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# Uppsala **REPORTS**

For everyone concerned with the issues of pharmacovigilance and toxicovigilance



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## MESSAGE FROM THE DIRECTOR

### Working with ISoP

I'm looking forward this year to a closer relationship between the WHO Programme for International Drug Monitoring and ISoP – the newly internationalised Society of Pharmacovigilance (previously ESOP), of which I was elected

President at the 2000 Annual Meeting in Verona.

ISoP's particular aim is to provide a forum for all those with an interest in the clinical and scientific aspects of drug safety, not just for full-time pharmacovigilance professionals. There are more details in the enclosed copy of the ISoP Star.

Staff at WHO headquarters have welcomed a closer association between ISoP and the WHO Programme. We'll try to arrange linked meetings, and wherever possible, back-to-back annual meetings (though it won't be possible this year). It seems most valuable that those involved in the various national pharmacovigilance centres in the Programme should have an extended opportunity for scientific debate with others committed to drug safety in their clinical work and research.

### Involving Everyone

Thinking about the future of the WHO Programme has occupied some of our time recently. We have to be sure our activities maintain the interest and commitment of developed countries, at the same time as providing essential service to developing countries as their national systems are established and begin to grow. We are always keen to be told how we can best develop to provide a service to all.

Communications issues (particularly getting benefit-risk information effectively out to clinicians) and the larger public health questions also remain at the heart of our concerns.

I hope we can continue to debate these matters together throughout the year, but especially at the ISoP Annual Meeting in Tunisia (17-20 October) and the WHO Programme Annual Meeting in New Zealand (20-22 November).



Ralph Edwards

## TUNISIA 2000 A FIRST IN AFRICA

**The 23rd Annual Meeting of the WHO Drug Monitoring Programme was held in Tunis 12-14 November 2000, with a pre-meeting tutorial on the 11th. This was the first time ever that the meeting had been held either in Africa or in an Arab country. Normally the meetings are held in English but this time simultaneous English-French translation was provided. The meeting was attended by 80 people from 40 countries around the world.**

### COMPREHENSIVE COVERAGE

#### Plenary sessions were devoted to:

- Crisis Management and the Importance of Good Communications Practice
- Pharmacovigilance and Rational Drug Use
- Case presentations on how epidemiological methods are applied by National Centres
- Adverse Effects in a Paediatric Population
- Adverse Reactions to Anti-HIV medication.

#### In working group sessions the meeting dealt with:

- Safety Monitoring of Herbal Preparations
- Vaccine Safety Surveillance
- ADR Terminologies
- Computer Software for Management of ADR Reports.

The working group on computer software formed a committee that will assess some existing report management systems used by National Centres with the aim of being able to recommend functional, low-cost computer support to newly established pharmacovigilance centres.

In addition to the subjects mentioned a variety of issues related to specific drugs were presented and discussed in the lively 'Drugs of Current Interest' sessions.

The annual meetings provide a unique forum for drug safety specialists to exchange information and views on safety problems of common concern. The meeting evaluation for Tunis 2000 revealed a high level of satisfaction among participants with both the professional content and the social side of the meeting.



## JOIN US!

### 24TH ANNUAL MEETING FOR NATIONAL REPRESENTATIVES NEW ZEALAND, 2001

This year's meeting will be taking place in **Dunedin University, New Zealand from 20-22 November**. David Coulter, Head of the Centre for Adverse Reactions Monitoring – and a familiar figure to those who've been to previous meetings – will be organising the event.



Otago Harbour, (courtesy Dunedin City Council)

The outline Programme looks like this:

<b>Pre-meeting tutorial for new member countries and new staff at National Centres</b>	<b>MONDAY 19 NOVEMBER</b>
<b>Welcome Event</b>	evening
<b>1st day's programme of discussions</b>	<b>TUESDAY 20 NOVEMBER</b>
<b>Mayoral Reception Conference Dinner</b>	afternoon evening
<b>Half day programme Half day excursion</b>	<b>WEDNESDAY 21 NOVEMBER</b>
<b>Full day's programme Free evening</b>	<b>THURSDAY 22 NOVEMBER</b>
<b>Excursion for those able to stay</b>	<b>FRIDAY 23 NOVEMBER</b>

## HELP SHAPE THE PROGRAMME!

*the UMC* is very keen that the programme should reflect your interests and priorities. If you haven't received or seen the questionnaire about the programme sent out by Sten Olsson –

- Please contact him and ask for one
- Send in your suggestions anyway by phone, fax or email (\*see below)

Whether or not you are expecting to attend the meeting, please let us know what you think are the priorities for discussion.

## IT'S A LONG WAY!

For some member countries travel to New Zealand may be a problem – we're only too aware of that. If you are keen to attend but fear you will have funding problems, please contact Sten Olsson\* at *the UMC*. No promises, but he'll do everything he can to help if at all possible.

## IT'S A GREAT MEETING

Last year's meeting in Tunisia was very enjoyable and productive. It set new standards for very effective use of the time together. There are going to be lots of important items on this year's agenda – and lots of great people! Do come!

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## Cuba

In March 2001 a one-week pharmacovigilance workshop was held in Cuba with participation from Dr Figueras, University of Barcelona and Mr Mariano Madurga, Spanish Medicines Agency. This workshop arose from the first National Meeting of Pharmacovigilance, which was held in Havana 19-20 September 2000, with participants from fourteen of the fifteen provinces of the country. Results of the reporting scheme were presented and thoroughly discussed. A series of recommendations for improvement of the pharmacovigilance system was adopted.

## Guatemala, Bolivia and Spain

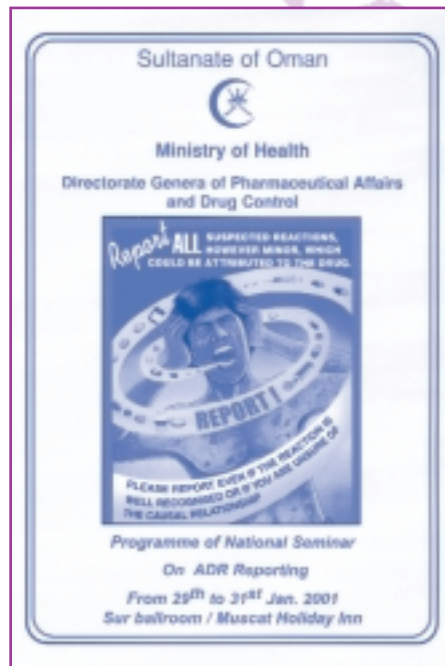
The Spanish International Cooperation Agency, AEI, is organizing a two-week training course in Pharmacovigilance and Pharmacoepidemiology in Antigua, Guatemala, 7-18 May, 2001. The course language is Spanish. The Spanish Medicines Agency and the Catalan Foundation of Pharmacology will provide the professional content. Course fee and accommodation are provided by AEI.

A similar course was held in July 2000 at Santa Cruz de la Sierra, Bolivia, with 32 participants from 12 Latin American countries. That course also had a module on quality control of pharmaceuticals. For more information about the course in Guatemala, please contact **Mariano Madurga Sanz**, the Spanish Medicines Agency, **Tel: +91-596 7711**, **Fax: +91-596 7891**, **E-mail: mmadurga@agedmed.es**

## Ireland

The Irish Medicines Board is making an effort to engage dentists in the reporting of adverse drug reactions. An article has been published in the Journal of the Irish Dental Association and meetings are being held with representatives of the profession. Reference: Flint S.R, O'Sullivan, C, Arthur N. An Update of Adverse Drug Reactions of Relevance to General Dental Practice. Journal of the Irish Dental Association **46: 67 - 70 (2000).**

## Oman



*New booklet produced in Oman skilfully adapting Malaysian poster*

An adverse reaction reporting programme was started in Oman in 1992 and in 1994 the country joined the WHO Programme. Because of low and even falling reporting rates from health professionals the Directorate General of Pharmaceutical Affairs decided to organize a National Seminar on ADR reporting 29-31 January, 2001.

Close to two hundred physicians and pharmacists from all parts of



*Dr Sawsan Ahmed Jaffer and Dr Dirk Deleu at the Oman Seminar*

the country attended this seminar at which prominent clinicians described their experiences. Ronald Meyboom and Sten Olsson from the UMC gave their perspectives on good pharmacovigilance practice and the need for adverse reaction reporting. Dr Wolfgang Schumann and Dr Patricia Fleuranceau-Morel provided views of the international pharmaceutical industry from Schering AG.

After three days of discussions it was concluded that:

- **local training seminars should be organised around the country**
- **pharmacovigilance should be introduced in education for healthcare professionals**
- **better coordination of present efforts should be attained**
- **involvement of clinical pharmacists and hospital drug and therapeutic committees should be encouraged**
- **the effects of the seminar should be followed up periodically.**

## Russia

The Pasteur Institute in St Petersburg, Russia, organised a seminar on *Monitoring of Vaccination Adverse Events* on 16 February 2001, in collaboration with the Nordic Council of Medicines. The objective was to promote spontaneous reporting of adverse events following immunisation to an audience of approximately 200 health professionals. Ms Kristin Kvande from the Norwegian Medicines Agency, Dr Hanna Nohynek from the National Public Health Institute in Finland and Dr Preben Aavitsland representing the National Institute of Public Health in Norway presented experiences from the Nordic countries. Sten Olsson from the UMC advocated international collaboration and pooling of data to facilitate early detection of rare events.

## United Kingdom

The London School of Hygiene and Tropical Medicine is running a post-graduate training course *Certificate in Pharmacoepidemiology & Pharmacovigilance* from 13 February - 2 July 2001. The course is part-time and comprises 55 hours of formal teaching and contact time, 70 hours of self-directed study and 50 hours of project work. Formal teaching is taking place in London during three sessions. Those interested in future courses should contact the course secretary **Deborah Curle**: **Tel: +44 (0)20 7927 2489**, **Fax: +44 (0)20 7637 3238**, **E-mail: d.curle@lshtm.ac.uk**

## Uruguay

Several activities were carried out in Montevideo, Uruguay, in early December 2000, to sensitise health professionals to the need for adverse reaction reporting. *Pharmacovigilance Days* were organised on 4, 5 and 6 December by the Coordinating Centre for Toxicology and Pharmacovigilance (Professors Mabel Burger and Carolina Seade) and the General Directorate for Health, Ministry of Public Health. In addition to presentations of the local situation Sten Olsson from the UMC gave his views on the need for pharmacovigilance and provided guidelines on how to set up a pharmacovigilance centre. Dr Gonzales Negri from ANMAT presented experiences from Argentina.

On 7 and 8 December the health organization COCEMI organized an *International Course on Drug Safety Monitoring* with some 200 participants from different parts of Uruguay. Lectures were given by experts from the pharmacovigilance centres in Argentina and Chile, from the UMC, and from Pharmacia Corporation, USA.

## Zimbabwe

In August 1998 the Medicines Control Authority arranged an international ADR training course in Kadoma, Zimbabwe. The results of the training activity were evaluated and described in an article which has now been published. Reference: Evaluation of a Training Course on Pharmacovigilance in Sub-Saharan Africa. *Pharmacoepidemiology and Drug Safety* **9: 133 - 138 (2000).**

## New members of the WHO Drug Monitoring Programme

**Welcome to two more countries**, Macedonia and Sri Lanka, who have now been admitted as formal members of the WHO International Drug Monitoring Programme. The total number of members is now **60**.

An application has also been received from Ministry of Health, Ghana. However, Ghana has not yet submitted any case reports in the agreed format and is regarded as an associate member country until the technical details have been sorted out. Ghana joins the five other associate members.

**Contact persons in the three countries are:**

### Ghana

Dr Alex Dodoo  
Centre for Tropical Clinical Pharmacology & Therapeutics  
University of Ghana Medical School  
Korle-Bu Teaching Hospital  
ACCRA, Ghana  
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### Macedonia

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### Sri Lanka

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**Fax: +94 1 695 230**  
**E-mail: phrm\_cmb@slt.lk**



**Meyler's Side Effects of Drugs - 14th edition**

The latest edition of this encyclopaedia was recently published by Elsevier Science (ISBN 0-444-50093-6). Dr Graham Dukes is famous for having edited this number-one source of annotated information of adverse drug reactions since the 8th edition in 1975. He is now doing it for the last time, sharing the burden with Dr Jeffrey Aronson and eight co-editors. The 1,870 pages are divided into 49 chapters. Each chapter covers medicines used in a specific therapeutic area and provides extensive referencing to the world literature. To each medicine a short adverse reaction pattern is given after which all significant reactions are listed, sorted by system-organ class. Ralph Edwards of *the UMC* is responsible for the introduction entitled, 'What are we doing in medicines safety?'

**Risk Communication and Public Health**

This book, edited by Peter Bennett and Kenneth Calman, brings together a wide variety of perspectives on risk communication, from the health professionals, campaigning organisations, governments and their advisory committees,

academia, consultancies. It should be of interest not only to those involved in risk-assessment and risk-communication but also to anyone interested in the role of science and the media in the political process. It is published by Oxford University Press 1999, ISBN 0-19-263037-7.

**Consumer Reports on Medicines - Policy and Practice**

A consensus document adopted by the first international conference on Consumer Reports on Medicines held in Sigtuna, Sweden, 29 September-1 October 2000 is now available. This 12-page document (which is being translated into Russian, French and Spanish) may be obtained from the organizers of the conference: Kilen, Kammakargatan 7, S-111 40 Stockholm, Fax: +46 8 6960110, E-mail: kilen@kilen-institutet.se.

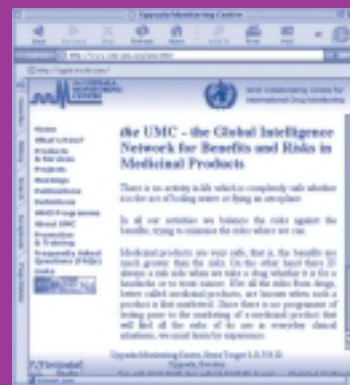
It may also be downloaded from the Internet web site [www.kilen.org](http://www.kilen.org)

In connection with the conference a 12-minute video recording was made. It includes interviews with leading opinion-makers about the need for adverse reaction reporting and consumer participation. The video may also be obtained from Kilen.

**Exchange of website addresses**

At *the UMC* we're keen to provide links from our web site to other relevant sites that people interested in drug safety and pharmacovigilance might want to know about. Naturally we wish to apply strict quality criteria when choosing sites. We would welcome suggestions from our readers of websites they

consider interesting and valuable from a pharmacovigilance perspective. Please submit your suggestions to [info@who-umc.org](mailto:info@who-umc.org). We would also recommend our partners to make sure that a link is provided from your website to ours. The URL is <http://www.who-umc.org>



**Useful Websites**

**Metabolic interactions**

It is not uncommon that adverse reactions or failing therapeutic efficacy are demonstrated to be due to metabolic interactions between medicines or between medicines and other agents. The following internet websites provide free search facilities for information on documented metabolic interaction. They may be valuable tools when assessing the plausibility of new adverse reaction signals.

**1. <http://www.gentest.com>**

Click on the 'Human P450 Metabolism Database'. This site is maintained by Professor Slobodan Rendic, Department of Pharmaceutical Chemistry, Faculty of Pharmacy and Biochemistry, University of Zagreb, PB 156. A. Kovacica 1, HR 10000 ZAGREB, Croatia.  
**Tel:** +385 1 481 8304, **Fax:** +385 1 485 6201  
**E-mail:** [rens@nana.pharma.hr](mailto:rens@nana.pharma.hr)

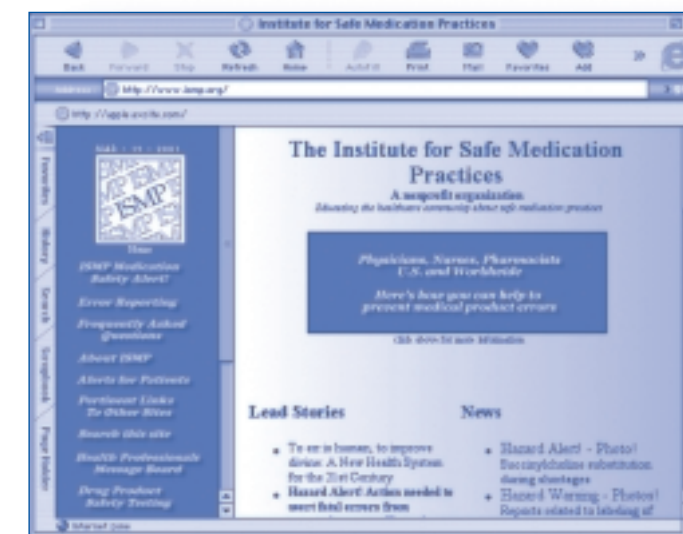
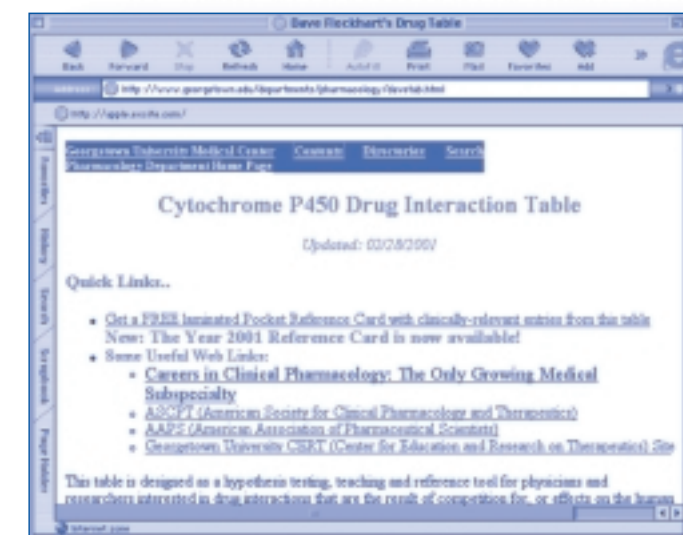
**2. <http://dml.georgetown.edu/depts/pharmacology/davetab.html>**

This site is maintained by Dr David A. Flockhart, in the Division of Clinical Pharmacology at Georgetown University, USA,  
**E-mail:** [flockhad@gusun.georgetown.edu](mailto:flockhad@gusun.georgetown.edu)

**Medication errors**

The Institute for Safe Medication Practices, a non-profit organisation located in Huntingdon Valley, Pennsylvania, USA maintains an Internet web site with the address <http://www.ismp.org/>. The site displays recent examples of medical errors and provides facilities for reporting of medical error experiences. It also provides contact details to institutions in Canada, Hong Kong, Israel, Spain, Sweden, United Kingdom and USA where reports of medical errors are welcome. From the site one may also subscribe to the ISMP Medication Safety alert, a newsletter published every other week.

The United States Pharmacopoeia has ceased operating its Drug Products Problem Reporting Programme. Those reporters who previously used this programme are encouraged to report drug quality problems to the FDA MedWatch programme.





# News *from* the Uppsala Monitoring Centre



## Uppsala awaits invasion...

### 6th International Pharmacovigilance Training Course in Uppsala

*the* UMC is again inviting health-care professionals who have recently started or will soon start in the practical operation of pharmacovigilance programmes to a two week training course in Uppsala from 7-18 May, 2001.

The first course of this kind was organized in 1993. This time we are focusing on methodological aspects of pharmacovigilance, cutting out some of the clinically-oriented lectures that were included in the five previous courses.

Module I is devoted to methods used in spontaneous adverse reaction monitoring, while module

II provides an introduction to pharmacoepidemiology.

Although *the* UMC has not been able to offer any fellowships to cover the costs of the training we were happy to receive a great number of applications. Some support was received from WHO headquarters to assist a few applicants from developing countries. In all 58 individuals from 35 countries applied for the 25 places available.

Selection of applicants to be admitted to the course was made on the basis of a series of criteria including:

- balanced geographical distribution
- representative mix of established and newcomer countries
- mix of institutional links e.g. regulatory/clinical/academia/industry
- relevant position and educational background
- balanced gender distribution.

The difficult selection process ended up in admitting 28 individuals altogether to one or other of the two modules. The participants represent 28 different countries from all six WHO regions.



Helena Sjöström, Jenny Eriksson and Jessica Nilsson

### More pharmacists joining *the* UMC team

In the previous issue of *Uppsala Reports* 13 we mentioned that Helena Sjöström was employed at the Centre last September to help with the processing of incoming adverse reaction reports. This time we have a picture!

Early this year the report processing and dictionary updating team was further strengthened by Jenny Eriksson and Jessica Nilsson joining us. They are all graduate pharmacists from the University of Uppsala. In addition Helena has taken pharmacy courses at the University of Pennsylvania, Philadelphia, USA.

### USA Vaccine ADRs added

In *Uppsala Reports* 13, we advised that a significant number of vaccine-related

adverse reactions reports had been received from the Centre for Disease Control (CDC) in the USA. Since then another batch of reports has arrived from CDC and we have now incorporated close to 120,000

case reports of vaccine-related adverse reactions from the USA in the WHO database, covering the period up to the end of 2000. We expect to receive regular contributions from CDC from now on.

## Inside the FDA

Cecilia Biriell and Ronald Meyboom from *the* UMC paid an extremely interesting two-day working visit to the FDA pharmacovigilance unit in Washington DC, 'Office of Post-marketing Drug Risk Assessment' (OPDRA) in October last year.

After being introduced to the new management, Drs Peter Honig and Martin Himmel, a presentation was given to an audience of some 60 people describing current developments at *the* UMC. Together with 'foreign affairs' Dr Andrea Neal, Cecilia and Ronald had talks with representatives of the many subsections of OPDRA.

### Matters of special interest were

- compatibility of the new OPDRA software and *the* UMC
- statistical signal detection
- MedDRA and WHOART
- communications between the centres

OPDRA is flourishing; it has now around 80 staff members, including 20 full-time safety assessors, who are primarily responsible for studying ADR case reports. As explained by Dr David Graham, much attention is now being paid to the testing of hypotheses and the follow-up of signals through the Co-operative Agreement Program. Also, a special system has been put in place for the reporting (i.e. stimulation, recording and evaluation) of medication errors, encompassing about ten trained experts.

*the* UMC delegation returned home with a wealth of information regarding new procedures, fields of interests and current priorities at OPDRA, useful for fine-tuning of the information to be provided by *the* UMC and for streamlining and intensifying collaboration.

Working visits will take place to other National Centres in due course. There is so much to learn from each other!

### Out and About...

A series of visits by a small delegation from *the* UMC is planned to various National Centres, in order to provide support and help in ensuring timely reporting to the WHO database.

Many developments and changes are continuously taking place at National Centres. New staff members come, tasks expand and priorities change. *the* UMC aims at the best collaboration and is keen on providing individual centres and their staff with information tailored to their needs and interests.

## Distinguished newcomers New signal reviewers joining *the* UMC panel

Last year we announced in this newsletter our need for additional volunteers to join our panel of signal reviewers. To our great satisfaction many eminent professionals have approached us stating their interest in taking part in *the* UMC signal review process. The following experts have now started helping us in assessing the clinical significance of the drug-reaction associations identified by our data-mining technique as being reported to the WHO data base more frequently than expected:

- Dr W Curt Appel, Kusuri Canada Corporation, Ottawa, Canada  
E-mail: wcappel@kusuricanada.ca
- Prof Dr Andrew Czeizel, Foundation for the Community Control of Hereditary Disease, Budapest, Hungary.  
E-mail: czeizel@mail.interware.hu
- Dr Nicholas R Dunn, Aldermoor Health Centre, Southampton, United Kingdom  
E-mail: nick.dunn@soton.ac.uk
- Prof Pierre Gillet, Laboratoire de Pharmacologie, Vandoeuvreles Nancy, France  
E-mail: gillet@medecine.uhp-nancy.fr
- Dr Alice Kuruvilla, Department of Pharmacology, PSG Institute of Medical Sciences and Research, Coimbatore, India  
E-mail: Psgimsr@md3.vsnl.net.in
- Dr Saad Shakir, Drug Safety Research Unit, Southampton, United Kingdom  
E-mail: saad.shakir@dsru.org
- Prof Krishnan C. Singhal, Department of Pharmacology, J N Medical College, Aligarh Muslim University, Aligarh, India  
E-mail: kcsinghal@VSNL.com
- Dr Myles Stephens, Bishop's Stortford, Herts, United Kingdom  
E-mail: stephmdb@lineone.net
- Prof Mabel E Valsecia, Catedra de Farmacología, Facultad Medicina, Universidad del Nordeste, Corrientes, Argentina  
E-mail: mvalsecia@med.unne.edu.ar



# GREAT PROGRESS

## Training course follow-up - achievement & obstacles

Exactly one year after the previous UMC pharmacovigilance training course in 1999, the participants received a follow-up questionnaire asking about achievements and obstacles in implementing the action plan they were requested to do during the course. Half of the participants responded to the questions put to them. The major achievements and obstacles mentioned were:

### Achievements:

- centre for drug information and pharmacovigilance established (**Mozambique, Venezuela**)
- pharmacovigilance programme adopted by authorities (**Sri Lanka**)
- new ADR reporting form designed and put to general use (**Kyrgyzstan, Latvia, Mozambique**)
- campaigning to achieve greater awareness about importance of ADR reporting (**Brazil, India, Sri Lanka, Kyrgyzstan, Mozambique, Venezuela, Zimbabwe**)
- publications on ADR monitoring (bulletins, newsletters, journal articles) (**China, Kyrgyzstan, Latvia, Malaysia, Mozambique, Poland, Sri Lanka, Zimbabwe**)
- pharmaceutical decision-makers realise importance of pharmacovigilance (**Singapore, Zimbabwe**)
- improved reporting rates (**India, Kyrgyzstan,**

### Malaysia, Poland, Zimbabwe)

- improved resources for pharmacovigilance centre (**Singapore**)
- legislation including pharmacovigilance adopted or proposed (**China, Latvia, Poland**)
- pharmacovigilance introduced in training curricula for health care professionals (**India, Venezuela**)
- Periodic Safety Update Reports requested from producers and evaluated (**Poland, Sri Lanka**)
- ADR database established (**China, CSL company, Poland**)
- ADR reports sent to *the* UMC (**China [more than before], Sri Lanka**)
- collaboration with national vaccination programme initiated (**Zimbabwe**)

### Obstacles, problems encountered

- occupied with many other tasks than pharmacovigilance (**Malaysia, Mozambique, Zimbabwe**)
- lack of financial resources or adequate staff (**Latvia, Mozambique, Zimbabwe**)
- organisational or administrative reforms (**China, Singapore**)
- things take much longer than expected (**CSL Company**)
- lack of response from health professionals (**Kyrgyzstan, Latvia, Venezuela**)
- lack of computer facilities (**Kyrgyzstan**)
- managing software for reporting to *the* UMC (**Sri Lanka**)
- pharmacovigilance low priority among decision makers (**Brazil, Latvia**).

## ANDREW ADVANCES

### UMC TEAM MEMBER NOW A PhD STUDENT

Andrew Bate was recently accepted as a PhD student by the Department of Clinical Pharmacology, University of Umeå, Sweden. His supervisor is Professor Rune Dahlqvist. Andrew has already been heavily involved in the development of the BCPNN -

methodology (Bayesian Confidence Propagation Neural Network) that *the* UMC now uses in the identification and analysis of new adverse reaction signals. He will continue refining this approach for his PhD thesis.



# BEYOND ADRs

## WHO and the future of pharmacovigilance



The team gathered in Geneva: Back row: Bruce Rowsell, Rachida Soulaymani-Bencheikh, Niamh Arthur, Yukiko Maruyama, Vladimir Lepakhin, Sten Olsson, Kenneth Hartigan-Go, Ralph Edwards, Kenich Tamiya, Lembit Rägo; Front row: Mary Couper, Nilima Kshirsager, Ushma Mehta, Peter Folb

**A**n international group of experts met on 19-20 October, 2000, in Geneva under WHO auspices to discuss the future destiny of pharmacovigilance. The hope is to develop the fundamental framework of the science of pharmacovigilance and shape the agenda for the next decade.

The meeting was initiated as a follow-up to the publication of a technical paper on how to set up a pharmacovigilance centre. The results of the discussion are being prepared for distribution.

During the discussions it became rapidly apparent that pharmacovigilance goes far beyond the strict definition of post-marketing surveillance. It is rather a process to secure the safest possible use of medicinal products for patients. It was recognised that this apparently simple aim involves a number of complex issues: for example, balancing effectiveness against risk and affordability.

Comparisons between medicinal products are not easy to make, and decisions that are in the interests of public health, may not serve the best interests of individual patients.

### Other demanding issues include:

- empowering patients to share responsibility for treatment – this involves a far greater degree of communication and education and is not a straightforward issue
- the influences affecting the use of medicinal products by health professionals
- the influences on good stewardship in safety matters in the pharmaceutical industry – this being a shared responsibility by the pharmaceutical industry, the prescribing doctors and the patients themselves.

There was also a large agenda of more detailed topics for future discussion, investigation and action. It is quite clear that there is much to be done in the future. The assembled group saw an urgent need for pharmacovigilance to develop way beyond trying to detect adverse reactions to newly marketed products.

It is hoped that the eventual text *The Value of Pharmacovigilance* will have a strong impact.

## JOB OPPORTUNITY AT the UMC

We are looking for a statistician, or a computer scientist with some statistical experience to work on the further development of the quantitative signal detection tool used by *the UMC* (the BCPNN). The person would preferably be interested in analytical and numerical statistical methods and want to develop further experience with neural networks and data-mining. The applicant should also have good written and oral English.

We would consider applicants available from a few months up to or exceeding a year. However, potential collaborators should be prepared to stay here in Uppsala for most of the time. Payment will be provided, and is negotiable but will depend on the qualifications and experience of the applicant.

Those interested should submit a CV, including background in statistics and computer science, to Andrew Bate, who will be happy to provide more information about the project.

**Apply to Andrew Bate, Programme Leader, Signal Research Methodology, *the UMC*, Stora Torget 3, S-753 20 Uppsala, Sweden. E-mail him at: [andrew.bate@who-umc.org](mailto:andrew.bate@who-umc.org)**

## UMC HEAD-CASE?

**Sten Olsson shows his international credentials by sporting very un-Swedish headgear!**



## END OF AN ERA *All change at the UMC board*



The 1998 Board retires: (left to right), Ms Margaretha Hammarberg, Dr Ellen Vinge, Mr Alf Nilsson (chairman) and Mr Thomas Norell.

***the Uppsala Monitoring Centre*** is a foundation formed by the Swedish government over twenty years ago. The government appointed a new board in July 1998 while the future administrative structure of the Centre and its links with WHO were being reviewed. The result of the review was presented in September 1999. The Government was considering the proposals and discussions were being held with WHO during last year.

The new management structure now awaits discussion by the WHO Executive Committee. To make way for the smooth implementation of a proposed new management structure the board that has served since 1998 resigned in December 2000.

We are very grateful for the diligent work and valuable contributions made by the four board members.

## Product News

### 4th Quarter 2000 Update

The new versions of the computerised WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 4th quarter of 2000 are now available. It was sent to subscribers during February 2001.

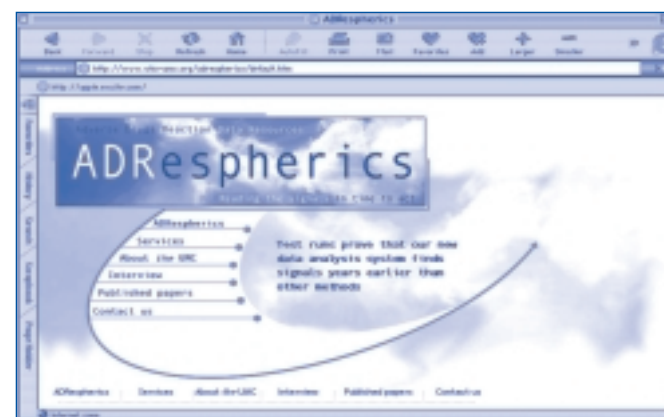
If you are a subscriber to either WHO DD or WHO-ART and have not yet received the update, please contact **Inger Forsell** ([inger.forsell@who-umc.org](mailto:inger.forsell@who-umc.org)).

Data files for the 1st Quarter of 2001 should be available by the end of May 2001.

### ADRespherics

ADRespherics, the commercial version of the BCPNN approach to data-mining using the WHO database for signal detection, is now an established standard service. Potential customers are invited to contact **Mats Persson** ([mats.persson@who-umc.org](mailto:mats.persson@who-umc.org)) for further information. The service was described in the May 2000 edition of *Uppsala Reports*. You can also find out more about ADRespherics on our website:

[www.who-umc.org/adrespherics/default.htm](http://www.who-umc.org/adrespherics/default.htm)



## UMC EXHIBITIONS

***the UMC has been represented at the following conferences during 2001:***

SMI conference, Pharmacovigilance, Perspectives and Future Directions, 21-22 February 2001, London, UK

DIA conference, Controversies in Drug Safety, 26-27 February 2001, Toronto, Canada

DIA conference, Annual Euro Meeting 2001, 6-9 March 2001, Barcelona, Spain

***the UMC plans on being represented at the following conferences during the rest of 2001:***

Applied Clinical Trials conference, European Summit, 14-16 May 2001, Paris, France

DIA conference, Safety Information & Labelling, 24-25 May 2001, New Orleans, US

DIA conference, 37th Annual Meeting, 8-12 July 2001, Denver, US

ISPE 17th International Conference on Pharmacoepidemiology, 24th -26th August, Toronto, Canada.

**We hope to meet many of our readers and friends at one or other of these events!**

## 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 customer 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](mailto:inger.forsell@who-umc.org)). We would also appreciate if you gave us your area of responsibility, for us to be able to target our information to the right users in the future.



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

1. A training programme with the title **Drug Safety Surveillance and Epidemiology** in Washington, USA, 23-25 April and in Philadelphia, USA, 15-17 October, 2001
2. A workshop on **Safety Information and Labelling** in New Orleans, USA, 24-25 May, 2001
3. The 37th Annual Meeting - Denver, USA on 8-12 July 2001. As in the Annual EuroMeeting, one of the session topics is Clinical Safety/Pharmacovigilance
4. A seminar on **Medical Approach in Diagnosis and Management of ADRs 2001**, in Paris, France, 25-26 October, 2001
5. A workshop on **Pharmacovigilance into 2002** in London, UK, 5-6 November, 2001

For more **information** on these 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**

- The Drug Safety Research Unit (DSRU) in Southampton, UK, will organise two different public events, a Workshop on **Medical Aspects of ADRs** in spring 2001 and the **1st Annual DSRU Conference on Pharmacovigilance** in June 2001. For **information** please contact Georgina Spragg:  
**Tel: +44 (0)23 8040 8600**  
**Fax: +44 (0)23 8040 8609**  
**E-mail: georgina.spragg@dsru.org**

- IPT (International Pharmaceutical Training) is organising an interactive training course with the title **Introduction to Adverse Event Reporting & Pharmacovigilance** in London, UK, 10 - 11 May and 20 - 21 September 2001. Course leader is Dr Curt Appel, formerly responsible for the ADR Monitoring Division at Health Canada. For further **information** contact IPT:  
**Tel: +44 (0)20 7915 5055**  
**Fax: +44 (0)20 7915 5056**  
**E-mail: registration@iir-conferences.com**

- The **1st Umeå International Summer Conference on Adverse Drug Reactions** will be held in Umeå, Sweden, 14-15 June, 2001. The subtitle is: Predicting, detecting, understanding and avoiding ADRs. The conference is organised by the Division of Clinical Pharmacology, Umeå University, S-901 85 Umeå, Sweden. For more **information** contact the Umeå Congress Bureau:  
**Tel: +46 90 130034/130035**  
**Fax: +46 90 130036**  
**E-mail: booking@umea-congress.se**

- **EPHAR 2001**, July 6th-9th Lyon, France. The Journées Françaises de Pharmacovigilance will take place in 2001 in Lyon, before the meeting of the Fédération des Sociétés Européennes de Pharmacologie. PACKAGE, 140, cours Charlemagne, 69002 Lyon, France.  
**Phone: +33 4 72 77 45 50**  
**Fax: +33 4 72 77 45 77**  
**E-mail: package@package.fr**

- **Introduction to Pharmacovigilance and Adverse Event Reporting** is a training course being organised by IBC 26-28 September 2001, in Brussels, Belgium. For **information** please contact IBC:  
**Tel: +44 (0)193 2893851**  
**Fax: +44 (0)193 2893893**  
**E-mail: cust.serv@informa.com**

- The **9th Annual Meeting of the International Society of Pharmacovigilance (ISoP)** will take place in Tunis, Tunisia, 17-20 October 2001. For further **information** and registration forms please contact the Centre National de Pharmacovigilance.  
**Tel: +216 1 562 098 or +216 1 564 763**  
**Fax: +216 1 578 196 +216 1 571 390**  
**E-mail: chalbi.belkahia@rns.tn**

- **2nd Course on Promoting Rational Drug Use in the Community**. Two-week training course aimed at health programme staff from ministries of health, universities, development agencies, non-governmental organizations. Course language: English. To be held in an African country during September/October of 2001. Exact dates and venue to be confirmed. For **information**, please contact: Daphne Fresle, Department of Essential Drugs and Medicines Policy, World Health Organization, CH-1211 Geneva 27, Switzerland.  
**E-mail: fresled@who.int**

## DISCOUNT DEAL ON REACTIONS WEEKLY



**National Centres participating in the WHO Drug Monitoring Programme now get discount subscriptions to the review journal *Reactions Weekly*.**

This results from an agreement between *the UMC* and Adis International, the publisher. According to the agreement, effective from 1 January 2001, *the UMC* makes a bulk subscription to *Reactions Weekly* for all its National Centres at one third of the list price. Many more countries can now keep up with world medical literature on adverse drug reactions at a very reasonable price. Some countries (Finland, Ireland, Norway and Switzerland) have generously agreed to pay for more than one discount subscription, thus allowing more National Centres to benefit.

### *Reactions Weekly*

- reviews about 1,800 medical journals worldwide for articles on adverse drug reactions
- provides summaries of the original publications in paper print and as an on-line service.

*the UMC* has agreed to supply Adis with copies of adverse reaction newsletters and bulletins from the National Centres taking part in the WHO Programme.

Translations into English of articles in Scandinavian languages will also be provided to Adis. National Centres also benefit from *the UMC* - Adis deal by having access to information from national adverse reaction bulletins on a weekly basis instead of quarterly as was the case when *the UMC* produced its own Adverse Reactions Newsletter. This newsletter is now discontinued.

## RECENT PUBLICATIONS from the UMC

1. Edwards I R, Lindquist M. Understanding and communication of key concepts in therapeutics. In: **Moments of truth - Communicating Drug Safety**. 2000. Verona, Italy: Elsevier Science.
2. Lindquist M. Signal detection using the WHO international database. In: **8th Annual Meeting European Society of Pharmacovigilance**. 2000. Verona, Italy: Elsevier.
3. Bate A, Lindquist M, Orre R, Meyboom R H B, Edwards I R. Automated classification of signals as group effects or drug specific on the WHO database. In: **8th Annual Meeting European Society of Pharmacovigilance**. 2000. Verona, Italy: Elsevier.
4. Meyboom R H B, Lindquist M, Flygare A K, Biriell C, Edwards I R. Should therapeutic ineffectiveness be reported as an adverse drug reaction? In: **8th Annual Meeting European Society of Pharmacovigilance**. 2000. Verona, Italy: Elsevier.
5. Pettersson M, Lindquist M, Edwards I R. Signal analysis using international ADR and drug utilization data. In: **8th Annual Meeting European Society of Pharmacovigilance**. 2000. Verona, Italy: Elsevier.
6. Meyboom R H B, Lindquist M, Eijgenraam M, Ståhl M. Loperamide and urinary retention - a new adverse effect of an old drug. In: **8th Annual Meeting European Society of Pharmacovigilance**. 2000. Verona, Italy: Elsevier.
7. Edwards I R, Aronson J K. Adverse drug reactions: definitions, diagnosis, and management. **Lancet**, 2000; 356: 1255-1259.
8. Meyboom R H B. The Case for Good Pharmacovigilance Practice. **Pharmacoepidemiology and Drug Safety**, 2000(9): 335-336.
9. Wiholm B-E, Olsson S, Moore N and Waller P. Spontaneous Reporting Systems Outside the US. In: **Pharmacoepidemiology**, Strom B L (Ed). 2000, John Wiley & Sons Ltd: West Sussex. 175-192.
10. Orre R, et al. Bayesian neural networks with confidence estimations applied to data mining. **Computational Statistics and Data Analysis**, 2000. 34(8): 473-493.
11. Lindquist M, Ståhl M, Bate A, Edwards I R, Meyboom R H B. A retrospective evaluation of a data mining approach to aid finding new adverse drug reaction signals in the WHO international database. **Drug Safety**, 2000. 23(6): p. 533-542.
12. Edwards I R. Introduction: What are we doing in medicines safety? A perspective from *the Uppsala Monitoring Centre*. In: **Meyler's Side Effects of Drugs**, Dukes G, Aronson J K, (Eds). 2000, Elsevier.
13. Olsson S, Edwards I R. The WHO International Drug Monitoring Programme. In: **Side Effects of Drugs Annual 23**, Aronsson J K (Ed). 2000, Elsevier. p. 524-529.
14. Coulter D M, Bate A, Meyboom R H B, Lindquist M, Edwards I R. Antipsychotics and heart muscle disorder in international pharmacovigilance; a data mining study. **BMJ** (in press).





## Obituary

*As a person Åke Liljestrand was modest, almost shy, talking with a rather quiet voice. He always had a funny story to share with his friends and colleagues.*

### Åke Liljestrand

**The first chairman and acting director of the WHO Collaborating Centre, Professor Åke Liljestrand, died late last year at the age of 83.**

He was instrumental in creating a modern drug control system in Sweden and was director of the Swedish drug control authority from 1970 until his retirement in 1982. He took an active part in the development of efficient systems for adverse reaction reporting both in Sweden and internationally. Åke Liljestrand became chairman of the European Society for the Study of Drug Toxicity in 1972. In 1974 he was appointed member of the WHO Expert Committee for Drug Evaluation.

In 1977 the WHO was planning to end the International Drug Monitoring Programme and he was



active in persuading the Swedish Government to take on the responsibility for running the Programme by creating the WHO Collaborating Centre for International Drug Monitoring based in Uppsala.

The agreement between WHO and the Swedish government was signed in January 1978 and Åke Liljestrand was appointed acting director and chairman of the Board. He then devoted much time and energy to the proper establishment of the Uppsala Centre and he organised the 1st Annual Meeting of Representatives of National Centres, held in Uppsala in November 1978.

As a person Åke Liljestrand was modest, almost shy, talking with a rather quiet voice. He always had a funny story to share with his friends and colleagues. He also had a strong temper, however, and fought hard for his views in scientific discussions.

We are indebted to Åke Liljestrand for being instrumental in establishing what is now known as *the* UMC. We remember him with warmth and gratitude.

## the Uppsala Team



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