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Uppsala REPORTS

For everyone concerned with the issues of pharmacovigilance and toxicovigilance



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MESSAGE FROM THE DIRECTOR

Drug safety is enjoying a surge of interest and activity worldwide and there are many exciting developments taking place.

Here are some of the current initiatives:

- Work on new analysis tools for spontaneous reporting databases
- Defining ADR terms in vaccine vigilance
- New interest in ADRs associated with biologicals and medical devices
- Growing international consumer activity
- New thinking about drug-related medical error.

Active support and finance needs to be found for all of these if they are to deliver their potential benefits, but I think an even greater challenge for us all is to make sure that these and many other efforts are actively communicated and co-ordinated. There is such a risk that time and resources will be wasted in duplicated effort, in 'reinventing the wheel', in going over old ground for little net gain.

WHO and *the* Uppsala Monitoring Centre have, as part of their core mandate, the responsibility to ensure that information and tools are freely and equally available to all member countries. My personal hope is that we can concentrate on making real collective progress.

To do this we need to be sharing our thinking and research, and concentrating on the enormous undiscovered territories of the science. Where the foundations are laid, we should build on them; when the house has a roof we should live in it; when we're at new frontiers, we should be planning and allocating resources with the greatest of care. There's too much to do for duplication and competition.

I and the team here in Sweden send our best wishes to you, and hope that many National Centres representatives are already planning to join us in Amsterdam for the next Annual Meeting in October, and that we'll see many more of you at the ISoP meeting later the same week.

Ralph Edwards

The ICD-ART project

Bringing together terminologies

the Uppsala Monitoring Centre is currently working on a project to bring together three existing terminologies used in ADR reporting: WHO-ART, ICD 9 and ICD 10. The project will create a system that can be browsed, searched and imported into other database systems. There will be a unified format in the output terminologies and inter-terminology links. Tools for browsing, searching and editing the terminologies and the inter-terminology links will also be available.

The purpose for creating these unified terminologies in XML (eXtensible Markup Language) is to:

- ⦿ comply with international standards
- ⦿ build a system that can be used 'as-is', or that can be imported into databases
- ⦿ facilitate the creation and modification of user interfaces for searching and browsing
- ⦿ make it possible to use an electronic seal, which will ensure that the user uses a validated and unmodified version of the terminology.

Benefits for ADR reporting

Linking these three terminologies is intended to:

- ⦿ assist comparison between databases and sources coded in different terminologies
- ⦿ facilitate the spreading of ADR reporting to regional centres and down to physician level (these users are

often familiar with ICD but not with WHO-ART. They can continue coding in an ICD-like environment but the reports will be coded with the corresponding WHOART term in our database.)

- ⦿ support co-ordination, co-operation and help to avoid unnecessary double work.

New format will emerge in phases

The ICD-ART project will be performed in two phases. In the first phase the two ICD terminologies will be put into a structured XML format. The new format will be validated via the print version. The second phase will be to put the WHO-ART terminology in the same format and to create inter-terminology links to the ICD terminologies.

Importance for National Centres - and others

This project will hopefully be of benefit to new National Centres, as well as National Centres that operate on a regional basis, and should be a valuable tool in both collecting and interpreting adverse drug reactions.

The system will be an important tool for epidemiology, where often, different data sets coded in different terminologies are compared.

The system will also help regulators, the pharmaceutical industry and clinical trial organisations to confirm that the validated and unmodified terminologies have been used in clinical trial and ADR reporting.

Welkom in Amsterdam!

Annual Meeting for Countries participating in the WHO Programme

13-16 October 2002

The 25th Annual Meeting for the WHO Programme for International Drug Monitoring comes to Europe, when Lareb (Netherlands Pharmacovigilance Foundation) will host the meeting in Amsterdam, capital of the Netherlands. Dr Yasuhiro Suzuki, Executive Director Health Technology and Pharmaceuticals, of the WHO, will open this, the 'silver jubilee' Meeting.

Though small, Amsterdam is a cosmopolitan city and has kept its cosy, historical town atmosphere while having the allure of a modern metropolis. Through the ages it has been a magnet for artists, thinkers and entrepreneurs, and is a popular setting for international conferences and festivals.

The Local Organiser is Kees van Grootheest of Lareb. The venue will be the Royal Tropical Institute (Koninklijk Instituut voor de Tropen); this neo-classical building is situated close to the Oosterpark at the periphery of what is known as Old Amsterdam.

On Sunday 13th October the programme will open with a Welcome Reception. There will then be two and a half days for the Meeting, followed by a half-day joint session on Wednesday 16th October with delegates at the 2002 International Society of Pharmacovigilance Annual Meeting. RAI Hotelservice has been appointed official agent for hotel accommodation and offers

reduced rates. National Centres delegates may book through RAI Hotelservice (but are free to contact any hotel or hostel in Amsterdam).

You may wish to view the ISO P 2002 site <http://www.isop2002.org/index.htm>, which has much information which will also be of interest to National Centre delegates. Hotel

booking may be made on-line, but you must make a separate registration if you also wish to attend the ISO P conference.



2002

Amsterdam





The Brazilian Pharmacovigilance Programme

Murilo Freitas Dias, (Manager of Pharmacovigilance Unit, Pharmacist, MSc Pharmacology) describes the work of a recent National Centre to join the Programme

The situation in Brazil

Pharmacovigilance monitoring of drugs by a regulatory body is nowadays an indispensable part of any healthcare system. In Brazil, our programme gained its strength during 2000 and 2001, leading to full membership of the WHO Programme.

Brazil is the largest country in South America with population of 170 million, and represents the ninth largest drug consumer market in the world. Brazil has a complex market, with more than 6,000 products (around 10,000 formulations) and 500 pharmaceutical companies. Until 1999, Brazil had no government programme for pharmacovigilance. During the 1980s and 90s pharmacovigilance awareness began through health schools, consumer defence bodies, drug information centres and health professionals associations.

In 1999 the National Health Surveillance Agency (ANVISA) was created. ANVISA is a government body with administrative independence, stability of its directors during period of office and also enjoys financial autonomy. In the Federal Public Administrative structure, ANVISA is closely bound to the Health Department.

In the 1960s the thalidomide disaster affected 300 babies in Brazil; and in 2000 another tragedy occurred in association with treatment of Leishmaniasis; the meglumine antimonate, caused 300 serious local adverse reactions, some resulting in death.

In 2000, we initiated a process to select technicians to work in the National Drug Monitoring Centre or Pharmacovigilance Unit (UFARM), but it was not easy to start a pharmacovigilance programme when there are many health problems that

Management of Post-marketing Products to offer a legal platform to expand our field of action. An Internet ADR form was elaborated in July 2001, and in August 2001 we sent 105 ADR reports to the Uppsala Monitoring Centre and Brazil was admitted as the



Brazilian Pharmacovigilance Team Photo

Back row (from left to right) Davi Rumel (Adjunct Director & General Manager of Health Products Post-Marketing), Celso Grisi Júnior (Pharmacy student), Marcus Tolentino Silva (Pharmacy student), Murilo Freitas Dias (Manager of Pharmacovigilance Unit), Catarina Juliana da Vila (Medical Analyst, Database Services), Clarice Alegre Petramale (Co-ordinator of Sentinels Hospitals Network Programme), Polliana Almeida Velloso (Team Support)

Front row (from left to right) Elaine Sanchez (Team Support), Gilvânia Melo (Programme Leader, Drug information analyst), Nair Ramos de Souza (Programme Leader, Market Review), Elenice Lacerda (Programme Leader, Customer Relations), Flávia Queiroz Leite (Programme Leader, Recall Monitoring & Pharmaceutical Registry), Patricia Mandali de Figueiredo (Programme Leader, Database Services)

must be solved at the same time. Because of that, in parallel with pharmacovigilance, ANVISA planned to improve drug regulatory legislation and put high investment in material and personal training, including the UMC training course in Pharmacovigilance in May 2001.

Safety, effectiveness and rationality

The Brazilian Pharmacovigilance Programme was planned with four principles in mind: safety, effectiveness, rationality and quality of marketed drugs.

In May 2001 UFARM was created by the Ministry of Health. The Pharmacovigilance Unit was implanted into the newly-created General

62nd country in the International Drug Monitoring Programme.

In September of 2001, the first Workshop of Hospital Safety Use of Drugs and Pharmacovigilance for 54 hospitals around Brazil took place with 180 health professionals (doctors, pharmacists and nurses) and participation of national and international experts. This meeting started a network called 'Sentinel Hospitals' with the intention of early detection of adverse drug reactions (without the confounding variable of medication error). In April 2002, a second Sentinel Hospitals workshop will take place with 50 more hospitals and 150 health professionals. Sentinel Hospitals will conduct not only the local pharmacovigilance programmes, but



also offer medical device surveillance (technovigilance) and blood surveillance (haemovigilance).

In May of 2002 the first training course in Rational Drug Use will take place, for 40 internal medicine doctors who are supervisors from Schools of Medicine.

Regional and international developments

In October 2001 UFARM supported the creation of the Regional Centre of Ceará (Federation State), third element of Pharmacovigilance System after the Regional Centre of São Paulo (created by regional government in 1998) and CEATOX (Special Centre, recognised by the WHO in 1998). It is planned that all 28 States in Brazil will have a Regional Centre for Pharmacovigilance. UFARM has made 15 National Pharmacovigilance Alerts and participated in 40 international pharmacovigilance meetings. It has also published 7 technical communications in Portuguese to improve rational use of drugs.

By the end of 2001, our database had 195 ADRs with assessed causality, and more than 2,000 ADR forms needing technical harmonisation with National System elements.

To improve the voluntary notification process, 97,000 ADR forms were sent to health professionals, supported by pharmaceutical manufacturers. During 2002 ANVISA will mail 60,000 more ADR official forms to health professionals.

UFARM are also directly involved in the general management of Inspection of Pharmaceutical Products in ANVISA in voluntary or obligatory drug recalls.

Since January 2001, UFARM e-mail service has been available, offering 340 technical answers each year. UFARM has a systems analyst who is developing the Brazilian

Pharmacovigilance Database (SISFARMACO) with notification, causality assessment and reports modules.

Other lines of investigation are the review of the drug market for screening irrational associations of active compounds, and biological materials used to produce medicines (specially identify high risk to BSE). We also plan to check banned drugs in other countries which may be officially registered in Brazil, and to start reviewing important drug legislation about package insert information leaflets.

We are creating a network of six laboratories around the country for drug blood level assay, to determine problems linked to therapeutic failure in some medicines.

Quality of drugs

Brazil's ADR form has two parts: 1 for the report, and 2 for complaints of technical quality problems. UFARM is a partner for quality problems and all forms which highlight this situation are sent to General Management of Inspection of Pharmaceutical Products in ANVISA to start an investigation process, - UFARM is directly involved when there are any noxious events related to patients.

At the end of 2000 UFARM was contacted by the National Health Foundation (FUNASA/MS), about reported serious local ADRs with meglumine antimonite. UFARM started an investigation to identify the problem; FUNASA made a case-control study and some laboratory analyses were made to elucidate this case. In the end, 300 serious local adverse reactions (some resulting in death) were identified, possibly due to heavy metal lead and arsenic contamination.

Other actions

The UFARM is frequently asked to make official statements on subjects related to drugs, for departments of ANVISA and for external bodies. In many cases UFARM gives technical internal support to ANVISA.

UFARM is about to start another network for drug surveillance of meglumin antimonate. This restricted network is called Sentinel Doctors and the goal is intensive pharmacovigilance. Brazil, as a member of MERCOSUR (Argentina, Uruguay, Paraguay and Brazil), proposes harmonisation of technical rules in the areas of pharmacovigilance dealing with relevant aspects in terminology and risk assessment.

The Team

Today the Pharmacovigilance Team consists of four clinical physicians, five pharmacists, one systems analyst, two team support persons and two *ad hoc* external consultants working by projects. UFARM has in addition four trainees from a school of pharmacy.

Conclusion

The Brazilian Pharmacovigilance Programme was born in 2000, but started to walk only in 2001. The hard birth and development were helped by specific interventions from government leaders about the potential and necessity of pharmacovigilance. We made many technical presentations for promotion during political meetings, and this strategy seems to have paid off. It is possible for all underdeveloped counties to confront the problems in the beginning to structured pharmacovigilance. After the first step the population will have better protection, and this is the biggest gift that we can give for all people in Brazil.

ANVISA will accomplish its mission: to protect and promote health, ensuring the sanitary health of products and services.



A South American journey

Erica Walette and Anne Kiuru recount their recent visits:

First stop Curacao

As a part of our personal vacation in South America we had the opportunity to visit people working in the pharmacovigilance area. Our first visit was to the beautiful island of Curacao, just off the coast of Venezuela, and the Bureau of Pharmaceutical Affairs in the capital Willemstaad. There we met the Director, Dr Peter Fontilus, and



Erica Walette, Dr Peter Fontilus, Zjumira Wout and Anne Kiuru at the Bureau of Pharmaceutical Affairs on Curacao.

Zjumira Wout, who currently works for a pharmaceutical company. She is however helping the centre until a replacement is found. Curacao is an associate member in the WHO Programme for International Drug Monitoring and is closely collaborating with Lareb in the Netherlands.

There is a good reporting network being established on the islands of the Netherlands Antilles, which includes quick feedback to the reporting doctor during the assessment period. A final conclusion of the specific drug-ADR problem is also sent to the rapporteur. Many of the reports received by the centre are problems common in the Caribbean, including ADRs on capsaicin containing drugs, polypharmacy and

different dermatological products. As with all pharmacovigilance centres there is a strong will to contribute to international drug monitoring, but lack of manpower and technical difficulties are obstacles.

Laying foundations in Ecuador

After three days on the hot and humid island and an adventurous flight over the Andes, we landed safely in Quito, the capital of Ecuador. In Ecuador there is, as yet, no established centre collaborating with the WHO. We met up with the Dean of the Medical faculty at the PUCE University (Pontificia Universidad Catholica Del Ecuador), Dr Jose Teran Puente, who is trying



Dr Jose Teran Puente, one of the driving forces of establishing pharmacovigilance activities in Ecuador.

to establish a collaboration between his faculty and the Military Hospital in Quito. We participated in one of these meetings and there was no doubting the interest and enthusiasm of those involved.

Welcoming Peru into the Programme

The last stop of our 9-week journey was in the capital of the most recent member country to join the program as a full member, Lima. We met Dra Susana Vasquez Lescano and her team at their offices at the Ministerio de Salud, where the Peruvian National Centre is located. In order to include more Hispanic countries in the Programme and to increase

their interactions and participation in information exchange, they believe that translating documents, articles and other sources of information into Spanish, is of great importance. It is obvious that the pharmacovigilance world is filled with knowledgeable and experienced professionals, however, the confusion caused by languages can sometimes be a problem.



*Left to right
Gina Huaraj Garcia
Dra Susana Vasquez Lescano
Lima, Peru*

Our journey in South America was a once in a lifetime experience, but one that we would be glad to do again! The beauty of the countries, the good food and people we met made everything truly unforgettable. We were received with great hospitality and warmth. Thank you to all!

Sten Olsson adds:

The WHO Programme continues to grow. As a result of Erica and Anne's visit to the Peruvian National Centre, we have now received the first batch of case reports from Peru and they are in the accepted format. Since Peru has already applied for membership that means that the number of full members should now be counted as 67. (With Bahrain counted as an Associate Member there are still 4 of them.)



Cuba taking the lead

In early March Helena Sjöström and Sten Olsson from *the UMC* visited Havana, Cuba, both to learn more about the Cuban pharmacovigilance system and to make presentations at the 'Jornada de Pharmacovigilancia'. This conference was held on 12 and 13 March. It was opened by vice-minister Enrique Comendeiro Hernandez and attracted participants from seven countries, mostly from Latin America. Helena gave her presentation to the conference in Spanish, which was appreciated by the audience. A great number of presentations were made during the two days, both orally and as posters, showing both the width and the depth of pharmacovigilance in Cuba and in Latin America.



Giset Jimenez and Francisco Debesa

We learned that through a very active training programme for doctors, pharmacists and nurses Cuba has attained the highest reporting rate in the world in the last few years. In 1999 and 2000, some 20,000 spontaneous reports of suspected adverse drug reactions were received per year through the regionalized pharmacoepidemiology network. For a population of 11 million this is an exceptionally good reporting rate. Part of the explanation might be that Cuba has a very high number of doctors/population. Unfortunately, because of capacity problems at the

pharmacovigilance Centre, only a fraction of these reports are currently available in the WHO database. The situation will be improved however with a new database being put into operation at the Centre.

The Cuban pharmacoepidemiology network combines adverse drug reaction reporting with provision of drug information service, continuous drug utilization studies and ad hoc case-control follow-up studies. Francisco Debesa and his team at the Cuban Centre have promised us a more detailed description of the Cuban system for a later issue of Uppsala Reports.

Training Course 2002 in Colombia

The Spanish Agency of International Cooperation (AECI), and the Spanish Medicines Agency, Ministry of Health, is organising its 3rd Training course on Pharmacovigilance in Cartagena de Indias, Colombia, 29 July- 9 August 2002. The organizations carried out courses on pharmacovigilance for Latin-American Countries and other Iberoamerican Training Centres in 2000 and 2001.

This course provides theoretical and practical training in pharmacovigilance methods. It is mainly targeted at Latin-American professionals considering establishing national pharmacovigilance centres, and at newcomers at National Centres.

If you want more information, please contact:

Centro Iberoamericano de Formación of the Agencia Española de Cooperación Internacional (e-mail: cartagena@cifaeci.org.co; <http://www.cifaeci.org.co/programa.htm>)

or Dr Mariano Madurga from the Spanish Medicines Agency (*Agencia Española del Medicamento*; e-mail: fvigilancia@agedmed.es; <http://www.agedmed.es>).

There will also be a pharmacovigilance course as part of the X Congress of the Organization of Ibero-Latinoamericans Pharmacists (OFIL) in Santa Cruz de la Sierra, Bolivia. The dates are 9th-11th May and the course, on the first day, will be run by Dr Mariano Madurga of the Spanish Medicines Agency. There is an informative (Spanish) website: <http://www.congresoofil.com/>



A group at the Cuban conference, including Vice-Minister Enrique Comendeiro Hernandez (1st from left), Julián Perez Peña, Director, Centre for Pharmacoepidemiology (5th from left), Francisco Debesa (8th from left) and Mariano Madurga (10th from left), along with staff of the Cuban National Centre, visitors from Guatemala and the UMC.



News *from* the Uppsala Monitor

At the Heart of the UMC: the Input Team

by Helena Fucik, Helena Sjöström and Jessica Nilsson

Within *the UMC*, our core activity is the collection and processing of reports of adverse drug reactions from around the world. With 67 countries now full members of the WHO Programme, this is a bigger task than ever before. The importance and potential of the WHO database to world-wide drug safety increases every day.

The database is updated weekly in the current system, and backed-up every night. In the new system, currently in its final test stages, the updating will be performed daily. Reports are processed within one week of arrival at *the UMC*. All reports must follow a specified format, whether submitted on paper forms or – which the vast majority or reports are – electronically.

Report inputting process

Inputting of reports into the database is often not a straightforward process. Sometimes, for very good reasons, countries are unable to submit their ADRs to us in Uppsala for a shorter or longer period. This

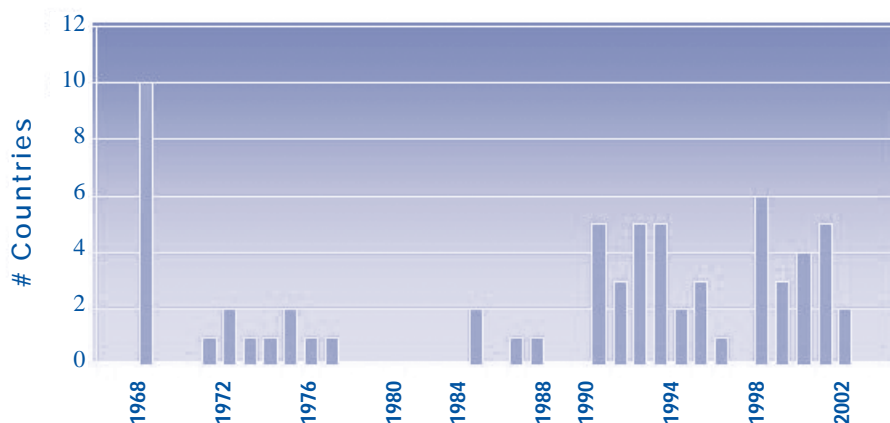
may mean a sudden surge in reports added during a following quarter. For example Vietnam has recently submitted a large number of reports in one such batch. It was also the case in the fall of 2000 when we processed a backlog of about 300,000 US reports. A common reason for such delayed reporting is often that the National Centres are changing to new IT-systems and /or developing new procedures to extract and transfer data to *the UMC*.

Upon receipt of reports the first processing is some computerised Quality Assurance (QA) tests of format and content.

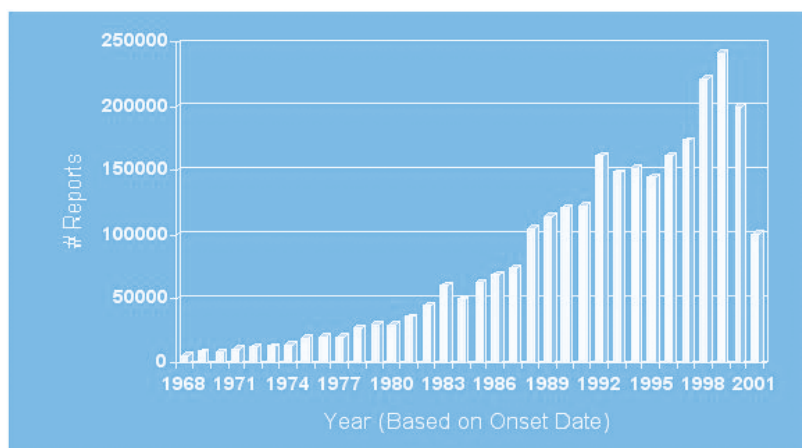
Checking reports

The process of adding in the ADR reports is also more than just putting them on the computer. Individual reports that don't fulfil format and/or QA controls must be checked meticulously by the person who receives the batch from a National Centre. Sometimes the reports must be referred back to the Centre that submitted them to assess coding or translation.

The most common reason for rejection to hinder reports being entered directly into the database is use of new drug names that are not yet defined in the WHO Drug Dictionary, – despite 2,000 new entries added each year.



New member countries joining the Programme by year



Number of ADR reports added to the WHO database by year

Common problems with reports:

- Delay in reporting
- Backlogs
- New staff at the NC
- E-mails and mail don't reach *the UMC*
- Not unique ID-number
- New drugs/terms
- Language barrier



Monitoring Centre

Reporting frequency

The receipt of reports at Uppsala is not a regular, predictable routine – just like healthcare itself, there are variations from week to week and from quarter to quarter. The aim is that reports should be submitted by each National Centre at least four times per year, though preferably once a month, but some report more often and some less.

Current reporting frequency

> 4 times/year	(25% of NCs)
1-3 times/year	(65%)
< 1 time/year	(10%)

For instance, in the 2nd quarter of 2001, most reports were received from the USA, followed by the UK, Canada, Australia and Spain; in the 3rd quarter, the 'top five' were UK, Thailand, Australia, Ireland and Netherlands.

Top 10 reporting countries - 2001

1. USA	107,178
2. UK	28,452
3. Australia	12,659
4. Germany	9,024
5. Spain	8,868
6. Canada	7,804
7. Thailand	7,684
8. Ireland	4,255
9. France	3,365
10. Sweden	3,222

To get an idea of 'effective' reporting rates, the quantities of reports should however be compared to the number of citizens in each country. From that perspective New Zealand over the past five years has the highest reporting per year, followed by Australia then the USA (although Australia's reporting rate is almost twice as high as the USA).

Quality process

Also, of course it is not just the quantity but the quality of reports which is important. Minimum requirements to identify unique cases are: a unique country code and case ID, one ADR and one suspected drug. But to be of value for signal assessment other additional data are needed – to give a hint of completeness and usefulness the system assigns a higher quality ranking depending on how many of the following are present: onset date of reaction(s), drug treatment dates, indication, outcome and positive rechallenge.

The future

An additional major task of the input team at present is the final quality testing of the new database system developed by *the* UMC. All the

existing ADR reports (until 01:2) have already been converted into this system and currently the two systems run in parallel. The plan is to close down INTDIS (the old system) by the end of the second quarter this year, and from then on all reports will be added only to the new system.

When the new database is up-and-running the WHO database will be able to store more details about each case. The system will also facilitate both the report input processes and the retrieval of data.

The present annual reporting rate to *the* UMC is around 160,000 ADR reports. As of the end of year 2001, there were 2,792,872 reports in the WHO database. The 3 million mark is not far off!

Herbals classification

WHO Collaborating Centre for International Drug Monitoring (*the* Uppsala Monitoring Centre) has just published draft Guidelines for Herbal ATC classification. Some herbal remedies have a longstanding use in medicine and their actions are well-defined. For various reasons it has been deemed impractical to incorporate hundreds of herbal remedies in the regular ATC classification. However, experience from the ATC system - particularly in connection with the monitoring of adverse effects of drugs - has shown that such a system would also be suitable for herbal remedies. In 1998, De Smet proposed a system for ATC classification of herbal remedies which is fully compatible with the regular system. With a few modifications this system has now been adopted and is given in these draft guidelines. The ATC Index lists ATC codes per substance, while this herbals guideline is a help to assign ATC codes to herbal remedies.

In both the ATC and the Herbal ATC systems remedies are divided into groups according to their therapeutic use. Whenever possible the level 1-4 codes in the herbal system are equal to the levels in the regular ATC system. If you are interested in this publication, please contact Anneli Lennartsson for a copy or more information.



News *from* the Uppsala Monitoring Centre

New phase of UMC collaboration with Reactions Weekly

Since the beginning of 2001 *the UMC* is collaborating with Reactions Weekly, the journal produced by Adis International that reviews the world literature for adverse reaction information on a weekly basis. *the UMC* contributes with news from National Pharmacovigilance Centres and in return National Centres may subscribe to the journal at a very favourable rate.

The Adis - UMC collaboration entered a new phase at the beginning of this year. Every time Adis literature reviewers find an article concerning a drug - reaction association that has not been described in literature before, the WHO database is consulted. If relevant reports are found in the database, the number of occurrences is given in Reactions Weekly.

Experience so far shows that relevant reports are often to be found in the WHO database when the first report occurs in literature, the definition being that no earlier descriptions are found in Medline or in the Adis literature database. To the 65 'first reports' published in the initial nine issues of Reactions Weekly in 2002, the WHO database held cases on 38 occasions.

Sometimes the number of unpublished reports was surprisingly high. When for example the first case of Stevens-Johnson syndrome to ofloxacin was published there were already 113 suspected cases in the WHO database. It is often difficult to determine whether the published cases and those described in the WHO database refer to the same patients.

Investigators interested in having access to the material in the WHO database should contact Erica Walette (erica.walette@who-umc.org) for assistance.

Product News

4th Quarter 2001 Update

The new versions of the computerised WHO Drug Dictionary and WHO Adverse Reaction Dictionary (WHO-ART), containing information for the 4th quarter of 2001 are now available. They were sent to subscribers during early February 2002.

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 1st quarter of 2002 should be available by April / May 2002.

Staff of *the UMC* will be attending the following conferences this summer:

- 38th Annual Meeting of the DIA, Chicago II, 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 of them beforehand, please contact Mats Persson - (mats.persson@who-umc.org)

Further details on UMC Products and Services are available on the back of *the UMC Basics* sheet, included with Uppsala Reports, or see *the UMC website* www.who-umc.org

Publications from *the UMC*

Marie Lindquist and Ralph Edwards have published an article in *The Journal of Rheumatology* 2001; 28:5 The WHO Programme for International Drug Monitoring, Its Database, and the Technical Support of *the Uppsala Monitoring Centre*.

A Data-Mining Approach for Signal Detection Analysis, Bate A, Lindquist M, Edwards IR, Orre R, in the journal *Drug Safety* (In Press).



Monitoring Centre

Launch of Viewpoint

the UMC's new publication '**Viewpoint**' (part 1) was launched at a press conference during the Drug Information Association conference in Basel in early March. The new booklet was also handed out from *the* UMC's stand at the conference to delegates. It is already attracting comment and interest. An article about '**Viewpoint**' (part 1) has appeared in the journal *Scrip*.

'**Viewpoint**' will also be distributed during the coming weeks to National Centres, to those working in the pharmaceutical industry, as well as to medical schools, consumer groups and other organisations.

The issues raised in '**Viewpoint**' will be the subject of discussions and presentations at future conferences this year.

If you do not receive a copy or know of someone else who would appreciate receiving one, please let *the* UMC know.



Inger Forsell, Mats Persson, Ralph Edwards, Cecilia Biriell on the Rhine as it passes the old city of Basel.

Inset: Ralph Edwards during the press conference to launch 'Viewpoint'

The following are the major sections in **Viewpoint**:

The risks of being alive

The ways in which we perceive and manage risk in our everyday lives and the way in which medical risk is communicated.

Viewpoint then examines

- absolute
- relative
- attributable, and
- reference

risk. These important distinctions are often poorly communicated and little understood.

Benefit, harm, effectiveness and risk in drugs are examined and discussed.

Finding out about the safety of drugs and Why ADRs are so important

- identifying new information about potential hazards, and
- preventing harm to patients.

The core activity of *the* Uppsala Monitoring Centre and of member countries of the WHO Programme.

Viewpoint examines the information about drug safety available through clinical trials, pharmacoepidemiology and other methods.

The importance and difficulties of vaccines monitoring is discussed.

Viewpoint – other topics

- responsibilities and dilemmas of drug regulatory authorities
- openness and transparency in drug safety communications
- impact of global pharmaceutical activity
- need for education and public debate
- *quality of life* for patients; patient empowerment
- counterfeit medicines and generic medicines
- safety of herbal and traditional medicines
- the widening scope of pharmcovigilance.

Viewpoint provides the basis for a new and reasonable debate about the realities and possibilities of safety in medicine. We hope this debate will acknowledge the huge benefits which drugs have brought, but it will also inspire better understanding of the risks associated with any medical intervention, and how they can best be understood and managed in the interests of patient welfare and public health.



Quality of Care: Patient Safety

A report by the Secretariat of WHO, presented to the WHO Executive Board in December 2001, highlights its commitment to patient safety as a key component of quality of global healthcare.

Interest in medical adverse events began to take off in the 1950s, while recent years have seen an important body of research on the subject, including pharmacovigilance.

The report includes a valuable table, which compares some of the research on adverse events in relation to hospital admissions. These range from a low but significant 3.2% admissions experiencing an adverse event, to 16.6% in one Australian study.

Clearly, action needs to be taken, and the report proposes a three-stage approach to the problem:

- Preventing adverse events
- Making them visible
- Mitigating their effects when they occur.

These will need:

- Increased ability to learn from mistakes, through better reporting systems, skilful investigation of incidents and responsible sharing of data
- Greater capacity to anticipate mistakes and probe systemic weaknesses
- Identify existing knowledge resources
- Improvements in the healthcare delivery system, with quality at the core of the system.

The report sees a pro-active leadership role for the WHO within a concerted international effort to reduce adverse events in medicine. 'The experience of countries that are heavily engaged in national efforts clearly demonstrates that although health care systems differ from country to country, many threats to patient safety have similar causes and often similar solutions. There is great scope for collaboration in designing and implementing systems for patient safety.'

Six urgent activities are listed at the end: developing common definitions of patient safety and adverse events; making patient safety the prime concern of healthcare system performance and quality management; establishing a comprehensive evidence base on how to classify, measure, report and prevent adverse events; drawing up a framework for WHO support across various activities related to improving performance in quality of care and preventing adverse events; establishing a network of collaborating institutions as centres of excellence; promoting partnerships between public and private sectors in developing responses to adverse events in healthcare.

In its response to this report, the WHO Executive Board has requested the Director General:

- 1) to develop global norms, standards and guidelines for the definition, measurement and reporting of adverse events and to provide support to countries in developing reporting systems, taking preventive action and implementing measures to reduce risks
- 2) to promote framing of evidence-based policies with particular emphasis on product safety, safe clinical practice and safe use of medical products and creation of a culture of safety within healthcare
- 3) to develop mechanisms to recognise the characteristics of health care providers that offer a benchmark for excellence in patient safety internationally
- 4) to encourage research into patient safety.

The report is a useful lobbying tool for all working in the area of drug safety. It is available as an Adobe Acrobat file from the WHO website: <http://www.who.int/gb/>

New staff

William Frempong, Annica Lundström

With more countries joining the WHO Programme and increasing demand for services from the Centre, *the UMC* has just taken on two more pharmacists to assist in the entry of new substance and drug entries in the WHO databases.



William Frempong was born in Liverpool, England, brought up in Ghana and also graduated from Uppsala University. Apart from his 5-year old son Moses (known as Mosquito) his passions are reading and football. But his new colleagues should beware: he is also fond of practical jokes...

Annica Lundström graduated from Uppsala University earlier this year. She comes originally from Arvidsjaur in the north of Sweden and is fond of travel, music and ostbagar (cheese doodles).



Agra hosts international meeting

Bruce Hugman writes:

The first annual meeting of the Society of Pharmacovigilance (India) was held in Agra on 8 and 9 February this year. It was a lively and interesting occasion held in SN Medical College, and attended by over 100 local and international specialists and students.

- ADR reporting and GPs
- Monitoring of herbal preparations
- Effective communications, and
- Post-marketing surveillance were covered, as well as a wide range of specific drug-related and disease-based topics.

Professor of Clinical Pharmacy in Mysore. He gave a vivid account of the enormous contribution being made to patient care and safety by clinical pharmacists working as therapeutic partners with consultants and doctors. Dr Ed Napke (Canada) promoted the case for excipients to be taken more seriously in pharmacovigilance – in his usual lively and passionate style. The guest of honour was Dr John Autian, an old friend of medical science in India.

One novel and productive element of the conference was a student pharmacovigilance poster prize competition. This produced some remarkably creative and memorable displays.

Professor K C Singhal, the moving force behind the Society and the Conference, declared himself well-pleased with the event, and is hoping that it will be the first of many – and the beginning of a new momentum in drug safety awareness and activity in India.



Prof K C Singhal (fifth from left) with some of his senior colleagues and guests at the Agra conference.

High level issues such as:

- The need for pharmacovigilance in India

One of the distinguished contributions was from Parthasarathi Gurumurthi,

UMC training course in Australia

the UMC will be organising its 7th international training course 'Pharmacovigilance – The Study of Adverse Drug Reactions', in conjunction with the Australian National Centre, from 4-15 November 2002 in Canberra, Australia.

The course is intended for healthcare professionals who have recently become engaged in the practical operation of programmes for spontaneous adverse reaction reporting in a hospital, regulatory or industry setting.

- Module I covers an introduction to ADRs and Spontaneous adverse reaction reporting;
- Module II offers an introduction to pharmacoepidemiology.

Theoretical and practical aspects of adverse drug reactions and pharmacovigilance are covered.

Theoretical parts include lectures, group discussions and poster presentations.; practical sessions include recording of case information and computerised retrieval of information from the database of the WHO Drug Monitoring Programme.

The course language will be English.

Course fees will be announced shortly.

For a full course programme and application form, please apply to:

Mrs Anneli Lennartsson
the Uppsala Monitoring Centre
Stora Torget 3
S 753-20 Uppsala
Sweden

Fax: +46 18 65 60 80

e-mail info@who-umc.org



New books

Adverse Drug Reactions

Anne Lee (Ed) of Glasgow Royal Infirmary, Scotland
Pharmaceutical Press
London 2001

An essential and practical guide to the reactions that affect particular organ systems. Chapters describe the common types of reaction, how to recognise these reactions, predisposing factors and the drugs that are implicated most often. Practical guidance is also given on the management strategies of suspected adverse reactions.

Medical Journalism - Exposing Fact, Fiction, Fraud

by Ragnar Levi
Studentlitteratur 2000

Preface by Deborah Blum, Professor of Journalism,
University of Wisconsin-Madison, USA

This useful book has chapters on
Media meets medicine
Scientific fact of science fiction?
Pitfalls in medical reporting
Critical medical journalism
Medical journalism online
References; Glossary; Index

Mr Levi is a medical editor with a background in both medicine and journalism. His book starts by discussing the basic who, what, when, where and how of medical reporting. Who reports on health and medicine? How are stories selected? What sources are used? Barriers to critical reporting. He then goes on to cover common problems in medical research, and distinguishing between strong and weak scientific evidence. After the 'ten pitfalls in medical reporting', the 4th chapter explores the concept of critical medical journalism and describes its main features – finding the truth, weighing the evidence, and watching for methodological 'red flags'. How can medical reporters deal with scientific uncertainty? What about self-deception among reporters?

Finally, he describes the emerging field of online medical journalism and how new media raise questions of confidentiality, currency and accuracy of information.



Pharmacovigilance from A to Z

Barton Cobert and Pierre Biron
Blackwell Science
2002

This handbook is aimed not only at professors and students in academic setting, but also at newcomers to the field of pharmacovigilance who must learn on their own the basics of this complex field. In his foreword, Ralph Edwards writes "If you are, quite reasonably, overwhelmed by the prospect of accessing key knowledge in pharmacovigilance, then this is a most valuable book for you."

Understanding, influencing and evaluating drug use

Jonathan G A Darnell
Therapeutic Guidelines Ltd
Melbourne 2001

Chapters include 'Understanding the drug use environment', 'Influencing drug use' and 'Evaluating drug use'. A resource for practitioners interested in drug usage evaluation and the wider community interested in ensuring that drug discovery and availability is translated into the best possible health outcomes.

Drug-induced Ocular Side Effects (5th edition) (with CD-ROM)

F T and FW Fraunfelder of Oregon Health Sciences
University, Portland
Butterworth-Heinemann
Boston 2001

Intended as a guide to help the clinician decide whether a visual problem is drug related. It is the intent of this book to compile and organise 'previous reports' into a format that the busy clinician may find useful.



Forthcoming Courses and Conferences

Date	Title	Place	Organiser / Contact
2-3 May 2002	Pharmacovigilance into 2003	Hotel Copthorne Tara London, UK	DIA European Office Tel: +41 61 386 9393 Fax: +41 61 386 9390 e-mail: diaeurope@diaeurope.org
5-8 May 2002	12th International Conference on Pharmaceutical Medicine 'The Future is Now' Symposium 5 – Pharmacovigilance in a Globalised World	Fiesta Americana Coral Beach Cancun, Mexico	Contact: B.P. SERVIMED Tel: +52 5575-9931 / 5575-9861 Fax: +52 5559-9497 / 5575-9937 01010 e-mail: info@servimed.com.mx
19-22 May 2002	7th Annual International ISPOR Meeting	Crystal City, Arlington, VA, USA	ISPOR Tel: +1 609 219-0773 Fax: +1 609 219-0774
9-11 June 2002	Convegno di Primavera SIFO 2002 Sicurezza del Paziente: Prevenzione e Monitoraggio delle Reazioni Avverse da Farmaci e Dispositivi Medici	Reggio Calabria, Italy	Emmezeta Congressi Tel: +39 (0)2 66802323 Fax: +39 (0)2 6686699 e-mail: sifo2002@mzcongressi.com
10-14 June 2002	Second Latin-American Pharmacovigilance Course	Santiago, Chile	Contact: Directora, Instituto de Salud Publica de Chile, Avda Marathon No 1000, Nunoa-Casilla 48, Santiago, Chile. Tel: +56 239 87 69 Fax: +56 239 87 60
12-13 June 2002	"How to Read a Paper – A Course on Critical Appraisal"	Southampton, UK	Contact: Jan Phillips, Drug Safety Research Unit e-mail: jan.phillips@dsru.org
18 July 2002	"Pharmacovigilance of Over-the-Counter Medicines"	Southampton, UK	Contact: Jan Phillips, Drug Safety Research Unit e-mail: jan.phillips@dsru.org
18-21 August 2002	18th ISPE Conference	Edinburgh, Scotland	Tel: +1 301 718 6500 Fax: +1 301 656 0989 e-mail: ispe@paimgmt.com
19-20 Sept 2002	Adverse Event Reporting and Pharmacovigilance	London, UK	IIR UK www.iir-lifesciences.com
2-3 Oct 2002	"Interpretation and Application of Pharmacoepidemiological Data"	Southampton, UK	Contact: Jan Phillips, Drug Safety Research Unit e-mail: jan.phillips@dsru.org
16-19 Oct 2002	ISoP Annual Meeting	Amsterdam, The Netherlands	Secretariat: Tel: +31 73 6469 704 Fax: +31 73 6426 136 www.isop2002.org
21-22 Oct 2002	Medical Approach in Diagnosis and Management of ADRs Training Course	Hotel Sofitel Paris Forum Paris, France	Contact: Training Administrator, DIA Tel: +1 215 628 2288 e-mail: Training@diahome.org
30 Oct – 1 Nov 2002	Drug Safety Surveillance & Epidemiology Training Course	Hyatt Regency Penn's Landing Philadelphia, PA, USA	Contact: Training Administrator Tel: +1 215 628 2288 e-mail: Training@diahome.org
3-5 Nov 2002	ISPOR - 5th European Congress	Rotterdam, The Netherlands	ISPOR Tel: +1 609 219-0773 Fax: +1 609 219-0774
6-7 Nov 2002	"Workshop on Case Narrative Writing"	Southampton, UK	Contact: Jan Phillips, Drug Safety Research Unit e-mail: jan.phillips@dsru.org
4-15 Nov 2002	Pharmacovigilance – the Study of Adverse Drug Reactions	Canberra, Australia	Contact: <i>the</i> Uppsala Monitoring Centre, Sten Olsson, Stora Torget 3, S-753 20 Uppsala, Sweden. Fax: +46 18 65 60 80 e-mail: sten.olsson@who-umc.org
12-23 May 2003	Pharmacovigilance – the Study of Adverse Drug Reactions	Uppsala, Sweden	Contact: <i>the</i> Uppsala Monitoring Centre, Sten Olsson, Stora Torget 3, S-753 20 Uppsala, Sweden. Fax: +46 18 65 60 80 e-mail: sten.olsson@who-umc.org

New Board of *the* UMC

On 11 December 2001 WHO and the Government of Sweden signed an update of the agreement from 1978 concerning the WHO International Drug Monitoring Programme and the operation of the foundation WHO Collaborating Centre for International Drug Monitoring (*the* UMC). The most important practical changes concern the governing body of the Foundation, the Board, and the financial situation of the Centre. The new Board consists of 6 members with an equal number of alternates. The Swedish Government and WHO each appoint 3 members for a period of 3 years. One of the members appointed by the Swedish side will act as chairman.

The new financial situation of *the* UMC is that there is no longer any funding from the Swedish state. *the* UMC will have to rely fully on sales and consultancy services to acquire the funding needed to operate the WHO Drug Monitoring Programme. In practical terms this is not a dramatic change since the Swedish contribution over the last few years has constituted only a small fraction of *the* UMC turnover.

The new Board of the Foundation had its first meeting in Uppsala on 22 March 2002, with an introductory seminar the day before (see photo). Chairman of the Board is Mr Ulf Westerberg, Director General of the National Board of Forensic Medicine, Sweden. His deputy is Assistant Professor Ellen Vingé, Clinical Pharmacologist, University of Lund. The other

members appointed by the Swedish Government are the Professors of Clinical Pharmacology Anders Rane and Marja-Liisa Dahl from the Karolinska Institute and Uppsala University respectively. Their deputies are clinical pharmacologists Ulf Bergman and Rolf Larsson. WHO has appointed Dr Lembit Rågo (alternate Dr Mary Couper) from WHO Headquarters, Professor Jürgen Beckmann (alternate Dr Norbert Paeschke) from the German Drug Control Agency, BfArM, and Professor Mohammed Hassar (alternate Dr Rachida Soulaymani-Bencheikh) from the Moroccan Institute of Hygiene.



the Uppsala Team



Communications information

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Postal Address:

the Uppsala Monitoring Centre,
Stora Torget 3, S-753 20 Uppsala, Sweden

Telephone: +46 18 65 60 60

Fax: +46 18 65 60 80

E-mail:

(general enquiries) info@who-umc.org
(sales & marketing enquiries) sales@who-umc.org
Personal e-mail messages may be sent to any member of the team by putting their name (e.g. ralph.edwards) in place of **info** or **sales**

Internet: <http://www.who-umc.org>

Ralph Edwards
**Professor in Medicine,
Director**

Sten Olsson
Head of External Affairs

Cecilia Biriell
Head of Internal Affairs

Marie Lindquist
**Head of Data Management & Research,
General Manager**

Mats Persson
**Head of Marketing & Sales, Business
Development Manager**

Mohamed Farah
**Programme Leader,
Traditional Medicines**

Malin Ståhl
**Programme Leader,
Signal Detection**

Andrew Bate
**Programme Leader,
Signal Research Methodology**

Helena Fucik
Data Processing Co-ordinator

Monica Pettersson
**Programme Leader,
Signal Analysis**

Malin Nord
Programme leader, Database Products

William Frempong
Pharmacist

Annica Lundström
Pharmacist

Erica Walette
Programme Leader, Database Services

Anna-Karin Flygare
Medical Terminologies

Jenny Ericsson
Data Management

Jessica Nilsson
Data Management

Anne Kiuru
Signal Detection & Analysis

Helena Sjöström
Data Management

Daniel von Sydow
Project Co-ordinator

Sven Purbe
**Data Management & Quality
Assurance Co-ordinator**

Anna Lindquist
Team Support, Web Editor

Inger Forsell
Sales & Customer Relations Executive

Maria Bergström
**Team Support,
Internal Affairs & Sales Assistant**

Anneli Lennartsson
Team Support, Internal Affairs

Geoffrey Bowring
External Affairs Co-ordinator