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Uppsala reports

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

- WHO Drug Dictionary
- New Centre in Russia
- News from Around the World
- DIA Annual Meeting, Montreal

MESSAGE FROM RALPH EDWARDS, DIRECTOR

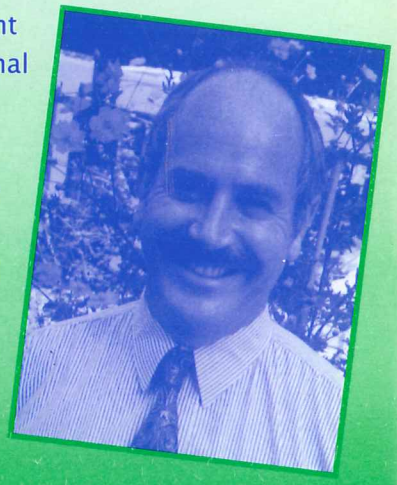
Dear Colleagues,

We have recently been thinking a great deal about issues of benefit-risk analysis and the communication of the results of such analyses to health professionals and patients. The more we have talked about it the more we have realised that the evidence-based approach, as it is currently understood, is not practical: there is simply not enough hard evidence!

Further thought has led us to the view that there are levels of evidence ranging from personal belief and anecdote, through uncontrolled case series, to fully documented controlled trials (looking at both benefit and risk). The problem is that all this evidence is never collected together to allow a body of knowledge to be built up. This is particularly true of the management of less common diseases.

To remedy this, where the main issue is that of risk and benefit analysis, we propose a structured Difficult Disease Treatment (DDT) web page. We suggest that information can be added by any interested party under various headings such as: *Personal Views/Comment; Case Reports For and Against; Case Series/Uncontrolled Studies; Retrospective Controlled Studies; Prospective Controlled Studies Completed and Underway; Meta-analyses; Reviews; Relevant Pharmacological, Physiological or Other Laboratory Studies.*

If we achieve this, we should be able to collect useful information with the strength of evidence being transparent within the headings under each DDT topic. Comprehensive published information might be accessible through journal and other links.



If you think this is a good idea we would love to hear from you. At the Uppsala Monitoring Centre we shall probably trial the scheme, and ask some of our expert consultants to review the material from time-to-time.

With best regards,

Ralph Edwards

Professor I Ralph Edwards
Director

P.S *An old colleague of mine offers international consultancy and advice on medical, and other relocation, services available in the UK. This service may be very useful to our colleagues visiting the UK, or if the need arises to find out about such services at other times. The contact address is:*

Mrs. M.B. O'Connor-Read, Managing Director Extra Mile Relocation, 58 Acacia Road, London NW8 6AG Phone: +44-171-586 4991 Fax: +44-171-722 2966

the UPPSALA MONITORING CENTRE

In their previous rural environment, the team could easily pop out of the office for a quick volley-ball match. Here are the cheerful athletes prior to a bruising encounter with local rivals

NOW IN NEW PREMISES

On August 15 we moved from our old office at the Medical Products Agency (MPA) in the outskirts of Uppsala to new, larger premises in the City Centre which can accommodate approximately 50% more staff than we have today. It is not without a certain feeling of regret that we leave the direct environment of the MPA. We have had a very good host!

Our new office is located in a house built in the 1930s by the central square (Stora Torget). In the past we had the forest, a golf course and a riding school as our neighbours, now we overlook the busy bus traffic, the shoppers and idle students walking across the square.

We apologise if you have noticed a decreased service level from our Centre in the past few months due to the planning and execution of the move. The new premises have injected a new dose of enthusiasm into the staff and you can soon expect more from us again.

the Uppsala Monitoring Centre
Stora Torget 3 S-753 20
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A NEW PHARMACOVIGILANCE CENTRE SET UP IN RUSSIA

On May 1, 1997, the Federal Centre for Adverse Drug Reactions Study was established in Moscow by the Russian Ministry of Health.

Professor V.K. Lepakhin was appointed director of the new centre and Dr A.V. Astachova became the executive director. The main objectives of the Centre are:

- to organise the work of recording and study of adverse drug reactions in Russia
- to analyse and systematise reports on ADRs
- to collect and analyse ADRs from medical literature
- to publish up-to-date information on ADRs for health professionals
- to make proposals to the regulatory agency (Pharmacological Committee) to undertake administrative measures to limit the risk for drug-induced disease

According to a governmental decree all regions of the country are obliged to set up a regional adverse reaction monitoring centre for which the Federal Centre will be the coordinating body. The Federal Centre will publish a bulletin "Safety of Drugs", publish articles in medical journals and newspapers and lecture about ADRs at different medical institutions in the various regions.

Professor Lepakhin and Dr Astachova visited the UMC on August 27. We got down to very practical details on how we may collaborate in the future and we anticipate the Russian centre joining the WHO Programme very soon. Germany has offered to give support to the development of the new Russian pharmacovigilance centre along the lines of a "twinning programme" that was discussed at the meeting of national centres in 1994.

Professor Lepakhin and Dr Astachova may be contacted at the following address

Federal Center for Adverse Drug Reaction Study, Ministry of Health of the Russian Federation, Mikluho-Maklaya str 8, Moscow 117198, Russia, tel +7-095-4335600, fax +7- 095-4340292.

First meeting of International Working Group on the ATC/DDD methodology held in Geneva, 28-30 April 1997

In May 1996, the World Health Organisation signed an agreement with the Government of Norway concerning the Anatomical Therapeutic Chemical (ATC) classification and the assignment of Defined Daily Doses (DDDs) for pharmaceuticals.

Since then, the WHO has been responsible for coordinating the international aspects of the procedure, and for dissemination of information. The technical work will continue to be carried out by the WHO Collaborating Centre for Drug Statistics Methodology, Oslo, Norway (WHO-Oslo).

To aid WHO-Oslo in assessing proposals for ATC codes/DDDs, an international working group has now been set up. The new group which replaces the previous European working group consists of 12 government and academic representatives, covering all the continents of the world, and includes experts with a background in drug utilisation, clinical pharmacology and epidemiology.

Together with representatives from WHO Headquarters, the Norwegian Government, WHO-Oslo and the Uppsala Monitoring Centre, the international expert panel had its first meeting in Geneva in April this year. A representative from the international pharmaceutical manufacturers' association (IFPMA) was also invited for the inaugural day.

The participants were greeted by the Assistant Director-General of the WHO, Dr F. Antezana, followed by Ms M. Andrew from the Norwegian Board of Health, and Dr. J. Idänpään-Heikkilä, Division of Drug Management and Policies, WHO.

After the welcome, the head and the staff of the WHO-Oslo Centre gave overviews of the history and principles of the ATC/DDD methodology, and some of the working group members presented their views on the use of the system.

Aided by the chairperson, Dr I. Trolin from the Medical Products Agency, Sweden, the participants discussed several topics, including the purpose and scope of the ATC/DDD system, the procedures for handling proposals and recommendations, and how the system can be promoted and used in different areas of the world.

It was agreed that the ATC/DDD methodology provides a useful tool to facilitate drug utilisation studies and drug surveillance, to give feedback to prescribers, and to aid the work towards a rational use of drugs.

The hope is that the system, under the auspices of the WHO, will continue to develop, and become a truly international classification system that will be accepted and used worldwide.

Marie Lindquist (Observer)

ADR MONITORING IN VIETNAM

A national ADR monitoring centre was officially inaugurated in Hanoi, Vietnam in December 1994. In June 1996 a regional centre was established in Ho Chi Minh City. Up to now approximately 2000 ADR case reports have been received by these two centres. In May this year Sten Olsson from *the* Uppsala Monitoring Centre carried out a three-day training course on ADR monitoring in Hanoi and visited the two Vietnamese pharmacovigilance centres. He was contracted by Ministry of Health to provide guidance as to how working routines and recording systems used might be improved. It is expected that Vietnam will soon apply for membership in the WHO Drug Monitoring Programme.

Contact information for the two centres:

Professor Hoàng Tich Huyên,
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Fax: +84-4-825 6911

Dr Cao Minh Quang,
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Do write to us!

We are always delighted to hear from our readers - but such delight is not very frequent just now!

Do let us have news, views, ideas, comments for or about *Uppsala Reports* to share with our worldwide readership. A quick, handwritten note will be more than acceptable!

Send contributions to Sten Olsson by fax (+46-18 65 60 80) or by e-mail (sten.olsson@who.pharmasoft.se).

Thank you.

The UMC at DIA

The Drug Information Association (DIA) held its 33rd Annual Meeting in Montreal, Canada, 22 - 26 June, 1997. Two presentations from *the* Uppsala Monitoring Centre were made in the safety track. Marie Lindquist presented the features of the new WHO adverse reactions data base that will become operational during 1998 and that will be compatible with newly developed CIOMS, ICH and CEN standards.

Sten Olsson co-chaired a session on Working Methods of National Adverse Drug Reaction Centres with Dr Martijn ten Ham, WHO, Geneva and made a presentation based on material collected for the publication *National Pharmacovigilance Centres* that was recently published by *the* UMC.

We also had a booth in the exhibition area where our products and services were exhibited.

Do you know any journalists?

We're keen to establish an international network of journalists who are interested in our activities and the questions of benefit and risk in medicinal drugs.

If you have contacts with editors or journalists in your country, would you be kind enough to let us know their names and communications details so that we can get in touch with them from time to time? Materials we send to them will not in any way relate to issues in your country, but only to matters of general, international concern.

Please contact Sten Olsson at *the* UMC by fax (+46-18 65 60 80) or e-mail (sten.olsson@who.pharmasoft.se)

RECENT PUBLICATIONS AND PAPERS FROM *the* UMC

In the previous issue of UPPSALA REPORTS we described the results of the ASAP project combining adverse reaction information from the WHO database with drug utilisation statistics from IMS. We were rightly criticised for not giving references to the published papers. Here they are:

1. M. Lindquist, J. Sanderson, C. Cleasson, J-L Imbs, A. Rohan, I.R. Edwards, New Pharmacovigilance Information on an Old Drug; An international Study of Spontaneous Reports on Digoxin, Drug Investigation 8, 73 - 80, 1994

2. M. Lindquist, M. Pettersson, I. Ralph Edwards, J. Sanderson, N. Taylor, P. Fletcher, J. Schou, F.T. Fraunfelder, Omeprazole and Visual Disorders: Seeing Alternatives, Pharmacoepidemiology and Drug Safety 5: 27 - 32, 1996

3. M. Lindquist, M. Pettersson, I.R. Edwards, J. Sanderson, N. Taylor, A.P. Fletcher, J.Schou, R. Savage, How Does Cystitis Affect a Comparative Risk Profile of Tiaprofenic Acid with Other Non-Steroidal Antiinflammatory Drugs? An International Study Based on Spontaneous Reports and Drug Use Data, Pharmacology & Toxicology 80, 211 - 217, 1997

4. M. Lindquist, I.R. Edwards, Risks of Non-Sedating Antihistamines. Lancet 1997; 349: 1322.

5. M.M.S. Stahl, M.Lindquist, M. Pettersson, I.R.Edwards, J.H. Sanderson, N.F.A. Taylor, A.P. Fletcher, J.S. Schou, Withdrawal Reactions with Selective Serotonin Reuptake Inhibitors (SSRI:s) as Reported to the WHO System, European Journal of Clinical Pharmacology (in press)

OTHER RECENT PAPERS FROM THE CENTRE:

1. C. Biriell, I.R Edwards, Reasons for Reporting Adverse Drug Reactions - Some Thoughts Based on an International Review. Pharmacoepidemiology and Drug Safety; 6: 21-26, 1997

2. I.Ralph Edwards, Adverse drug reactions: Finding the needle in the haystack (editorial), British Medical Journal 315: 500, 1997

3. I.Ralph Edwards, Who cares about pharmacovigilance?, Drug Safety (in press)

4. I. Ralph Edwards and Bruce Hugman: The challenge of Effective Benefit-Risk Communication, Drug Safety (in press)

WHO ADVERSE REACTION TERMINOLOGY

We have now developed a new computer software called WHOART-Access which allows retrievals in the WHO Adverse Reaction Terminology. WHOART-Access allows you to follow the hierarchical structure, look for terms and synonyms, choose among the available languages (English, French, Spanish, German, Portuguese) and print relevant parts. The software runs on PCs with a 486 processor or faster, Windows 3.1 or Windows95 and 4Mb internal memory. The software will be provided free of charge to national pharmacovigilance centres.

PRODUCT NEWS

WHO Drug Dictionary

You can now have access to a completely new product providing support to WHO Drug Dictionary users. The new product consists of three computer files that contains all changes made to the WHO Drug Dictionary since the first quarter of 1992, including changes in ingredients and ATC codes. These cumulative files are intended to aid those who wish to keep track of records that have been changed between different versions of the WHO Drug Dictionary database. The regular additions are not recorded since they can be extracted from the current version of the complete database. The new files will be updated on a three monthly basis.

WHO Dictionary Users' Group?

In the past we have enjoyed having access to a WHO Dictionary Users' Group that provided us with feed-back on our products and services, mainly WHOART and WHO Drug Dictionary. User Group meetings have been convened once or twice a year, normally in connection with major events organised by DIA (Drug Information Association) in the USA or in Europe. The Users' Group used to have a coordinator who organised and chaired the meetings and was the main spokesperson providing feedback to *the* UMC. At present there is no-one to coordinate the activities of the Users' Group which we feel is a great loss. If you should be interested in taking on this role or if you wish to be a member of the Users Group, please contact Liza Storm at *the* UMC. She will be happy to give the Group the support it needs.

News from Around the World

ARGENTINA

Dr Guillermo Lombardo has moved from the department of pharmacovigilance to medical device monitoring within ANMAT, the authority responsible for control of medicines, food and medical technology. His e-mail address is unchanged (glombard@anmat.gov.ar) but his new fax number is +54-1-3400800. Dr Lombardo has stated that he may still be available for training activities in pharmacovigilance in Latin America. He has played a major part in such activities the past few years.

AUSTRALIA

Dr Alain Rohan recently left the national pharmacovigilance centre at TGA, the regulatory authority of Australia. His new position has not yet been confirmed. Dr Rohan has made many valuable contributions to the WHO Drug Monitoring Programme over the years. Among many other things he has served as rapporteur and as chairman at annual WHO meetings and he has been a much valued member of faculty at one of the Uppsala courses in ADR monitoring. He has made a major contribution to the development of the national pharmacovigilance system in the Philippines.

CANADA

Ms Carole Bouchard has moved from pharmacovigilance to another assignment within the Therapeutic Products Directorate. She is currently the associate director for the Bureau of Policy and Coordination and will not be with the Bureau of Drug Surveillance for the next seven months. Carol Langlois is the acting head for the ADR reporting unit. His e-mail address is Carol_Langlois@inet.hwc.ca. He can be reached at +1-613-957-0337. The fax number is +1-613-957-0335.

MALAYSIA

Ms Zoriah Aziz is presently on leave from the national monitoring centre in Malaysia for PhD studies in pharmacoepidemiology at the University of Nottingham in the United Kingdom. Ms Aziz attended the Uppsala training course on ADR monitoring in 1995.

KUWAIT

The WHO Regional Office for the Eastern Mediterranean Region has assigned Sten Olsson of *the* Uppsala Monitoring Centre for a short-term consultancy to formulate a plan of action for the establishment of an adverse drug reaction centre which will serve Kuwait and all the Gulf region. The short-term consultancy will be carried out 25 October to 7 November, 1997

SAUDI ARABIA

The Saudi Ministry of Health is collaborating with the Food and Drug Administration of the United States in an effort to set up a pharmacovigilance programme in Saudi Arabia. The manager of the pharmacovigilance unit, Dr. Adnan Jenaidi is scheduled to visit FDA for a few weeks in October followed by a visit to *the* Uppsala Monitoring Centre for approximately one week.

POLAND

Professor Andrzej Czarnecki, who has been the director of the Polish pharmacovigilance centre for many years, recently moved to the United Kingdom to work at the Post Licence Division of the Medicines Control Agency. The contact person at the Polish centre is now Ms Agata Maciejzyk.

SURVEY CARRIED OUT IN CANADA

A sample of 1200 general physicians, 1200 specialists and 600 pharmacists in Canada is being asked to respond to a questionnaire sent out by the Bureau of Drug Surveillance with the aim of

- assessing the tools or mechanisms currently used to disseminate information on ADRs
- confirming the essential data required for an ADR report
- segmenting potential reporter groups and defining their needs so that useful marketing measures may be developed
- determining appropriate tools for the promotion and reporting of ADRs

Responsible for the study, planned to be completed by October 1997, is Ms Carole Bouchard, Bureau of Drug Policy and Coordination, Health Canada, tel +1-613-9415513, fax +1-613-9411812

PHARMACOVIGILANCE MEETINGS

IBC USA Conferences is organising two events during the next few months:

- A conference with the title "Manage Global Pharmacovigilance; Re-Engineer the Adverse Event Process to Meet Emerging Regulatory and Business Requirements" at the Watergate Hotel, Washington D.C., USA, 23 - 24 October, 1997
- An executive forum entitled "Reducing Adverse Drug Events & Medical Errors", 24-25 November, 1997, at Boston Park Plaza Hotel, Boston, USA,

Further information may be obtained from IBC USA Conferences on tel +1-508-4816400, fax +1-508-4817911, e-mail: reg@ibcusa.com

India does not have a national pharmacovigilance centre.

There are, however, many centres in India working with pharmacovigilance and many of them have been in touch with our centre, asking for support and collaboration. Up to now we have not had any formal mechanism by which we could establish working relationships with centres not officially designated as national centres by the Ministry of Health. WHO is an inter-governmental organisation that has to work through governmental bodies.

The present database does provide a good picture on what complications may occur when drugs are being used in different populations, under different cultural circumstances and in different health care systems, but it is in need of more information on drug problems being encountered in developing countries.

Relations with pharmacovigilance centres in India established

In agreement with WHO Headquarters, Geneva and the Indian Drugs Controller General it was recently decided to establish working relationships with two centres in India as "special centres" collaborating with the WHO Drug Monitoring Programme.

1. Department of Clinical Pharmacology, Seth G.S. Medical College and K.E.M Hospital, Parel, Mumbai (Bombay) 400 012. The Director is professor N.A. Kshirsagar who, during a number of years, has published scientific papers on ADR issues and in January this year took on a coordinating role by convening a conference in Mumbai on Adverse Reaction Monitoring, Prevention and Treatment. Spontaneous ADR reports are expected to arrive soon in Uppsala from the Mumbai centre. Telephone and fax numbers to Professor Kshirsagar's department are +91-22-4143505 and +91-22-4143435 respectively.

2. Department of Pharmacology, J.N Medical College, Aligarh Muslim University, Aligarh 202002. This department directed by Professor K.C Singhal coordinates an intensive hospitals monitoring programme, funded by the Indian Council of Medical Research and carried out at 12 different centres in India. During a three year period information on more than 60 000 patients has been collected. Professor Singhal may be contacted on telephone no +91-571-400584 and on fax no +91-571-400123.

The present arrangement is to be seen as temporary until such time that the Indian Ministry of Health will designate a national pharmacovigilance centre.

the Uppsala Team

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