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Uppsala reports

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

MESSAGE FROM THE DIRECTOR

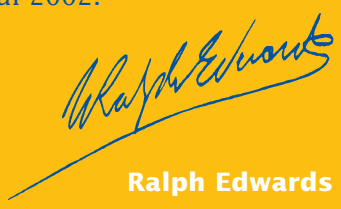
Springtime in New Zealand was changeable for our Annual Meeting in November, but the magnificent South Island scenery provided the lovely backdrop for a memorable and useful conference. With representatives from 35 countries, a substantial agenda was covered and many items of common interest discovered and discussed.

Details will be reported elsewhere, but here are a couple of things which struck me very forcibly. First, we had a number of distinguished presentations from developing countries, covering challenges special to them, but which have global relevance. Especially challenging were the monitoring of new drugs used for tropical diseases, and herbal and traditional medicines. The influence of true globalisation on the Programme is set to become more and more powerful and exciting; that is beyond doubt.

Second was the subject of improper external pressures on regulators and scientists in pharmacovigilance – an unprogrammed item which emerged as an issue of great concern to many participants. The discussion provoked a number of anecdotes, which have serious implications. This is an issue that demands attention, starting by collecting the available substantive evidence, before full consideration and appropriate action.

David Coulter and his team managed to attract a great deal of media coverage during the few days of the meeting – radio, TV and newspaper – a reminder to us all of the continuing challenge of getting our information and knowledge out to a wider audience.

I hope we shall see many of you at next year's meeting in Amsterdam. In the meantime, from all of us at the UMC, very best wishes for a happy and successful 2002.



Ralph Edwards

Ground-breaking Collaboration in Drug Safety Data

World-wide drug safety is soon to become available on the web for commercial customers and for member countries of the World Health Organisation (WHO) Programme for International Drug Monitoring. It offers access to a range of data previously exclusive or relatively inaccessible.

Software developed by QED Inc., includes up-to-the-minute search and analysis tools providing invaluable resources for national regulatory authorities, pharmaceutical companies and medical scientists wishing to examine the safety profile of drugs in clinical use. The software, QScan is already available to pharmaceutical companies for use on their own databases, and on data released by the US regulatory authority (FDA) under Freedom of Information legislation. *the* Uppsala Monitoring Centre will be making available data from the WHO world-wide database of drug safety information (including over three million reports) which will be accessible alongside the US data.

The real benefit of this collaboration to future users is the simple, user-friendly web-access to the data and the practical search and analysis tools. Previously the WHO data has been available only with relatively unsophisticated search and analysis tools, or via service requests to *the* UMC. The service will be developed further and made available after summer 2002.

Ralph Edwards believes the collaboration will provide invaluable new opportunities for member countries and for commercial customers: "The WHO database is a unique resource providing an international perspective on the safety profile of thousands of drugs. Now its data can be searched and analysed more readily and effectively than ever before. We hope it will make a further contribution to the reduction of harm to patients from the effects of drugs and to the improvement of patient care world-wide."

For further information on this collaboration, please contact Daniel von Sydow at *the* UMC.

With this edition of Uppsala Reports you will find a paper by S Z Rahman and K C Singhal on 'Problems in Pharmacovigilance of Medicinal Products of Herbals Origin and Means to Minimise Them'.

Dunedin on our minds

Report by Sten Olsson

It was not without certain worries that we accepted the invitation from New Zealand to host the 24th Annual Meeting of Representatives of National Centres participating in the WHO International Drug Monitoring Programme. Not that we had any reason for doubting the quality of the programme or the hospitality. However, for most people involved in our network, going to New Zealand requires some considerable long-distance travelling which is associated with higher than normal costs. It was only fair however that the New Zealand centre, being one of the founding members of the WHO Programme and contributing more actively to its progress than most, should get the attention it deserves from the international community by hosting the meeting. For once the New Zealand representatives did not have to make the annual long-haul trip! After the events of 11 September we feared that the attendance rate at the Dunedin meeting would be exceptionally low. However, we severely misjudged the attraction power of New Zealand, Dunedin and the Annual WHO Meeting. Approximately 80 representatives of 35 countries attended the meeting, which is a very good outcome under the circumstances.

Judging from comments from delegates and statements in the meeting evaluation form, the 24th Annual Meeting was one of the best ever. The mix of the high standard professional programme and the unique social events were exceptionally rewarding. There was something for everyone in the programme offered.

Some of the topics highlighted during the meeting were:

- The risks of transmitting Bovine Spongiform Encephalopathy via pharmaceuticals and blood products (Professor Jürgen Beckman, Germany and Dr Elwyn Griffiths, WHO)
- Safety monitoring of borderline substances
  - Dietary supplements (Ms Margaret Carlson, FDA, USA)
  - Non-allopathic Indian medicines (Dr Nithya Gogtay, Mumbai, India)
  - Herbal medicines (Ms Abida Syed Haq, Malaysia)
- Effects of regulatory decisions (Dr Paul Seligman, FDA, USA)
- Principles of benefit/harm assessment (Ralph Edwards, UMC)
- Pharmacovigilance and Public Health (Dr Rachida Soulaymani, Morocco/ Nithya Gogtay, India).

One morning was devoted to methods and concerns given particular attention in New Zealand:

- The Intensive Medicines Monitoring Programme (Dr David Coulter)
- Linking adverse reaction reporting with a Medical Warning System (Dr Michael Tatley)
- Brand substitution - national implications for pharmacovigilance (Prof Tim Maling/Dr Natasha Rafter).

In one session the meeting split into four parallel working groups. The subjects discussed were:

- Approaches to promoting ADR reporting
- Present and future benefits of being a member of the WHO Programme
- Linking pharmacovigilance to rational drug use
- Consumer reporting.

Intermingled with the topics mentioned above were sessions devoted to discussions on individual drug problems of current concern.

David Coulter, Mary Couper, and the host for 2002, Kees van Grootheest alongside the Taieri Gorge railway

Bruce Hugman was in charge of managing the meeting process, which he did with his customary elegance, humour and firmness. The host team, under the direction of Dr David Coulter, provided delegates with the most favourable conditions for professional discussion and social encounters. In addition to a Maori welcome ceremony, receptions with the University and the Mayor of Dunedin, we were taken for penguin and seal watching (albatrosses were hatching and could not be visited). There was also the most spectacular train ride into the surroundings of Dunedin, including a visit to a sheep farm with 25,000 sheep.

If you travel half-way around the globe you wish to experience something exceptional - and so we all did. Thank you, David and team, for your efficiency, warmth and generosity.

The Annual Meeting is always a good opportunity to meet old friends and make new ones, to catch up on developments and discuss common problems and share solutions. For UMC staff members, travelling such a long distance to be in attendance at Dunedin meant stop-overs which were put to great use in up-dating us on what is happening in several Asia-Pacific countries. We pass on our experiences to Uppsala Reports in the following pages.

A return to the challenges of Vietnam

I have had the privilege to follow the development of drug safety monitoring activities in Vietnam since the early 1990s (writes Sten Olsson). The Drug Monitoring Centre in Hanoi was formally inaugurated in December 1994 and in June 1996 a second centre was established in Ho Chi Minh City. Both centres are located within the premises of the drug quality control laboratories.

Dr Tran Thi Nhung

Since the establishment of the monitoring centres a lot of effort has been made running training courses and other promotional activities in the various provinces of Vietnam. Professor Hoang Tich Huyên in the north and Dr Cao Minh Quang in the south have been initiators of these out-reach activities. Their efforts have not been without results. Adverse reactions case reports are now being received from all provinces, in all some 5,000 reports have been collected. Reports from physicians account for some 60%, while reports from pharmacists account for around 35%. The vast majority of reports refer to adverse reactions from the use of antibiotics. This time I met with Dr Tran Thi Nhung, who is running the everyday business of the Hanoi drug monitoring centre, and Professor Huyên, now retired from the Medical School but still active in promoting pharmacovigilance. Their main concern is the lack of suitable computer software for processing and analysis of the case information they receive. There have been earlier attempts to install commercial computer software for managing this task but for various reasons the systems have never become operational. Because of this lack of proper tools for analysis of data, the information collected has been seriously under-utilised. Feedback has been provided mainly as individual responses to reporters and overall reporting statistics. The Ho Chi Minh City centre publishes its own bulletin, and in the north messages are distributed to health professionals through articles in the journal Clinical Pharmacy.

I encouraged Dr Nhung and Professor Huyên to ensure that all reports are submitted to the WHO database without delay, using the reporting software provided by the UMC. From *the* UMC the Vietnamese centre may then receive a detailed account of their reports, sorted by product, by reaction or by any other parameter. Once the Vietnamese centre has its own database in operation old reports may be retrieved from the WHO database.

It is of major importance for us working at *the* UMC to visit National Centres from time to time to be faced with the challenges our partners in the Programme are confronted with. We can only provide support and assistance if we know what the everyday problems are! I'm very grateful to Dr Nhung in particular for taking the time to explain to me in detail about the working routines of the Vietnamese Centre and sharing with me her aspirations and hopes for future development.

New Zealand and Thailand

Monica Pettersson visited the National Centres in Dunedin and in Bangkok, during her travel from the National Centres meeting in New Zealand.

"Before I left New Zealand I spent a day at the National Centre in Dunedin, with Ms Janelle Ashton. We discussed some of the technical aspects of reporting to the WHO database. I also had some follow-up questions from the presentation that Dr Michael Tatley and Janelle Ashton made during the National Centres meeting. We also spent some time discussing the IMMP (Intensive Medicines Monitoring Programme). On my way home from Dunedin I had the pleasure to stop for half a day at the National Centre in Bangkok, Thailand. I was invited to have lunch with the team in the APR (Adverse Product Reaction) Monitoring Centre, four very keen pharmacists and the new Head of the APR Monitoring Centre, Ms Pornpit Silkavute. It was a very nice lunch, (though the food was hotter than I am used to in Sweden!) I discussed general issues about the Programme, with Ms Pornpit.

Later, I met her staff and discussed important technical issues regarding reporting to the WHO Adverse Drug Reaction database.

The Thai system has developed impressively, to include 23 regional centres in hospital settings. They now have some 11,000 case reports a year."

Visit to the Safety Division, Pharmaceutical and Food Safety Bureau, Tokyo

On 13 November, Dr Mary Couper from WHO Headquarters and Cecilia Biriell from *the* UMC visited the National Adverse Reaction Centre in Tokyo, Japan, reports Cecilia.
The purpose of the visit was to increase the communication and co-operation between the Japanese centre and the WHO Programme, given Japan's importance in the Programme.
The head of the Safety Division, Dr Tatsuo Kurokawa, welcomed us. The Safety Division consists of around 30 people, of whom 8 work on the safety of pharmaceuticals. Our agenda was long and we had a full day meeting with all the staff of the pharmaceuticals safety section, with Mr Tamaki Fushimi leading the discussions.

Mary Couper presented the WHO's new strategy in pharmacovigilance work and I presented the current activities of *the* UMC. One of the main topics of the day was how reporting to the WHO database from Japan can be improved both in terms of number of reports and speed of submission. A new database for industry reports in the ICH-format is planned, and this would enable submission of industry reports from Japan to WHO.
Improved communication of safety information was also discussed. The WHO could possibly help in the translation of material from the Japanese language, since there exists a significant language barrier.
The meeting was very fruitful and a preliminary invitation was made for some of the Tokyo staff to visit *the* UMC in the spring to further develop the co-operation.

Data-mining in Australasia

Andrew Bate presented a paper entitled "Quantitative signal detection in the WHO database" at the 1st Annual DIA Workshop In Japan For Global Pharmacovigilance on 1-2 November at Aioi Sonpo Shinjuku Hall, Tokyo, Japan.
The objective of the meeting was 'to share basic and fundamental knowledge about the mechanisms of pharmacovigilance among specialists from the US, Europe and Asia to reveal differences and similarities between practices internationally'.
Other participants included Dr David Coulter from New Zealand, and Dr Tatsuo Kurokawa from the Ministry of Health in Japan.
In connection with the National Centres meting in Dunedin, Andrew also had discussions with Dr Ian McDonald and his colleagues from the computer science department at Dunedin University who have an interest in data-mining.

Article continued overleaf

*Adis International, publishers of **Reactions Weekly** and **Drug Safety**, have their main office in Auckland, New Zealand, so the Annual Meeting offered UMC staff a chance to meet our contacts in their natural habitat!*
The reprint collection 'Pharmacovigilance in Focus' is still available from the UMC (price US$7) - contact Inger Forsell for details: inger.forsell@who-umc.org
In the Adis office - Sam Masters, Rosie Stather, John McKeogh.

Ian Boyd, Andrew Bate and Pat Purcell outside the TGA Canberra

Andrew also held discussions about data-mining while in Australia following the Dunedin meeting. On December 3rd he had productive meetings with a group lead by Dr John Yearwood from the School of Information Technology and Mathematical Sciences at the University of Ballarat, near Melbourne. Following some initial work undertaken by Dr Pat Purcell, they have begun a collaborative research project on data-mining the Australian database of drug adverse reactions. They were keen to hear more about the UMC's recent experiences of data-mining the WHO database.

The following day, Andrew flew from Melbourne to Canberra, to make another presentation and hold discussions about the UMC data-mining project with the Australian National Centre Therapeutic Goods Administration (TGA). This meeting involved Dr Ian Boyd and Dr Pat Purcell, who gave Andrew a guided tour around the TGA building and described more about their activities. He also introduced the newer members of staff in the ADR unit at TGA.

A New Adverse Drug Reactions Unit for Canberra

On the way to the Annual National Centres meeting, there was a chance for Mary Couper and Cecilia Biriell to visit the National Centre in Canberra, Australia, writes Cecilia.

"It was good to revisit Canberra and the Australian National Centre, (where the National Centres meeting was held in 1987). The TGA (Therapeutic Goods Administration) now has new, very attractive premises in the outskirts of Canberra, (where they said you can see kangaroos hopping around.) We were introduced to all staff by the head of the centre Dr John McEwen."

The Australian centre currently has a staff of around ten people, and has recently recruited two new medical officers. The Australian centre makes much use of its very active Adverse Reactions Committee, which meets eight times a year. It was encouraging to see that 'Sending reports to WHO' is regularly ticked off on the big chart on the wall after each committee meeting.

"I was introduced to the Australian way of automated signal detection by Dr Patrick Purcell, and explained *the* UMC's combinations database to some of the newer staff". Further co-operation between the TGA and *the* UMC in this area will be developed, involving Andrew Bate from *the* UMC (see page 5).

Australia has from the start of the WHO programme been one of its most active members, and we have every reason to believe that this will continue in the future.

Medical Toxicology Congress in Penang

Ralph Edwards was a key-note speaker at the Third International Congress of the Asia-Pacific Association of Medical Toxicology, held in Penang, Malaysia, from 12-15 November 2001.

In the section 'Information and communication technology', he spoke on the need for international co-operation between those collecting and interpreting adverse drug reaction reports, and the reports held at poison control centres.

This WHO Programme experience has been used to alert health professionals to new adverse drug reactions. Reports to poison control centres contain a wealth of clinical detail, and about a third of poisonings in many centres are due to drugs.

Ralph foresaw great potential in:

- Structured information on poisoning/chemical injury cases, to allow for better epidemiology and assessment of public health impact, as well as giving vital clinical information on trends and treatment outcomes. Data-mining can be applied to detailed case information and give insights into the effects of treatment.

- Better case details in pharmacovigilance, to improve the diagnosis and management of ADRs. Information on overdose can be crucial in the consideration of the safety of certain drugs, such as antidepressants.
- Exchange of staff and pooling of some resources would invigorate and improve the efficiency of each of the disciplines of clinical toxicology and pharmacoepidemiology.

Visit to 'Lion City'

On our way to the other side of the world (from a Swedish perspective that is New Zealand) and the 24th Annual National Centre Meeting, Marie Lindquist and myself took the opportunity to visit the National Centre in Singapore (writes Helena Sjöström).

From cold wintry Sweden, we arrived late at night to a warm and humid city, where Chan Cheng Leng (Head, Pharmacovigilance and Information & Research, Centre for Pharmaceutical Administration) welcomed us and drove us to the hotel. After a good night's sleep and a hearty breakfast, we were prepared for a day at the Centre for Pharmaceutical Administration within the Health Sciences Authority (HSA). Together with Cheng Leng and her team we discussed several issues concerning ADR reporting as well as reviewing their publications within the pharmacovigilance area.
We also had the great opportunity to attend Kenneth Hartigan-Go's lecture on "Linking Pharmacovigilance with Rational Drug Use" where he brought experiences from drug safety monitoring in the Philippines mixed with interesting drug related examples.

We were pleased to meet Dr. Clarence Tan (Chief Executive, Health Sciences Authority) and his team, over a scrumptious lunch at the restaurant Xin Cuisine.
The afternoon started with a refreshing and very interesting walking tour around the National University Hospital (NUH), guided by Suwarin Chaturapit (Deputy Director for Pharmacovigilance, Communications & Research). The hospital holds 935 beds and is government-owned.
The rest of the day was spent at the National Centre, where we continued the discussions on ADR reporting with a contribution from Henry Soh, an IT and technical expert.

Lunch at Xin Cuisine, Singapore
From top left: Suwarin Chaturapit, Marie Lindquist, Dr Kenneth Hartigan-Go (Department of Pharmacology & Toxicology, University of the Philippines), Dr. Clarence Tan, Cathy Hartigan-Go (wife of Kenneth), Ang Pei San (Pharmacist, Pharmacovigilance, Centre for Pharmaceutical Administration); front left: Chan Cheng Leng, Professor Edmund Lee (Pharmacology Department, National University of Singapore), Dr. John C W Lim (Director, Centre for Pharmaceutical Administration), Helena Sjöström.

Seminar in Suva

One of the most isolated members of the WHO Programme was visited by Helena Sjöström and Cecilia Biriell after the National Centres Meeting. They had been invited by Mr Peter Zinck, chief pharmacist at the Government Pharmacy in Suva, the capital of Fiji, to hold a seminar in adverse reaction monitoring. The audience consisted of physicians, pharmacists and nurses from all over Fiji, mostly from the main island Viti Levu.
Fiji has been a member of the WHO Programme since 1999, but due to lack of resources and because one key staff member has left, drug monitoring is at present virtually non-existent in Fiji.

The purpose of the seminar was to introduce the concept of adverse reaction monitoring and its place in the rational use of drugs to all the participants, and to inspire them to be active in the development of reporting in Fiji.
The seminar was held over two days at the Colonial War Memorial Hospital in Suva. Lectures were mixed with working groups on how drug monitoring can be developed in Fiji and how information should be communicated. The participants were very active in the working groups and came up with many good ideas for the development of pharmacovigilance in Fiji, despite the very limited resources.
Reports from the working groups will form the basis of a document from the Government Pharmacy, which will hopefully mean a fresh start for drug monitoring in Fiji.

New strategy for detection of signals in the WHO Database

Signal Detection

Early detection of signals of international drug safety problems is an important role for *the* Uppsala Monitoring Centre. With more than 250,000 reports per year entered into the WHO Database, an automated way of picking up drug-ADR combinations for assessment is essential. Previously, in the signal detection process *the* UMC used the BCPNN methodology (Bayesian Confidence Propagation Neural Network – the data-mining used by *the* UMC) to produce quarterly line listings of new associations and then sent to members of *the* UMC international expert review panel. They chose drug-ADRs of potential interest and requested case reports from *the* UMC. If the reviewer after assessing the cases found the issue worth signalling, a summary was written for inclusion in the restricted document 'SIGNAL'.

Drawbacks with the old system

The BCPNN generates more than 2,000 new associations every quarter. This is too many for individual review and the process of sending line-listings, case reports and other information back and forth between the reviewers and *the* UMC creates extra administrative work, is time consuming and ineffective.

New Approach

From late 2002, *the* UMC will modify the approach to the detection of signals in the WHO Database. As before the selection of drug-ADR combinations to assess will be largely based on the associations highlighted by the BCPNN. However, *the* UMC will further refine the likelihood of picking up important signals by using a triage strategy. The triage will focus on the detection of serious ADRs with newer drugs and drug-ADR combinations with rapid increase in the IC value.The checking of the product information for highlighted drugs will be done at *the* UMC as part of the triage system. Potential signals, ie, adverse effects not described for the drug in the available sources, will be sent to the expert reviewers for assessment together with the case reports.

The triage strategy

Every quarter the WHO Database will be scanned using the BCPNN methodology (as before) to produce the Combinations Database. *the* UMC will then apply a set of different algorithms, on the Combinations Database to decrease the number of drug-ADRs to assess, and to increase the likelihood of finding the most important signals.

Seriousness and rapid reporting increase - new algorithm

the UMC will put its greatest efforts into never missing early signals concerning serious, potentially fatal reactions with new drugs. Introducing the following algorithm on the Combinations Database will likely help in filtering out the relevant drug-ADR combinations:

- Drug first entered into the database in the last one or two years

Figure 1

Old

- the BCPNN methodology produced quarterly line listings of new associations
- Associations sent to members of the UMC review panel
- Panel members chose drug-ADRs of potential interest.
- Reviewers requested case reports from the UMC
- UMC retrieved requested case reports from the WHO Database.
- If reviewer (after assessing cases) found the issue worth signalling, a summary was written
- Summary included in SIGNAL

itoring Centre

- The ADR is serious, ie a WHO-ART critical term
- At least one report having fatal outcome; and
- The drug-ADR combination exceeds the statistical threshold for review, ie having a lower 95% confidence limit of the IC above zero
- Few reports on the combination

Figure 1 shows the filters applied on the relevant drug-ADR combinations on the Combinations Database. *the* UMC is also concerned with drug-ADR combinations with rapid increase in the IC value indicating disproportionately increased reporting of the combination to the WHO Database. We intend to investigate closely combinations fulfilling the following criteria:

- The drug-ADR combination exceeds the statistical threshold for review, (ie having a lower 95% confidence limit of the IC above zero); and
- the IC has increased by 2 or more since the last quarter.

Special attention will be given to important drug-related reactions and terms of special interest (such as Stevens-Johnson syndrome or Lyells's syndrome, agranulocytosis or rhabdomyolysis).

International signals

A signal is more credible if the drug-ADR is reported from several countries. This is achieved by filtering on any of the above algorithms if more than one country has reported the combination.

The new approach in practice

The combinations filtered out by any of the above algorithms will be checked at *the* UMC for occurrence in the available product information literature. For drugs where the reaction is not found or not described well enough, case reports will be retrieved from the WHO Database. *the* UMC will then send the cases to the most appropriate experts in the review panel to assess the evidence for the reaction being related to the suspected drug. As before, the reviewer will draft a signal text and *the* UMC will include it in SIGNAL for distribution to all National Centres.

While human review is essential, a combination of the above triage strategies or similar approaches is necessary when attempting analysis of large amounts of data. With this new signal detection system in place we think we can make the signalling process more effective. The expert reviewers' time and competence is better used by leaving UMC to handle the triage strategies while the expert consultants use their clinical and pharmacological knowledge and experience in the assessment of the case data.

The triage strategies described above will start to be used on the Combinations Database from the second quarter in 2002. By definition, the use of triage strategies may exclude some potential signals from consideration, although the intention is to improve the chances of detection by focussing on areas of greatest importance. *the* UMC will as always be open to receive ideas for improvements.

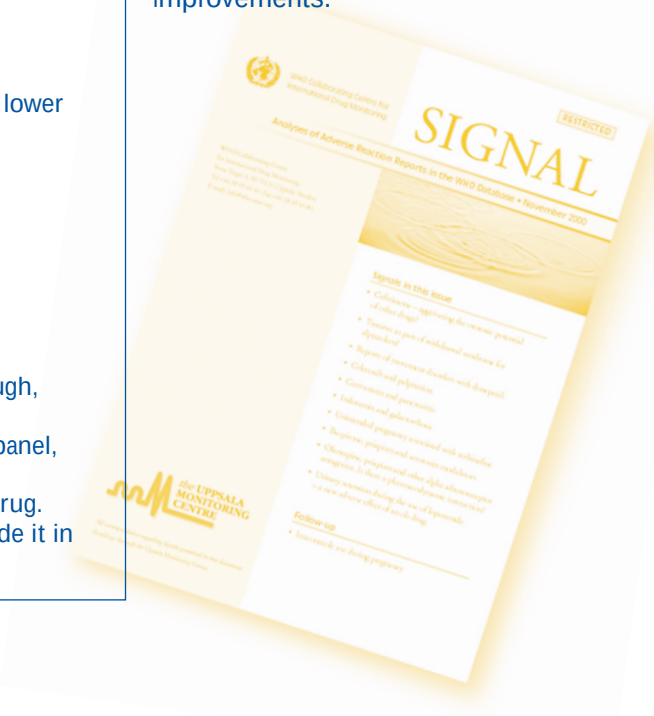
New

Every quarter the WHO Database will be scanned as before using the BCPNN methodology with a choice of new filters:

- Drug first entered in database in the last one or two years
- the ADR is serious, ie WHO-ART critical term
- term of special interst
- drug-ADR combination exceeds the statistical threshold, (ie having a lower 95% confidence limit of the IC above zero)
- few reports on the combination
- more than one country reported the drug ADR.

The following actions are then taken:

- Combinations filtered out are checked at the UMC for occurrence in product information literature;
- for drugs where the reaction is not found or not described well enough, case reports retrieved from WHO Database
- the UMC sends cases to the most appropriate experts in the review panel, who
- assess the evidence for the reaction being related to the suspected drug.
- As before, the reviewer will draft a signal text and the UMC will include it in SIGNAL



News *from the* Uppsala Moni

Corporate Portfolio – major new publication from *the* UMC

That no drug is 100% safe for all people in all circumstances (in other words that risk in medicines cannot be reduced to zero), is a truth little discussed or understood. The commonest and most familiar drugs like paracetamol and aspirin – with billions of doses taken every year –have the potential for serious harm in some circumstances and at some levels of dose.

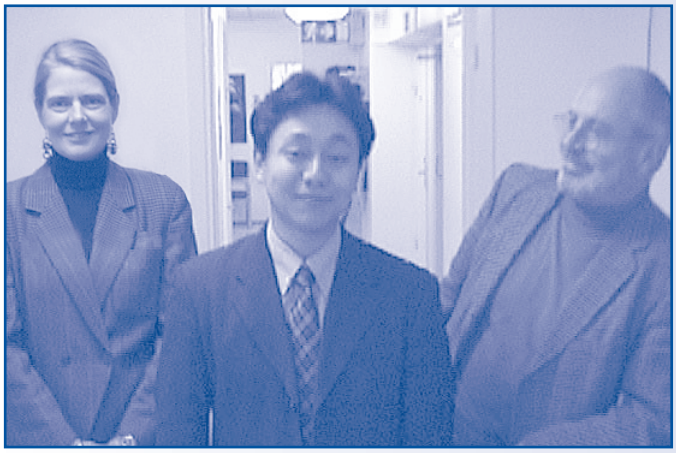
New drugs are marketed after thorough clinical trial testing, but on relatively small numbers of subjects, only maybe two or three thousand. It's likely therefore that an adverse reaction with a frequency of, say, 1 in 10,000 may not be revealed in the trial. Information about such reactions can be gathered only once the drug is generally available. This information comes through adverse reaction reporting systems.

Most drugs are known to have side-effects of varying degrees of severity. There needs to be negotiation between the doctor and patient as to whether or not the benefits of a particular drug outweigh the harm which are known sometimes to occur. These are some critical issues for patients: is there enough good information about these things, do doctors know enough about them and do doctors involve patients in the decision to use one drug or another?

the UMC believes the subject needs to be widely discussed and understood if patients are to get the best deal from their medical care, if public health is to be protected, and the occurrence of serious – and costly – adverse reactions is to be reduced. Two major new publications from *the* UMC will address these and other critical issues. Viewpoint Part 1 aimed at a general and wide audience, will seek to open up these questions to debate. Viewpoint Part 2 will be published later in 2002, and will provide a comprehensive and detailed technical account of the work of *the* UMC and the WHO in the science of pharmacovigilance – the scientific study of drug safety. This will be of greater interest to technical and medical specialists, and to member countries of the WHO Programme for International Drug Monitoring. However, the concerned layperson will also find much of interest after having read Part 1.

Japanese visitor

Mr Kenichi Tamiya, Associate Professional Officer in the Quality Assurance and Safety: Medicines department at WHO, Geneva visited *the* UMC from 3rd – 14th December. His purpose was to learn about *the* UMC's activities, and take the opportunity to get acquainted with the staff at *the* UMC and their work. In doing so he compiled a report to help Lembit Rägo and Mary Couper in Geneva better understand *the* UMC's activities, and prepare for closer collaboration between WHO and *the* UMC.



Marie Lindquist, Kenichi Tamiya and Ralph Edwards at the UMC

then on to the Arctic Circle…

As well as experiencing the very Swedish winter, (with glögg, ginger cookies, Lucia, snaps, beautiful Christmas illuminations), after his serious work was over Ken went to Gallivare in the Arctic Circle to see the aurora borealis (northern lights). Ken sent us a great description of what he saw.

"How lucky we were! We stayed there for three nights and the weather was fine every night. Around 11pm on the second night, we saw a light like a search light in the northern part of the sky. Then another white light appeared in the east sky just above the horizon and the light spread as a horizontal line. The white line then spread vertically and made a sort of curtain. It changed its figure very quickly and it was just like the curtain swung by the wind …we were spellbound by this mysterious natural phenomenon. It lasted around one hour. On the third night, a dim aurora like the Milky Way began to appear over the sky at 4:30pm and we could see it on and off until 11pm. A brighter curtain with light green colour appeared around 8pm over the mountain. It was fantastic. We went outside the hotel every 30 minutes to check the sky - with a lot of clothes inside our skiwear, thick gloves, a warm cap and a face mask - but it was worth doing it! We regret that we could not see the bright and red aurora, but we heard that one is very rare."

itoring Centre

Forthcoming Courses and Conferences

The Certificate in Pharmacoepidemiology & Pharmacovigilance will be running on the following dates in 2002:
12-15 February 9-11 April, 5-7 June, 1 July (exam)
Deborah Curle
Health Promotion Research Unit
London School of Hygiene & Tropical Medicine
Tel: + 44 (0) 20 7927 2489
Fax: + 44 (0) 20 7637 3238
email: deborah.curle@lshtm.ac.uk

14/15 February
EGA's annual regulatory affairs conference
London
Management Forum: Fax +44 1483 536424
e-mail registrations@management-forum.co.uk

5-8 March 2002
DIA Annual Euro Meeting: The Patient is Waiting (Track 4, Effective Pharmacovigilance)
Convention Centre, Basel, Switzerland
Contact: Tel +41 61 386 9393 Fax +41 61 386 9390 or diaeurope@diaeurope.org

10-12 April 2002
Drug Safety Surveillance & Epidemiology Training Course
Park Hyatt Washington, Washington, DC, USA

April/May
Liver Injury
Oxford, UK
ISoP Administration, PO Box 32974, London, SW19 8YG, UK
Email: administration@isoponline.org;
Phone / fax: +44 (0)20 8286 1888

19-22 May 2002
7th Annual International ISPOR (International Society for Pharmacoeconomics and Outcomes Research) Meeting
Crystal City, Arlington, VA ISPOR
Phone: (609) 219-0773
Fax: (609) 219-0774

18-21 August 2002
18th ISPE Conference
Edinburgh Conference Centre
Heriot-Watt University
Edinburgh, Scotland

3-5 November 2002
5th European Congress
de Doelen Congress Center,
Rotterdam, The Netherlands
ISPOR (International Society for Pharmacoeconomics and Outcomes Research)
Phone: (609) 219-0773
Fax: (609) 219-0774

Recent publication

Drug Benefits and Risks:

International Textbook of Clinical Pharmacology

Editors: Chris van Boxtel, Budiono Santoso, Ralph Edwards

ISBN: 0-471-89927-5, 734 pages, published November 2001

This new book looks at practical therapeutics and the surrounding general and pharmaceutical knowledge: an inclusive reference to the scientific basis and practice of drug therapy.
The key concept is looking at the balance between the benefits and risks of drugs and the social impact which drugs have in modern societies. Taking an evidence-based approach to the problem, the practice of clinical pharmacology and pharmacotherapy in the developing as well as the developed world is examined.

For this purpose the book

- Covers general clinical pharmacology, pharmacology of various drug groups and the treatments specific to various diseases
- Gives guidance on how doctors should act so that drugs can be used effectively and safely
- Encourages the rational use of drugs in society

This book will be invaluable for anyone working within, or associated with, the field of clinical pharmacology and pharmacotherapy - undergraduates, postgraduates, regulatory authorities and the pharmaceutical industry.

Through sponsorship by the Dutch Rad-Ar council 800 free copies will be made available for emerging countries via the member National Centres of the WHO Programme for International Drug Monitoring (see UR13 p11).

Product News

3rd Quarter 2001 Update

The new versions of the computerised WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 3rd quarter of 2001 are now available. It was sent to subscribers during early December 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 4th quarter of 2001 should be available by February/March 2002.

After attending conferences during the summer and autumn of 2001 we have received a number of requests regarding our signal detection using the BCPNN methodology. If you are interested in starting using or subscribing to the commercial version of the BCPNN - ADRespherics please do contact Mats Persson (mats.persson@who-umc.org) to set up a telephone conference to discuss more about ADRespherics and what it could do for you and your organisation.

Staff of *the* UMC will be attending at the following conferences during 2002:

- Contemporary Pharmacovigilance and Risk Management Strategies, Washington DC, USA, 14-17 January
- DIA Euro meeting, Basel, Switzerland, 5-8 March
- 17th Annual DIA Conference on Clinical Data Management, Charleston SC, USA, 17-20 March
- 38th Annual Meeting of the DIA, Chicago Il, USA, 16-19 June
- 18th ISPE Annual Meeting, Edinburgh, Scotland, 17-21 August

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

the Uppsala Team

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