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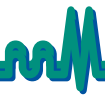
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Uppsala REPORTS

For everyone concerned with the issues of pharmacovigilance and toxicovigilance



- **What does *the* UMC do?** *page 4*
- **National Centre opens in Ghana** *page 10*
- **Hard work and fun at *the* UMC training course** *page 6*
- **INSERTS: UMC Basics and reader questionnaire**



MESSAGE FROM THE DIRECTOR

MAKING THE MOST OF EXPERIENCE

In this edition of *Uppsala Reports* we publish a summary of the achievements and activities of *the UMC* since 1978 (page 4). The extent of our work is not well-known everywhere (something we are working on!)

and it concerns me that sometimes new ideas or initiatives in pharmacovigilance may duplicate the work we are doing, or fail to capitalise on the experience and learning of the WHO Programme. We are much more interested in collaboration than competition, and very keen to help prevent scarce resources being wasted in covering old or familiar ground.

BEYOND REGULATION

Any healthcare professional submitting a report is demonstrating their concern about their patient's welfare. If regulation is the only purpose of pharmacovigilance, then reports on familiar ADRs may be judged as uninteresting and unimportant.

But if pharmacovigilance is about improving patient therapy and public health, then we should see any ADR report as having clinical and educational value: yes, this report may record 'only' a known reaction - but is there anything unusual about it? Could better information about the drug, or a deeper knowledge of the patient have prevented it? What does it tell us about the effectiveness of drug information and medical training?

If a healthcare professional bothers to write a report we should be grateful and should certainly ensure that the response is more than a routine thank you letter. We need to encourage and reward anyone who is committed enough to report, and be sure we don't inhibit them by suggesting that anything at all is uninteresting or unimportant. Since under-reporting is still regarded as a major drawback in pharmacovigilance such encouragement for reporters seems worth the extra work in National Centres.

MEETING UP

Decision-time for attending annual meetings is around the corner: will you be joining us in Tunis for ISoP? Or in Dunedin for our own Annual Meeting of Member Countries? I hope so!

Ralph Edwards

Who's who at the UMC?



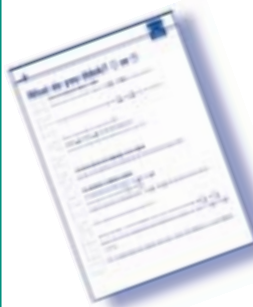
With this copy of *Uppsala Reports* you'll find a sheet giving details of everyone in *the UMC* team and what they do.

We hope you'll find this useful and that it will help to make contact with us simpler.

It will appear with every *Uppsala Reports*, updated each time BUT - if you want to contact us, don't worry too much about who you choose, we'll make sure your enquiry gets into the right hands!

We need your views!

Please help us make *Uppsala Reports* more relevant and interesting for you!



You'll find a reader comment form with this edition - Please take a few moments to complete it and return to us. We promise to listen and respond!

Contributions and suggestions welcome!

Please send us news and views from your country! The occasional photograph would be very welcome, too!

Uppsala Reports is distributed to around two thousand people worldwide - the more news and information we have from you all - the better *Uppsala Reports* will be!

Please fax, e-mail or post your contributions - however short - to Sten Olsson here at *the UMC*.

Mary Couper WHO-HQ reports on the work of the WHO delegation at the ICH in Tokyo

A team of five people (see photo) representing WHO attended an ICH meeting in Tokyo from 19 to 24 May 2001. Among the topics discussed there were two which had importance for the WHO International Drug Monitoring Programme. These were a two-day meeting of the Board of the MedDRA Management Services Support Organization (MSSO) and a one-day brain-storming session on items of post-marketing surveillance issues. A paper on the activities of *the* Uppsala Monitoring Centre and a discussion paper on the pharmacovigilance activities in WHO were handed out and were welcomed by the participants. Copies can be obtained from either *the* UMC or WHO-HQ.



Prof Ralph Edwards, Dr Lembit Rāgo, Dr Sabine Kopp Kubel, Dr Mary Couper (not pictured Mr Kenicha Tamiya)

One of the items on the agenda of the Board meeting of the MSSO was collaboration with WHO on the implementation of MedDRA in non-ICH countries. Recommendations from the Annual Centres' meeting in Tunisia had not been implemented. The MSSO had decided that it was not feasible to maintain a pharmacovigilance subset based on WHO-ART within MedDRA and a review to validate the terminology had been undertaken without consulting WHO. It was therefore decided that

WHO-ART should be retained by WHO and further developed together with ICD 10. Dialogue between the MedDRA MSSO and WHO will continue.

The one-day meeting on postmarketing surveillance concentrated on three main issues: the harmonisation of Periodic Safety Update Reports (PSURs), the development of early postmarketing pharmacovigilance and the standardisation of case reporting based on existing documents.

It is important that WHO remains as an observer in these meetings in order to be able to actively steer the activities.

WANTED

Photos and cuttings!

We are producing a new brochure about the work of *the* UMC and about the issues of benefit and risk in medicine, for publication in October.

We hope the material will raise the debate about the major issues in pharmacovigilance, particularly the understanding and communication of uncertainty. In that respect, we are planning for the brochure to have an educational, even campaigning element to it. Please help us!

We are very keen for the brochure to have international appeal, and to include pictures and information from our worldwide collaborators.

If you can contribute any documentary-type photographs of local people in medical or non-medical settings, especially with some strong human or emotional interest content (mothers and kids; teachers with students; doctors or nurses with patients and so on), please contact Cecilia Biriell. We would also like any press cuttings or interesting drug-related facts, experiences or crises for inclusion in the brochure.



What do we do with Products, service

From time to time people tell us that they

● Processing of over **200,000 individual ADR case reports per year**, submitted by National Centres. Processing includes quality control and coding of information on drugs and reactions.

● Maintaining the **WHO ADR database**: currently holding 2.7 million reports from 60 countries since 1968. The database is used without restriction by the member National Centres, and has several search strategies built into its tools. Ad hoc special searches are done by UMC staff on request.

● The production of formatted outputs:

- Type A: annual tabular listing of reactions reported during previous 3 years with cumulative totals
- Combinations Database indicating significance of new reactions
- Reporting statistics produced annually.

All output formats are based on suggestions by the WHO Programme members and are thoroughly tested and quality assured.

● Organising, in collaboration with WHO Headquarters, the **Annual Meeting of member countries of the Programme**, setting and maintaining worldwide harmonised standards, relating to definitions, communication and confidentiality of data. Scientific discussions, including those relating to individual drug problems, form a prominent part of the agenda.

● Operation of international **expert review panel** to monitor and evaluate signals and signalling processes. Around 40 international domain experts aid *the* UMC and Programme members in finding and evaluating new drug safety signals. International standards for signal reviewers have been developed.

● Publication and updating of the **WHO Drug Dictionary**. This has become the standard drug reference database accepted by all member countries, including the EMEA, and most pharmaceutical companies. It is updated regularly on a quarterly basis, though immediate ad hoc requests for updates are done at a small charge.

● Publication and updating of the **WHO Adverse Reaction Terminology (WHO-ART)**. This has been the standard drug safety and chemical safety dictionary of medical terms throughout the Programme. Links with the ICD versions 9 and 10 are already in place and will be enhanced.

● Publication of **SIGNAL**. For over a decade this has been the vehicle for informing Programme members on evaluated signals from the international data. It has recently been made available to single, international market authorisation holders for their own products.



● The **ADR Signal Analysis Project (ASAP)** - collaboration with IMS using international spontaneous report rates in combination with international drug sales statistics, achieved after a period of extensive research.

● Development of **Bayesian Confidence Propagation Neural Network (BCPNN)** data-mining process, capable of much earlier and more sophisticated signal detection.



● Promotion of the study and communication of the benefits and risks of drugs as a core activity in pharmacovigilance.

● Frequent **training activities** in pharmacovigilance theory and practice centrally (in Sweden) for international participants and locally around the world. Annual international and regional training courses in pharmacovigilance are undertaken by *the* UMC, in co-operation and alone. Some training material is available from *the* UMC and on *the* UMC website.



Does *the* UMC do? Tasks and achievements

are not clear about the range of UMC activities and achievements.

- Research and development of a single, **worldwide herbals classification** and preparation for integrating herbals into the global pharmacovigilance process. The classification of all the herbal product/ADR information in the WHO database is complete. A herbal ATC is being developed in cooperation with the WHO Collaborating Centre for Drug Statistics Methodology, Oslo. The classification will continue to be maintained by *the* UMC.

- Publication of **National Pharmacovigilance Systems**. This is the only record in the world of the processes of the National Pharmacovigilance Centres of all member countries of the WHO Programme.



- Publication of the **WHO Pharmaceuticals Newsletter**. The *Newsletter* is a much valued information source on international drug regulatory decisions and safety concerns, produced by WHO with UMC support.

- **Reactions Weekly** (ADIS International). An agreement between *the* UMC and ADIS has allowed this synopsis of drug safety issues in most major international and national medical journals to be available to Programme members. Drug Safety Newsletters, produced by National Centres are quoted in *Reactions*.

- Quarterly publication of **Uppsala Reports** - *the* UMC's and member countries of the Programme's 'house magazine'.



- Contribution to **CIOMS** initiatives. *the* UMC has been an active contributor to all the CIOMS publications in drug safety except for the first. *the* UMC initiated and chaired the work on CIOMS 1a which was later the basis for the ICH E2B guideline on data transmission and storage. The conceptual work on benefit-risk was generated in *the* UMC with some collaborators and published before being used by CIOMS.
- **New WHO report database**. This work has been used to develop an ICH E2B compatible database for the WHO Programme reports including all of the WHO historic data. The new database also uses a drug file which was based upon the CEN pre-standard. This new Drug Dictionary contains all the historic data from the previous WHO-DD, but can store many more useful data fields as future drug information is added.
- **WHO partnering** with industry in the development of new drugs. WHO now has very close relationships with various industry partners in developing and promoting drug therapies for, usually, tropical diseases. In such a partnership, WHO has a very strong obligation to collect and analyse drug safety information in order to satisfy its public health role in drug safety.
- The **Vigimed** e-mail conferencing system allows all National Centres in the programme to discuss issues of interest.

There is no other official body in the world which has a truly independent and global perspective on drug safety other than the WHO and its collaborating centre, *the* UMC. International harmonisation (understanding and allowing variation when justified, or in situations of uncertainty) and standardisation (applying agreed and preferably optimal practices in the same way, without variation) are difficult to achieve without consensus. It is the WHO's general mandate to do this work, and the record of achievement in the field is now substantial, authoritative and widely-recognised.



Biannual Training course gets the

Productive and sociable time in Uppsala

This year's training course in Uppsala was characterised by hard work and the making of new friends.

31 participants from 27 countries descended on Uppsala for the start of the fortnight's course on 7 May. They came from all corners of the globe - South America, Africa, Europe Central and South East Asia - and rapidly settled in under the Swedish spring sunshine (which gave way to Swedish spring rain after the first week!)

The two modules of the course covered every aspect of pharmacovigilance and pharmacoepidemiology, as usual. Lectures and presentations were given by members of *the UMC* team and by many guest speakers.

Participants ranged from senior and experienced scientists, academics and pharmacovigilance professionals, to more recent arrivals at National Centres in member and associate member countries.

The audience was unusually lively and participative - making time-keeping a real problem as the questions and comments poured out after each session. UMC staff and lecturers were very impressed at the energy and commitment shown day after day.

Social pleasures

The group was no less energetic in its social activities, conversation and the making of new friendships. After the informal welcome party many of the group met early each evening at *the UMC* before exploring a new restaurant for dinner. The course dinner was held in a restaurant overlooking the river Fyrisån - and was followed (for a dedicated few) by dancing way into the night. At the weekend there were local trips and a tour of Stockholm.

It was a remarkably sociable group - and everyone involved seemed to have a very good time professionally and personally.

In their own words:

We asked participants to comment on the course for *Uppsala Reports*. Here are some of the things they wrote:

The opportunity for people from different parts of the world from various disciplines to share their experience and concerns must be invaluable. The objective of this course to provide the required knowledge has been achieved.

Clive Chan, Hong Kong

Excellent training programme. I would recommend it to anyone working in pharmacovigilance. The clubs and restaurants of Uppsala aren't bad either.

Alex Dodoo, Ghana

Excellent training course, excellent classmates, excellent teachers. It was a fantastic experience for me, and I'm sure will serve my country.

Alejandro Maria Goyret, Uruguay

Five Star training course! When I first saw the programme I thought it would be very difficult to give my best... because it seemed too intensive... (but) it didn't happen... it was a great privilege to learn so much and (have) contact with such different cultures (and make some friends too!)

Ana Araújo, Portugal

...reinforces... our decision to continue working in pharmacovigilance. Thank you for this beautiful experience.

Leticia Rodriguez, Mexico

Thank you very much for your astonishing, informative, attractive course... For me as a senior scientist I think I got a great deal of experience which will help me establish pharmacovigilance in Jordan.

Al-Hakam Al-Hadidi, Jordan

I would like to thank the UMC for providing such a pleasant atmosphere to meet, exchange views and share thoughts and findings.

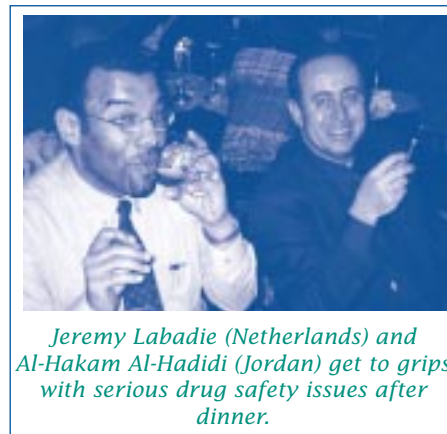
Chunhua Tian, PR China

There were some criticisms, which *the UMC* team is taking very seriously:

- for those with English as a second or third language there were some problems
- some important sessions were thought to be rushed and too short
- there were some calls for lecture notes and presentation print-outs to be more reliably circulated before sessions
- given the very wide range of experience of participants, some sessions were too elementary for some, too advanced for others.



Clive Chan (Hong Kong), Tarn Yeong Goh (Singapore)



Jeremy Labadie (Netherlands) and Al-Hakam Al-Hadidi (Jordan) get to grips with serious drug safety issues after dinner.

The next Uppsala Training Course in Pharmacovigilance will be held in Spring 2003. Sten Olsson is the co-ordinator.

Posters from participating countries in the Training Course are now available to view on *the UMC* website, under promotion and training.



... thumbs up from participants



*Front row:
Chua Kui Hong, Ralph Edwards, Leticia Rodriquez,
Cecilia Morgado-Cadiz, Embaye Andom*

*Back row:
Elvira Ivanova, Vladimir Lepakhin, Alejandro Sacarelo,
Helena Prazská, Clive Chan, Alex Dodoo, Tarn Yeong Goh,
Jeremy Labadie, Mohan Joshi, Elena Kozhukova,
Al-Hakam Al-Hadidi, Murilo Dias, Ana Araújo, Priya Bahri,
Oscar Simooya, Chunhua Tian, Amra Cabaravdic, Sten Olsson, Gloria
Shalviri, Alison Bond*

*(Not present): Elaf Khalil Kamel, Marja-Leena Nurminen, Monika Schutte,
Suresh Gupta, Deven Parmar, Amina Tebaa, Simona Gatti, Helle Kieler*



*Jeremy Labadie
(Netherlands),
Helena Fucik (UMC),
Alex Dodoo (Ghana)
and, in front,
Mohan Joshi (Nepal)*



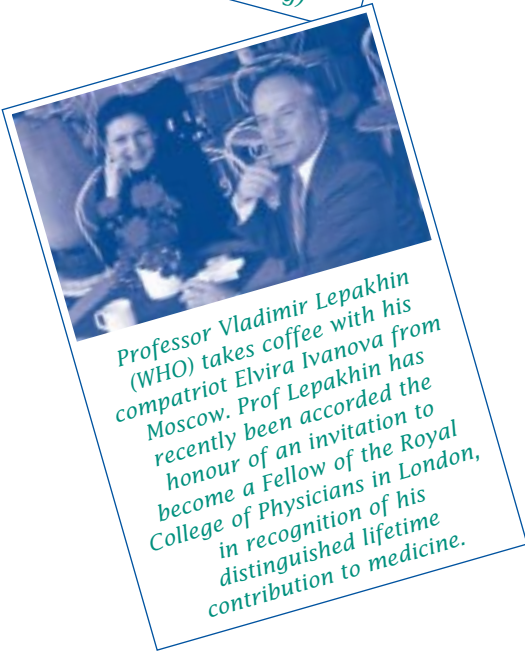
*Amra Cabaravdic,
(Bosnia-Herzegovina)
Alejandro Goyret
(Uruguay)*



*The course dinner -
Maria Bergström (UMC) enjoys a
post-dinner drink with
Alex Dodoo (Ghana) and
Clive Chan (Hong Kong)*



*At work: Alejandro Goyret (Uruguay),
Ana Araújo (Portugal),
Mohan Joshi (Nepal)*



*Professor Vladimir Lepakhin
(WHO) takes coffee with his
compatriot Elvira Ivanova from
Moscow. Prof Lepakhin has
recently been accorded the
honour of an invitation to
become a Fellow of the Royal
College of Physicians in London,
in recognition of his
distinguished lifetime
contribution to medicine.*



*Not only were course members
hard-working and sociable -
but elegant, too, as you can see
from this coffee-time shot at
the conference hotel.*

*(left to right)
Cecilia Morgado-Cadiz (Chile),
Chua Kui Hong (Brunei) and
Leticia Rodriguez (Mexico)*

Participants List

- Amra Cabaravdic, Bosnia-Herzegovina
- Murilo Freitas Dias, Brazil
- Chua Kui Hong, Brunei
- Cecilia Morgado-Cadiz, Chile
- Chunhua Tian, China
- Helena Prazská, Czech Republic
- Elaf Khalil Kamel, Egypt
- Embaye Andom, Eritrea
- Marja-Leena Nurminen, Finland
- Monika Schutte, Germany
- Alex Dodoo, Ghana
- Clive Chan, Hong Kong
- Suresh K Gupta, India
- Deven Parmar, India
- Gloria Shalviri, Iran
- Al-Hakam Al-Hadidi, Jordan
- Juana Leticia Rodriguez y Betancourt, Mexico
- Amina Tebaa, Morocco
- Mohan P Joshi, Nepal
- Jeremy Labadie, Netherlands
- Ana Araújo, Portugal
- Elvira Ivanova, Russia
- Elena Kozhukova, Russia
- Tarn Yeong Goh, Singapore
- Helle Kieler, Sweden
- Simona Gatti, Switzerland
- Priya Bahri, United Kingdom
- Alison Patricia Bond, United Kingdom
- Alejandro Maria Goyret Sacarelo, Uruguay
- Oscar Simooya, Zambia



WHO Pharmaceuticals Newsletter

The WHO Pharmaceuticals Newsletter, produced by the QSM (Quality Assurance and Safety: Medicines) team at WHO headquarters, Geneva, is now also available on the Internet.

This WHO Newsletter is a bi-monthly publication which is distributed to drug information officers and key professionals in all WHO member states. The aim is to disseminate topical information on the safety and efficacy of pharmaceutical products, received from WHO partners and other sources. *the UMC* is contributing to the drug safety section of the Newsletter.

Ms Charmian Common, who was the editor of WHO Pharmaceuticals Newsletter for several years, recently retired from the organisation.

Dr Shanthi Pal, New Delhi, India, is joining the QSM temporarily to take on the task of editing the WHO Pharmaceuticals Newsletter. The URL is www.who.int/medicines/organization/qsm/activities/drugsafety/orgpharmanews.html

Fundamentos de Farmacoepidemiologia

The Brazilian organization GRUPURAM (Group for Research into Rational Use of Medicines), published a 180 page book in Portuguese on the basics of pharmacoepidemiology in October 2000.

The editor is Professor Lia Lusitana Cardozo de Castro, Faculty of Clinical Pharmacy, University of São Paulo. The book has 5 chapters with extensive reference lists. Please contact Dr. Lisa L C de Castro at lusitana@vol.com.br if you are interested in obtaining a copy.

Free Medical Journals

Did you know about the Internet site www.freemedicaljournals.com? It currently provides links to some 650 biomedical journals that are provided free in full-text versions on the Internet. Some are made available free immediately after

publication, some only after some months (1-24). The free journals are listed on this Internet site, either alphabetically or by category. There are 20 journals mentioned both under the headings 'pharmacology' and 'pharmacy', among them the WHO Drug Information and the WHO Pharmaceuticals Newsletter. Journals in 10 different languages are currently listed.

Free Medical Journals.com



The International Society of Pharmacovigilance will soon be on the Internet. A simple site, giving basic information about the Society and details of its forthcoming Annual Meeting in Carthage-Tunis will soon be accessible at www.isoponline.org. Later it is hoped to add a forum for discussion of pharmacovigilance topics.





Health Database Resources

DGI Center for Health Research and Education, Inc provides an Internet service called BRIDGE-on-line, describing epidemiological data resources from mainly North America and Europe. Currently, the databases comprise approximately 85 resource profiles, including each of the following elements:

- ☐ Contact and accessibility information for each database
- ☐ Population characteristics (e.g. size, geographical location)
- ☐ Demographic data
- ☐ Vital statistics information
- ☐ Diagnosis data (i.e., coding practices)
- ☐ Procedure data (i.e., coding practices)
- ☐ Drug data (e.g. coding, dosage)
- ☐ Laboratory tests
- ☐ Economic data (e.g. cost of drugs)
- ☐ Database linkage capabilities to various other sources
- ☐ References of published studies using the data
- ☐ Relevant links to web sites.

The databases fall into one of the following categories:

- ☐ Population Databases: Diagnoses & Drugs - Longitudinal
- ☐ Population Databases: Diagnoses & Drugs - Cross-Sectional
- ☐ Population Databases: Drug Data Only
- ☐ Population Databases: Diagnosis Data Only
- ☐ Population Databases: Diagnosis Specific
- ☐ Spontaneous Reporting Systems
- ☐ Large Clinical Trials
- ☐ Other Databases.

DGI charges a subscription fee for searching the data sources.
The URL is <http://www.dgi.org>

Forthcoming Courses & Meetings in Pharmacovigilance

The International Society for Pharmacoepidemiology (ISPE) is organising the 17th International Conference on Pharmacoepidemiology in Toronto, Canada on 23-26 August 2001.

For further information contact the ISPE office at
Fax: +1 301 656 0989

The Drug Information Association (DIA) is organising the following events of interest to drug safety and pharmacovigilance:

- A training course entitled *Applied Epidemiology* in Edinburgh, UK on 1-2 October 2001. This is the first time this course is held in Europe
- A training course on *Medical Approach in Diagnosis and Management of ADRs 2001* in Paris, France, 25-26 October 2001
- A training course on *Drug Safety Surveillance and Epidemiology* in Philadelphia, USA on 15-17 October 2001. The course provides an overview of domestic and international safety surveillance, from both the industry and the FDA perspectives
- The 14th Annual EuroMeeting *The Patient is Waiting* held in Basel, Switzerland on 5-9 March 2002. One of the themes is Effective Pharmacovigilance

For more information on the DIA events contact:
Tel: +1 215 628 2288 Fax: +1 215 641 1229
E-mail: dia@diahome.org
Or
Tel: +41 61 386 93 93 Fax: +41 61 386 93 90
E-mail: dia@diaeurope.org

Management Forum is organising an intensive course on *Medical Aspects of Drug Safety & Pharmacovigilance* on September 20-21, 2001. They are also organizing a seminar on Pharmacovigilance - Quality Assurance and Compliance on October 31, 2001

For more information contact Management Forum at

Fax: +44 1483 536424
E-mail: registrations@management-forum.co.uk

Continued on page 13



Italy

The Ministry of Health has recently taken measures to improve pharmacovigilance activities carried out by the Medicines Evaluation and Pharmacovigilance General Direction. The pharmacovigilance office now has Dr Roberto Raschetti as its head.

He may be reached at the Ministry of Health, Medicines Evaluation and Pharmacovigilance General Direction, Pharmacovigilance Office, Viale della Civiltà Romana, 700144, Roma
Fax: +39 06 5994 3554
E-mail: roras@iss.it

Cyprus

The pharmacovigilance centre in Cyprus will be organising a promotional seminar on 29 September 2001, aimed at physicians, pharmacists and nurses.

The objective is to educate the participants on the role of pharmacovigilance, the need for active participation from the health professionals and how to report ADRs. Representatives from *the* UMC will contribute to the seminar.

Dr Athos Tsinontides is responsible for the meeting, e-mail: dipcc@cytanet.com.cy

Canada

Dr Heather Sutcliffe recently left the Canadian pharmacovigilance centre for other duties within Health Canada.

The new acting head of the Adverse reaction Information Unit is Dr Robert Leitch.

Ghana

The Ghana National Pharmacovigilance Centre in Accra was officially inaugurated on 11 June 2001.

Speeches were delivered by the Deputy Minister for Health and the WHO Country Representative.

The launch of the Centre was carefully planned and prepared

on 20th October 2000, to collaborate in the setting up of a national centre for pharmacovigilance. In January 2001 a draft proposal for the centre was discussed and the plan of work for 2001 agreed upon.

Preparing the ground

As part of this plan and with funding from the FDB, Sten



Dr T.C. Corquaye, Chief Executive, Food and Drugs Board, Ghana giving the Welcome address at the launch of the National Centre for Pharmacovigilance

for. The Food and Drugs Board of Ghana (FDB) and the Centre for Clinical Tropical Pharmacology and Therapeutics (CTCPT) of the University of Ghana agreed, at a meeting held



Dr Alex Dodoo, Co-ordinator, Ghana National Centre for Pharmacovigilance explaining the spontaneous reporting system to the audience

Olsson of *the* UMC was invited to Ghana to provide technical assistance and to give recommendations as to how to establish and develop effective pharmacovigilance activities in the country. During a very busy week 1-7 April, 2001, Sten and his two local partners, Alex Dodoo and Selassie Haybor, had discussions with relevant authorities, teaching institutions, hospital departments, professional associations, representatives of pharmaceutical manufacturers and the media. At these meetings the concept of pharmacovigilance was explained and the need for setting up a national pharmacovigilance system in Ghana emphasised. The team and its message were very well received.

continued →



Traditional medicines

Only a minority of medicines consumed in Ghana are prescribed by physicians. In most cases patients seek advice and buy medicines from pharmacists, chemists, traditional medical practitioners or unqualified drug dealers. Traditional herbal medicines constitute a major part of the consumption of therapeutic remedies, often in combination with orthodox medicines. Innovative ways of collecting safety information from this kind of practice will have to be initiated.

The FDB has appointed an Adverse Reactions Advisory Committee to assist the National Centre for which Alex Dodoo is the coordinator (alexooo@yahoo.com).

The Ghana National Drugs Programme is being supported by 5-year ear-marked funding from the Dutch Government.

Ghana was admitted to the WHO Programme as an associate member country last year.



Kenneth Hartigan-Go

The Philippines

A prominent person in the WHO pharmacovigilance programme, Dr Kenneth Hartigan-Go, left the Bureau of Food & Drugs in the Philippines on 31 May, 2001,

where he had the position as Deputy Director.

He has rejoined the University of the Philippines, College of Medicine, Department of Pharmacology and Toxicology and has also become the Executive Director of the Zuellig Foundation. This is a non-governmental organisation focussing on public health issues in the Philippines.

The national ADR unit will continue to operate at the Bureau of Food and Drugs with Dr Marissa Macaraeg as contact person.

The new contact details for Dr Hartigan-Go are:
Zuellig Foundation
5F Zuellig Building
Sen. Gil Puyat Avenue
Makati City, Philippines
Tel: +63 2 845 7204
Fax: +63 2 843 1495

European Union

At its meeting on 27 February - 1 March, 2001, the EU Committee for Proprietary Medicinal Products (CPMP) appointed Dr Fernando Garcia Alonso, Spain, as the new chairperson of its Pharmacovigilance Working Party. Dr Garcia Alonso is replacing Dr Patrick Waller from the UK.

India

A workshop on ADR Monitoring was organised in Mysore, India, 30 March - 1 April by the Central Drugs Control Organization and the WHO country office.

Around 30 delegates involved in drug safety monitoring in India participated. The main objective was to initiate steps for establishing a viable and sustainable pharmacovigilance programme in India.

People's Republic of China

The National Center for ADR Monitoring was founded in 1989 and joined the WHO International Drug Monitoring Programme nine years later.

In this, the most populous country on earth, there are eleven regional centres based in major cities around China which collect and collate ADR cases for onward reporting to the National Center. Other provincial centres are planned to open shortly. China is establishing a National Pharmacovigilance Information Net (NPIN) to link the eleven regional centres and the UMC; there is a local area network at the National Center.

Since 1998, an Adverse Drug Reactions Newsletter has been published in Chinese, and from June 2001 a version in English will be produced - mainly for the benefit of colleagues from countries in the WHO Programme. There are also plans for a Chinese Adverse Drug Reaction Information Bulletin.

Some important academic training meetings have been arranged around the country (two more this year in Hangzhou in June and Changsha in September), while over 1,000 participants have attended Regional Center training courses over the last few years.

Clearly impressive and steady progress from Director Shaoli Li and his seven colleagues!



News *from* the Uppsala Mon

New type of software solution for National Centres

the UMC has, together with a group of IT consultancy companies, performed a feasibility study for a new form of on-line service based on the technology of *the UMC* database. The pre-study was funded by the Swiss Drug Regulatory Agency, the IKS. The agency will be funding the development of the first version. The planned system will replace the present pharmacovigilance software module used by the Swiss National Centre. With the new system the Swiss Centre will be working over the Internet and will be storing all data directly in *the UMC* database. The system will be developed during the remaining part of 2001. A number of additional functionalities will have to be developed and added to the current system, such as security and user authentication.

Our plan is to invite other National Centres to use *the UMC* database as their repository for ADR data. For each additional centre there will be some additional development but the goal is that this solution will be a cost efficient alternative for National Centres. It will also improve the reporting frequency to the WHO database since the reports will be made available for search and analysis directly after the final assessment of the National Centre.

We will inform you about the development of this project in future issues of *Uppsala Reports*. If you want to know more about the project please contact Daniel von Sydow: daniel.von-sydow@who-umc.org.

Pharmacovigilance in Focus

A collaboration project between *the UMC* and Adis International has resulted in a publication entitled *Pharmacovigilance in Focus- the Theory and Practice of Pharmacovigilance*. This book of approximately 450 pages contains a selection of 12 review articles, earlier published by Adis mainly in the journal Drug Safety. The articles, by Ralph Edwards, Marie Lindquist, Ronald Meyboom, Sten Olsson and others, are divided into the following sections:

- Introduction
- General Issues
- Practical Issues: National Centre Context
- Practical Issues: International
- Pharmacovigilance
- From Data to Rational Drug Use
- Perspective.

Ron Meyboom from *the UMC* and Rosie Stather from Adis have put this reprint collection together. It may be obtained from *the UMC*; the price is US\$7 per copy. Contact Inger Forsell (inger.forsell@who-umc.org)

Recent publications from *the UMC*

1. Olsson S. Pharmacovigilance and the need for medical specialist participation. UEMS Compendium of Medical Specialists 2001, 2001(2): p163-165
2. Olsson S. The Need for Pharmacovigilance, in Pharmacology and Therapeutics in the New Millennium, Gupta S K, Editor. 2001: p 502-508
3. Coulter D M, Bate A, Meyboom R H B, Lindquist M, Edwards I R. Antipsychotic drugs and heart muscle disorder in international pharmacovigilance: data-mining study. Br Med J, 2001. 322(7296): p1207-9
4. Fucik H, Farah M H, Meyboom R H B, Lindquist M, Edwards I R, Olsson S. Vigilance of Herbal Medicines at *the Uppsala Monitoring Centre*. Minerva Medica, 2001. 92: p 24-26



Monitoring Centre

Thinking and planning:

In April *the* UMC team spent two days away from the office for a team planning conference in Uppsala.

Here they are relaxing in bright Swedish sunshine between sessions.



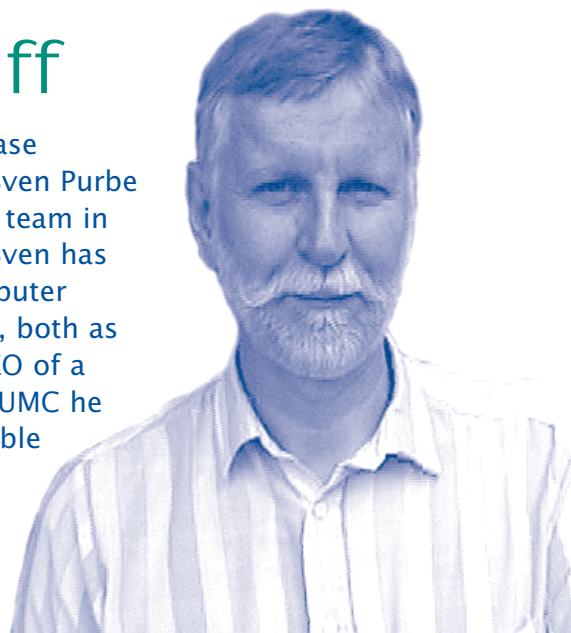
For most of the conference the team was split up into smaller working groups, and had very lively and fruitful discussions on various topics, including:

- priorities and coordination of the many projects that team members are involved in;
- commercial interests versus scientific work; the need for a balance between the two;
- relationships with different partners in the UMC's world-wide network.

This was a profitable two days, both for individuals and for the whole team.

New Staff

We've got a new database manager! His name is Sven Purbe and he joined *the* UMC team in early May. In the past Sven has worked with both computer hardware and software, both as an employee and as CEO of a small company. At *the* UMC he will mainly be responsible for development and maintenance of the Drug Dictionary database.



Forthcoming Courses & Meetings in Pharmacovigilance

Continued from page 9

IIR is organizing the following events:

- A 2-day interactive training course titled *Introduction to Adverse Event Reporting & Pharmacovigilance* in London, UK on 20-21 September 2001
- A conference on *Optimising Blood Product and Substitute Safety* in London, UK on 26-28 September 2001

For registration contact Customer Services on:
Tel: +44 (0)20 7915 5055
Fax: +44 (0)20 7915 5056.

The 9th Annual Meeting of the International Society of Pharmacovigilance (ISoP) will take place in Carthage-Tunis, Tunisia, 17-20 October 2001.

The first day 17 October is dedicated to a workshop on standardising casualty assessment.

For further information contact:

Tunisia Convention Bureau
Tel: +216 (1) 860 202
Fax: +216 (1) 860 130
E-mail: tcb@planet.tn

The Informa Pharmaceutical Academy is organizing a 3-day course with the title *An Introduction to Pharmacovigilance and Adverse Event Reporting* in Brussels, Belgium on 26-28 September 2001

For more information call the bookings hotline:
Tel: +44 1932 893851



More News *from the Upps*

Conferences

Mohamed Farah and Helena Fucik have attended three recent scientific meetings where *the UMC's* activities on monitoring of herbal preparations were presented:

'Rational Phytotherapy - Clinical Trial on Herbal Medicinal Products', organised by the Swedish Academy of Pharmaceutical Sciences in Stockholm, 14 February 2001

'Natural Products 2001 & Cosmeceuticals', organised in London by IBC Global Conferences, 28-29 February 2001

'Herbal Medicines and Cancer', organised by the University of Florence, Departments of Oncology and of Clinical Medicine in Florence, 8-9 June 2001,

In all meetings the presentation by *the UMC* stressed the need of using a standardised nomenclature (genus+species+author) for identification of herbal substances.

Visitors from China

A six-member delegation from the State Drug Administration (SDA) of the P.R.China visited *the UMC* on 19 March, 2001. Head of the delegation was Professor Bian Zhen Jia, Deputy Director General of the SDA.

The programme included presentations of activities and priorities of the SDA and *the UMC* in pharmacovigilance, leading into a discussion on the scope for further collaboration. In particular discussions focussed on the need for training and communications.

Recent events in *the UMC herbarium*

Dr Xiaorui Zhang, Acting Co-ordinator for Traditional Medicines at the Department of Essential Drugs and Medicines Policy, WHO, Geneva visited *the UMC* 30 May - 1 June. Mohamed Farah presented the work done so far with regard to herbal classifications and safety monitoring of medicinal products of herbal origin.

Discussions were also held about further integration of the work done at *the UMC* with activities coordinated by the WHO regarding traditional medicines. Dr Zhang invited a representative of *the UMC* to attend the Third WHO Consultation on Selected Medicinal Plants and The WHO Informal Meeting on Methodologies for Quality Control of Finished Herbal Products.

Both meetings are being held in Ottawa, Canada, in July 2001, *the UMC* will be represented by Mohamed Farah. Dr Zhang visited the Department of Pharmacognosy, University of Uppsala and listened as UMC staff members Helena Fucik and Jenny Ericsson presented their theses for Bachelor of Pharmacy. The title of Helena's paper is 'Building a Computerised Herbal Substance Register for Implementation and Use in the WHO International Drug Monitoring Programme'. Jenny wrote her thesis on 'Drugs of Natural Origin in Sweden'.

The final session of Dr Zhang's stay was devoted to a visit at the estate of Carl Linnaeus, the father of systematic botany, in the outskirts of Uppsala.



Uppsala Monitoring Centre

Product News

1st Quarter 2001 Update

The new versions of the computerised WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 1st quarter of 2001 are now available. It was sent to subscribers during May 2001.

If you are a subscriber to either WHO DD or WHO-ART and have not yet received the update, please contact Inger Forsell (inger.forsell@who-umc.org).

Data files for the 2nd quarter of 2001 should be available by August/September 2001.

Umeå International Summer Conference

Anne Kiuru reports:

The 1st Umeå International Summer Conference on Adverse Drug Reactions was held in Umeå, northern Sweden on the 14th and 15th June. The 158 participants from 15 different countries came from academia, industry, health care and regulatory agencies. The two conference days were filled with interesting symposia and posters where subjects within the ADR panorama and its evaluation were discussed.

Andrew Bate and Ralph Edwards from *the UMC* presented and discussed the signal generation process using neural network data-mining. Pharmacogenetics of ADRs, communication about drug risks, new databases and criteria for taking drugs off the market were also among the topics discussed.

Ralph Edwards chaired the afternoon session on drug risk communication, which included a presentation on modern communication skills by Bruce Hugman, one of *the UMC's* consultants. The audience expressed strong commitment to this important area of learning and development.

Where are you? We need your help!

Due to mergers and acquisitions and new contact persons or new addresses, there is a risk that our ongoing subscribers and other customers do not receive their ordered products.

We need your help to keep our files up-to-date. Please inform us about your current communication details by post, fax or email (inger.forsell@who-umc.org).

We would also appreciate if you gave us your current area of responsibility, for us to be able to target our information to the right users in the future.



And finally... (with caution)

as a service to readers, we are pleased to reproduce useful advice devised by three doctors from British Columbia, and set out in a letter to the *Annals of Pharmacotherapy* in 1993:

A number of products available on the market today contain a combination of ingredients and, although a few combination products are useful, such as trimethoprim/sulfamethoxazole, most are unnecessary and do not allow for flexible dosing, which is important in dosing medications to the individual patient. Although we do not intend to promote the use of combination products, there is apparently an ingredient that, if added to all single-entity drugs, would revolutionize the use of and improve the safety of all medications. Almost without exception, recommendations in drug monographs, drug reviews, etc., state that in certain instances drugs be "taken with caution" or "use with care". To us it makes sense that either caution or care, in varying doses, should be added to all drugs. It may be that this combination is not presently available because no one really knows how much caution or care to use. This is evidenced by the fact that drugs, in general, are rarely prescribed with enough caution or care. Presented below are guidelines to help practitioners decide how much caution/care should be added to drugs. Once these drugs have been given with appropriate doses of caution or care, then the clinician must properly monitor the drug therapy. Quotations come from actual recommendations from a variety of drug review articles and monographs published in the Physician's Desk Reference.

"Use with caution"

A normal dose (1 g) of caution should be given with this drug to prevent toxicity from occurring.

"Special precautions should be taken"

Give a unique/special dose (3.14159 g) of caution in a sustained-release preparation at least six hours before administering the drug.

"Administer with caution"

Give the drug with an extra large dose (4 g) of caution, because this drug is so toxic that it must be given with a member of the clergy present (add minister?).

"Caution should be exercised"

Give the drug with a healthy dose (8 g) of caution and suggest a weekly exercise program to prevent excess toxicity from occurring.

"Use with extreme caution"

This drug is so toxic that it requires a dose of caution so large (14 kg) that, in fact, the amount of caution may cause toxicity (or at least damage should the tablet fall on the patient). Therefore, the drug should likely not be used at all.

"Administration should be performed with extreme caution"

This, to our knowledge, has nothing to do with drugs, but is a warning to all hospital administrators, that their duties should be done with extreme caution in order to avoid annoying clinicians

"Applied with caution"

This is for topical preparations, and one must mix in an equal amount of caution before applying this drug to any surface area.

"Care should be taken"

If one does not have any caution handy, or a combination product with caution is not available, then this drug can be used with care, which is an effective alternative to caution.

"Watch closely"

Drugs with this warning must be prescribed only if one has keen eyesight and is willing to chaperone the patient 24 hours a day to identify potentially strange "goings on". Aging clinicians with presbyopia should, for obvious reasons, not use this drug.

"Monitor closely"

This warning suggests that these drugs have specific toxicities that can be identified only by placing a monitor (e.g. a CT scan) on or close to the patient at all times (infinitely long extension cords or battery packs may be required).

"Monitor periodically"

For energy-conscious clinicians or those without extension cords, these drugs may be monitored by reading journals or other publications.

"Measured periodically"

Drugs with caution have the potential to cause loss of weight but, unfortunately, at the expense of height. Patient who find it becomes difficult getting on rides at amusement parks should be taken off the drug, measured, and then watched closely (see above).

"Monitoring must be done at regular intervals"

Many things should be done at regular intervals (e.g., sleeping, eating, sexual intercourse) and the appropriate regular intervals are determined by the ease of giving these drugs during these activities.

"Should be given with great care and under close observation"

This requires that only mothers or grade-school teachers must give these drugs.

Terms such as those presented above provide little useful information.

We encourage authors not to use terms such as "monitor closely" or "use with caution". These terms are likely used because it is often difficult to be concise and specific about such issues. Despite this, drug companies/authors/clinicians should attempt to provide recommendations that are more meaningful and allow the clinician to use and monitor drug therapy more effectively.

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