

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

We very much hope that you enjoy reading this 'new look' edition of *Uppsala Reports*.

As always, we want to make it as useful and interesting as possible for all of our readers - so if you have any suggestions or queries, we would be delighted to hear from you.



Some time ago, over twenty countries requested that we support the handling of CIOMS I reports from industry, and produce summarised information from the reports at intervals. The response to enquiries from industry was lukewarm because of two main drawbacks: that the limitations of our current database meant that they might need to answer frequent requests for additional data, and that inputs, outputs, changes and accesses must all be logged.

We decided to wait for the development of our new database to fully answer the challenges

posed. Our new database for ADRs is now under trial. It is based on the CIOMS Ia and ICH E2B proposals with some additions. Certainly there is a comprehensive set of fields and the workflow software provides adequate audit, thus answering the objections above.

We will be very interested to hear from national centres and industry who feel their workload may benefit from using a service for CIOMS I, industry and case reports (which will be annotated as direct from industry in the new database). It is clear that there will be some duplication between these reports

and the industry reports forwarded through national centres. Such duplication occurs with the current situation, and it is hoped that the use of the same database will facilitate checking between the two sets of data.

Please let us know if you wish to join a trial of our new database. We need at least one national centre and one international company to do this. So do get in touch!

Ralph Edwards
Director

A Simpler Form of Address



'The WHO Collaborating Centre for International Drug Monitoring' has always been a bit of a mouthful for everyday use. Now we've shortened and simplified it to 'The Uppsala Monitoring Centre' and adopted a new logo to reflect the change.

We still hold full responsibility for all activities and services associated with the WHO Programme on International Drug Monitoring and for providing general and technical support to member countries. On the other hand, the abbreviated title is not only more convenient, but it also recognises that we have activities in addition to those of the WHO Programme.

We hope you will associate this new image with our vision for the future of quality in service and our expanding range of activities, products and services.

Visit our Home Page

A full account of the Uppsala Monitoring Centre, its vision, activities, products, staff - almost everything you might want to know! - can be found on our Home Page, <http://www.who.pharmasoft.se>. Do visit us!

ADR Signal Analysis Project - 'ASAP'

This research project which combines the features of the database of the WHO drug monitoring programme with drug utilisation statistics from IMS International and official demographic statistics, got a two-year research grant from the Biomed fund of the European Union. The final report of the research project was presented to the EU in January 1997.

Results

The main purpose of the project was to examine the use of the WHO ADR database, the IMS drug utilisation database and international demographics for the investigation of drug safety signals. Although no definitive algorithms could be applied to every analysis,

a number of standard tabulations were developed, together with methods to bring together the data and recalculate sales and prescription figures into internationally comparable measurements.

The analyses made showed that the methodology can be used for a wide range of drug safety problems. Both the technological and scientific findings made will add to existing international pharmacovigilance practices. Some of the analyses have led to publications in reputable journals, and the ASAP team suggests a way to develop the strategy as a new pharmacovigilance service, which should benefit administrators, prescribers, manufacturers, and, above all, patients.

Major Scientific Breakthroughs and/or Industrial Applications

The comparison of adverse reaction reporting rates, as compared with raw numbers of reports, across countries and over time has never been achieved before, and could only be achieved in this way, with the cooperation of the participating experts and the two international databases.

There are direct drug safety benefits of the project: the results show that the methodology is a cheap and quick way of analysing international ADR signals, and that it can provide information that adds to existing knowledge.

Reporting *adverse drug reactions*

WHY DO (SOME) DOCTORS ACTUALLY TAKE THE TIME TO DO IT?

The Uppsala Monitoring Centre has made a pilot study to find out why some physicians and pharmacists take the time to report adverse reactions. Previous studies have tended to concentrate on why they do not report. The National Drug Monitoring Centres in the WHO programme were asked to send a letter to 20 reporters, with a copy of one of their own reports, to ask why they had chosen to report that particular reaction. They were also asked to give comments about adverse reaction reporting in general, and their own habits in particular.

Twelve countries replied and gave information about the habits and views of the reporters of 177 cases. Since this was an explorative pilot study the letter to reporters had only an open question about reasons for reporting.

The responses were categorised at the WHO Collaborating Centre into 14 groups, with the great majority in the top six:

- Ψ **motivation to contribute to medical knowledge**
- Ψ **reaction previously unknown to reporter**
- Ψ **reaction to new drug**
- Ψ **reporter reports all significant reactions**
- Ψ **known association between drug and reaction**
- Ψ **severity of reaction**

From the responses some useful - if obvious! - recommendations can be made. The proposals are based on comments from doctors who have reported, but who represent only a small proportion of professionals who are keener and more aware than the majority.

- Ψ **actively promote the professional and public health benefits of ADR reporting**
- Ψ **consider the needs of particular professional groups in promotional activities**

- Ψ **focus attention on new drugs, observed possible ADRs, and on the most important categories of reactions (severe reactions rather than serious)**
- Ψ **develop simple, accessible forms and systems for reporting and follow-up**
- Ψ **give personal encouragement, recognition and feed-back for those who submit reports**
- Ψ **give evidence of the usefulness of submitted reports in publications, bulletins, notified regulatory decisions etc.**

Cecilia Biriell, Ralph Edwards: Reasons for Reporting Adverse Drug Reactions - Some Thoughts Based on an International Review, Pharmacology and Drug Safety 6: 21-26 (1997)

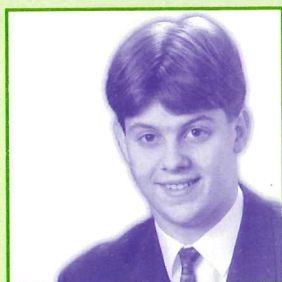
Please contact the Uppsala Monitoring Centre for a full copy of the publication.

Ψ Since mid March Jonathan Edwards has been a member of our team. His main task is to be



in charge of maintenance of our computer hardware and software. Jonathan will also be responsible for the development of new software to support us and our clients.

Ψ Andrew Bate has been working with us as a research assistant since January this year. In addition to his collaborative work on



artificial neural networks with the Royal Institute of Technology, Stockholm, he helps take care of incoming adverse reaction reports.

Ψ From September this year we will not have the capability to receive or produce any magnetic tapes. The computer with a tape

station is now old-fashioned and expensive to maintain, and we shall not be replacing it. If you have submitted adverse reaction reports to us on magnetic tape or have got any of our computerised registers on that medium, please consider using diskettes or direct file transfer instead. If this causes you problems, please call us to discuss possible alternatives.

Ψ During the summer, tentatively in August this year, we expect to move to new premises in central Uppsala. This is the result of the expansion of our tasks and our staff which has taken place over the last few years. Up to now our landlord, the Medical Products Agency, has managed to provide us with the office space we need but now we have reached the limit of what the present premises can accommodate. In April our Board decided that we can move to new premises located at Stora Torget 3. The new office, overlooking the Central Square, provides excellent working conditions and very good communications for visitors. For everyone working at the Centre this is a very positive development. We will let you know as soon as we have details of our new postal address and telephone number - and hope to welcome some of you to our new home.

Ψ Last year Ralph Edwards and

Sten Olsson from the Centre gave lectures to audiences in Melbourne and in Sydney, Australia, though a video-conference connection. Unfortunately the studio used in Uppsala was closed down shortly afterwards with the effect that this service could not be offered to others. However, we have now got access to another video-conferencing facility in Uppsala. Consequently we can now offer this facility as a cheaper alternative to our travelling to course venues around the world. The technology allows for discussions and simultaneous display of illustrations to all parties.

Ψ We recently established a list of e-mail addresses called "Vigimed" that includes pharmacovigilance professionals associated with the WHO Programme. The list is meant to provide a forum for rapid exchange of information on drug safety issues to a limited number of concerned individuals. An e-mail message sent to "Vigimed" will automatically be distributed to everyone included on the list. If you are collaborating with the WHO Drug Monitoring Programme, have an e-mail address and are still not on the Vigimed mailing list, please contact Sten Olsson at sten.olsson@who.pharmasoft.se

"NATIONAL PHARMACOVIGILANCE SYSTEMS" NOW AVAILABLE

This attractive and comprehensive publication offers the first detailed overview of national pharmacovigilance systems throughout the world. It can be used in a variety of different ways:

- Ψ **To gain an insight into how the national pharmacovigilance system is set up and operated in a particular country**
- Ψ **To get a global overview of how systems resemble each other or differ, including variations in national**

adverse reaction reporting forms

- Ψ **To understand how national centres collaborate and interact globally under the auspices of the World Health Organization**

The publication will benefit health care practitioners, professionals working within the pharmaceutical industry, drug regulators and all those interested in pharmacovigilance. It covers details of 45 national systems over 235 pages. It also provides a

comprehensive directory of names, addresses and communication details, which should contribute towards intensifying world-wide communications on issues of drug safety and pharmacovigilance practices.

Annual up-dates will be provided, so that the dynamic and changing systems outlined in the directory can be kept as up to the minute as possible.

For further details, please contact Sten Olsson at the Uppsala Monitoring Centre.

News *from Around the World*

EU

Mr Philippe Meyer who was the principal administrator at the Commission of the European Union, Brussels, in charge of pharmacovigilance affairs, has moved on to the external relations department within the Commission.

Iran

The national pharmacovigilance centre in Iran has been moved from the quality control laboratory to National Drug Information Centre (NDIC). Dr Mahlegha Mahmoodi is director of NDIC while Dr Mohammad Shafzadeh is in charge of the pharmacovigilance unit. The contact address is: Iranian Drug Information Center, ADR unit,

Under Secretary for Curative and Drug Affairs, Building No 3, Fakhre Razi, Enghlab Ave, Tehran 13145
fax +98-21-675868

Japan

The new head of the Japanese national pharmacovigilance centre is Mr Koichi Ishii who has succeeded Mr Tatsuo Kurokawa, now the director of the food chemistry division within the Ministry of Health and Welfare.

Portugal

Dr António Faria Vaz has been appointed head of the national pharmacovigilance centre at INFARMED, the Portuguese drug control authority, replacing Dr Ana

Maria Corría Nunes.

Dr Faria Vaz and colleagues paid a short visit to Uppsala in early April.

Venezuela

The present head of the national pharmacovigilance centre is Dr Carmen Lozada Aranguren. She has replaced Dr Evelyn Uzcátegui. The contact address is Instituto Nacional de Higiene "Rafael Rangel", Sección de Farmacología Sanitaria, Apartado Postal 60.412-Oficina del Este, Caracas, tel +58-2-662 4797, fax +58-2-6625074

The Philippines

The second National ADR Training Workshop is being held in Manila 14-15 May 1997.

WHO Dictionaries Users' Group Meetings

The next Users' group meeting will be held at the annual DIA meeting in Montreal on Monday June 22.

The Centre's representatives at the meeting will be Marie Lindquist, Research and Development Manager, and Liza Storm, Marketing Manager.

Unfortunately there was no Users' group meeting at the Philadelphia DIA meeting in March. However, those of you who have not received the minutes from the London meeting, held in November last year, please contact us and we will send you a copy.

Once again we would like to remind you of the fact that a new chairperson/convenor for the Users Group has not yet been elected. We think it is very important to have an active users' group, so if you have any suggestions for a suitable person, please let us or the DIA know.

FTP

As we have mentioned earlier, we plan to introduce the capability of delivering the Dictionaries files by direct file transfer (FTP). This option will be available from September/October this year. Those of you who are interested in receiving the files by FTP, please contact us.

Product *News*

The Drug Dictionary

The development of the structure of the new Drug Dictionary proceeds as planned. To get continuous information about progress, please look at our homepage (see below for details) where you will find current information. We will, of course, also give you up-to-date information at the next Users' group meeting.

The printed version of the Drug Dictionary (the former WHO Drug Reference List) will be produced and available during May/June this year. It will contain information up to and including the first quarter of 1997. As the new ATC codes are not available until the beginning of the year and as we find it important to have them added to the new edition we decided to postpone the production by a few months. We hope the delay in availability will not be of any inconvenience for you.

The Adverse Reaction Terminology

The new printed versions of the Adverse Reaction Terminology (English, French, Spanish and

Portuguese) are now available for distribution.

Jonathan Edwards has recently started the development of an Adverse Reaction Terminology product containing software with search facilities like the DD Access product provides for the Drug Dictionary. The new product is likely to be available for sale in September/October this year.

The current computerised versions of the Dictionaries contain information up to and including the fourth quarter of 1996. The next versions, containing information as per the first quarter of 1997, will be ready for distribution during May/June.

The new updated DD and ART information leaflets are now also available in French.

For current information on our products and activities we would like to remind you of our homepage (see address below) which is updated regularly, and of course you are welcome to contact us as soon as you have any queries at all regarding our products and/or services.

<http://www.who.pharmasoft.se>

Pharmacovigilance Meetings

Ψ The 9th Annual Euromeeting of the Drug Information Association (DIA) will be held in Düsseldorf, Germany, May 26-28, 1997.

The pharmacovigilance track will have three main themes:

1. Maturation of pharmacovigilance in an international environment moving towards harmonization
2. Practical issues facing the pharmaceutical industry
3. Risk management in a global regulatory environment.

More information may be obtained from DIA European office, fax +41-61 3829050, e-mail: diaeurope@stepnet.de

Ψ Management Forum will arrange a basic training course on Pharmacovigilance for Those Working on Drug Safety Monitoring in the EU in London, UK, June 4-6, 1997. Please fax +44-1483 536424 for additional information

Ψ The Drug Information Association will have its 33rd Annual Meeting in Montreal, Canada, June 22-26, 1997. One of the main tracks concerns drug safety. The session topics are as follows:

1. Black box warnings
2. The challenges of managing the serious adverse event database from IND to NDA
3. CIOMS update and benefit risk analysis
4. Working methods of national adverse drug reaction centres
5. ICH M1 medical terminology
6. EU safety update

7. Electronic transfer and management of safety data
8. Pre- and post-marketing adverse event handling - the daily challenge
9. US FDA safety update
10. ICH update
11. Communicating safety information effectively
12. Signal identification and follow up.

More information may be obtained from DIA, fax +1-215 641 1229, e-mail dia@diahome.org

Ψ Instituto Nacional de Higiene "Rafael Rangel", Caracas, Venezuela, will organize an international workshop on pharmacovigilance 10 - 11 July, 1997. Please fax Dr Carmen Lozada +58-2-6934967 for further information.

Ψ ISPE, the International Society for Pharmacoepidemiology, will have its 13th International Conference at Walt Disney World Dolphin Hotel, Orlando, Florida, USA on August 24-27, 1997. More information about the conference may be obtained from Professor Stanley Edlavitch, fax +1-913-588-2791, e-mail: ispe@kumc.edu, website: <http://www.kumc.edu/ISPE/>

Ψ European Society on Pharmacovigilance (ESOP) will hold its fifth annual meeting in Berlin, Germany, September 15-16, 1997. Topics will include

1. Would we prevent the thalidomide disaster today?
2. Delayed allergy-like reactions to x-ray contrast media

3. Allergy, toxicity and resistance - the problems with anti-bacterials

4. Risks of long-term suppression of HCl-secretion

5. Pro-arrhythmic effects of drugs

6. Contribution of drug-utilisation studies to pharmacovigilance.

For more information contact Dr Jürgen Beckmann, Federal Institute for Drugs and Medical Devices, fax +49-30 45483515

Ψ The 2nd Congress of the European Association for Clinical Pharmacology and Therapeutics will also be held in Berlin, September 17-20, 1997. One symposium will be on adverse drug reactions with the following themes:

1. Mechanisms of "idiosyncratic" drug toxicity

2. Hepatotoxicity

3. Assessment of oral contraceptives

4. Pharmacoepidemiology in pharmacovigilance

For more information contact FGU Berlin, fax +49-30 21295420

Ψ SOBRAVIME (Sociedade Brasileira de Vigilância de Medicamentos) will organize its IV Brazilian Congress on Pharmacovigilance in Curitiba, Brazil, 23 - 26 September, 1997. Further information and a draft programme may be obtained from the SOBRAVIME secretariate, fax +55-11-2584241, e-mail:sobravim@eu.ansp.br

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