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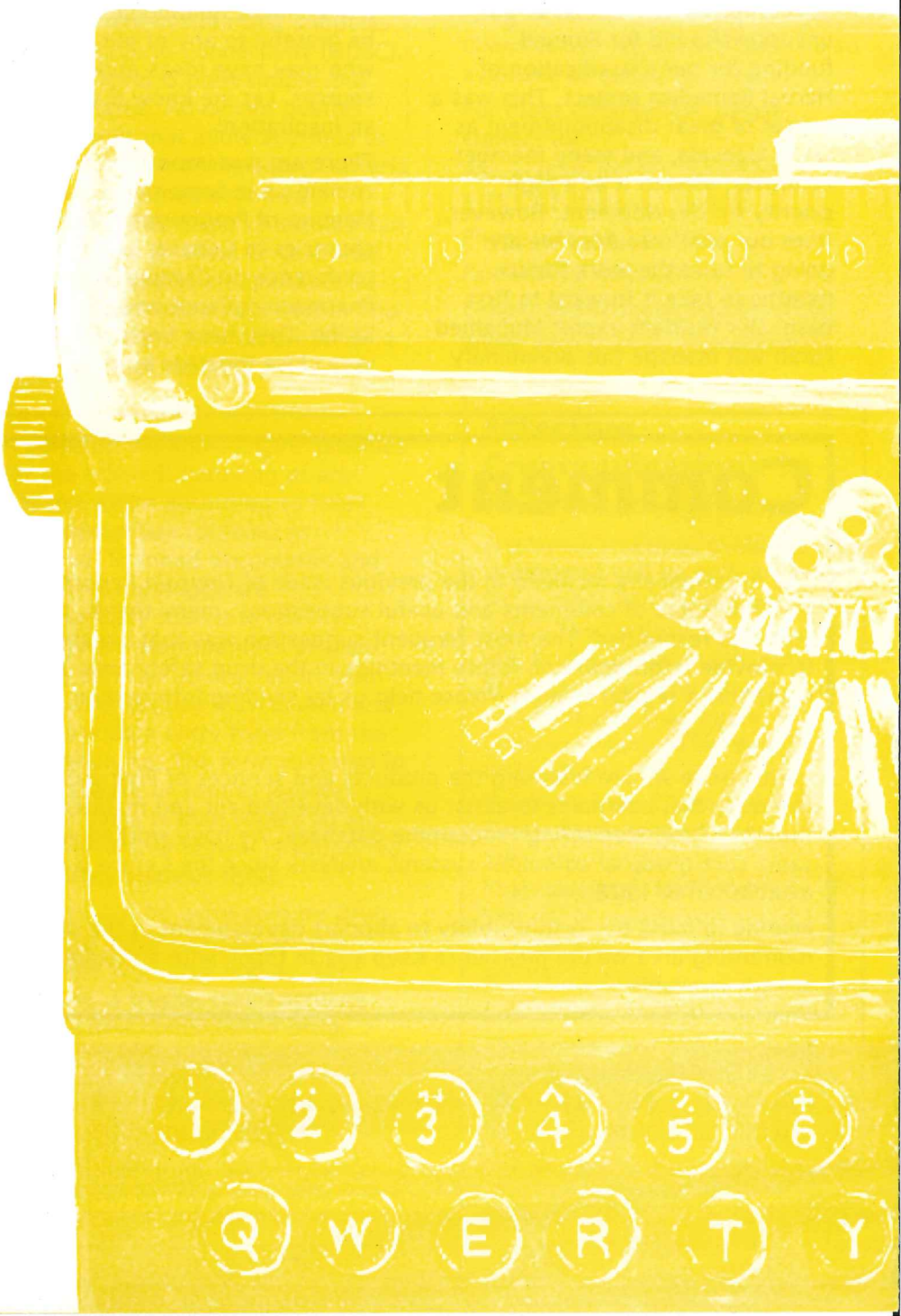
Uppsala reports

For everyone concerned with the issues of pharmacovigilance and toxicovigilance



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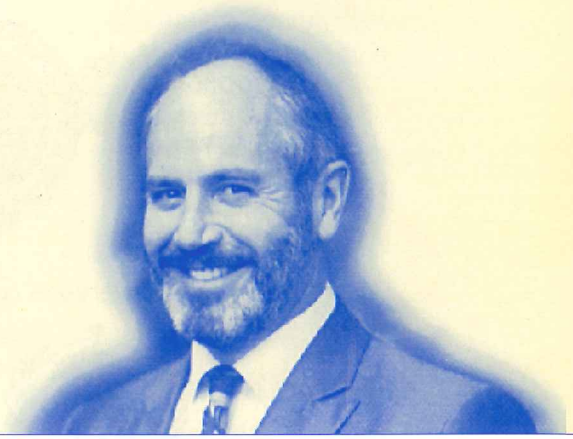
Greetings from *Uppsala*

A Message from Ralph Edwards, Director

The Uppsala Monitoring Centre

We were delighted to hear from so many of you in response to our request for your views about *Uppsala Reports*. We were even more delighted that almost all of you felt it was an interesting and useful publication. Please do continue letting us know how we can improve it further.



There's reference elsewhere in *Uppsala Reports* (page 3) to our unsuccessful bid for Biomed funding for our Classification of Herbal Remedies project. This was a matter of great disappointment as we in Uppsala, and many member countries, viewed it as a high priority for development. However, from our own resources we are going to fund the work for six months to take it forward to first base. Our resident expert Mohamed Farah will manage this preliminary phase. Beyond that, we shall need independent funding, and we shall be grateful to any of our readers who may have ideas about possible sources. Let me know if you have an inspiration!

There are two important events coming up in September - our Annual Meeting of Programme member countries in Geneva, and a notable conference on Communications in Pharmacovigilance to be held in Sicily. They have been scheduled very close together so that colleagues from other continents may have the chance of attending both. Dates and places appear elsewhere in this newsletter, and full details will be circulated soon. Do mark them in your diaries!

Best wishes to you all for 1997!

Ralph Edwards
Director

Comment

Your views

The questionnaire included in the previous issue of *Uppsala Reports* generated lots of comments and useful suggestions: many thanks to all of you who responded. The most frequent suggestion was that we should try to provide information on future meetings in the drug safety area. We shall make this a regular feature. Please help us by sending information to us.

Software

In this issue we are featuring the products and services of PharmaSoft, the company that continues to assist us with development and maintenance of the WHO Drug Monitoring Programme database. We have worked with the same core group of computer systems analysts since the Centre was established in 1978.

Bearing in mind our responsibility to support development in the drug monitoring area we are pleased to keep you in touch with software that is already available.

PRODUCT NEWS

- The WHO Adverse Reaction Terminology (WHOART) is now available in a Portuguese version. The Portuguese text is now part of the file you get if you order the computerized WHOART. It is available also in paper print. The Portuguese terms were originally worked out by the Portuguese national centre in Lisbon.
- The French version of WHOART is now available in a new edition. Another 350 terms already incorporated in the English WHOART have now been given French equivalents with the aid of the French national pharmacovigilance centre.

...Continued on the back page

A N N U A L M E E T I N G 1 9 9 7

The 20th Annual Meeting of National Centres participating in the Programme will be held in Geneva from 30 September to 3 October 1997. Full details will be circulated in February.

Communications Workshop

Verona September 1996

Twenty-five professionals from a wide range of disciplines gathered in Verona in late September to discuss *Communications in Pharmacovigilance.* They were there at the invitation of Professor Giampaolo Velo of the City's University Institute of Pharmacology.

Doctors, nurses, lawyers, journalists, consumer representatives, academics and pharmacists examined a range of problems and priorities in relation to the communication of drug safety information among professionals, regulators, drug companies and to the public. A model of ideal communications practice was proposed and some of the common communications traffic in pharmacovigilance was measured against it.

It was clear to all participants that there was much fruitful work to be done. The groundwork was laid for for application for the issues to be taken to a CIOMS working party (since accepted), and, separately, to an international conference in 1997 (Sicily, 24-27 September. See page 5).

Anyone interested in taking part in these activities or contributing to them is welcome to inform the conference organisers, c/o Bruce Hugman, EQUUS, 10/11 The Stableyard, Broomgrove Road, LONDON SW9 9TL, UK;
Fax: +44 171 733 3600;
e-mail: equus@dircon.co.uk.

NEWS FROM THE UPPSALA MONITORING CENTRE

- Malin Zaar joined our team in early December 1996. Her services as a pharmaceutical officer are much needed, particularly since Monica Pettersson is about to take maternity leave. Malin will mainly be working with quality checking of incoming ADR reports and recording of drug names for the WHO Drug Dictionary.
- Every three months we produce an Adverse Reactions Newsletter, containing reviews of national adverse reaction bulletins, information on regulatory decisions and other types of drug safety communications submitted to us. The ADR Newsletter is restricted in its circulation primarily because it contains figures taken from the WHO adverse reactions database. We have now however, made a special issue of the ADR Newsletter 96:3 in which only material already in the public domain is reviewed. This version is available only on Internet. The URL is http://www.who.pharmasoft.se/newsletter/news963.htm
- The training course in Adverse Reactions and Adverse Reaction Monitoring that we have organized in Uppsala over the last four years will not be held in 1997. The main reason is that many regional courses will be held and we do not want to compete with these but rather support and take part in them. The courses we know of at the moment are:
  - Buenos Aires, Argentina 23 - 25 April, 1997, Pharmacovigilance in Latin America organized by the drug control authority ANMAT. Contact person Dr Guillermo Lombardo, Av. de Mayo 869, 1084 Buenos Aires, fax +54-1-3457135, e-mail: glombard@anmat.gov.ar. Sten Olsson from our centre is scheduled to contribute to this activity.
  - Manila, the Philippines, May 1997. Organized by the national centre in the Phillippines, coordinated by Dr Kenneth Hartigan-Go, Dept of Pharmacology, College of Medicine, 547 Pedro Gil St., Ermita, Manila 1000.
    fax: +63-521-8251,
    e-mail: Hartigan@kulog.upm.edu.ph
  - Southern Africa, tentatively in Zimbabwe November 1997, organized jointly by the national centres in South Africa and Zimbabwe. Contact persons: Ushma Mehra, fax: +27-21-4486181, e-mail umehta@uctgsh1.uct,ac.za and Gugu Mahlangu, fax: +263-4-736980
  - Possibly one course in the Eastern Mediterranean Region. The date and place are not yet settled. If you are interested you may contact Dr Abdel Aziz Saleh at the WHO Regional Office for the Eastern Mediterranean Region, P.O. Box 1571, Alexandria 21511, Egypt, fax: +203-48 38916, e-mail: postmaster@who.sci.eg
- Sten Olsson, General Manager at the Centre, will take part in a national conference on adverse reaction monitoring in Bombay, India, 25 - 26 January, 1996. One of the aims of the conference, which will be attended by the Indian Drugs Controller General, is to attain national coordination of pharmacovigilance activities in India. The chief organizer is Professor N.A. Kshirsagar at Dept of Clinical Pharmacology, Seth G.S. Medical College, Bombay.
- Immediately following the conference in Bombay Sten Olsson will assist in the promotion of an adverse drug reaction monitoring programme for Bangladesh. The national programme is coordinated by Mr Salim Barami at the Directorate of Drug Administration, Dhaka. He attended the Uppsala ADR training course in 1995.

Maria Bergström who recently joined the Uppsala team

ANNUAL WHO MEETING IN LISBON

The Nineteenth Annual Meeting of National Centres Participating in the WHO Programme for International Drug Monitoring was held in Lisbon, Portugal from September 15 to 18, 1996. There were 97 participants from 51 countries, the largest and most representative attendance ever at one of these meetings.

The meeting began with a welcoming address from Dr. Ana Maria Corrêa Nunes, Head of the Pharmacovigilance Centre of INFARMED and Chair of the Organising Committee.

WHO Activities

Dr Martijn Ten Ham (WHO Geneva) discussed development activities in Oman, Pakistan, Chile, Costa Rica, Brazil, the Philippines, and Eastern Europe.

Ralph Edwards referred to some highlights of the activities at the Uppsala Monitoring Centre. These included the publication of the signal review in the *Drug Information Journal*, the documentation of various national pharmacovigilance systems, communication via the Internet, and a new database model with increased data fields and a new drug dictionary.

The meeting had three sessions on *Drugs of Current Interest*, and as in the past few years, these proved particularly interesting and stimulated much discussion.

The Portuguese Contribution

On the second day delegates were welcomed by the President of the Portuguese National Institute of Pharmacy and Medicines, Dr Aranda da Silva, by Dr Martijn Ten Ham on behalf of the WHO, and by the Minister of Health of Portugal, Dr. Maria de Belem Roseira. All three speakers stressed the great developments made by Portugal in the area of pharmacovigilance and the importance of the Portuguese programme and the current meeting to Portugal and the WHO.

The United States centre then presented a session on the *ICH and ADR Monitoring*. The session was introduced by Dr Robert Nelson who outlined the rationale for the development of the ICH processes. Dr Nelson noted that a goal of the ICH was to agree to common standards, processes, principles and regulations in the US, Europe and Japan (see below right).

Definitions

Professor Edwards made a presentation on *Definitions*. The question was asked whether there was a wish to change any of our current definitions regarding adverse drug reaction, side effect, adverse event, causality definitions, seriousness and severity. This was particularly important regarding the work of the ICH. A working group was established to consider the issue. A report of its progress will be published in a future edition of *Uppsala Reports*.

Influencing Drug Policy

A session entitled *From Signals to Drug Policy* was introduced by Ralph Edwards who presented the result of a questionnaire to national centres on the SIGNAL document. Professor Edwards indicated that the issue of the process of moving from signals to drug policy was one which was highlighted by many national centres and the meeting divided into working groups to consider this issue. The purpose of the group meetings was to develop and agree on the concepts and/or guidelines for the actions to be taken once a signal is identified. Each group presented their findings to the meeting and the Uppsala Monitoring Centre has undertaken to summarize these and provide a discussion paper based on the work of the various groups.

Workshops

The group then broke into six workshops - *Herbal Medicines, Vaccines, Technical Issues, Poison Information, Drug Utilisation and ADR Frequency*, and *Polypharmacy* and each group reported back to the meeting.

There was a session on *Abuse Related ADRs* with presentations from Estonia, Argentina, India, the Philippines, Iran and Brazil. There was also a session on *Counterfeit Drugs*. Recent examples were discussed including fake polio vaccine in India and diethylene glycol contamination in Haiti, Bangladesh, Nigeria and Argentina.

Productive Time

In their evaluations, almost all participants said that they felt the event had been very productive and that their investment of time and money in attending had been worthwhile.

ICH AND ADR MONITORING - FURTHER DETAILS

There were five ICH initiatives as follows - M1(Nomenclature), M2 (Electronic Transmission Vehicle), E2A (Expedited Adverse Drug Reactions), E2B (Electronic Data Format) and E2C (Periodic Safety Updates). Speakers from the US discussed each of these topics in some detail. Particular attention was given to the concept of International Medical Terminology (IMT) including the CIOMS decision in September 1994 to build from MEDDRA and the process which has evolved since that time

Dr. Nelson discussed the application of the ICH PMS initiatives in the FDA's adverse event reporting system (AERS). This application has provided the opportunity to re-engineer the whole US system. Dr. Nelson indicated that in the US, 75-80% of reports are submitted by industry, unlike the situation in most other countries. The current FDA database has only limited data available on each report and the revised system will provide a full data system. The revised system will allow for both electronic and paper submission and will not be dissimilar to the current ADROIT system operating in the UK. The use of IMT will be required and regulations are being written to mandate this use.

Dr Ian Boyd, Australia, was the wonderfully efficient rapporteur for the meeting and contributed this summary.

We wish to thank Ana Maria Nunes and her colleagues for organising a remarkable meeting, both from a scientific and social point of view

PharmaSoft

The Global company that provides IT to Pharmaceuticals

PharmaSoft has more than twenty years' experience in the development, implementation and maintenance of system solutions to drug regulatory authorities and pharmaceutical companies. PharmaSoft products and services include product database systems, ADR systems, document management, workflow and SGML. The company expertise is based in equal measure on professional experience in the pharmaceutical arena and information technology.

WHO Collaboration

One of PharmaSoft's main customers is the Uppsala Monitoring Centre. PharmaSoft has been maintaining and enhancing WHO's international ADR database. The system is now being updated and the Drug Watch 2.0 system is about to be implemented at the Centre.

Introducing Drug Watch 2.0

Pharmacovigilance is an increasing challenge for all drug organizations, the demands are getting higher and the volume is getting bigger. Both pharmaceutical companies and regulatory authorities are keen to ensure worldwide safety in drug treatment. The challenge is global and so is the solution that PharmaSoft is now presenting: Drug Watch 2.0.

Drug Watch 2.0 is developed in two different versions, one for industry and one for authorities.

International Standards

The core of Drug Watch 2.0 is an ADR database designed co-operatively with the WHO Centre. It is based on international standards from the ICH and CIOMS.

The ADR database model is linked to PharmaSoft's standard product database that handles information about drugs. The latter adheres to the CEN standard and its specification of medical products.

PharmEDI

As with all PharmaSoft's products, Drug Watch adheres to the PharmEDI standard (set of six ISO standards) and all reports can be saved in SGML format (Standard Generalized Markup Language). This ensures a complete compliance with international standards as well as future requirements such as Electronic Data Interchange (EDI).

Use of several dictionaries

The flexibility of the system also lies in its ability to handle several terminologies for both drugs, diseases and ADR classification. WHO-ART, ATC, ICD, COSTART and MEDDRA (pending approval) are among the main terminologies that can be used in Drug Watch. Furthermore, local classifications may be added.

Advanced Search Function

The database model can be implemented on any database management system that supports Open Data Base Connectivity (ODBC). Data retrieval is both simple and sophisticated. Advanced queries can be built that allow any field to be used as part of the search criteria which can also be saved as a bookmark. The result of a query can be displayed in a text or graphical format. All charts are clickable so that you can refine your search and drill down from an ADR profile to a specific set of reports.

Powerful Workflow System

A powerful workflow engine provides for the efficient handling of any adverse event according to rules and appropriate routeing as required. Scanned documents and electronic messages are automatically routed to the appropriate staff member or team. A user can call up any report from the queue, display it on screen and fill in the data entry form from the core database. The form is stored in the database or sent to another person. Data is then routed to an assessor whose review is supported with many analysis tools.

Triggers can be generated by Drug Watch to initiate certain actions using the workflow engine. For example, a trigger could activate when a new combination drug-adverse reaction is entered.

Direct access to WHO database

Drug Watch 2.0 will simplify communication by national authorities with the WHO ADR database when sending new reports in a secure way through EDI.

Drug Watch also includes a direct connection to the WHO ADR database allowing statistics and reports to be easily retrieved. Seamless connections are also provided for MEDLINE and DECC (Drug Effects in Clinical Chemistry).

Full Audit Trail

An audit trail records the time and day for each user as changes and tasks are performed. Drug Watch features, therefore, a very reliable and detailed version handling, registering all events: what changes have been made, who made them and when. Any version of the report can easily be retrieved and displayed.

Drug Watch is a Windows compliant client/server application and is also available as single PC version.

For more information, please contact us!

PharmaSoft AB, P.O. Box 1237
S-751 42 Uppsala, Sweden

Phone +46 18 185400

Fax +46 18 109200

E-mail: marketing@pharmasoft.se

WWW: http://www.pharmasoft.se

Effective Communications in Pharmacovigilance

A ground-breaking, working conference will be held in Erice, Sicily, from 24-27 September 1997. The conference organisers are: Professor Ralph Edwards, Bruce Hugman, Martijn ten Ham and Professor Giampaolo Velo. It is being organised by the International School of Pharmacology, Ettore Majorana Centre for Scientific Culture, Erice; the Institute of Pharmacology, The University of Verona; in collaboration with The Uppsala Monitoring Centre and WHO Geneva.

Full details will be mailed soon.

This conference finishes three days before the Annual Meeting in Geneva and it is very much hoped that many of our colleagues will be able to attend both.

News from Around the World

People's Republic of China

A new journal, The Chinese Journal of Adverse Drug Reactions, will appear with its first issue around 1 January 1997. The Beijing Center for Adverse Drug Reactions Monitoring, headed by Dr Cheng Jinghua, is responsible for the journal. The contact address is No 13, Ditan Park, An Ding Men, Beijing 100011, fax +86-10-64266618.

Malaysia

Dr Ahmad bin Mahmud has left the National Pharmaceutical Control Bureau and is now attached to another division within Ministry of Health. He is succeeded as the contact person for the national drug monitoring centre by Dr Anis bin Ahmad.

Estonia

The State Agency of Medicines has started, in collaboration with the Tartu University, a campaign to explain the importance of ADR reporting. The campaign involves special two-hour lectures for undergraduates and for doctors during refresher courses. An ADR reporting form has been developed that is distributed to hospitals and included in the national drug compendium. It is expected that Estonia will join the WHO Programme during 1997.

Germany

Dr Annekarin Bertelsmann, who was in charge of pharmacovigilance activities at the European Medicines Evaluation Agency (EMEA) for one year, has returned to the German drug control authority in Berlin where she is now head of the section for pharmacoepidemiology.

Czech Republic

Dr Dana Štolbová is our new contact person at the national monitoring centre at the State Institute for Drug Control in Prague.

United Kingdom

We have been informed by Dr Ivan Stockley, Medical School, Nottingham, England, that the 4th edition of his standard reference book *Drug Interactions* has just been published by the Pharmaceutical Press, London.

PRODUCT NEWS

continued from page 2

In addition to English, French and Portuguese, WHOART is available in German and Spanish. The Spanish version is still incomplete however, containing only the preferred terms. The Spanish national pharmacovigilance centre is currently working on updating the Spanish version. It should be mentioned that the Ministry of Health and Welfare in Japan has a Japanese version of WHOART. It is presently not available from the Centre in Uppsala however.

PHARMACOVIGILANCE MEETINGS

The 9th annual Euromeeting of the Drug Information Association (DIA) in Düsseldorf, Germany, 26 - 28 May, 1997 will have pharmacovigilance as one of its four parallel tracks. For more information please contact DIA, Postfach 4012, 4012 Basel, Switzerland fax: +41-61-3829050, e-mail: diaeurope@stepnet.de

The DIA annual meeting will take place from 22 - 26 June 1997 in Montreal, Canada.

Management Forum, London, organises the 9th Annual Conference on Pharmacovigilance, 3-4 March, 1997. Contact, fax +44 1483 36424.

University of Surrey, UK will hold a meeting on Pharmacoepidemiology and Pharmacovigilance 9 - 11 April 1997. Contact Marie Braisher, fax +44 1483 418453.

The Uppsala Team

Director: Professor Ralph Edwards
General Manager: Sten Olsson
Research and Development Manager: Marie Lindquist
Science and Quality Assurance Manager: Cecilia Biriell
Sales Manager: Liza Storm
Sales and Promotions Manager: Mats Persson
Expert, Herbals Project: Mohamed H. Farah
Pharmaceutical Officers: Helena Fucik, Anna-Karin Flygare, Monica Pettersson, Malin Zaar
Secretaries: Anna Lindquist, Maria Bergström

Communications information

Uppsala Reports © The Uppsala Monitoring Centre 1997
Postal Address:
The Uppsala Monitoring Centre,
Box 26, S-751 03 Uppsala, Sweden
Telephone:
+46 (18) 17 48 50
Fax:
+46 (18) 50 78 40
e-mail:
who.drugs@who.pharmasoft.se
Personal e-mail messages may be sent to members of the team by substituting the name of the addressee (e.g. ralph.edwards or liza.storm for who.drugs)
Internet:
http://www.who.pharmasoft.se