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Uppsala reports

For everyone concerned with the issues of pharmacovigilance and toxicovigilance

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MESSAGE FROM THE DIRECTOR

What do you think of us?

This is the question we asked National Centres and some of our customers in a survey earlier in the year. The responses were not entirely comforting!

More people than we would wish were unsure about what we did at *the* UMC. Many said that they contacted us only 'occasionally' or 'rarely' because of this uncertainty. Many had not visited and did not know about our website **(www.who-umc.org)**. Some have had problems getting through to us, or with their orders for products, or with the speed of our response. So, it seems we have a lot of work to do to achieve the 100% awareness and quality we seek.

There were many positive and appreciative comments too, so the picture is far from all negative – but our users and customers have presented us with a real challenge which we must address.

We have made efforts over the years to raise our profile and make contact with everyone to whom we might be useful (*Uppsala Reports* is part of that effort), but clearly there is still much work to be done.

Our mission is to serve the interests of pharmacovigilance throughout the world: any organisation or individual who feels we might be able to help them should contact us without hesitation.

the UMC is in a unique position to help develop integrated and harmonised international technical services which could get WHO backing. We're very keen to be asked about and involved in any idea or project which could improve drug safety and patient therapy, and to offer our long experience and considerable expertise wherever they can be useful.

Listening to one's customers is not always entirely comforting, but it shows we are very much alive and determined to meet the needs of those who have a right to expect the very best from us.

If you have any thoughts about how we can raise our profile, disseminate information about what we do, extend our influence and usefulness – please let me know!

Ralph Edwards

TUNISIA FACT FILE

Tunisia is a presidential republic with an emerging economy. Tunis, an ancient city whose past is linked to an even more ancient civilization, has become a major financial centre and an important international destination reflected by its splendid conference and leisure facilities. Visitors will be delighted with the standards of service and the warmth of the welcome! *Tunisia is 1 hour ahead of Greenwich Mean Time (GMT) from October to April.*

LANGUAGE

The official language is Arabic but almost everyone speaks some degree of French; English is not commonly spoken outside major tourist areas.

CLIMATE

North Tunisia has a Mediterranean climate with a temperature of around 20ºC in November. The further south you go the hotter and drier it becomes with summer temperatures of over 40ºC.

CURRENCY

The unit of currency is the dinar, (1 dinar = 1,000 millimes) and can only be obtained in Tunisia. Travellers' cheques and credit cards are accepted in urban and tourist areas in Tunisia.

ELECTRICAL APPLIANCES

Electric power is supplied at 50 cycles at 220 volts, 50 cycles AC, and transformers are available in hotels and shops.

SHOPPING

The working week is Monday to Saturday. Most stores are closed on Sunday, except in resort areas, where many remain open. In the bazaars and souqs (markets), inflated prices will give you the pleasure of bargaining and a chance to exhibit your talent as an actor!

EATING OUT

Local cuisine which is based on a centuries-old tradition – briq à l'oeuf, couscous, tajines, pastries and mint tea – or international cuisine, can be enjoyed at a number of friendly restaurants, some of which provide the ever popular malouf music.

GETTING AROUND IN TUNIS

One of the best modes of public transport is the Tunis Metro – a new modern facility which also serves the new quarters. Taxi prices are very cheap.

SAFETY

The people in Tunis, and in fact throughout Tunisia, are very friendly and are always willing to help. Do however be cautious and well aware of your personal space at all times.

HISTORY AND SIGHTS

Archaeological visits should include Dougga, Carthage (near Tunis), one of the best preserved Roman towns in Tunisia, and the old Islamic town of Kairouan, Tunisia's holy city, which has fine examples of Islamic architecture. The Bardo Museum in Tunis is famous for its collection of Roman mosaics. Matmata is a major tourist attraction with its lunar landscape and troglodyte pit homes of its Berber inhabitants.

BEACHES AND ACTIVITIES

The best beaches are in the north around Tabarka, Bizerte and Sidi Ali el-Mekki and on all the coast: Hammamet, Sousse Mahdia, Zarzis and Jerba. Besides scrambling around ancient Berber and Roman ruins, in the desert areas there are activities available such as camel trekking, sand-skiing and ballooning. Colourful and exotic reefs and marine life make snorkelling or scuba diving a real pleasure.

Enjoy your visit!

(All the above information should be taken as a guide only)

Professor Chalbi Belkahia

WHO Drug Monitoring Programme

23rd Annual Meeting (11-14 November, 2000)

"It will be our great pleasure to welcome friends and colleagues from around the world to Tunis for the 23rd Annual Meeting of the National Centres of the WHO Drug Monitoring Programme. This is the first time that the National Centres have met in Africa or the Arab world and my colleagues and I here are delighted at the prospect of greeting you at our Institute, and also offering the opportunity of enjoying all the rich experiences of Tunisia past and present."

The objectives of the annual meeting are:

- to provide a forum for countries participating in the programme to meet and discuss issues of current concern
- for latest developments, best practice and methodology in pharmacovigilance to be explained, promoted and discussed
- for *the* UMC to exercise its accountability to member countries and seek their advice as to future directions, service levels and research priorities
- to provide a supportive, informative, sociable event in the pursuit of more effective pharmacovigilance worldwide and in developing productive relationships between member countries and other key players.

The meeting will be held at the **Institut National Sciences Appliquées et Technologie (INSAT), Tunis** (see photo below). Three levels of hotel standard are available and to benefit from the lower reservations rate you should already have booked via the Tunisia Convention Bureau. They will confirm the hotel you have been booked in and send a map helping you to get there and to the INSAT.

All representatives from National Centres and other invitees should already have received a mailing in July containing the latest programme, hotel booking forms and information on Tunisia, together with material on the Mediterranean Congress of Clinical Pharmacology which takes place just before the WHO meeting.

In September, a general request for issues to be discussed under the heading 'Drugs of Current Interest' and further preparatory material was sent out. Newcomers to the WHO Drug Monitoring Programme are invited to present their systems and activities as posters, allowing for stimulating and intense discussions with colleagues. During plenary sessions simultaneous translation English - French will be provided, and facilities are available for transparency, slide and computer presentations.

An official opening ceremony will take place on 11 November, in the presence of the Minister and the Deputy Minister of Health.

'In spite of the fact that we now have access to faxes, e-mails, Internet, satellite conferences etc for exchanging information, no means of communication can replace the personal encounter face-to-face. Also, in the scientific world personal confidence plays a significant role in decision making. For 23 years now, the annual meeting of National Centres has been the forum at which newcomers and experienced professionals on the drug safety arena have met, exchanged views and information, become friends and brought the science of pharmacovigilance and the WHO Programme forward. The programme for this year's meeting looks very interesting. Don't miss the chance of attending this first annual meeting on the African continent, and meeting your colleagues in a most attractive environment'.

Sten Olsson, Head of External Affairs, the UMC

WHO am I?

Lembit Rägo

Dr Lembit Rägo joined the World Health Organization (WHO) in December 1999 as Coordinator of Quality Assurance and Safety: Medicines (QSM). This position includes responsibility for the WHO International Drug Monitoring Programme, and for *the* UMC. We interviewed Dr Rägo to introduce him to our readers.

1. Uppsala Reports: *Dr Rägo, you came to WHO from Estonia. What's your professional background and what did you do before joining WHO?*

I graduated from Tartu University, Estonia as a medical doctor in 1979. My postgraduate studies and research resulted in a PhD from Tartu University, and later from Kuopio University, Finland. From 1982 to 1992 I taught pharmacology at Tartu University. Then in 1992 I was elected Professor of Clinical Pharmacology there. From 1989 until 1999 I was adviser on pharmacology, first with the Ministry of Health and then, after the ministries were combined, the Ministry of Social Affairs.

This was an interesting position as it covered everything related to drugs. No other adviser was responsible for policy issues such as planning and implementing pharmaceutical sector reform, creating and implementing national drug legislation, a reimbursement scheme or starting a pharmacovigilance system. As all this had to be achieved quickly after the country re-established its independence in 1991, I was also the founder and first head of the Estonian Drug Regulatory Authority 1991-1999.

In 1999 the State Medicines Agency moved into brand new premises and nowadays has 45 full-time staff (more information at www.sam.ee). During these years drug utilization monitoring using the ATC/DDD guidelines at a national level was started, and the Drug Information Bulletin and annual data sheet compendium Pharmaca Estica were launched.

I have always been lucky in working with wonderful people. One could say that Estonian pharmaceutical sector reform, building from scratch to a fully functioning drug regulatory system, was largely driven by two people supported by committed younger colleagues joining in step-by-step. This would have been impossible without the commitment of my close friend, Dr Raul Kiivet (now Professor of Health Management and Head of the Institute of Public Health at Tartu University).

During 1998-1999, I was also President of the Estonian Society of Pharmacology and an observer member of the European Commission Pharmaceuticals Committee on behalf of the Collaboration Agreement of Drug Regulatory Authorities in European Associated Countries, CADREAC. In 1999 I became a member of the Executive Board of the European Association of Clinical Pharmacology and Therapeutics.

Not unnaturally, the university part of my work suffered from my other commitments; however, we believed that there was no place for clinical pharmacology if drug regulation did not work. I published quite a substantial number of international articles on experimental and clinical pharmacology and also regulatory affairs. For many years the scientific papers mostly reflected the successful work of the small team of postgraduate students and younger colleagues I had in the University.

2. UR: *Being Coordinator of the Quality Assurance and Safety: Medicines team at WHO seems like a very broad area of responsibility. What are the main tasks included in your job description and what is the range of products coming under your management?*

"QSM is no longer responsible for quality assurance and safety of biologicals and blood products. These are now localized in other specific departments of Health Technologies and Pharmaceuticals"

In fact, the QSM team includes most of the activities of the former Department of Drug Management and Policies (DMP). This department was merged with another dealing with drugs (Drug Action Programme). The Essential Drugs and Medicines Policy Department (EDM) (Director Dr Jonathan Quick) was created in the cluster of Health Technologies and Pharmaceuticals (HTP), under Executive Director, Dr Yasuhiro Suzuki.

QSM is no longer responsible for quality assurance and safety of biologicals and blood products. These are now in localized in other specific departments of HTP. However, I am responsible for cross-cluster coordination of quality assurance and safety issues. Also, QSM no longer deals with the Essential Drug List and treatment guidelines, as this is taken care of by the Policy Access and Rational Use (PAR) team in EDM.

QSM concentrates mostly on three areas:

(1) normative functions in the area of quality assurance,
(2) safety of medicines, and
(3) information exchange and regulatory support to member countries. On the quality assurance side, one should mention International Nonproprietary Names (INNs), International Pharmacopoeia, and numerous regulatory guidelines for quality assurance adopted by the WHO Expert Committee on Specifications for Pharmaceutical Preparations. The WHO Collaborating Centre for Drug Statistics Methodology in Oslo, which takes care of operating the Anatomic, Therapeutic and Chemical classification and designation of Daily Defined Doses (ATC/DDD) also works under QSM supervision.

An important part of the work is information exchange that is directly linked with safety issues. QSM organizes:

- the biennial International Conference of Drug Regulatory Authorities (ICDRA)
- quarterly WHO Drug Information sheet, together with *the* UMC and other respective units in HTP,
- the WHO Pharmaceuticals Newsletter, communicating newly discovered drug safety problems as WHO Drug Alerts, etc.
- critical review of psychoactive substances and prepares recommendations to the UN Commission on Narcotic Drugs on behalf of WHO.

The work in quality assurance together with safety and information exchange supports a very important area: regulatory support to member countries. QSM has provided the WHO model system for computer-assisted drug registration (SIAMED) in order to help regulatory authorities to maintain updated databases of registered drugs. QSM is also trying to promote the implementation of regulatory guidelines and good regulatory practices.

In addition I have some personal appointments such as the official WHO Observer to the ICH Steering Committee, and Secretary of SCRIHS (Secretariat Committee on Research Involving Human Subjects), these also backed by the team.

3. UR: *In the WHO Drug Monitoring Programme there is a division of responsibilities between WHO headquarters and the UMC. How do you perceive their respective roles and do you see any problems in this arrangement today or in the future?*

The responsibilities and balances in the WHO Drug Monitoring Programme have been clearly in favour of *the* UMC as the major operational arm of WHO headquarters in the field of drug safety. It is difficult to overestimate the considerable progress made by *the* UMC during past decades. Due to its very limited resources, WHO headquarters has been restricted in its actions. WHO headquarters was going through difficult times when Martijn ten Ham, the chief of the former Drug Safety Unit in DMP, retired in 1998. The post was not filled and, Martijn's obligations were added to the QSM team coordinator's job description. However, Dr Mary Couper from QSM helped to continue the ongoing activities. Now she is fully on board and safety issues will become her major activity. Recently, the post of clinical advisor to EDM/QSM was created and Dr Vladimir Lepakhin has joined our small team on the safety side. So, finally after the reforms, in terms of posts, the safety area has been strengthened in headquarters.

WHO headquarters should probably be more active in overall policy issues as well as in advocacy and promotion of the safety of all medicinal products. More intensive cooperation between headquarters and *the* UMC is important in order to use the very limited resources in an efficient way. A good example of this cooperation is the recent merger of the WHO and UMC newsletters, thus eliminating duplication and giving the clear added value of joint effort. Naturally there are some problems related to the status of *the* UMC after the review by the Swedish Government but I would not like to concentrate on possible problems, but rather work for better solutions. My impression is that *the* UMC is a very good partner in trying to solve the problems.

4. UR: *At the forthcoming meeting of ICH (International Conference on Harmonisation) in San Diego in November 2000, pharmacovigilance will be on the agenda. Do you think there are potential conflicts of interests between the ICH countries and WHO in the area of pharmacovigilance?*

Again, we should concentrate on common interests rather than on potential conflicts. Naturally WHO should take into consideration the interests of all countries and not only those of the ICH regions. We are currently, together with *the* UMC, trying to find ways in which we could cooperate for the benefit of all countries in the field of pharmacovigilance. It will not be easy but we should try. When we fail to cooperate on the basis of mutual respect for each other's interests, and when we feel that there is a threat to global public health matters, we should make our position very clear in order to get strong support from member states.

"Many countries will have joined the Programme to swell the numbers to more than 80 from the present 59"

5. UR: *What role will the WHO Drug Monitoring Programme and the UMC be playing in the WHO strategy for achieving rational use of drugs throughout the world?*

It is difficult to over-estimate the role of the WHO Drug Monitoring Programme and *the* UMC in the rational use of drugs. However, unfortunately only a minority of WHO member states have joined the Programme. The WHO Medicines Strategy: Framework for Action in Essential Drugs and Medicines Policy 2000-2003 (final draft) lists under section 5.3 Quality and Safety (Component 8) "Access to international adverse reaction monitoring system extended to drug regulatory authorities of additional countries". Under 'challenges' the same section lists guidelines such as Safety Monitoring of New Drugs in the Immediate Postmarketing Phase, Guidelines on Safe Use of Drugs in Pregnancy and Guidelines on Safe Use of Drug Combinations. However, much depends on the finances that will be available. Financing really sets priorities and for the time being, regulatory issues like norms and standards including safety issues, are not priorities for WHO. We need much better promotion of our activities, including pharmacovigilance, in order to get support from the governments of member states.

6. UR: *The cost of medicines and medical treatment is getting a lot of attention these days. Do you think this will lead to pharmacovigilance getting higher priority within WHO as a means of limiting the expensive treatment of iatrogenic diseases?*

Actually there is very little evidence about the costs of iatrogenic diseases from the developing countries. Most of the data originate from the most developed countries. One can easily argue that in the conditions where access to drugs is a major problem (many countries spend less than $1 per person for drugs annually) adverse effects of drugs are not a big problem. Again, it is an issue that needs studies for evidence and evidence for advocacy.

7. UR: *If you were to get a 100% increase on your budget for drug safety activities, how do you think the increase should be used?*

I am very sad to say that for the time being I cannot answer this question (mathematically 100% increase of zero is still zero!) Due to recent "efficacy cutting" for priority areas we lost the budget line "International adverse reaction monitoring system: support to national drug regulatory authorities for adverse drug reaction monitoring" worth $30,000 in the previous budget. We are currently working on how to redistribute the funds within QSM in order to maintain at least some safety-related activities.

"We need much better promotion of our activities, including pharmacovigilance, in order to get support from the governments of member states"

8. UR: *What is your vision for the WHO Drug Monitoring Programme? What role will it have five years from now?*

In five years from now: the WHO Drug Monitoring Programme will have overcome the situation of being a low priority and low-funded activity and it will be considered a high priority programme by all WHO member states. Many countries will have joined the Programme to swell the numbers to more than 80 from the present 59. Cooperation between countries in the field of pharma-covigilance will have steadily improved and several global initiatives will be developing under WHO leadership.

News from Around the World

BANGLADESH

the UMC recently received an update report on pharmacovigilance activities in Bangladesh from Mr Salim Barami, who attended *the* UMC ADR training course in 1995.

Mr Barami, who is presently Superintendent of Drugs at the Directorate of Drug Administration (DDA) in Dhaka, submitted a proposal in 1995 for the establishment of a pharmacovigilance system in Bangladesh. Due to a series of reorganizations at the DDA his proposal was not acted upon immediately. The Ministry of Health and Family Welfare has now, however, constituted an Adverse Drug Reaction Advisory Committee, including experts from different medical and pharmaceutical disciplines and relevant associations.

The committee, together with the DDA and the local WHO office, organized a workshop for creating awareness regarding ADRs and ADR monitoring (3 - 4 June, 2000), in Dhaka. Doctors and pharmacists from nine medical colleges and the DDA attended. Papers on the following topics were presented:

- the necessity and objectives of ADR monitoring
- pharmacological basis of ADRs
- methods and benefits of ADR monitoring.

The ADR monitoring cell of the DDA has published notices in daily newspapers and participated in radio broadcasts to advocate rational use of medicines and has also produced posters and stickers in Bengali.

USA

The Center for Drug Evaluation and Research (CDER) of the US Food and Drug Administration recently issued draft guidelines on 'Content and Format of the Adverse Reaction Section of Labeling for Prescription Drugs and Biologics'. The guidance document, distributed for comment, is intended to assist drug manufacturers in developing the adverse reactions section of drug labelling and to bring greater consistency to the content and format. The document is available from the FDA website at: **http://www.fda.gov/cder/guidance/1888dft.htm** or can be obtained from CDER, FDA, 5600 Fishers Lane, Rockville, MD 20857, USA

PERU

In August 2000 the Ministry of Health, Peru, submitted its application to WHO for joining the WHO Drug Monitoring Programme.

A National Centre for Pharmacovigilance and Drug Information (CENAFIM) has been established within the drug control authority, Direccion General de Medicamentos, Insumos y Drogas. In its functions CENAFIM will be assisted by reference centres and a technical pharmacovigilance committee.

The pharmacovigilance centre will be collecting spontaneous ADR reports and will also be carrying out hospital surveys and epidemiological studies. During 1999 and 2000 some 200 reports have been received from manufacturers, health professionals and patients. When these reports have been submitted to *the* UMC in the agreed format, Peru will become the 60th member country of the WHO Programme.

Contact person is **Dr Susana Vásques**, CENAFIM, Avda Arenales 1302 - Of 319, Jesus Maria, Lima, Peru, **Tel: +51-14-716 246 Fax: +51-14-716 353**
E-mail: cenafim@digemid.gob.pe Internet: http://www.minsa.gob.pe

INDIA

Professor N Kshirsagar of the BYL Nair Hospital & TN Medical College, Mumbai, which is a WHO Special Pharmacovigilance Centre, has reported to *the* UMC about the postal survey method they are using for detection of specific ADRs.

Questionnaires are sent out to 500 - 1000 physicians, either to get safety information on a drug 1-2 years after it has been introduced or to answer a specific question.

The response rate has varied between 10 and 20%. Adverse events identified using this method include:

- ciprofloxacin-induced arthropathy
- convulsions in non-epileptics due to mefloquine-fluoroquinolone co-administration and aggravation of bronchial asthma, and,
- angioedema due to nimesulide.

Professor Kshirsagar and her team recommend this method particularly in countries where ADR monitoring is not well developed. It serves the purposes of creating awareness about ADRs, signal generation, detecting ADRs peculiar to the country's population as well as helping establishing a reporting culture. The method is described in greater detail in Gogtay N.J, Mangalvedhekar S.S, Kshirsagar N.A **Adverse Drug Reaction (ADR) Monitoring in India and the Postal Survey as a Useful Tool for ADR Detection** Pharmacoepidemiology and Drug Safety 9: 235 - 236 (2000).

NETHERLANDS ANTILLES

In Uppsala Reports 10, August 99, we reported the pharmacovigilance activities carried out in Netherlands Antilles. In April this year the Ministry of Public Health and Environmental Hygiene formally submitted its application to join the WHO Drug Monitoring Programme.

Since the system was created in close collaboration with Dutch colleagues it has been decided that ADR reports will be processed by the LAREB foundation in the Netherlands and sent on to *the* UMC by them. Our contact person at the centre is **Ms Zjumira G.M. Wout**, Bureau of Pharmaceutical Affairs, Fokkerwek #26, P.O. 3824, Curaçao, Netherlands Antilles.
Tel: +599-9-614 877
Fax: +599-9-614 879
E-mail: zwout@ibm.net

CHINA

Dr Cheng Jinghua of the Beijing regional centre for adverse reaction monitoring recently advised *the* UMC of the establishment in China of a Drug Safety Information Group which is a nation-wide academic group under the Pharmacy Administration Commmission. The main tasks of the Group are:

- holding symposia and conducting training courses on drug safety
- communicating drug safety information and providing drug information service
- investigating and reassessing some key medicines
- carrying out popular education on drug safety.

(See page 8 for more news on Ralph Edwards' visit to China in April)

PHILIPPINES

The Bureau of Food and Drugs recently produced a 10 minute educational video about Adverse Effects Following Immun-ization (AEFI). The film explains the different kinds of AEFIs and why they need to be monitored and how reporting should be carried out.

The Bureau has also produced a series of educational audio cassettes on adverse drug reactions. Volume I covers neurology and obstetrics, Volume II dermatology and reactions in the elderly, Volume III cardiology and psychology.

Copies of the video and audio cassettes may be obtained from *the* UMC. Please contact **Anneli Lennartsson**.

News *from the* Uppsala Monitoring Centre

Dr Saad Shakir, Head of DSRU

COLLABORATION WITH DRUG SAFETY RESEARCH UNIT

There is a clear need to extend *the* UMC network with new partners, particularly those with the power to analyse drug safety signals. As a further step in this direction *the* UMC and the Drug Safety Research Unit (DSRU) in Southampton, UK, have agreed to collaborate on signal detection and analysis. In the near future we will explore advanced methods of analysis, combining the breadth of international spontaneous data with the depth of information and denominator data available from the DSRU. This adds to the already existing collaboration with the International Medicines Monitoring Programme (IMMP) in New Zealand.

REVIEW PANEL MEETING AT *the* UMC

On September 13-15, 2000 the second reviewer meeting was held at *the* UMC in Uppsala. The first review panel meeting took place here in Uppsala in August last year with 13 panel members participating.

This year we are very happy that the number of participants has increased to 25, 12 of whom are new to the panel. The aim of the meeting is for reviewers to share experiences of signal detection work and to learn how to make best use of the information in the WHO Database. We hope the results of meeting together will be a more harmonized approach to signal analysis and a higher quality of signals reported in the SIGNAL document.

Our signal reviewers are now presented individually with a short CV on our Internet website. Please visit us at **www.who-umc.org** and get to know our partners!

BACKLOG OF US REPORTS NOW IN WHO DATABASE

As the United States Food and Drug Administration introduced its new AERS database in 1997, the transfer of adverse reaction reports to the WHO Programme was initially interrupted in the absence of interface software. *the* UMC later received a backlog amounting to approximately 258,000 adverse reaction case reports.

In the new data set adverse reactions were recorded according to the MedDRA terminology instead of WHO-ART used previously and still used by all other member countries. The medicinal products and ADR terms which occur most frequently on the reports have now been checked for occurrence in the WHO Drug Dictionary and WHO-ART. In total there were approximately 70,000 and 6,000 unique deviations in medicinal products and ADR terms respectively.

It was later found out that a significant number of the US records were follow-up reports to cases notified earlier. FDA then supplied *the* UMC with a file allowing the identification of follow-up cases, thus avoiding duplicate reports. Once this preparation processing was accomplished a procedure for updating the WHO database with this vast volume of material was set up.

By the end of October 2000 most of the backlog from 1998 up to and including reports for the first quarter 2000 will be in the WHO database.

As from now we expect a regular contribution from the FDA. Since the US data is a large part of the total annual input, the WHO database being up-to-date with US reports is of major importance for improving the chances of *the* UMC identifying new adverse reaction signals through its data-mining techniques.

NEW PROJECT - IMPROVED COMMUNICATIONS WITH NATIONAL CENTRES

Although *the* UMC has frequent contacts with National Centres participating in the WHO Programme, we still feel that communications can be improved and so increase the commitment and involvement of member countries to the Programme.

A special project, headed by Cecilia Biriell, on finding new ways of improving communications was recently started at *the* UMC.

ADR Reporting

The aim of the project is to make sure that all people at National Centres are aware of the services that the WHO Programme can provide for them, and also what obligations national centres have to make the Programme work. The most important of these is to prompt the regular sending of adverse reaction reports to *the* Uppsala Monitoring Centre.

Communications Data

There can be no communication without correct names, addresses, fax numbers etc. The first task the project group has undertaken is to upgrade *the* UMC's address register of National Centres. This may seem like a simple task, but it is in fact quite difficult. Many names of people who don't work at National Centres any longer are still in *the* UMC address register. We urge all National Centres to respond to our questionnaire and to keep us informed of any changes taking place.

Guidelines

In cooperation with WHO headquarters, a document has been developed stating the obligations for National Centres and explaining services such as database searches, the SIGNAL review and National Centres meetings. This paper will be sent to all National Centres shortly, to make sure that all heads know about this. In the future the paper will be sent out each time we hear about the appointment of a new Centre head.

Newcomers

In the past we have not had the resources to make sure that all people at National Centres are aware of services provided by the Programme. But now we are putting some of our resources into making an **information pack** for all newcomers, containing an overview of the Programme, some recent and relevant published articles from *the* UMC, information about the Drug Dictionary and the WHO-ART etc. There will be different information packs tailored for Centre heads, technical contact people and information contacts. More ways for keeping communications open are planned and we will be back to you later about this project. If you have more ideas in this area, please tell us.

Visit to China

The third Chinese National ADR Meeting, 'Clinical Drug Safety - 2000' was held in Hangzhou, April 18 - 22, 2000. The meeting was organized for the first time jointly by the Pharmacy Administration Committee of the National Institute of Hospital Administration, and the editorial office of the national 'ADR Journal'.

CHANGE

China, like many other countries, is going through a major reorganisation of its health services. The national centre is in the process of being moved from the Health Ministry to the State Drug Administration. There is considerable interest in the further development in a rational drugs policy and this includes the consideration of the cost impact of ADRs.

NEW ARRANGEMENTS

At the meeting a formal group of the 10 regional centres was formed. This will further the scientific and professional activities in drug safety and act as an advisory group to the National Centre. The National Centre is an administrative and regulatory body which does not involve itself in the collection or use of the ADR report data in any other way than for regulation. With the new bipartite system, the regional centres will be responsible for th collection of reports, promotion of reporting, the analysis of data and the publication of information in the new ADR Journal.

The meeting had a full and comprehensive agenda, but did not discuss the economic impact of ADRs. There was considerable interest in the two UMC presentations, one on Clinical Diagnosis of ADRs (Ralph Edwards) and the other on Monitoring of Herbals (Mohamed Farah).

the UMC team was accompanied by Dr Cheng Jinghua and Mr. Wang Da-you. They visited a tea plantation and helped in the harvest of tea

Mohamed and Ralph (in the hat!) demonstrate their commitment to the principle that herbal classification must be done in the field. 'There will always be questions about the quality of materials purchased in bulk when they are collected in the field by ordinary people unfamiliar with herbals,' says Mohamed. 'It's essential that manufacturers verify the identity of herbals delivered to them.'

leaves. The correct identification of this plant is: **Camellia sinensis** var. **sinensis** (L.) Kuntze = Camellia theifera Griffith = Camellia thea Link = Thea bohea L.= Thea sinensis L. = Thea viridis L. - all these different names are correct.

APOLOGIES!

We would like to apologise to Dr Cheng Jinghua for the incorrect spelling of his surname in the last issue of Uppsala Reports. We hope this didn't cause Dr Jinghua any embarrassment.

UMC WITH 'BEST POSTER' AT CPT CONFERENCE 2000

The CPT 2000 (Clinical Pharmacology and Therapeutics) conference was held in Florence, Italy on 15-20 July. Ralph Edwards, Mohamed Farah, Malin Ståhl and Marie Lindquist attended from *the* UMC.

In the session on communications and drug safety, Ralph Edwards gave a talk about communication of the benefit/risk balance of medicinal products. In this section there were also presentations by Dr Kenneth Hartigan-Go (Philippines); Dr Tony Wong (Brazil); and Bruce Hugman (EQUUS, UK).

The Communications Presentation Team: from (right to left) Dr Tony Wong, Dr Andrew Herxheimer, Bruce Hugman, Dr Kenneth Hartigan-Go, Prof Ralph Edwards accompanied by Dr Ellen Vinge

Mohamed Farah made a presentation about the monitoring of herbal medicines. He stressed the need for using binomial names instead of common names in the reporting of herbals to avoid confusion.

Malin Ståhl represented *the* UMC with a poster entitled 'Recent Improvements of International Signal Detection'. This showed results of validations of *the* UMC´s new signalling system. It was selected as the best poster in the post-marketing drug surveillance session during a guided poster tour conducted by Prof René-Jean Royer and Sir Michael Rawlins.

16th ISPE CONFERENCE IN BARCELONA

The International Society for Pharmacoepidemiology (ISPE) holds its yearly meetings alternately in North America and in Europe. This time, Barcelona (21-23 August) was the host city for the conference. 550 delegates attended the meeting - a new record!

New Approach

The conference had a big programme, organised differently from previously - in the mornings longer plenary lectures with ample time for discussion, both about methodology and specific drug safety issues. The keynote address was presented by Dr Patrick Waller from the Medicines Control Agency (MCA), UK who talked about 'Pharmacoepidemiology - A Tool for Public Health'.

ADRespherics

Many of the normal short presentations were replaced by plenty of posters on all three days. There was also time for discussion with colleagues and friends in the breaks. *the* UMC participated with an exhibition and demonstration of 'ADRespherics', the new method for signal detection and analysis using data-mining techniques.

Andrew Bate from the Centre was one of the speakers in a workshop on 'Signal Identification' and presented how *the* UMC data-mining method for signal detection has been validated. The session was well attended and evoked a lot of interest and questions. The whole session will be published in the journal 'Pharmacoepidemiology and Drug Safety'.

In a so-called 'council meeting' a discussion was held on how people in countries where pharmacoepidemiology is not yet well developed can get proper training in the subject. It was decided that a tentative plan should be developed and presented to ISPE's executive committee in early 2001. Whether ISPE should try to get status as an NGO (Non-Governmental Organisation) to enable closer cooperation with the WHO, was also discussed.

Toronto 2001

Next year's conference will be held in Toronto, Canada. In 2002 the ISPE delegates will visit Edinburgh, Scotland.

CONSUMER REPORTS ON MEDICINES

The Swedish foundation KILEN - Consumer Institute for Medicines and Health organized a first international conference on Consumer Reports on Medicines in Sigtuna, just outside Stockholm, Sweden, 29 September - 1 October 2000 in co-operation with several partners including *the* UMC. An introductory address was made by Dr Mary Couper of WHO, Geneva. Sten Olsson from *the* UMC provided an overview of pharmacovigilance activities as they are carried out in different parts of the world. The ambition of the organizers is to create an international network for exchange of drug experience reports originating from patients themselves. Proceedings from this conference may be obtained from **Ms Lena Westin, KILEN, Fax: +46-8-6960110, E-mail: kilen@kilen-institutet.se Internet: http://www.kilen.org**

UPPSALA PHARMACOVIGILANCE TRAINING COURSE 2001

The 6th international training course on Adverse Reactions and Adverse Reaction Monitoring will be held in Uppsala 7 - 18 May, 2001.

The course provides basic theoretical and practical training in pharmacovigilance methodology and an introduction to pharmacoepidemiology. It is mainly targeted at newcomers at national pharmacovigilance centres and professionals considering establishing such centres. Some participants from industry are also admitted. Invitations will be distributed in November 2000. If you want to be sure to get an invitation, please contact Anneli Lennartsson at *the* UMC.

US VACCINES DATA NOW IN WHO DATABASE

The Centre for Disease Control (CDC) in USA recently submitted all the adverse reaction case reports in their VAERS database to the WHO programme in the required format. The reports, amounting to some 108,000, are attributed to 129 different vaccine products. They will be incorporated into the WHO database by the end of October, 2000.

STAFF CHANGES

In July 2000 Jonathan Edwards, who has been responsible for IT (Information Technology) strategy and internal IT support at *the* UMC since 1997, decided to leave our Centre. He took up a new position at a company in Uppsala developing Internet-based software.

We have employed a new pharmacist, **Ms Helena Sjöström**, who joined *the* UMC team at the end of September. To start with she will mainly be working with processing of incoming adverse reaction reports and recording of drug names, occurring on such reports. Look out for her picture in Uppsala Reports 14.

RECENT PUBLICATIONS FROM the UMC

1. Lindquist M, Edwards R I, Bate A, Fucik H, Nunes A M, Ståhl M. **From Association to Alert - a revised approach to International Signal Analysis** Pharmacoepidemiology and Drug Safety, 1999. **8:** S15 - S25.
2. Meyboom R H B, Edwards R I, Egberts A C G. **Mirtazepine and the granulocytes - so far so good**. New Zealand Medical Journal 1999. **112**: 104.
3. Edwards R I. **Spontaneous reporting - of what? Clinical concerns about drugs** Br J Clin Pharmacol, 1999. **48**: 138 - 141.
4. Fraunfelder F W, Fraunfelder F T, Edwards R I. **Diplopia and HMG-CoA Reductase Inhibitors**. J Toxicol - Cut & Ocular Toxicol, 1999. **18 (4)**: 287 - 289.
5. Edwards R I. **The accelerating need for pharmacovigilance**. J R Coll Physicians Lond 2000;34:48-51.
6. Edwards R I. **Pharmacovigilance - beyond 2000**. Reactions Weakly 2000, No. 783.
7. Farah H M, Edwards R, Lindquist M, Leon C, Shaw D. **International Monitoring of Adverse Health Effects Associated with Herbal Medicines**. Pharmacoepidemiology and Drug Safety 2000 **9:** 105-112.
8. Meyboom R H B, Lindquist M, Egberts A C G. **An ABC of Drug-Related Problems**. Drug Safety 2000; 22 (6): 415-423.
9. Meyboom R H B, Lindquist M, Flygare A-K, Biriell C, Edwards R I. **The Value of Reporting Therapeutic Ineffectiveness as an Adverse Drug Reaction** Drug Safety 2000; **23(2):** 95 - 99.
10. Edwards R I. **Spontaneous ADR Reporting and Drug Safety Signal Induction in Perspective**. Pharmacology & Toxicology 2000; **86:** Supplement 1, 16-19.
11. Edwards R I. **The management of adverse drug reactions: from diagnosis to signals**. Adverse Drug Reaction Journal Vol..2, No. 2, 103-105, 2000 (In Chinese).
12. Farah M H. **Key issues in herbal pharmacovigilance**. Adverse Drug Reaction Journal Vol.2, No. 2, 105-109, 2000 (In Chinese).
13. Lindquist M, Ståhl M, Bate A, Edwards R I, Meyboom R H B. **A retrospective evaluation of a data-mining approach to aid the finding of new adverse drug reaction signals in the WHO International Programme of Drug Monitoring database**. Drug Safety (in press).

Copies of the papers listed above may be obtained from **Anneli Lennartsson** at *the* UMC.

VISITS TO KUWAIT AND INDIA

Sten Olsson from *the* UMC was invited by Kuwait University to give a lecture on adverse drug reactions at a therapeutic update course in early May 2000. He also visited the national pharmacovigilance centre in New Delhi, India and gave lectures at the All India Institute of Medical Sciences and at the Hamdard University.

'UMC TRAINING COURSE 2001' see above left

COURSES & MEETINGS in PHARMACOVIGILANCE

- IIR is arranging a conference on **Blood Product Safety**, 16-17 October 2000, London, UK. For **information** contact IIR at
  Tel: +1-888-670 8200
  Fax: +1-941-365 2507

- Instituto Nacional de Higiene "Rafael Rangel" in Caracas, Venezuela, is organizing its VIII International Course on **Normative and Regulatory Aspects of Registration and Control of Drugs** 25 September - 20 October, 2000. As part of this course a workshop on pharmacovigilance will be held 18-20 October. Course manager is Ms Gerda Ackerman
  Fax: +58-2-6624 797
  E-mail: lottyack@cantv.net

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

  - A training programme on **Medical Approach in Diagnosis and Management of Adverse Drug Reactions** in Paris, France, 12-13 October, 2000
  - A training programme with the title **Drug Safety Surveillance and Epidemiology** in Washington, USA, 23-25 October, 2000
  - A workshop with the title **MedDRA - A Practical Approach to Implementation** 30-31 October, 2000, Washington DC, USA
  - A training course in **Applied Epidemiology**, 2-3 November, Philadelphia, USA
  - A workshop on **Pharmacovigilance into 2001**, in London, UK, 15-16 November 2000
  - A workshop on **Improving Pharmacovigilance Working Practices: The CIOMS V Initiative** in Washington DC, USA 11-12 December, 2000
  - **Adverse Experience Workshop** in Washington DC, USA on 8-10 January, 2001
  - A workshop on **Safety Information and Labelling** in New Orleans, USA, 12-13 February, 2001

  For more **information** on the DIA events contact:
  Tel: +1-215-628 2288
  Fax: +1-215-641 1229
  E-mail: dia@diahome.org
  or
  Tel: +41-61-386 9393
  Fax: +41-61-386 9390
  E-mail: diaeurope@stepnet.de

- The **III Brazilian Congress of Hospital Pharmacy** will be held in Salvador, Bahia, Brazil, 5-8 November, 2000. Pharmacovigilance will be one of the main topics of this congress. For more **information**, please contact Professor Lúcia Noblat
  E-mail: lacb@ufba.br

- The Drug Safety Research Unit (DSRU) in Southampton, UK, will organize three different public events, a Workshop on **Narrative Writing** in December 2000, 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: +44-1703-408 600
  Fax: +44-1703-408 609
  E-mail: georgina.spragg@dsru.org

- Rostrum will organize a training programme on **Pharmacovigilance and Adverse Event Reporting** on 11 April, 2001.
  For **information** please contact Rostrum:
  Fax: +44-1708-734876/725413
  E-mail: rostrum@pils.com
  Internet: www.rostrumtraining.co.uk

- 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 organized by the Division of Clinical Pharmacology, Umeå University, S-901 85 Umeå, Sweden. For more **information** contact Ms Aina Mattsson
  Fax: +46-90-120 430
  Email: aina.mattsson@pharm.umu.se

BOOKS *and other* PUBLICATIONS

NEW GERMAN HANDBOOK ON ADVERSE DRUG REACTIONS

Handbuch der unerwünschten Arzneimittelwirkungen, edited by B. Müller-Oerlinghausen, R. Lasek, H. Düppenbecker and K-H Munter is published by Urban & Fischer, München, 1999 (ISBN 3-437-21240-0). The first part of this (750 page) book of is divided into 21 chapters, each covering one therapeutic group of medicines. To each generic substance an overview of known adverse reactions is provided with frequency estimates given. The second part has eight general chapters on such topics as mechanisms, methods of detection and study, and special concerns regarding herbal preparations and biologicals.

DRUG RISKS IN MEDICAL PRACTICE

This book in the Slovak language (Riziko Liekov v Medicínskej Praxi), edited by Professor Milan Kriška, was published earlier this year by the Slovak Academic Press, Bratislava (ISBN 80-88908-58-2). The initial hundred pages cover general subjects of pharmacovigilance and drug risks. The remaining 375 pages provide summary information on adverse reactions by therapeutic group, specified on substance level.

MONITORING DRUG SAFETY - A SHARED RESPONSIBILITY

This is a 15 minute VHS-video produced by the Drug Information Association (DIA) explaining why adverse reactions occur and how drug risks are detected, through the phases of development of a new medicine and after marketing. It emphasizes the need for close collaboration between patients, health professionals, producers and authorities to ensure that drugs are used safely and risks are detected early. Professional advice for the production of this video has been provided by Bruce Rowsell, Health Canada and Win Castle, SmithKlineBeecham. The video can be acquired from DIA at a price of USD $25. Contact Sue Greco,
Fax no +1-215-6411229
E-mail: grecos@diahome.org

DON'T TELL THE PATIENT - BEHIND THE DRUG SAFETY NET *by Bill Inman*

This is an autobiography and a description of the early developments in post-marketing drug safety monitoring by one of the pioneers who was instrumental in the establishment of the 'Yellow card' system and later created the Prescription Event Monitoring scheme in the UK.

Highland Park Productions, Bishops Waltham, UK,
ISBN 0-9675812-0-6

DRUG BENEFITS AND RISKS

A new multi-author, international textbook edited by Profs. Chris van Boxtel, Budiono Santosa and Ralph Edwards. Published by Wiley, UK

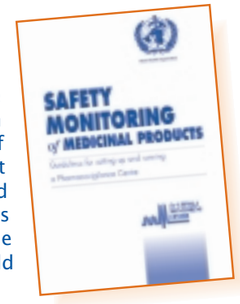
This is a book about practical therapeutics and the surrounding general and pharmacological knowledge. The aim of the book is to give expert guidance on how to treat patients. Whilst the book is concerned with the best possible evidence-based therapy and information, it also aims to be a practical and useful guide wherever in the world patients are treated. To achieve this, authors of the various sections have been brought together from around the world, and have peer-reviewed each other's contributions.

The publishers have tried to keep the price low, so allowing as many as possible to have access to the book. The style and kinds of questions which could be asked to reinforce learning will vary all over the world, and the addition of highlights could also draw emphasis to text inappropriately. For all these reasons also the book is standard in its format. Teachers will need to formulate their own strategy for using this book in their teaching.

The editors would claim that part of problem-based learning is to have a starting point where practical information is given and also some of the surrounding philosophy. Where problem-based learning has been developed, the discussion and interaction with a local expert is usually an initial part of the exercise. Sadly, there are many places in the world where this practical expert advice is not easily available for a variety of reasons, neither are many textbooks available. The aim of this book is allow experts to say, in their own way, what they think is important in their discipline.

Through sponsorship by the Dutch Rad-Ar council 800 free copies will be made available for emerging countries via the member National Centers of the WHO Programme for International Drug Monitoring. It is hoped they will find it useful, and even promote its use in their countries.

SAFETY MONITORING OF MEDICINAL PRODUCTS



Guidelines for setting up and running a Pharmacovigilance Centre, published by *the* UMC in 2000. There is a limited number of copies available of the first printing. The guide will be reprinted and translated into other languages to ensure wide availability. Please contact **Sten Olsson** if you would like a copy.

POISONING, POISON CONTROL AND ENVIRONMENTAL TOXICOLOGY

This book (95 pages) is edited by Professor S.K Gupta, Professor of Pharmacology at the All India Institute of Medical Sciences and head of the Indian national pharmacovigilance centre. The book is based on presentations made at a symposium under the aegis of the International Congress on Frontiers in Pharmacology and Therapeutics in the 21st Century in New Delhi 1-4 December, 1999. It is divided into three sections

I. Problem of poisoning and its management
II. Environmental toxicology
III. Rules and regulations

The book is published by Utkarsh Prints, New Delhi, and may be obtained from Professor S.K Gupta,
Fax: +91-11-686 2662
E-mail: skgupta@medinst.ernet.in

Product News

WEB-BASED TRAINING COURSES

WHO Drug Dictionary and WHO-ART

As previously advised, *the* UMC has developed web-based training courses for users of the WHO Drug Dictionary and the WHO Adverse Reaction Terminology. The courses, providing video and audio presentations, include descriptions of the features of the thesauri and how they may be used. Self tests are included. They can be found on *the* UMC website **http://www.who-umc.org** The website has now also got the added facility of answers to Frequently Asked Questions (FAQs). Contact Liza Storm at *the* UMC to get your passwords to the courses.

2ND QUARTER 2000 UPDATE

The new versions of the computerized WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 2nd quarter of 2000 are now available.

DO WE HAVE YOUR DETAILS CORRECT ?

We hope that your received this issue of Uppsala Reports correctly addressed to you. If we have incorrectly spelt/omitted your name, parts of your address or your title, please do let us know. It is vital that we have your correct communications details and we need your help in ensuring this. It would also be very useful to us if you could reconfirm your telephone, fax, email and website details – you can do this by sending us your most up-to-date communications details by post, fax, or email c/o **Anneli Lennartsson** at *the* UMC.

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