Improving the quality of medical editing

Reducing publication bias, avoiding conflicts of interest, redefining authorship and improving peer review practices: these are some of the aspects covered by medical editing, a field that has become the object of an increasing number of articles, research, and meetings.

Several associations of science editors have emerged in recent years (see below). In the biomedical field the development of these associations is mainly driven by those in charge of the most influential international journals, particularly The Lancet, the British Medical Journal, and JAMA. Some ISDB bulletins have been involved in these associations.

Co-operation among editors aims at improving the quality of biomedical publications, i.e. their reliability, relevance, and adaptability to current needs. Medical editing also involves standardising articles: structure of abstracts, format of tables, style and references. It also tackles ethical issues, such as disclosing financial interests of authors, fighting scientific fraud, and relations with industry/advertising.

Promoting medical editing is not a new fad. It is justified by the key role biomedical publications have come to play in the information process, which eventually allows health professionals to make evidence-based decisions.

Improving medical editing involves the readers. Indeed, critical appraisal of the medical literature always starts with identifying the source of publication (who? why? type of funding?) and the editorial method used (how?).

We recommend the following associations, whose resources are available on the Internet:

• Council of Science Editors (CSE): www.councilscienceeditors.org
• European Association of Science Editors (EASE): www.ease.org.uk
• World Association of Medical Editors (WAME): www.wame.org

[Adapted from la revue Prescrire May 2000, n° 206]

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THE ISDB COMMITTEE

You will find below some details about each committee member. Feel free to contact them with suggestions for activities or any questions you may have.

In alphabetical order:

DZULKIFLI ABDUL RAZAK
Pharmacist/Pharmacologist (Academic)
Editor of PRN8099, and PenawaRacun (Malaysia)
National Poison Centre
Universiti Sains Malaysia
11800 Penang
Malaysia
Tel: 604 6570099
Fax: 604 6568417
E-mail: dzul@usm.my

HIROKUNI BEPPU
Editor of The Informed Prescriber (Japan)
1-43-8-404, Nishikoigakubo Kokubunji
Tokyo 185-0013
Japan
Tel: 81 4 23 25 6983
Fax: 81 4 23 25 5148
E-mail: beppu@nihs.go.jp

MARIA FONT
Community practising General Practitioner
Editorial board member of Dialogo sui Farmaci (Italy)
Servizio Farmaceutico ULSS 20
Via Poloni, 1
37122 Verona
Italy
Tel: 39 45 591705
Fax: 39 45 8075607
E-mail: mfont@mei.it

MARY HEMMING
Pharmacist (not practising)/Epidemiologist
Chief Executive Officer of Therapeutic Guidelines (Australia)
Level 2
55 Fleming Rd
North Melbourne, Victoria 3051
Australia
Tel: 61 3 93 26 63 24
Fax: 61 3 93 26 63 20
E-mail: mhemming@tg.com.au

CHRISTOPHE KOPP
General Practitioner, practising in Paris community
Editor of Prescrire International, the English edition of la revue Prescrire (France)
BP 459
75527 Paris Cedex 11
France
Tel: 33 1 47 70 86 06
Fax: 33 1 47 70 52 04
E-mail: christophe.kopp@wanadoo.fr

KSENJA MAKAR AUSPERGER
General practitioner (not practising)
Co-editor of the hospital drug bulletin Farmacologia (Croatia)
University Hospital Rebro
12 Kispaticeva
10000 Zagreb
Croatia
Tel/Fax: 385 1 213861
E-mail: vrhovac@rebro.mef.hr

JOSE MARIA RECALDE-MANRIQUE
Doctor (not practising)
Editor of Boletin Térapeutico Andaluz (Spain)
Escuela Andaluza de Salud Publica
Campus Universitario de Cartuja
Apdo. de Correos 2070
E-18080 Granada
Spain
Tel: 34 95 816 1044
Fax: 34 95 816 1142
E-mail: cadime@easp.es

PIJUS KANTI SARKAR
Doctor (not practising)
Editor of Bulletin On Drug & health Information (BODHI) (India)
P 254 - Block B
Lake Town
Calcutta 700 089
India
Tel: 91 33 5216878
Fax: 91 33 2414915
E-mail: fha@cal.vsnl.net.in

ANDREA TARR
Pharmacist (not practising)
Associate editor at the Drug and Therapeutics Bulletin (United Kingdom).
2 Marylebone Road
London
NW1 4DF
United Kingdom
Tel: 44 20 7770 7571
Fax: 44 20 7770 7665
E-mail: andrea.tarr@virgin.net

KRISANTHA WEEARASURYA
Doctor, practising in hospital
Member of the editorial board of Sri Lanka Prescriber (Sri Lanka)
Dept of Pharmacology
Faculty of Medical Sciences
University of Sri Jayawardenepura
Gangodawila, Nugegoda
Sri Lanka
Tel/Fax: 94 1 695 230
E-mail: kw_twcp@slt.lk

Regional coordinators

Ksenija Makar Ausperger for Central and Eastern Europe
Maria Font for Western Europe
José Maria Recalde for Latin and North Americas
Welcome to New full Members

RDU Update from the Phillipines
1000 copies per issue, 4 issues per year
Distributed free
Commenced publishing: 1991
Language: English
Geographical spread: national
Source of funding: Government
Editor: Isidro Sia
Dept of Pharmacology, College of Medicine
University of the Phillipines Manila
547 Pedro Gil St
Manila 1000, Phillipines
Tel: 63 2 526 4384
Fax: 63 2 521 8251 / 63 2 526 4384
E-mail: pharma@pchrd.dost.gov.ph / pharma_health@yahoo.com

PreMeC Medicines Information Bulletin from New Zealand
4000 copies per issue, 12 issues per year
Distributed free
Commenced publishing: 1991
Language: English
Geographical spread: national
Source of funding: The Pharmaceutical Management Agency Ltd (a subsidiary of the Health Funding Authority)
Editor: Neville Dickson
PreMeC
PO Box 10 545 The Terrace
Wellington, New Zealand
Tel: 64 4 496 5960
Fax: 64 4 496 5961
E-mail: neville@premec.org.nz
Web site: www.premec.org.nz

Farmakon from Slovenia
1500 copies per issue, 4 issues per year
Distributed to subscribers
Commenced publishing: 1998
Language: Slovene
Geographical spread: national
Source of funding: subscriptions
Editor: Jelka Dolinar
Slovenian Pharmaceutical Society
Dunajska 65, SI-1000 Ljubljana
Slovenia
Tel: 386 61 136 2440
Fax: 386 61 136 2443
E-mail: jelka.dolinar@guest.arnes.si
Web site: www2.arnes.si/~ljslfd1

FOLLOW-UP ON WHO-INDUSTRY PARTNERSHIP

We have already reported on the questionable hypertension guidelines published by the World Health Organization and the International Society of Hypertension (ISH) (see Newsletter December 1999). On May 1 & 2 In Geneva, Switzerland, Margaret Ewen delivered a speech on behalf of ISDB at the WHO/Public Health NGO Pharmaceuticals Roundtable Meeting. She presented ISDB’s perspective about WHO interactions with commercial enterprises. Based on her report the ISDB executive committee sent an electronic letter to the BMJ, expressing our standpoint on WHO guidelines (see below). We have been informed lately that WHO and its Management of Noncommunicable Disease department intend to review the WHO/ISH Hypertension Guidelines. They said a new methodology will be used, putting more emphasis on the evidence and public health implications in developing countries.

Industry-WHO partnership should also be seen in the broader context of a deliberate policy devised a few years ago by United Nation (UN) authorities regarding relations with transnational corporations. A worrying side effect of this policy is the case of WHO censorship of experts on infant feeding as reported below in a paper from Pharma-Brief (Germany). See also “Unicef accused of forming alliance with baby food industry” in the BMJ http://bmj.com/cgi/content/full/321/7254/132

For a more comprehensive view on risky partnership between UN agencies and transnational corporations, visit Corporate Europe Observatory web site and its section ‘UN and Corporations Update’ at: http://www.xs4all.nl/~ceo/.

Who-industry partnership in the hot seat

In the BMJ 20 issue Annabel Ferriman raises the possibility of WHO recommendations on infant feeding being influenced by the baby food industry. But certain direct and indirect interactions with pharmaceutical companies have already tarnished WHO’s credibility as an organisation and detracted from the documents it produces. For example, several of the recommendations in the 1999 WHO/ISH guidelines on the management of hypertension (1) have been said to not represent the evidence (2,3). One recommendation is a target reduction in blood pressure close to normotension rather than the more widely accepted slightly higher target. Another recommendation is for indiscriminate use of antihypertensive drug classes for initial use, thus conflicting with authoritative sources (4-7). The consequences of following these guidelines could be needless drug treatment, over-medication, and the increased potential for adverse reactions. Obvious beneficiaries are pharmaceutical companies who market antihypertensives. It has been suggested the advice stems from a misinterpretation of the evidence. There are several possible reasons for this misinterpretation, including an honest error or a conflict of interest on the part of the experts. Because the press release of the guidelines was sponsored by Astra, who stand to profit from their use, one tends to put more weight on a conflict of interest being involved.

Following much criticism, WHO has stated they will review the hypertension guidelines. Yet so far the guidelines are still being distributed.

WHO appears to be convinced that partnerships with commercial enterprises are beneficial and overlooks the inherent conflict of interest between public health and commercial goals.

We fail to see how any sort of company involvement in the development of guidelines is in the interest of public health.
A case of censorship by WHO

Information provided by its own consultants for an expert meeting has been censored by WHO.

The experts went public now. See the paper “WHO accused of stifling debate about infant feeding” in the British Medical Journal 20 (May 2000, p.1362).

Current WHO advice is that babies should get additional food from 4-6 month onwards. This recommendation makes the baby food industry happy because their products are used only for a short period of time and so the earlier the mothers start to supplement breastfeeding with other food the better for industry. Scientific evidence shows that giving supplemental food before the babies are 6 months old increases mortality under conditions found in developing countries. At a joint expert meeting of WHO and UNICEF, papers which demanded to take this evidence into account for future recommendations have been censored by the WHO secretariat. WHO did not want to discuss lifting the age for introducing supplementary food and dismissed a paper which argued that the baby food industry should not be involved in decision making because of its commercial interests. Furthermore recommendations to improve the code on mother milk substitutes were deleted in the discussion papers. 20 of the 28 invited experts protested against the censorship in a joint open letter to WHO director general Gro Harlem Brundtland and against the fact that they were not even allowed to discuss the lifting of the age for supplementary diet in the meeting.

WHO tried to justify its behaviour claiming its high “standards of scientific objectivity”. “With the regard to the suggestion that the WHO is getting too chummy with industry, it is in fact the mandated role to bring all legitimate players together on a given public health issue. The food industry continues to play an important and constructive role in relation to infant feeding.”

The position of WHO increases the doubts about the new “public-private partnership” ideology of this UN agency. Instead of defending the interests of small children, coming so close with industry leads to hazardous compromises. In this case they will lead to unnecessary deaths among babies in developing countries.

[Translated from Pharma-Brief by Jörg Schaaber]

Accepting donations from companies places WHO in a compromised position, and could jeopardise the value of the advice and image of the organisation. It would be naive to not recognise that the donor company will be expecting a quid pro quo such as financial gain or being seen as one of the “good guys”. The only way to ensure the credibility of any WHO guidelines or recommendations is to exclude all commercial enterprises from the development process.

Likewise, WHO should not permit commercial enterprises of any sort to directly fund publications as the information may be compromised or may be regarded as compromised. Prescribers will likely disregard information if it is distributed by a pharmaceutical company, and believe it trivialised if any other company, such as an insurance company or travel company, sponsors it. It is essential that WHO retains its editorial and publishing autonomy, and remains independent of company involvement. Christophe Kopp, Andrea Tarr

[Visit the BMJ web site for background papers: http://bmj.com/cgi/eletters/320/7246/1362#EL1]
Drug bulletins publish useful information about drugs and therapeutics. Other organisations may wish to use this information. John Dowden (Australian Prescriber) carried out a short survey to find out what bulletins do when another organisation wants to use information published in the bulletins. Overall the bulletins that replied want any ISDB policy on reprints to be a guideline rather than a regulation. This will be further discussed at the next general assembly 2002.

The response rate was rather small. Only 15 bulletins responded. Perhaps this is because few bulletins are asked for reprints. Most bulletins give permission if people want to copy their articles. This permission is usually controlled by the publisher. Often the publisher owns the copyright, but the articles of some bulletins are not protected by copyright. Bulletins are more likely to charge a fee if a drug company asks to copy an article. La Revue Prescrire has the most detailed policy for reprints. Most of the bulletins would like ISDB to develop a policy or guidelines for controlling the use of articles by drug companies.

### Results of the survey

#### 1. Is the content of your bulletin protected by copyright?
- Yes ...................................................10
- No ....................................................3

#### 2. Who holds the copyright?
- Publisher .............................................7
- Editorial Committee .................................1
- Ed Com/Editor ........................................1
- Institute ..............................................1

#### 3 (a) If someone wishes to reprint an article which your bulletin has published, do they need permission?
- Yes ...................................................12
- No ....................................................3

#### 3 (b) Who gives this permission
- Publisher .............................................4
- Editor ................................................2
- Editorial Committee .................................3
- Editor/Publisher ....................................2
- Ed/Ed Comm ..........................................1

#### 4. How often do other people ask about reproducing/reprinting articles per year?
- 1-5 ...................................................5
- 5-10 ................................................4
- 10-20 ................................................2
- 20-50 ................................................1
- >50 ...................................................2
- Rarely ................................................1
- Never ...............................................2

#### 5. Does your bulletin have a written policy for responding to requests to reproduce/reprint articles?
- Yes ...................................................2
- No ....................................................12
- No response .........................................1

#### 6. Does your bulletin provide reprints of articles?
- Yes ...................................................8
- No ....................................................7

#### 7. If a university asks permission to make copies of an article and give them to students, do you
- a) agree to the request?
  - Yes ...................................................12
  - N/A ....................................................3
- b) offer to reprint copies of the article?
  - Yes ...................................................7
  - No ....................................................7
  - Sometimes ..........................................1
- c) charge a fee?
  - Yes ...................................................12
  - No ....................................................4
  - N/A ....................................................3

#### 6. If a drug company asks permission to make copies of an article and give them to doctors, do you
- a) agree to the request?
  - Yes ...................................................7
  - No ....................................................7
  - Sometimes ..........................................1
- b) offer to reprint copies of the article?
  - Yes ...................................................4
  - No ....................................................4
  - N/A ....................................................6
- c) charge a fee?
  - Yes ...................................................7
  - No ....................................................2
  - N/A ....................................................6

#### 9. If your bulletin charges a fee, for allowing articles to be copied, how is the fee calculated?
- N/A ....................................................9
- Royalty per copy ....................................3
- Printing cost + %: ...................................2
- Non financial compensation: .................1

#### 10. Should the ISDB have a policy controlling the use of bulletin articles by drug companies?
- Yes ...................................................13
- Some bulletins would prefer guidelines rather than regulations.
- Maybe ...............................................1
CONTACTS WITH OTHER COLLEAGUES AND ORGANISATIONS

The following persons have contacted us.

RUSSIA

- Elena Ushkalova
  Coordinator of All Russia Drug Information Network (ARDIN)
  Vucheticha Str., 12, 125206, Moscow, Russia
  Tel: 7 095 138-0413
  e-mail: ardin@dol.ru

All Russia Drug Information Network has published the first issue of the ARDIN bulletin in March 2000. Its name is “Bulletin of All Russia Drug Information Network”. It was distributed at the annual National Congress “Man and Drug” and to the 12 Centres making up ARDIN.

ARDIN takes an active part in the project “Antimicrobial Resistance”.

The goal of the Antimicrobial Resistance Project is to achieve improvement in utilization of antibacterial agents through education for medical practitioners and students in medical and pharmacy schools.

Project objectives:

1. To provide health professionals and students from medical and pharmacy schools with reliable and unbiased information on antibacterial agents, taking into account data on prevalence of resistant bacteria strains and evidence-based medicine developments.

2. To supply health professionals and trainers in medical and pharmacy schools with training and methodological literature to conduct sessions on rational use of antibacterials.

3. To improve medical personnel’s qualification in clinical pharmacology of antibacterial agents through delivering schools on rational use of antibacterials.

4. To evaluate effectiveness of an information and educational program on antibacterials through surveys among trainees of a school of rational use of antibacterials before and after the training course.

Development of the project will follow a number of steps:

1. Development and publication of a manual on antimicrobial therapy (20,000 copies) for free and targeted dissemination among health care facilities, medical and pharmacy schools, regional health care authorities and other organizations which need this manual for practical work.

2. Development, publication and targeted dissemination of methodological guidelines based on materials from the above manual (1,000 copies). This will assist in delivering workshops on rational use of antibacterials.

3. Organization of workshops on rational use of antibacterials in St. Petersburg, Ryazan, Novgorod, Pskov, Tomsk, Vladivostok and Moldova.

Both the book and workshops had enormous success not only in Russia but in all NIS countries though the number of copies for them was very limited: 20 000 copies is insufficient even for Russia. It is the first book of such kind in all NIS countries. Now we are looking for funds for additional copies. May be pharmaceutical companies will help us. Though the information is absolutely unbiased and drugs are included under generic names companies are also of high opinion about it.

Novgorod center informed us that physicians would like to reprint the book on their own money.

I think that the book is used as national guidelines in antibacterial therapy of systemic infections. The majority of authors and editors (39 persons) are leading clinical pharmacologists and clinicians.

In all regions the workshops also got a very high appraisal both from physicians and administrators of regional health care. Our centre in St. Petersburg was asked by city health care administration to conduct the workshops monthly. They have planned 6
workshops (6 hours each) beginning September. Vladivostok Centre was the pioneer among our centers in these activities. They have done such workshops for about 1.5 years (1-1.5 hours weekly). Tomsk and Novgorod Medical Universities are also willing to continue these activities.

THE ARDIN CENTRES:

Russian Center for Pharmaceutical and Medico-Technical Information of the Ministry of Health of the Russian Federation (PHARMEDINFO)
Attn. Galina Shashkova
Ul. Vucheticha, 12 Moscow, Russia 125206
Phone/Fax: (095) 211-5356
frmdin@dol.ru

Scientific Library of the Ural State Academy
Attn. Sergey Kolotvinov
Kluchevskaya street 5A Yekaterinburg, Russia 620109
Phone/Fax: (3432) 425288
svk@mail.ur.ru

Vladivostok Central Krai Hospital
Attn. Oksana Dmitrenok
Ul. Aleutskaya, 57 Vladivostok, Russia 690000
Phone:(4232) 257725
Fax: (4232) 251288
craevaya@online.vladivostok.ru

Tomsk Cardiology Institute
Attn. Elena Karakalova
Ul. Kievskaia, 111 Tomsk, Russia 634012
Phone: (3822) 558263
Fax: (3822) 558410
druginf@cardio.tsu.ru

St.-Petersburg Pavlov Medical University
Attn. Oleg Karpov
Ul. L. Tolstogo, 6/8 Saint Petersburg, Russia 197089
Phone/Fax: (812) 346-3417
Phcentre@spmu.rssi.ru

Moscow Medical Academy
Attn. Alexander Arzamastcev
Nikitsky Boul., 13 Moscow, Russia 121019
Phone/Fax: (095) 291-44-46
mnapharma@online.ru

Ryazan Central Oblast Hospital
Attn. Tatiana Dobrovolskaya
Ul. Internatsionalnaya, 3A Ryazan, Russia 390039
Phone/Fax: (0912) 360332
info@org.etr.ru

Ryazan State Medical University
Attn. Valentina Makarova
Ul. Visokovoltnaya, 9 Ryazan, Russia 391000
Phone: (0912) 767175
Fax: (0912) 760466
makarova@pharm.ryazan.ru

Novgorod Central Oblast Hospital
Attn. Svetlana Egorova
Kolmovo, d. 6 Novgorod, Russia
Phone/Fax: (81622) 28407
infmed@mail.natm.ru

ZAO Strakhovaia Apteka Drug Information Center
Attn. Maya Sviridenko
Ul. Novoluchanskaya 28/1, Novgorod 173003
Phone: (8162) 132043
Fax: (8162) 71562
mfic@telecom.nov.ru

Pskov Central Oblast Hospital
Attn. Irina Demchenko or Andrey Nikolaev
Ul. Maliasova, 2 Pskov, Russia 180640
Phone: (8112) 466489
Fax: (8112) 466423
inpharm@psk.sovintel.ru

Velikie Luki Central City Hospital
Attn. Igor Potapov
Bolnichnaya, 10 Pskov Oblast Velikie Luki, 182100
Phone/Fax: (8153) 74484
velmed@ellink.ru

MACEDONIA
- Simona Chorliet
Pharmaceutical Adviser
National Drug Information Centre (NDIC)
WHO Humanitarian Assistance Office

Mirka Ginova 17, 91000 Skopje, FYR Macedonia
E-mail: slc@who.org.mk
Tel./fax: +389-91-364.299, 362.879

Some perspectives and future goals of the Macedonian NDIC:
• Development of a national formulary
• Workshop on rational drug use and rational prescribing for GPs, in collaboration with the Centre for clinical pharmacology of the University in Pittsburgh, USA
• Establishing sustainable independent funding of the NDIC and Editorial board
• Issuing four Drug bulletins per year on a regular basis
• Developing closer contacts with other Drug information centres (for example in Croatia) with the perspective of joining the International Network of Drug Information Centres and the International Society of Drug Bulletins.

ZIMBABWE
- Kiran Bhagat
Professor of Clinical Pharmacology and consultant cardiologist
University of Zimbabwe
Activities:
Teaching: medical students, pharmacists, physiotherapists, nurses and basic science students
Research: cardiovascular pharmacology
MSc and PhD students
Other posts held:
Vice chairman of the National Drug and Therapeutics advisory committee
Editor of Cardiovascular Update Newsletter
Co-editor of Journal for Primary Care Physicians
Consultant advisor for World Health Organisation regional Headquarters in Harare
Department of Clinical Pharmacology
Health Science Building University of Zimbabwe PO Box A178, Avondale Harare Zimbabwe
Fax: 00-263-4-724346
Tel: 00-263-777-911
E-mail: kbhagat@healthnet.zw
Prescrire’s reps monitoring network in 1999-2000

Several years ago la revue Prescrire set up a network of subscribers to monitor the activity of sales representatives. The findings of the network are regularly published in la revue Prescrire.

More focused visits, but not more informative.
A report on the first eight years of the medical sales representatives (reps) monitoring network of la revue Prescrire triggered many reactions (1,2). A year later, the Network had not observed any improvements in reps visits (3). Are there any new trends in the report for 1999-2000? Here are some of the quantitative and qualitative findings prepared by the coordinator for the members of the Network.

Reps focused on new preparations, but still the information was lacking. Network members received fewer visits from sales reps presenting old preparations. Visits no longer involved entire product lines, or entire company catalogues, but one name or ‘concept’. A not so surprising trend: companies are increasingly merging, subcontracting of sales visits is more widespread, and reps are asked to concentrate their efforts on certain drugs (4). This trend, however, might have been due to some members of the Network asking reps to limit their visits to new products only.

Even so, prescribers are not receiving higher quality information. In 20% of the visits reported, the Summary of Product Characteristics (SPC) was not handed to Network members, although it is mandatory to do so in France. Though compulsory the Transparency Commission report that theoretically enables prescribers to better compare the drug to its competitors is only given in 10% of the visits. It is slightly better than in 1998-1999 when this figure reached 2.5%, but it is still inadequate.

Claimed benefits are still exaggerated, and risks are played down. During the 1999-2000 period, clinical indications claimed by sales reps were consistent with the SPC in about 70% of cases and partially consistent in 23%. Nevertheless, in 7% of the visits the indication was still totally different from that in the SPC. Dosage was consistent in 85% of cases.

All data on drug-associated risks were omitted in almost two out of three visits. No mention was made of adverse effects in 60% of cases, of contraindications in 63%, and of drug interactions in 67%. Even worse, in 3% of visits, this information was denied.

Network members do have a sharp critical judgment, but these figures should enlighten those who still consider sales reps as a source of reliable information.

Gifts: a non-representative network. In 41% of the visits reported this year, Network members felt they were strongly persuaded to prescribe the drugs, sometimes improperly, particularly for old preparations (54% of cases vs. 31% for new products).

Prescribers were given samples without asking for them, mainly for new preparations (27% of cases) and small gifts in 16% of cases, such as stationery, gadgets, and minor medical devices.

As before, proposals to take part in paid clinical trials were scarce this year: only 1% of cases. This unrealistic percentage is probably due to the type of Network, members of which discourage such proposals. Likewise, careful reps note the characteristics of doctors such as membership of professional organisations, prescriber of generic drugs (4). Reps might even notice if the prescriber reads la revue Prescrire (left on the desk) and if so, if they are dealing with a 'fan of the readers' test or with a fussy perfectionist.

Members not convinced by medical reps, and sometimes exasperated. To the question “Did you find the representative convincing?”, Network observers answered “not much” in 27% of cases and “not at all” in 54% of cases. Those who retired from the Network last year (as part of a process of relaying observers) are in general tired of poor quality visits. One observer who recently retired remarked “I was exposed to the risk of ‘continuous medical miseducation’ and tried to limit its effects as much as possible by systematically consulting the data sheet compendium during all drug presentations [...]. I am therefore getting rid of that risk [...] and will make better use of my time taking care of my patients”.

Among the new preparations presented in 1999, which most particularly irritated the members of the Network, there is zanamivir (Glaxo Wellcome). Certainly a promotional overdose (see page 77 comment on the French release of zanamivir).

[ Adapted from La revue Prescrire ]

A kind of direct-to-consumer advertising!

Direct-to-consumer advertising of prescription drugs is not authorised in Europe. It doesn’t prevent industry getting around the problem, as in the French release of zanamivir in 1999.

Things are by no means perfect when it comes to freedom of information in the field of pharmaceutical information. With others, we have criticised the exaggerated media launches of drugs like sumatriptan, sildenafil and orlistat, to cite but a few examples.

All these campaigns involved drugs available on prescription only, and released with advertising worthy of the planet-wide launch of a blockbuster, well before the drugs were officially marketed!

How can we explain the herd-like behaviour and lack of critical appraisal of the lay media? Indeed, so many journalists seem submissive to the drug companies.

Worst of all is the apathy of the French regulatory authorities. Have they simply given up trying to enforce the regulation which states that “drug advertising targeting the general public is only authorised if the product in question is available without a prescription (…)”? Take the recent example of zanamivir. For weeks, newspapers have carried full-page advertisements, with further ads on radio health programmes. Zanamivir was hyped to the point of a cure-all, despite its very limited clinical effects and the possibility that the people most at risk from influenza might stop getting vaccinated (see la revue Prescrire n° 200 and Prescrire International n°45). And for whose benefit?

Zanamivir is not covered by French social security, which is no excuse. Especially as its prescription requires a visit to a doctor, paid for by the health system.

If this type of advertising campaign is allowed to develop, even under the cover of informing or empowering consumers, prescribers and patients alike will be manipulated by press agents and the media. And health-care providers will have to pay the price.

We must act now, and ensure that well informed health professionals, not the media acting under industry’s orders, decide which drugs benefit which patients. [Adapted from la revue Prescrire November 1999 n° 200]

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**TRAINING COURSE**

An editor from Burkina Faso came to the revue Prescrire

L a revue Prescrire (France) and Mario Negri Institute (Italy) provide technical support to the Centre de Documentation et d’Information sur le Médicament (CEDIM) in Ouagadougou. So a junior editor spent 2 weeks training at la revue Prescrire in Paris in June 2000.

Patrice Zabsonré is a cardiologist in Bobo-Diolasso and a staff member of the bulletin La Lettre du CEDIM. The training course aimed at increasing his critical appraisal of drugs and countering promotional claims.

Reliable sources of drug information were dealt with in the first week: identifying and accessing the sources, using reliable information to appraise unreliable or exaggerate claims from drug companies.

In the second week he trained in reviewing the evidence in clinical evaluation dossiers of the New Drug section.

In his conclusion on the course Patrice Zabsonré identified several key elements (among others) for producing quality information:

- independence again and again!
- long term commitment of editors (rather a small and regularly published bulletin than irregular publication)
- the English language is a basic requirement (In Burkina Faso as in France this is still an obstacle) (a).

This training course was funded by the WHO Essential Drugs and other Medicines unit. Another one is scheduled end of 2000 for training of a CEDIM documentation officer.

Danielle Bardelay
La revue Prescrire

CEDIM PO box 7002, Ouagadougou 03
Burkina Faso
Tel/fax: 226 32 46 59
E-mail: cedim@cenatrin.bf

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**DECKER AWARD FOR A CONTINUING EDUCATION PAPER ON LA REVUE PRESCRIRE’S READERS TEST**

A paper on Prescrire’s readers test has been granted the Decker Award for the best paper in 1999 on research in continuing medical education. The title is: “Quasi-experimental Study on the Effectiveness of the Readers’ Test in the Medical Journal la revue Prescrire”.

The paper is published in the Journal of Continuing Education in the Health Profession (vol 18, n°2) and is available at http://www.jcehp.com/v18broc.htm
WORST PILLS, BEST PILLS FROM THE USA

Worst Pills, Best Pills News May 2000 warned consumers on the withdrawal for safety reason of cisapride and troglitazone from the US market. These recent withdrawals come after those of grepafloxacin, bromfenac, mibefradil and dexfenfluramine.

They take this opportunity to remind us of their five-year wait-and-see attitude.

Six Drug Withdrawals In 30 Months On Safety Grounds
Why The Five-Year Rule Is More Important Than Ever

You should wait at least five years from the date of release to take any new drug unless it is one of those rare “breakthrough” drugs that offers you a documented therapeutic advantage over older proven drugs. New drugs are tested in a relatively small number of people before being approved, and serious adverse effects or life-threatening drug interactions may not be detected until the new drug has been taken by hundreds of thousands of people. A number of new drugs have been withdrawn within their first five years after approval. Also, serious new adverse reaction warnings have been added to the labeling of a number of drugs, or new interactions have been detected, usually within the first five years after a drug’s release (…).

None of the drugs listed above can be regarded as “breakthrough” drugs and the safety problems that resulted in their removal from the market were known, in most cases, before their approval. In addition, multiple treatment options were available to doctors and patients to treat the conditions for which these drugs were approved.

To remain attractive to investors, particularly institutional investors, companies must promise ever-increasing stock prices and a greater proportion of their profits to shareholders. In order to meet Wall Street’s expectations, the drug industry must have their “pipelines” full of potential new drugs. Since important therapeutic advances in drug therapy are exceedingly rare some companies are marketing their mistakes, like the drugs mentioned above, to keep their economic performance indicators appealing to investors, and the public is paying the price in avoidable adverse drug reactions.

For more information visit the Public Citizen Health Research Group web site: http://www.citizen.org/hrg/

PHARMA SELECTA FROM THE NETHERLANDS

Pharma Selecta has been an ISDB recognised correspondent for several years. The journal publishes a special issue this summer for its 15th anniversary. You can visit their web site at: http://www.pharmaselecta.nl.

We translate an editorial from issue 8, vol 16.

High expectations
Why are expectations often so high when it comes to new, innovative drugs? I can think of a number of reasons:
— an appealing theoretical concept
— wishful thinking: we really would like to have better drugs
HTTP://WWW.CITIZEN.ORG/

eLETTER:

Public Citizen Health Research Group launches ‘eLetter’ web site on prescription drugs for the seriously mentally ill

The eLetter on Drugs for Severe Psychiatric Illnesses was established in May 2000 to provide objective and updated information on these drugs to psychiatrists and other mental health professionals, individuals affected with these illnesses, and their families. The eLetter covers antipsychotic, antidepressant, and mood stabilizer medications that are used to treat schizophrenia, manic-depressive illness, severe depression, and some other disorders. Although basic information on serious mental illness is included, the principal focus is to alert you to new information about the risks of older drugs and to inform you about new drugs as they come onto the market.

The establishment of the eLetter is all the more important as pharmaceutical companies have had an increasingly influential effect on the prescribing habits of psychiatric professionals. As recently documented, pharmaceutical companies provide gifts, free meals, and travel subsides to psychiatric residents and psychiatrists, leading them to prescribe those companies’ products. A. Wazana, Physicians and the Pharmaceutical Industry: Is a Gift ever Just a Gift? JAMA 283:373–380, 2000). Influen-
tial psychiatrists are paid up to $10,000 by pharmaceutical companies to give a single talk; repeat performances are implicitly dependent on the psychiatrist saying the right thing about the company’s product. Some phase 3 trials of new antipsychotic and antidepressant medications have been compromised by unethical professionals who report incorrect information to the pharmaceutical company in order to make more money. Even advocacy groups of families and patients have been unduly influenced by accepting financial support from the pharmaceutical companies, making them less likely to protest high prices or unethical corporate policies.

The purpose of the eLetter is therefore to collect the most recent and objective information available on antipsychotic, antidepressant, and mood stabilizer medications and make it available without charge. The eLetter is neither pro-pharmaceutical industry nor anti-pharmaceutical industry. It recognizes the fact that such medications are critical for the treatment of severe psychiatric illnesses and that many lives are being improved by taking these medications. It also recognizes the fact that these medications are often prescribed for people who do not need them, that their adverse effects are being underreported, and that the high cost of many of the medications makes them unavailable to those who need them.

Funding for the eLetter comes from an anonymous individual. No funding from pharmaceutical companies is accepted.

[Adapted from Worst Pills Best Pills June 2000, vol 6, n° 6]

INFORMAZIONE SUI FARMACI FROM ITALY

Gianni Tognoni is going back and forth between the past and present situation of drug information in Italy. Between blurred identity and inevitable questions...

The French colleagues who publish la revue Prescribe have recently initiated – with the usual creativity – an interesting exercise with their readers: a year of work, reflections and initiatives to celebrate the 20th birthday of the Bulletin. We obviously immediately sent our congratulations declaring our willingness to take part in this long celebration, while realising that our roots are more ancient, making our Bulletin next year a candidate for a silver wedding with information.

Being faced with the memory of our identity has accelerated the crystallisation and the translation into an operative proposal of an invitation for early November:

a) to all journals who – with Informazione sui Farmaci – currently provide drug information in Italy;

b) their more or less faithful readers, voluntary or institutional, and

c) more generally all those who, in health care or society, are directly or indirectly involved in this field,

pecially and the instrument to compare hypotheses rather than a juxtaposition of more or less accurate and self-congratulatory reports.

1. Drug information in Italy has never been as rich, varied and of quality, at the national, (inter)regional and local level: coming from bodies and boards representing the full spectrum of public and private resources, of institutions and academies, of pharmacists, pharmacologists, general practitioners and specialists; printed paper still central, albeit with increasing excursions in the world of e-communication: oriented to research and transfer, to clinical practice, to epidemiology, to economics. If – as “doyen” and wardens of memory – we go back to the early stages, “only” a quarter of a century

ISDB Newsletters Vol. 14, N°2, October 2000 • Page 11
ago, we could say that everything has changed.

2. The greatest novelty (or is it the only one?) is undoubtedly at the governmental level:
a) owing to institutional choices in terms of drug approval and registration, which have quickly consolidated in Italy, and to the increasingly leading European scenario;
b) owing to the revolution in the ministerial Bulletin, appearing now to have achieved authority and relevance which had been endlessly hoped for.

3) The “new” situation has changed the terms of reference for drug bulletins: the aim of limiting successful epidemics of none-sense-irrationality has been replaced (at least for prescriptions within the NHS) by that of rationalising and optimising the use of drugs generally evaluated according to the principles of “evidence”. The centrality of drugs has been accompanied by increasing attention to problems and populations. Information as a product of “experts” has been complemented with information as a product of mixed working groups, in which (at least in principle) work is carried out taking into account qualifications and the necessary flexibility.

4) The “informal” area has enormously increased, or the area of self-medication, ortho- and heterodox, alternative-complementary, as a soft remedy and as a fashion, as a free choice in the area of “natural” options or as compliance with the market of illusions. Is it a “new” area on which to exercise critical appraisal so as to limit irrational treatment? Is it a “different” territory, to be respected or pitied, or commented upon occasionally, with the sympathy, condescension, disappointment, curiosity, or the disapproval with which one attends the political-cultural-ideological vulgar conflict between the gay pride and the political-religious orthodoxy of the Jubilee?

5) The many bulletins that have been created and try to grow share consistent contents and styles. Is it a measure of a positive “outcome”, deriving from the quality of common “procedures”? Is it an indicator (worrying? obvious? redundant? to be reinforced?) of a substantial lack of imagination? Is it a proof of the widening sphere of influence of rationality? or is it an expression of a lack of co-ordination of professional minorities who are bound to be confined to minorities of readers?

6) The “form” of information has deeply changed, as well as access to professionals and even more to lay people. The methodology and the market of drug information are increasingly and strongly intertwined with the overall dynamics of the “wide market” of information: that of present goods and future developments in health care, consumption, safety, quality of life, willingness to pay and buy well-being. Is the informative specialisation of bulletins – more or less editorially renewed and competitive – a guarantee, a handicap, a potential, a limit? Should it be considered as a privileged partner, a possible ally, or a hermit resembling nostalgic lovers of “nature and bio” in times of biotechnology? Or is it a strict guardian of cognitive specificity (possibly enriched by hypertexts) in a market privileging post-scientific information, virtual, more or less positively or negatively “transgenic”?

7) Intersecting these questions, all factual and not merely realistic, the old term independence (which was an ID card for bulletins) resembles an ancient earthenware pot.

In times and cultures of global information (registrations, refundability, legislation, experimentation, economics, patents, inequality), independence cannot be satisfied by external accreditation or self-certification. And we cannot be satisfied of being differently and competitively independent, possibly finding in this a justification for an undoubtedly dignified and respectable existence.

8) The question is certainly not new, but its relevance is proportional to the changes in the context where it is posed. The problem concerns the existence and the formulation of a “drug information” project with respect to the (lack of?) planning of health care and of society. Are there priorities, hierarchies, complementarities, incompatibilities between:
- rational objectives (of choices, uses, practices)?
- needs and appropriateness measures (of information strategies, of measures of acceptability, of accreditation for continuing education roles)
- “ceilings”, containment, projections and sharing of expenses (public, private, essential, optional, innovative, equivalent)?

9) Is there room for a reasoned, positively chosen, translation of independence in terms of:
- research, affirmation, experimentation of intelligence of what is happening?
- a disenchanted exercise of dialectics, of sorting out questions, in a culture prone to ready made and fast answers?

Gianni Tognoni

[Adapted from an editorial in Informazione sui Farmaci n°2, 2000]
Ritchie M Hao has given news of the National Drug Information Centre

The National Drug Information Center (NDIC) was created in 1993 to help promote rational drug use in the country. It was created as a component project of the Philippine National Drug Policy Program of the Department of Health. Since its creation, the NDIC continues to carry out its mandate by providing accurate and reliable drug information to its varied clientele. We participate in various drug intervention studies and conduct training on rational drug use. We also collaborate with different government and non-governmental institutions in many health promotion activities particularly on rational drug use.

The provision of reliable drug information is a key NDIC activity. To this day, the NDIC continues to collect and collate relevant information on drugs and related topics. Aside from its in-house databases, the NDIC has begun to exploit the limitless possibilities of the Internet. As it aims to expand in knowledge base and to cater to a larger clientele, the NDIC has taken a more proactive stance in information dissemination. Not only does the NDIC provide drug information by way of clients using its library and computer databases, the NDIC continues to churn out community-oriented reading materials. It has also become more active in the provision of information to policy makers by way of its advisors and press releases on relevant and pressing drug and health-related issues. The NDIC also continues to quarterly publish the drug bulletin, RDU Update, which has recently been accepted as full member of the International Society of Drug Bulletins (ISDB).

There is a need for many relevant research activities in the country. Drug use and drug intervention studies remain important research issues today. Being a repository of relevant drug information in the country, it is incumbent upon the NDIC to expand on this role by contributing to this information data pool. Community intervention studies are currently being conducted by the NDIC in Cupertino, with the Drug Use Study Group of the National Institutes of Health University of the Philippines Manila. In the future, the NDIC hopes to translate the results of these studies into relevant information materials for use by the community at large as well as information which may be of help to health policy makers.

Corollary to the above-mentioned activities, the NDIC also provides training activities on rational drug use for interested groups and organizations. Seminars and lectures further elucidate how the NDIC is able to carry out its mandate.

The NDIC remains steadfast in its commitment to promote rational drug use in the country. To strengthen its role in this respect, the NDIC continues to collaborate with various government and non-governmental agencies. The NDIC maintains close ties with the National Poisons Control Information Service, the Bureau of Food and Drugs, among others. The NDIC has also begun to streamline its activities according to the activities of the Department of Health.

Within the next years to come, the NDIC hopes to become the hub of drug information in the country. It has and will continue to be a key promoter of rational drug use. The NDIC will soon have started to implement its 5-year plan. This plan entails tri-media and Internet exposure, nationwide linkage, and expansion of existing NDIC facilities and services. As these plans begin to materialize, the NDIC will remain committed to its mandate and be strengthened by its cause.

Ritchie M Hao, MD
SLEEPING SICKNESS SEeks SPONSOR

The World Health Organization and drug companies failed to meet essential needs.

The current outbreak of human African trypanosomiasis, or sleeping sickness, affects around 450,000 out of the 60 million persons exposed in West and Central Africa (1). The first stage of the disease involves the lymph node and blood systems followed by meningoencephalitis, coma, and death. Two very old drugs are used in the first stage: suramin sodium and pentamidine. The price of pentamidine increased tenfold when it was reformulated for the prevention of Pneumocystis carinii pneumonia in patients with AIDS (2). Rhône-Poulenc Rorer (now part of the Aventis Group) agreed for some time to provide WHO with pentamidine for its sleeping sickness control programs. However, the company announced that the agreement is reaching its term and that the price will gradually match the price of the drug on the international market (3).

As for suramine, Bayer announced they were considering stopping production (1,3).

Melarsoprol, marketed in 1949, is the first-line treatment for sleeping sickness since it is effective in the two stages of the disease. This arsenical drug induces often fatal encephalopathy in 5% of patients, and almost one fourth of patients in some areas no longer respond to melarsoprol (4).

There is, however, a more recent drug, eflornithine, which is safer and more effective, but it is no longer produced due to its high cost (over $600 per treatment) (3). Marion Merell Dow (now part of the Aventis Group) had produced eflornithine jointly with WHO and since 1986 had considered giving up their rights; WHO was to find a way to produce the drug at a lower price (3). After several years of limited and unsuccessful efforts, this was the situation at the beginning of this year.

Through its work in Central Africa, chiefly in the Democratic Republic of Congo, Médecins sans frontières (MSF) has become one of the main observers of the outbreak of sleeping sickness. For many years, MSF’s has pushed for eflornithine to be manufactured again. The drug is in a good position in MSF’s campaign for access to essential drugs, as an example of drugs that are not accessible for lack of research and development. MSF has repeatedly called upon WHO and Hoechst Marion Roussel (Marion Merell Dow is now part of this group) to start manufacturing eflornithine again.

MSF was in charge of managing the remaining thousands of vials of the eflornithine stock through its centers for sleeping sickness treatment in Uganda. At the time when the last doses were going to be used, WHO and Hoechst Marion Roussel signed a licence agreement (December 6, 1999) whereby the company agreed to transfer the technology, and WHO would be responsible for the production of eflornithine. MSF is due to implement the agreement, that is, ensuring production, marketing, and registration of eflornithine in Africa and Europe (5).

A primary role that MSF has been forced to accept in an attempt to solve the problem, thus underlining WHO’s operational deficiencies and the failure of the pharmaceutical industry to meet essential health needs.

[Translated from la revue Prescrire June 2000, n° 207]

Extract from Prescrire’s literature watch.


Too often, drug efficacy is claimed on the basis of placebo controlled clinical trials that show a statistically significant difference in surrogate end points. But clinical relevance is rarely discussed. Indeed, efficacy should mean real clinical advantages to patients.

Safety questions raised by clinical trials or animal studies sometimes receive extremely optimistic answers, leading to hasty drug marketing. For instance, was it so urgent to market a drug that induces modest weight loss on the long term, when the studies intended to determine whether there is or not a risk of breast cancer have not been concluded? Relying on postmarketing pharmacovigilance follow-ups is not enough guarantee. Witness the failure of the survey carried out in France to document the true ocular toxicity of vigabatrin.

A key concept is disappearing unnoticed: innovation. For instance, when the World Health Organization (WHO) publishes recommendations for hypertension treatment that places all antihypertensive drugs on the same level, whether they offer or not true benefits in terms of cardiovascular prevention. Increasingly medicine agencies grant marketing approval based on placebo controlled clinical trials, without requiring comparative trials with reference treatments (drug based or not).

It’s as if regulatory authorities, confronted with market rules, have given up their responsibilities in favour of free competition between drug companies.

A true innovation is a drug that, for a given indication, provides advantages over existing treatments in terms of risks and benefits and/or convenience.

[Adapted from la revue Prescrire April 2000, n°205]
LONG OVERDUE REGULATION ON ORPHAN MEDICINAL PRODUCTS HAS BEEN APPROVED IN EUROPE

After the United States of America, Japan, Singapore, and Australia, the European Union has finally adopted a policy to provide incentives for marketing orphan drugs (1,2).

Regulation CE 141/2000, adopted by the Parliament and the Council of the European Union on December 16, 1999, came into effect upon its publication in the Official Journal of European Communities on January 22, 2000 (3). The implementation of this regulation now depends on procedures, such as designating an ad hoc committee and drawing up guidelines for its implementation (3,4).

The European regulation, as previous models in other countries, defines the eligibility requirements for the “orphan medicinal product” status and the advantages such status offers to manufacturers.

An orphan medicinal product “is intended for diagnosing, preventing or treating a life-threatening or chronically debilitating condition that affects less than five in 10 thousand persons in the Community when the application is made […], while there is no satisfactory method of diagnosis, prevention, or treatment of the condition that has been authorised in the Community or, if such method exists, the medicinal product will be of significant benefit to those affected by the condition” (3).

The designation of orphan medicinal products by an ad hoc committee offers three advantages: technical support from the European Medicines Evaluation Agency, a partial or total removal of the fees required for applications for European marketing approval, and marketing exclusivity for a ten year period (3). Member States are invited to share with the European Commission any additional incentives they may offer to pharmaceutical companies (3).

The European regulation includes what has turned out to be the most effective factor in other countries: marketing exclusivity. There are, however, several measures to limit potential problems that may arise from a ten-year exclusivity.

Such measures include refusing orphan drug status at the last moment before approval if the drug no longer meets the requirements; for instance, if the prevalence has changed and the condition is no longer rare. Exclusivity may be lowered to six years, if after five years the drug no longer meets the status criteria and if the product has been shown to be sufficiently profitable. A “similar” drug may be granted a marketing authorisation for the same indication as the initial orphan drug (despite market exclusivity) if the holder of the market exclusivity does not produce enough quantities of the product and if the second drug is safer or more effective than the first one.

At least on paper, this regulation on orphan drugs offers a fair balance between private and public interests. We extend our best wishes of success.

[Translated from la revue Prescrire May 2000, n°206]

Extract from Prescrire’s literature watch.

WE NEED INDEPENDENT FUNDING FOR CLINICAL RESEARCH

Widespread funding of research by industry is filling the public budget gap. As a result research priorities and findings are biased.

A British team specialised in knee osteoarthritis research calls our attention once more to the problem of predominant financing of clinical trials by pharmaceutical companies.

After many years of evaluating knee osteoarthritis treatments and searching the literature, they drew conclusions from their experience (1).

They identified 509 comparative clinical trials of all types of interventions for knee osteoarthritis: 414 (81.3%) of these trials involved drugs and many trials addressed poorly relevant questions. In contrast surgery, physiotherapy and life style measures were rarely studied. This is hardly surprising as pharmaceutical companies give funding priority to studies that interest them directly.

They also found that published clinical trials are often favourable to the sponsoring companies. Indeed, they showed a statistically significant correlation between industry funding and favourable results for the sponsor. This correlation was also found in meta-analyses (on all topics) published from 1993 to 1997 in eight authoritative medical journals: 16 (88%) of 18 meta-analyses spon- sored by drug companies favoured the treatment studied vs 81 (69%) of the 117 meta-analyses financed through other or unknown sources (statistically significant difference) (1).

They believe drug companies have “undue influence on the research agenda and distorts the body of published evidence”. They call upon health professionals and consumers to define research priorities and then to raise funds, instead of submitting to industry priorities.

We agree with these authors. A more independent and transparent medical research is needed. Unfortunately health and academic authorities are leaning in the opposite direction today, with funds from industry filling the void left by inadequate public budgets. Public authorities probably think they are saving money. They are actually mistaking the interests of the private and public sectors.

Health professionals and public health authorities should define research priorities according to the needs of the population. Funding for public interest research should come from government budgets and organisations independent of industry.

[Adapted and translated from la revue Prescrire April 2000, n°205]

EDITORIAL METHODS

HOW TO PRODUCE AN ARTICLE IN ISDB BULLETINS

We reprint here papers on how the Drug and Therapeutics Bulletin and la revue Prescrire, both founders of ISDB, produce their articles. Please send any corresponding material about your bulletin to Christophe Kopp.

HOW DRUG AND THERAPEUTICS BULLETIN PRODUCES ARTICLES

Articles in Drug and Therapeutics Bulletin (DTB) aim to provide practical and impartial advice on treatment. Since it started in 1962, the way that DTB produces articles has been gradually refined but the essential principles remain unchanged. While each article starts as a draft commissioned by one of our editorial team and written by an expert, the finished article is the result of detailed scrutiny, collaboration and revision involving a wide range of commentators and several editing stages. The resulting article, no longer attributable to any one source, is published unsigned. Here we describe our approach to producing articles and discuss some of the difficulties they pose.

Principles of Drug Bulletins

The purpose of a drug bulletin is to provide informed and unbiased assessments of drugs or treatments (their efficacy, safety and cost), to comment on how they should be used and assess their place in overall management. Related aims are to comment on how treatments are marketed and promoted, on the quality of the information available to prescribers and patients, and on the way a treatment has been licensed for use. To achieve these aims, a drug bulletin needs to be wholly independent of industry, advertising or any other form of commercial sponsorship, and independent of Government and licensing authorities. The International Society of Drug Bulletins, of which DTB is a founder member, is governed by these principles.

Government health departments exercise no influence over editorial policy of DTB. They have for many years paid for the subscription and distribution of DTB to hospital doctors, general practitioners, NHS advisers, final year medical students and teachers of clinical pharmacology throughout the UK and Eire. All contributors to DTB articles are asked to declare whether they have any interests or relationships which they think might influence their comments, and these are taken into account during the editing.

Commissioning Articles

DTB has a permanent in-house editorial team of doctors, pharmacists and pharmacologists, who work closely with an Advisory Council and Editorial Board, comprising experienced specialists. Once a year each specialist meets with the editorial team to consider articles for the forthcoming 12 months. Ideas for articles arise from reports in medical and pharmaceutical journals (we routinely scan over 40 journals), licensing authority announcements, drug company promotion, lay media items, problems encountered in clinical practice, readers letters and issues arising from previous DTB articles. After discussion, the list of possible topics is narrowed down to those that are considered most timely or useful. The specialist identifies possible authors from his or her knowledge of experts in the field and a detailed brief is agreed for the commissioning letter. Once a draft has been written, the specialist has a key role as ‘lead editor’ for the article, advising on each step of its development until it is published.

An article can take 6 months to a year to produce from the time of commissioning. Impromptu consultations with our specialists provide scope for ‘fast track’ articles where there is a particular development that calls for a swift response, for instance, when significant new data suggest a ‘Paper to change practice’.

Editing

Once a commissioned article is received, the first task is to check that it adheres fully to the commissioning brief. This is done by the Deputy Editor working closely with the specialist lead editor and with the author. The article is then allocated to one of the in-house editorial team (the ‘in-house editor’), who will steer the article through all subsequent consultation until publication. The in-house editor checks the references, reorganises the draft according to house style and may add text and references if more background or more detailed presentation of the data is required.

The draft is then circulated, unsigned, to 10-12 independent experts nominated by the author and the lead editor or identified from published work, and to representatives from the information departments of each company whose drugs have been mentioned. Comments are also invited from the Editorial Board and Advisory Council, the Department of Health, the Medicines Control Agency, the Royal Pharmaceutical Society of Great Britain (currently from the British National Formulary; BNF) and from relevant consumer and patient groups. The draft is also studied by a lawyer. Those sent drafts are asked for “comments and criticisms,
whether fact or judgment" and are request-
ed to send references wherever possible. The identity of authors and commentators remains confidential throughout.

This process, involving some 30-40 commentators, reveals areas of both agreement and disagreement. It identifies relevant data not covered in the draft, highlights issues of interest to non-specialists, pinpoints areas of controversy and often exposes the lack of evidence behind accepted dogma. It is the in-house editor's task, working with the Editor, Deputy Editor, specialist lead editor and author, to consider all the comments and to integrate relevant points and data into an amended provisional final draft. This is then circulated to 10-12 key commentators, some of whom will be newly nominated experts who will be seeing the draft for the first time, before final amendment.

In the last 2-3 weeks before the article finally goes to press, the draft is again scrutinised meticulously. Even at this late stage, the text will need updating if new data are published. The article is checked to ensure that the main text and conclusion accurately reflect the evidence, and that answers to difficult questions are not fudged.

Source Material

With very few exceptions, DTB only uses source material that is published (or very occasionally in press) and available to our readers for independent assessment. Most reliance is placed on information obtained from randomised, double-blind, controlled trials or meta-analyses that have been published in full in peer-reviewed journals.

Articles will usually refer to important consensus statements made by professional bodies (such as the British Thoracic Society). "Consensus statements" and 'clinical guidelines' now abound, however, and not all bodies producing them are independent of industry, so any recommendations are scrutinised critically and may be questioned. We also place reliance on reviews by national bodies (such as those in the BNF) and legal documents (such as summaries of product characteristics, data sheets and European Public Assessment Reports). Again, we may question accepted positions or draw attention to apparent inconsistencies.

We try to avoid using data published only as abstracts or held 'on file' with a drug company. We may do so exceptionally if no other data exist and the information appears to add insight in, for instance, a rapidly developing field. Data from the proceedings of company-sponsored meetings are commonly included when discussing a new drug but we are not prepared to base conclusions on such data alone; when they have been used, their status has been identified in the references by use of the symbol 'S', although in future we will draw attention to it only in the text.

Opinion

Our commentators' opinions are an important component of the editing process. As well as raising points about the interpretation of trial data, they can provide personal insights from those using or receiving treatments, and, where problems are defined, can offer solutions. Where no reliable data exist on a particular point the article must make this clear but, in this situation, opinion and insights may sometimes suggest a way forward with practical clinical decisions. Assessing the value of an opinion requires impartial judgment by the editorial team as to whether the idea is sound, has objective support and how widely it is held.

Consensus or Weighted Assessment?

While the resulting article may reflect consensus, this is not necessarily a primary objective: when consensus amongst our commentators is at odds with the published data, the scientific evidence, especially that from well-controlled clinical trials, prevails. Quite commonly, our commentators are divided about the interpretation of data, while some issues are so complex and specialised that an attempt to paint a broad consensus would be misleading. Occasionally, others may be persuaded about a point but we demand more rigorous evidence and resist a consensus amongst our commentators. Finally, where current consensus has failed to resolve a problem, a novel solution may be required.

While we often have to discuss opposing, supportable arguments, the message of the article, as reflected in the conclusion, aims to be clear, unambiguous and implementable. Ultimately, the responsibility for producing a clear message based on a weighted assessment of all the evidence and opinion gathered, lies with the Editor, conferring closely with the in-house editor and specialist lead editor who have assembled, evaluated and distilled the data for the final version.

Post-publication Letters

About two-thirds of the articles we publish stimulate correspondence. Usually the issues raised will have been considered during the consultative stages of producing the article. It is unusual to encounter scientific data that have been overlooked during the editorial process but correspondents may take a different view of the way the data should be interpreted. Some letters raise fresh issues that call for clarification or suggest an idea for a follow-up article. A correction is published if an error has occurred. Occasionally, the importance of the criticism calls for a fuller response, as in our next issue (see Drug-induced agranulocytosis: monitoring antithyroid treatment. DTB 1997; 35: 88).

Conclusion

Articles in Drug and Therapeutics Bulletin are produced after wide consultation. The editing process puts most store on data from scientifically valid clinical trials; the opinions of commentators are also taken into account. The conclusions reflect interpretation by a team of impartial editors and aim to provide the best available advice on treatment; they represent a weighted assessment but not necessarily a consensus. To allow others to make independent interpretations, the facts on which each conclusion is based are given in the text and references.

[Reprint from the DTB web site (http://www.which.net/health/dtb/main.html)]
HOW LA REVUE PRESCRIRE PRODUCES ARTICLES

At la revue Prescrire, articles are prepared through collective editorial work, a complex process gradually implemented along the years. As a rule, articles are originated and written by our own editorial staff.

The Editor as Part of a Team

La revue Prescrire’s editorial process relies on four types of actors: editors, literature search experts, reviewers, and quality control editors.

Nearly all editors are doctors or pharmacists who dedicate most of their time to their clinical practice. They have all received extensive training in the preparation of articles published by the journal.

Regardless of their previous professional experience, those wishing to join the staff undergo approximately six months of training, including critical appraisal of draft articles and in house editorial rules and methods. Once the training has been completed, they join the staff as junior editors, supervised by another editor acting as their tutor, and start working mostly on short articles. Usually, they only become senior editor after two or three years of experience.

Senior editors are trained and can be recruited to become section editors, executive editors and chief editor.

Throughout the years, la revue Prescrire has confronted difficulties working with outside authors. Our procedures are special and demanding. These require technical skills (up-to-date knowledge and ability to critically appraise the literature), willingness to accept criticism, and qualifications which are only acquired through long term training and work. Today, articles written by an outside author are very rare.

Editorial Teamwork

The topics of future articles are selected during meetings of editors, section editors, executive editors and the chief editor. The purpose of these meetings includes: preparing a list of topics chosen according to their relevance to practitioners; defining the main editorial directions; identifying the initial elements for the literature search (main sources considered); and designating an editor who will be in charge of each article.

Each project is then fine-tuned in order to define better its goals, limits, and conditions. A checklist is drawn up by the editor in charge of the project. Primarily, it will cover the objectives to be achieved by the article and the questions it will try to answer; the topics that will not be addressed; the framework for the literature search; and names of suggested reviewers. The checklist is submitted to other editors for comments and to a “reference editor” chosen according to the subject of the article. This allows the project editor to refine the checklist.

The editor prepares a literature search order, to be carried out by our documentation centre, then he or she proceeds to write the first draft of the article. The documentation centre applies retrospective and prospective procedures of literature search involving published and unpublished information.

The draft is submitted to the reference editor (sometimes to several reference editors) who will comment on the design, and will check that the arguments have been developed clearly and consistently. The reference editor also appraises the literature search, helps to separate established facts from hypotheses, and suggests amendments and/or further material.

The draft is then submitted to the corresponding section editor, along with checklist, the literature search method, all the referenced papers, including those provided by our documentation centre but not used, and all other preliminary drafts. The section editor reviews the draft for the first time, references in hand, and makes any necessary amendments, before finally giving the go ahead for submitting to reviewers.

Rewriting and Quality Control: still Teamwork

Reviewers do not always play the same role with regards to the final quality of the article. It may seem a modest contribution when the draft submitted has been well polished, yet confirming the quality of the text

Extensive Multidisciplinary Review Process

The draft is submitted anonymously to a panel of reviewers who will criticize the reliability, relevance and adaptability to practice as well as the structure, style and legibility.

Panel of reviewers, made up of 10 to 40 reviewers according to the nature and scope of the article, are “customized” for each paper. Reviewers fall under three categories: outside experts on the subject, methodologists, and practitioners representing the journal’s readership (mainly doctors and pharmacists, general practitioners, and specialists). Staff members complete the panel of reviewers. They bring their own expertise and maintain good coordination between the different sections.

The number of people involved in the review process is exceptionally high. Many continuing education journals mention a “scientific committee” or a “sponsoring committee” that are essentially honorary and take no active part in the journal. In primary publication journals, a few reviewers, often only two per article, review the manuscripts submitted.

Only a few journals publishing quality drug information have reviewing procedures similar to ours. The Drug and Therapeutics Bulletin, for instance, uses a similar number of reviewers (see above).

The list of all outside reviewers who contributed to one or several articles published in an issue is included in the colophon on the last page (with the exception of those reviewers who wish to remain anonymous). For the February 2000 issue (N° 203), for instance, 120 outside reviewers were involved in the reviewing process of one article at least.

As we said we do not ask hospital specialists or academic teachers to write articles for the journal. But these experts do play a key role in the review process where their contribution is often decisive.
is nevertheless essential. Or it may be a more important and determining role for long and complex articles or controversial topics dealing with sparse data or information not easily accessible.

Of course, the quality of the review process also depends on the reviewers, their updated knowledge, availability, and critical judgment. Our editors, taking into account the scope of reviewers’ comments on form and content assess their contribution.

Reviewers who never (or rarely) respond, who simply criticize without arguments, or whose contribution is limited or irrelevant are excluded. On the contrary, some reviewers are regularly solicited because they provide constructive and relevant criticism, back up their arguments with references, and notice important errors.

Reviewers chosen among our readership are renewed regularly, mainly, to obtain a “fresh look”, but also to relieve those who have done extensive reviewing.

The project editor writes a new draft, using comments of reviewers and the updated literature.

This new draft undergoes another control, all related documents in hand, this time by the section editor, followed by the corresponding executive editor who has also the comments of the chief editor and a report from the quality control editor. Before layout and proofing proofs, the quality control editor checks the wording of references, verifies that the article and reference contents are consistent, confirms the accuracy of citations, and makes sure there are no contradictions between the text and tables, notes, insets and figures.

Once laid out, a proofreader looks for any misprints, typos, or spelling errors. The chief editor may then give the go ahead for publication.

**Collective Signature**

The word “editor” has been chosen instead of “author” to underline the teamwork behind the articles published by la revue Prescrire, totally different from an authored opinion. For that same reason, most of the time the articles are signed: “© LRP” or ©PI for Prescrire international.

The “signature” of articles has been the object of serious thought. With time, signing conditions have evolved. When la revue Prescrire was created early in the 1980’s, the staff had wanted to publish all articles without any type of signature to emphasise the fact they had been written through teamwork. But the question came up soon: would authors be motivated to contribute to the journal, particularly specialists in hospitals and academics?

For quite a long time afterwards, a more or less detailed list of author names was used. The name of the author of the first draft appeared for articles in “Reviews”, “We have read”, and “Editorials” sections. No names appeared for articles under “New Products” and “Adverse Effects”, to stress the teamwork behind them, but also to protect editors from pharmaceutical companies.

As years went by, the “collective authorship” of the articles published by la revue Prescrire grew even more, and naming authors became at the same time unfair for most of the contributors and a source of confusion for the readers. Therefore, in 1996, signatures were modified to clearly show the multidisciplinary work required for our articles.

The symbol ©LRP and ©PI at the end of articles stands for all the guarantees provided by the journal’s staff and ultimately by the chief editor.

Publishing the full name of the person in charge of big articles under “Reviews” seem justified to the editorial staff since a note explicitly acknowledges that “the article is the result of editorial teamwork”.

A list of all the staff members, and of all those involved in each issue is published in the colophon on the last page.

**The Price of Collective Editorial Work**

The editorial teamwork follows a complex and demanding procedure. Its objective is to publish reliable up-to-date articles that satisfy the needs of our readers.

This editorial process has a price in terms of time. For the process to run smoothly, time cannot be reduced: many months will go by between the moment the article is commissioned and its publication. It is difficult to shorten this period to several weeks for articles that must be published urgently.

The process also has a price financially because of the thorough literature search, logistics expenses (circulating drafts, reviewing process etc.), time invested in training, and fees paid to literature search specialists, editors, outside reviewers, and quality control editors.

La revue Prescrire has no free subscriptions. Its financial costs, fully supported by subscribers, are directly related to the results: information as reliable as possible.

[Adapted from la Revue Prescrire May 2000, n°206, p 386-388]
BNF ONLINE

The British National Formulary has launched its web site (http://bnf.org/). We take this opportunity to reprint from one of its sections an introduction to this widely appreciated formulary.

British National Formulary: construction of a national prescribing resource

The British National Formulary is a joint publication of the British Medical Association and the Royal Pharmaceutical Society of Great Britain. It is under continuous revision and a new edition is produced in March and September each year for distribution primarily to doctors and pharmacists working for the National Health Service (NHS) and to all NHS hospitals.

The BNF has its roots in the health insurance formularies of the 1930s. Following the outbreak of the Second World War these were united into a National War Formulary, which provided formulas incorporating substitutes for scarce, imported ingredients.

The first BNF proper was produced in 1949 following the inception of the NHS. Coverage in the early BNFs was highly selective and was revised every two-and-a-half years, this new edition produced (for the period 1976-78) a need had been detected for a more comprehensive formulary incorporating a much wider range of preparations while still providing informed advice on their relative merits. A new style of BNF was therefore designed to respond to these needs. Whereas the old BNF had been selective and was revised every two-and-a-half years, this new BNF would be comprehensive with a new edition every six months. The first of these new BNFs was published in 1981.

Today, the BNF is an up-to-date pocket book, for rapid reference by practising healthcare professionals, which encourages sensible, cost-effective and safe use of medicines. It is also an educational tool for medical and pharmacy students. A Dental Practitioners' Formulary and a Nurse Prescribers' Formulary are available to cater for the special requirements of other prescribers.

Constructing the BNF

Numerous changes are made between editions. The more important changes are listed at the front of each edition.

Joint Formulary Committee

The Joint Formulary Committee is responsible for the content of the BNF. Doctors and pharmacists on the Committee (nominated by the British Medical Association, the Department of Health and the Royal Pharmaceutical Society of Great Britain) decide on matters of policy and review amendments to the BNF in the light of new evidence and expert advice.

The Committee meets quarterly and each member also receives proofs of all BNF chapters before publication.

Editorial team

BNF staff editors are pharmacists with a sound understanding of how drugs are used in clinical practice. Each staff editor is responsible for maintaining and updating specific sections of the BNF.

During the publication cycle the staff editors test information in the BNF against a variety of sources (see below). Amendments to the text are drafted when the staff editors (together with the executive editor) are satisfied that any new information is reliable and relevant. The draft amendments are passed to expert advisers for comment and then presented to the Joint Formulary Committee for approval.

Additionally, for each edition, sections are chosen from every chapter for thorough review. These planned reviews aim to verify all the facts in the selected sections and to draft any amendments to reflect the current best practice.

Staff editors prepare the text for publication and undertake a number of checks on the data at various stages of the production.

Expert advisers

The BNF uses over fifty expert clinical advisers (including nurses and dental surgeons) throughout the UK to help with the production of each edition. The role of these expert advisers is to review existing text and to comment on amendments drafted by the staff editors.

The BNF also works closely with a number of expert bodies that produce clinical guidelines. These clinical experts help to ensure that the BNF remains reliable in a number of ways:

- by commenting on the relevance of the text in the context of best clinical practice in the UK
- by checking draft amendments for appropriate interpretation of any new evidence
- by providing expert opinion in areas of controversy or where reliable evidence is lacking
- by advising on areas where the BNF diverges from product data sheets or summaries of product characteristics
- by providing independent advice on drug interactions, prescribing in hepatic impairment, renal impairment, pregnancy, breastfeeding, children, elderly, palliative care and the emergency treatment of poisoning.

In addition to regular advisers, the BNF is always able to call upon other clinical specialists for specific projects (recent projects have included management of shock, of myocardial infarction, and the management of conditions such as constipation and gastro-oesophageal reflux disease in children). The BNF also works closely with a number of expert bodies that produce clinical guidelines. Drafts or pre-publication copies of guidelines are routinely received for comment and for assimilation into the BNF.

Sources of BNF information

The BNF uses a variety of sources for its information; the main ones are shown below.
Summaries of product characteristics

The BNF receives summaries of product characteristics (SPCs) of all new products as well as revised SPCs for existing products. The SPCs are the principal source of product information and are carefully processed, despite the ever-increasing volume of information being issued by the pharmaceutical industry. (Some 400 SPCs were sent to the BNF over the last 4-5 months of 1998 - an increase of nearly 50% over the same period in the previous year.) Such processing involves:

- verifying the approved names of all relevant ingredients including ‘non-active’ ingredients (the BNF is committed to using approved names and descriptions as laid down by the Medicines Act)
- comparing the indications, cautions, contraindications and side-effects with similar existing drugs. Where these are different from the expected pattern, justification is sought for their inclusion or exclusion
- seeking independent data on the use of drugs in pregnancy and breast-feeding
- incorporating the information into the BNF using established criteria for the presentation and inclusion of the data
- checking the interpretation of the information by two staff editors before submitting to executive editor; changes relating to doses receive an extra check
- identifying potential clinical problems or omissions and seeking further information from manufacturers or from expert advisers
- careful validation of any areas of divergence from the SPC before discussion by the Committee (in the light of supporting evidence)
- constructing, with the help of expert advisers, a comment on the role of the drug in the context of similar drugs.

Much of this processing is applicable to the following sources as well.

Expert advisers

The role of expert clinical advisers (including nurses and dental surgeons) in providing the appropriate clinical context for all BNF information is discussed above.

Literature

Staff editors monitor core medical and pharmaceutical journals. Research papers and reviews relating to drug therapy are carefully processed. Where a difference between the advice in the BNF and the paper is noted, the new information is assessed for reliability and relevance to UK clinical practice. If necessary, new text is drafted and discussed with expert advisers and the Joint Formulary Committee. The BNF works closely with the Drug and Therapeutics Bulletin and has informal links with the MeReC Bulletin.

Systematic reviews

The BNF has access to various databases of systematic reviews (including the Cochrane Library and various web-based resources). These are used for answering specific queries, for reviewing existing text and for constructing new text. Staff editors receive training in critical appraisal, literature evaluation and search skills.

Consensus guidelines

The BNF’s advice is checked against consensus guidelines produced by expert bodies. A number of bodies make drafts or pre-publication copies of the guidelines available to the BNF; it is therefore possible to ensure that a consistent message is disseminated.

Reference books

Textbooks and reference sources are used to provide background information for the review of existing text or for the construction of new text.

The BNF team works very closely with the Martindale editorial team. BNF has access to Martindale information resources and each team keeps the other informed of significant developments and shifts in the trends of drug use.

Statutory information

The BNF routinely processes relevant information from various Government bodies including Statutory Instruments and regulations affecting the Prescription only Medicines Order. Official compendia such as the British Pharmacopoeia and its addenda are processed routinely to ensure that the BNF complies with the relevant sections of the Medicines Act. (The BNF itself is named as an official compendium in the Medicines Act.)

The BNF maintains close links with the Home Office (in relation to controlled drug regulations) and the Medicines Control Agency (including the British Pharmacopoeia Commission). Safety warnings issued by the MCA and guidelines on drug use issued by the Department of Health are processed as a matter of routine.

Relevant professional statements issued by the Royal Pharmaceutical Society of Great Britain are included in the BNF as are guidelines from bodies such as the Joint Computing Group (of the General Practitioners’ Committee and the Royal College of General Practitioners).

The BNF also reflects information from the Drug Tariff, the Scottish Drug Tariff and the Northern Ireland Drug Tariff.

Pricing information

The Prescription Pricing Authority provides information on prices of medicinal products and appliances in the BNF. The BNF also receives and processes price lists from product suppliers.

Comments from readers

Readers of the BNF are invited to send in comments. Numerous letters are received for each edition. Such feedback helps to ensure that the BNF provides practical and clinically relevant information. Many changes in the presentation and scope of the BNF have resulted from comments sent in by users.

Comments from industry

Each manufacturer is provided with a complimentary copy of the BNF and invited to comment on it. Close scrutiny of the BNF by the manufacturers provides an additional check and allows them an opportunity to raise issues about the BNF’s presentation of the role of various drugs; this is yet another check on the balance of the BNF’s advice. All comments are looked at with care and, where necessary, additional information and expert advice are sought.

The BNF is an independent professional publication that is kept up-to-date and which addresses the day-to-day prescribing information needs of healthcare professionals. Use of this resource throughout the health service helps to ensure that medicines are used safely, effectively and appropriately.
The Uppsala Monitoring Centre is a WHO Collaborating Centre for international Drug Monitoring. The UMC provides a number of services. We asked Sten Olsson, Head of External Affairs, what ISDB bulletins can expect from UMC as an information resource on adverse drug reactions. For more information you can contact Sten Olsson at: 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: info@who-umc.org, Internet: http://www.who-umc.org

The WHO database and the WHO centre are primarily established to provide service to National Centres participating in the WHO International Drug Monitoring Programme. The policy for use of information from the WHO database is set in a document (available on request to Christophe Kopp): adopted by the World Health Assembly in 1992. This document includes guidelines on provision of information to third parties, one of them being ISDB bulletins. In addition our Centre is bound by policy decisions made by authorities in each of the participating countries.

What information from the WHO adverse reaction database ISDB bulletins are entitled to access?

In practical terms ISDB bulletins may request information from the WHO database on any specific drug related issue. Such requests should be directed to us at the Uppsala Monitoring Centre, att. Ms Erica Walette, head of database services. We are entitled to provide summary quantitative information from the database e.g. number of reports on each adverse reaction term specified by reporting country. Individual case descriptions can only be provided from those countries, presently around 30 (see box page 22), which have agreed to making such information available to any inquirer. All output from the WHO database will be accompanied by a Caveat Document (appended) which clarifies the nature of the data collected and what precautions have to be taken when using it, including requirements for publication. Normally a response to an inquiry will be received within one week.

A signal detection service based on data mining is developed for National Centres and is now also made available to commercial customers under the name ADReSpheronics. It is difficult to imagine that this range of services would be of primary interest to ISDB bulletins and since a considerable effort in terms of analytical power and staff time goes into providing this service there are no plans of offering it at a lower than commercial rate.

What is the charge for information from the WHO data base for ISDB bulletins?

Since the WHO database and the UMC are established to serve National Centres only those centres have free access to the data base and UMC services. All other parties will have to pay a consultancy fee for the time required to carry out the customised database retrieval. The UMC keeps a price list at two levels, one for inquirers representing commercial enterprises and one for non-commercial organisations. ISDB bulletins will fall into the latter category. To give an example the cost of a standard listing of the number of reports/reaction and country for one drug would be 900 Swedish Crowns today for a non-commercial customer. Prices will vary with the complexity of the search. Each time a retrieval is requested a price should be asked for.

Are other products and services provided by the UMC available to ISDB bulletins?

ISDB bulletins have access to all public documents and software products provided by the UMC (see Publications section on the web site):

Uppsala Reports (free periodic newsletter available as Adobe Acrobat document)
WHO Adverse Reaction Terminology (available in English, German, French, Spanish, Portuguese and Italian)
WHOART Access (Adverse Reaction Terminology with software)
WHO Drug Dictionary (paper print or ASCII files)
WHO DD Access (WHO Drug Dictionary with software)
National Pharmacovigilance Systems (book describing pharmacovigilance in 57 countries)
Effective Communications in Pharmacovigilance (book, proceedings of Erice conference)
WHO Guidelines for setting up and running a pharmacovigilance centre (booklet) This guide of 25 pages is a good basic text for use in teaching pharmacovigilance. If you would like a personal copy, you can download it for free (Adobe Acrobat document) or contact Mrs Anneli Lennartsson at the UMC.
Pharmacovigilance training material (file developed to support a 3 day training course)

Possibly also the WHO Pharmaceuticals Newsletter, published by WHO headquarters in collaboration with UMC, may be made available to ISDB bulletins. The distribution policy for the new edition of this newsletter is still being determined.

The UMC can also be contacted for guidance and advice regarding pharmacovigilance activities around the world.
### WHO Collaborating Centre for International Drug Monitoring

**Release of data to others than National Centres**

August 1999

National Centres have been asked if they accept the release of case information from the WHO database. Countries indicated by an asterisk on the following list have agreed to ‘automatic release’ of such information, without their prior consent in each instance. It is understood that the agreed Caveat Document will be supplied with each response.

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— in the column for comments means that there has been no answer or inconclusive answer to the questionnaire

### Specific conditions

**Denmark:** Automatic release accepted if more than one brand of the relevant drug is marketed in Denmark. Information to be given on generic name level only. Country case identification number not to be revealed.

**Indonesia:** Automatic release to other government institutions. Indonesian data could be included in compilations of data where individual countries are not identified. In all other cases the National Centre should be consulted.
ACCESS TO ESSENTIAL DRUG INFORMATION

Access to essential medicines has been much debated lately. But less care has been devoted to access to no less essential information on the rational use of these substances. Comparative information on efficacy and safety of essential medicines should also be part of the ‘essential drug’ concept. And procurement of essential drugs should not be separated from procurement of information on their rational use, as illustrated in the two papers below.

The World Bank and pharmaceuticals

Torkel Falkenberg and Göran Tomson
Department of Public Health Science, Unit of International Health Care Research (IHCAR), Karolinska Institute, Stockholm, Sweden
[Abstract of a paper from the British journal Health Policy & Planning, reproduced from their web site http://intl-heapol.oupjournals.org/. The full version of the paper is available through subscription in the March issue, 2000 15:52-58]

Within less than a decade the World Bank has become the largest single source of finance (loans) for health in low and middle income countries as well as a major player in the field of pharmaceuticals. Often 20–50% of the recurrent government health budget in developing countries is used to procure drugs. Drugs are among the most salient and cost-effective elements of health care and often a key factor for the success of a health sector reform. However, pharmaceuticals are frequently being used irrationally, mainly due to market imperfections in health care, such as information asymmetries, leading to serious health problems and a heavy financial burden on the health system. Lending priorities set by the World Bank could be used to promote public health sector reform, leading to the rational use of affordable and available drugs of good quality in developing countries. This report provides the first analysis of World Bank activity in the pharmaceutical sector worldwide. The analysis of 77 staff appraisal reports, describing the planning phase of World Bank country projects, shows that 16% of the total World Bank health, nutrition and population budget, or approximately US$1.3 billion, has been committed to loans or credits supporting pharmaceutical activities in the programme countries between 1989–95. Roughly US$1.05 billion has been committed to procurement of drugs and medical equipment. Only 5% of the total pharmaceutical sector lending is committed to software components such as drug policy work and rational use of drugs. No more than 45% of the projects were developed in collaboration with pharmaceutical expertise. The World Bank is recommended to improve its pharmaceutical sector involvement by promoting drug policy research and development including national and international dialogue on pharmaceutical issues to ensure rational use of both drugs and loans. In this, the World Bank has an advantage given its expertise in health economics, and lastly its ability to be listened to by governments through its power.

Essential drug information in Vietnam

[Taken from the E-drug discussion group, March 3,2000]

The issue of promoting essential drugs has long been a key element in WHO’s policy to ensure equity in care and health for all. We all know that this is not enough, also essential drugs can be used wrongly, irrationally and unsafely. In Vietnam, the essential drug process has been included in our National drug policy. Over the past years, supply of essential drugs has also improved. A real challenge now is to address the use of these drugs, to achieve as much positive contribution to health, as possible. From a wider economical perspective, this is also much needed since ill health is becoming a serious poverty-trap for households with small marginals.

Drug-spending take a considerable proportion of the cost of illness now. Spent household-resources therefore need to give best possible value for money, to limit duration of illness and time with lost income. Thus, evidence based treatment guidelines and reliable drug information are clearly needed, to promote the ideals of Equity and Health for all!

Reading the E-drug debate input from Philippa Saunders, I wish to give my strong support to her idea of a more visible “campaign” to improve access to Essential Drug information. It is well known that information-access in many developing countries is difficult. In Vietnam this is also a challenge.

The ongoing restructuring of the economical system, with Doi moi market economy has clearly brought a new need for strengthened independent drug information. Evidence based treatment guidelines is only one aspect of this need. Here commercial advertising is now very active, promoting a plethora of “new” drugs for Vietnam. This needs to be balanced with the help of a strengthened independent drug-information system. Such a system is taking form in Vietnam now. There are now many actors and processes; such as our drug information centers, treatment-guidelines, a National physicians drug-use reference book, an ADR-monitoring network, Drug and therapy committees and a Poison information center. These structures and staff need now both to increase capacity and competence. They would benefit much from opportunities to establish long-lasting experience-exchange, with colleagues abroad. A stronger essential drug information collaboration & experience exchange program for drug-information professionals, would now be very beneficial, both for the health-professionals and for their patients.

Sam Tomquist
Adviser, rational and safe use of drugs
ADPC office, Ministry of Health, Hanoi, Vietnam
138 B Giang Vo street
Tel +844-8446059
Fax +844-8231253
E-mail: adpc@netnam.org.vn