams of data. Research – and its benefits – knows few national boundaries. Ethics, policy, and law are being severely challenged to keep up."

The author goes on "what I have tried to do in this report is to critique the issues surrounding privacy and research on existing data, and to survey the ways we all benefit from this research. Privacy is a deeply felt value and must be respected. We must find ways to pursue improved knowledge and privacy simultaneously."

COURSES & CONFERENCES

DATES	TITLE	PLACE	ORGANISER/CONTACT
9-10 May 2003	II Pharmacovigilance Conference	Coimbra Portugal	Núcleo de Farmacovigilância do Centro Ap. 3020, 3001-401 Coimbra Tel: +351 239 851830 Fax: +351 239 851839 E-mail: farmacovigilancia@nfc.pt www.nfc.pt
12-23 May 2003	Pharmacovigilance – the Study of Adverse Drug Reactions	Uppsala Sweden	Sten Olsson, <i>the Uppsala Monitoring Centre</i> , Stora Torget 3, S-753 20 Uppsala, Sweden E-mail: sten.olsson@who-umc.org
7-8 May 2003	QT prolongation and Safety Pharmacology	Barcelona Spain	Tel: +44 (0)20 7953 7450 Fax: +44 (0)20 7953 7453 E-mail: postmaster1@visioninbusiness.com www.visioninbusiness.com
8-9 May 2003	Monitoring Safety in Clinical Drug Development	Southampton UK	Jan Phillips, Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
9-11 June 2003	Pharmacovigilance course	London UK	Management Forum Ltd Fax: +44 (0)1483 536424 registration@management-forum.co.uk
11-12 June 2003	Signal Generation & Interpretation – What's New?	Southampton UK	Jan Phillips, Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
15-19 June 2003	39 th Annual Meeting, DIA	San Antonio USA	DIA Tel: +1 215 628 2288 Fax: +1 215 641 1229 www.diahome.org
23 June 2003	Adverse Event Reporting and Pharmacovigilance	London UK	Rostrum Tel: +44 (0)118 933 5343 E-mail: rostrum@mdsps.com www.rostrumtraining.com
24-28 June 2003	6 th Congress of EACPT. <i>There is a 'pharmacovigilance and communication' workshop.</i>	Istanbul Turkey	Flap Tour Tel: +90 312 442 07 00 Fax: +90 312 440 77 99 E-mail: flaptour@6theacpt.org
1-2 July 2003	Prepare to meet MedDRA challenges	London UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
21-22 July 2003	Adverse Event Reporting and Pharmacovigilance	London UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
21-24 August 2003	19 th ISPE Conference and the 1 st International Conference on Therapeutic Risk Management	Philadelphia USA	Tel: +1 301 718 6500 Fax: +1 301 656 0989 E-mail: ispe@paimgmt.com
3-4 September 2003	Evaluating Signals from Postmarketing Reports	Southampton UK	Jan Phillips, Drug Safety Research Unit Tel: +44 (0)23 8040 8621 E-mail: jan.phillips@dsru.org www.dsru.org
18-19 September 2003	Adverse Event Reporting and Pharmacovigilance	London UK	Pharmaceutical Training International Tel: +44 (0)20 7915 5055 Fax: +44 (0)20 7915 5056 E-mail: registration@pti-courses.com
29 September – 1 October 2003	Pharmacovigilance in the EU in 2003	Paris France	Fax: +41 61 225 51 52 www.diahome.org
9-11 October 2003	ISoP Annual Meeting (preceded by training courses)	Marrakech Morocco	Conference secretariat Fax: +212 37 75 60 87 www.isop2003.org

News round-up

Updates – 4th Quarter 2002

The new versions of the WHO Drug Dictionary (WHO-DD) and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 4th quarter of 2002 are now available and were sent to subscribers during March 2003. The WHO-DD pack contains the updated version of WHO-DD. If you have not yet received the update, please contact Inger Forsell (inger.forsell@who-umc.org).

Questionnaire feedback

We are very grateful to all those WHO-DD users who took the trouble to complete and return our recent questionnaire. The responses were full of invaluable comments which we will be following up. If you have not returned your Drug Dictionary Questionnaire, we are still very happy to receive replies up to the end of May 2003. Please send responses to Elizabeth Bengtsson, who can also send a blank questionnaire to anyone who did not receive the original form.

User Group meets in Rome

During the meeting in Rome, Mats Persson and Daniel von Sydow ran a WHO-DD Users Group meeting. This offered the opportunity to report on the results so far of the questionnaire and enabled DD users to ask questions and raise current concerns directly with UMC staff.

New UMC leaflet

the UMC displayed a new exhibition stand at the Rome meeting and gave away a new information leaflet, which describes the work of *the* UMC and products and services we can supply. Copies of the leaflet are also available from Elizabeth Bengtsson (elizabeth.bengtsson@who-umc.org).

Need help?

If you have any queries about the new format of the WHO-DD, or need further information about your current subscription or how to upgrade it, do call *the* UMC.

You can e-mail:

drugdictionary@who-umc.org - for comments about the DD, corrections, additions, and
inger.forsell@who-umc.org - for queries about your subscription.

If you are a subscriber to either WHO-DD or WHO-ART and do not receive your updates, please contact Inger Forsell.

Data files for the 1st quarter of 2003 should be available during May 2003.

Forthcoming exhibitions

UMC staff are planning to attend the following conferences in 2003:

- DIA Annual Meeting – San Antonio, TX, June 15-19
- ISPE – Philadelphia, August 21-24

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

Our Collaborations

the UMC is collaborating with a variety of external organisations in provision of pharmacovigilance services and products. This is a summary of current collaborators:

- DBMS Consulting – for developing the official TMS loading script for the WHO Drug Dictionary and the WHO Adverse Reaction Terminology
- Galt – offering the WHO DD loading in to the Galt dsNavigator™ Browser
- QED – organizations which license Qscan™ World can access the data and analysis tools continuously and program their system to alert them when drug safety cases that are relevant to their drug products are reported
- PSI International Inc – Pharmacovigilance training and Drug Dictionary training
- Software Technics Ltd – offering the WHO-DD, WHO-ART, ICD9/10 loading into the MediCoder and AutoEncoder Dictionary Browser

Have you moved?

Please help us! We'd like to keep our mailing lists in top condition, so do let us know if you haven't received post you are expecting from us, if there are mistakes on our labels, or if you have changed your position or address. Thank you!

Who to contact

For queries about your subscription or if you have not received something you should have, please contact Inger Forsell

inger.forsell@who-umc.org

For questionnaires and UMC leaflets, please contact Elizabeth Bengtsson

elizabeth.bengtsson@who-umc.org

For comments about the Drug Dictionary, additions or corrections, please contact

drugdictionary@who-umc.org



Inger Forsell, Rose C Wilkeson, RN, MSN, of Genzyme Corporation, USA and Mats Persson at the UMC stand in Rome.



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Malin Ståhl
Programme Leader, Signal Detection

Kristina Star
Signal Detection & Analysis

Daniel von Sydow
Project Co-ordinator

Erica Walette
Programme Leader, Database Services

Magnus Wallberg
Programme Leader, Systems Development

Job Opportunity in New Zealand

The Intensive Medicines Monitoring Programme in New Zealand, part of Centre for Adverse Reactions Monitoring (the New Zealand National Monitoring Centre), is currently advertising a vacancy for the position of Head: Intensive Medicines Monitoring Programme. This is only one of 2 similar programmes internationally and its research efforts have attained international recognition. The closing date for applications will be 16 May 2003 and the full job description may be obtained from www.otago.ac.nz/jobs or michael.tatley@stonebow.otago.ac.nz or phone +64 3 479 7247.



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