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Starting or Strengthening a Drug Bulletin

A Practical Manual

2005

International Society of Drug Bulletins

World Health Organization

Starting or strengthening a drug bulletin
A practical manual

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Preface

Using medicines safely and effectively requires that information is available to prescribers and others who give advice about medicines and also to patients or the public. This is true for developed, transitional and developing countries. Exactly what information is needed will depend on the local context and situation. Providing information in an impartial, objective and accessible way is a challenge. One effective approach is local production of a drug bulletin, and this manual aims to show global experiences in starting or strengthening such a bulletin. To achieve this goal the World Health Organization (WHO) and the International Society of Drug Bulletins (ISDB) have worked together on the project to develop and publish this manual.

ISDB is a worldwide network of independent bulletins that promote rational prescribing. Bulletins provide reliable comparative information on drugs and therapeutics that is in the context of local needs and local use. These ideals are very much in accord with those of WHO, so working together with ISDB to produce a manual on starting or strengthening a drug bulletin was a natural development.

From the outset, each organization's role in producing the manual was clear. The text was to be drafted and edited by ISDB members, who had final responsibility for the 'message'. WHO would advise and comment on content, and help with publication and distribution. This collaboration builds on a long history of shared ideals and mutual respect, and it was not by chance that when the Society was launched in 1986 it was with support from the WHO Regional Office for Europe. The manual continues this tradition, and we are delighted to publish it. We have no doubt that it will be a help to those wishing to start on the bumpy road to bulletin publication, and will strengthen those who are already active in the field.

Impartial, clear, reliable and up-to-date advice and information about treatments are invaluable. They have an added advantage if delivered in a local context by local experts. Working in this context, independent bulletins can be a key means of improving patient and public health. By strengthening the provision of advice at local level, the manual will benefit health workers, patients and community members alike. In recent years the concept of the empowered patient and the informed community has grown. This development has been mirrored by drug bulletins, which initially focused on prescribers and pharmacists, but have since broadened, with many now producing materials for patients and consumers. We hope that our manual will encourage the trend in providing impartial information to health professionals and consumers.

Joe Collier
Chair of ISDB

Richard Laing
Medical Officer
Medicines Policy and Standards
WHO

How the manual was produced

In 1998, ISDB, in collaboration with WHO, embarked on a joint project to develop and publish a manual aimed at helping people start or strengthen a drug bulletin. ISDB and WHO share a commitment to promoting rational drug use and see drug bulletins as important tools in this respect. WHO has worked together with ISDB in a number of areas and has supported ISDB training schools and regional meetings, in particular enabling people working on drug bulletins in developing countries to participate. Ideas for the manual grew out of this collaboration.

The aim of the manual project was to harness the insights of those with day-to-day experience of producing independent drug bulletins. It was agreed that the best way of reflecting the diversity of drug bulletins was to involve many people working in different countries for a variety of bulletins. The process of drafting and reviewing the manual has therefore depended on the active participation of many people, mainly editors from ISDB member bulletins.

Much of the writing and reviewing had been done by September 1999, when unfortunately, work on the manual stopped. At the 2002 general assembly of ISDB in Dubrovnik, regrets were expressed that the manual had not been published and it was agreed that efforts should be made to complete the project. A manual editorial team was formed in 2003 to do that. Working in collaboration with the Department of Medicines Policy and Standards at WHO, the editorial team has brought the text up-to-date and added new sections.

People who have worked on the manual

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Also:
Warren Kaplan, Center for International Health and Development, Boston University School of Public Health, USA; Kate Hawkins, Market Research, Which Ltd. UK; Neil Pakenham-Walsh, International Network for Access to Scientific Publications (INASP); Richard Laing, Kath Hurst, Department of Medicines Policy and Standards, WHO.

Manual coordinator in 1998/9

The first phase of work on the manual was coordinated by Daphne Fresle (working for WHO in the unit formerly known as the Action Programme on Essential Drugs). Ellen 't Hoen and Catherine Hodgkin also worked on the manual during this phase.

Manual editorial team (from 2003)

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About ISDB

The International Society of Drug Bulletins (ISDB) is a worldwide network of bulletins on drugs and therapeutics, which are financially and intellectually independent of the pharmaceutical industry. ISDB was founded in 1986 with the support of the WHO Regional Office for Europe, and particularly of Graham Dukes and Inga Lunde. Its overall aim is to assist the development of independent drug bulletins and to facilitate cooperation among them.

People producing independent drug bulletins face common difficulties. These include the challenge of starting and sustaining a publication with few resources, working in isolation and perhaps being a lone voice in promoting rational prescribing of medicines. Being a member of ISDB means being part of a worldwide network of like-minded individuals and organizations who face similar challenges, and who can share experiences, ideas and resources, support each other and act together. The Society is a membership organization, governed by a general assembly, which meets every three years. The primary sources of funding of ISDB are the annual membership fees and members' donations. Other funding, which has traditionally been ad hoc, has come from WHO and, for general assemblies, workshops and summer schools, from other organizations such as Health Action International, various non-governmental organizations (NGOs) and from local bodies (e.g. universities, public health schools, ministries, city councils).

To be eligible for membership of ISDB, a bulletin must meet certain criteria that demonstrate its independence:

- It must be run by an independent editorial team, working within an organizational structure capable of guaranteeing editorial independence.
- It must have financial resources that guarantee independence, such as public financing through a national or local government, financing by a non-governmental organization or self-financing through reader subscriptions or membership fees.
- It must carry no advertising relating to therapeutic or diagnostic activities.

ISDB has over 50 members representing 30 countries around the world. Member bulletins can carry the Society's logo on the publication as a mark of quality and independence. ISDB publishes a newsletter to inform members of the Society's business. It is published three times per year and distributed free of charge to all members. The Society's web site (**http://www.isdbweb.org**) contains the constitution, a directory of members and links to members' web sites, details of how to join the Society and a password-protected area accessible only to members.

To find out more about ISDB, including how to join, visit the web site **http://www.isdbweb.org**.

Executive summary

Drug bulletins have special characteristics: independence is a fundamental basis for their work and they provide information with a practical orientation. These characteristics help practitioners make rational decisions about treatments and also make drug bulletins a fundamental tool for promoting their rational use.

Producing a drug bulletin involves many challenges. These include starting and sustaining a publication without resources from drug companies, working in isolation, and perhaps being a lone voice in promoting rational prescribing of medicines.

Until now, there has been little written information about the work of drug bulletins and few opportunities for people doing this work to share experiences. This manual helps to rectify that situation. It is a practical tool, drawing from the experience of people who produce independent drug bulletins. The manual identifies some of the choices that face those involved in bulletins, describes the many ways to set up and run a drug bulletin, provides examples from a variety of bulletins in different parts of the world, gives tips and warns of common pitfalls. As well as being useful for people taking the first steps towards producing a bulletin, the manual contains a wealth of information for those involved with established bulletins.

After the introductory section, a chapter on the rational use of medicines explores the reasons why making rational choices can be problematical. It also describes how the special characteristics of drug bulletins help practitioners make rational decisions and also make bulletins a fundamental tool for promoting rational use of medicines.

The following chapters focus on what makes a bulletin independent, how to define the aims, target and type of bulletin and how to plan resources to start or sustain a bulletin. Chapters 6 and 7 look at planning, production and the editorial process. There is detailed discussion about books and journals that are useful to drug bulletins and suggestions of key references for bulletins with limited finances.

Chapter 8 outlines the principles of evaluating a new drug. The chapter is mainly intended for editors of established bulletins looking to develop their working practices or evaluating medicines that are new in their country. An annexe to the chapter provides more information on assessing the risk of harm, including assessing causation and using animal data.

Design, production and distribution issues are critical to bulletins' success and are addressed in depth by the authors. Establishing a sound organizational structure and considering possible legal issues are important, but sometimes overlooked, areas on which the manual also provides information and advice. Chapter 12 outlines the benefits and difficulties of undertaking evaluation of a bulletin – an essential component of establishing and maintaining its quality and usefulness. Three approaches are discussed – audit, feedback and impact assessment.

The importance of supportive partners at national, regional and international levels is highlighted in Chapter 13. Regardless of its stage of development, every bulletin can gain strength through the support of other similar publications, and the possibilities for twinning arrangements, joint training sessions and collaborative research are discussed here.

Finally, the manual underscores the importance of good record keeping, to ensure that information can be readily retrieved when needed. Details are given of what to keep and record, how to create an organizational memory and starting an archive.

The manual is an invaluable guide for:

- anyone thinking of starting a drug bulletin.
- all those running an established drug bulletin.

It will also interest:

- health professionals, including doctors and pharmacists, who contribute to the work of drug bulletins and are their primary users;
- organizations which sponsor or fund a drug bulletin, such as public and private health maintenance organizations;
- organizations that can make use of drug bulletins' work, for example, national and international regulatory agencies and health insurance organizations;
- patients and members of the public with a particular interest in health issues, especially in the rational use of medicines.

The manual is a tool-book not a rule-book, and ISDB and WHO urge all readers to provide their feedback on the form included at the end of the manual. The information, opinions and ideas received will be of great value when updating the manual.

1. Introduction

1.1 Are you starting or developing a bulletin?

You may be involved in running an established independent drug bulletin. You may be involved in the development of a new bulletin or exploring the possibility of setting up a drug bulletin. Or maybe you are interested in providing support to an independent drug bulletin. If so, this manual has been written with you in mind, and we hope that it will be a useful and practical tool.

There are many ways to set up and run a drug bulletin and many different types of good bulletin. This manual does not provide a 'blueprint' but it should be a helpful 'road-map' for those involved in drug bulletins. In other words it does not describe one 'right' way to produce a drug bulletin but illustrates various ways. It identifies some of the choices that face those involved in bulletins and it gives examples from a variety of bulletins in different parts of the world. It gives tips and warns of common pitfalls. Above all, this manual aims to draw from the experience of others involved in independent drug bulletins, and to present their experience in such a way that others can use it and benefit from it.

If you are involved in starting or strengthening a drug bulletin this manual should help you to take the decisions that are most appropriate for your work. It should make your tasks easier and help you to perform them more effectively.

1.2 Objectives of this manual

This manual aims to:

- reflect the diversity to be found among drug bulletins;
- help people to make choices about what is appropriate for their bulletin;
- illustrate useful methods and models;
- help people to learn from the successes and failures of others;
- help people to decide whether to set up a bulletin, how to set up a bulletin or how to strengthen their bulletin.

1.3 The need for the manual

Those involved in prescribing and using drugs need access to information which will enable them to use drugs, when they are needed, in ways which maximise the potential benefits and minimise the risks. Independent drug bulletins provide valuable information in a summarised and readable form which can help those involved in decisions about drugs to make those decisions wisely. The first few independent drug bulletins were established in the 1960s and the International Society of Drug Bulletins (ISDB) was founded in 1986.

Over the last 20 years many new drug bulletins have been established both in developing and industrialised countries and in the Newly Independent States. Many of these new bulletins have received advice and support from existing bulletins and from ISDB. In addition, ISDB has organized several training schools and regional meetings at which participants exchange experiences and develop the skills necessary to develop and run a quality drug bulletin (see **http://www.isdbweb.org**). Apart from these training schools and the informal contacts between members there have been few opportunities to share experiences and there is a lack of written information about the specific work of drug bulletins. This has made it difficult for those involved in new bulletins to benefit from the work of others. Often they have to discover for themselves the methods and procedures which have already been tried and tested by others. Unnecessary duplication of effort wastes time and resources. Sharing skills and experiences not only reduces this waste but it also contributes to the development of high quality bulletins and to a shared philosophy and common understanding of goals. Working together is one way of maintaining both quality and commitment. This manual is produced as a result of collaboration, and should strengthen future collaboration between bulletins.

1.4 The importance of feedback

This manual is a tool-book not a rule-book. Tell us what you have found useful and helpful, what you have found confusing, or what you would have liked to find but could not find in the manual. If you do this we will be able to add to and improve a future edition of the manual. At the end of the manual you will find a feedback form, which you can complete to let us know how you have used it and how you think it could be improved.

Please visit the ISDB web site: **www.isdbweb.org** for details on where to send feedback.

This manual, together with relevant articles will also be available on the WHO web site at: **http://mednet2.who.int/DrugBulletinProject/**

WHO address: World Health Organization, Medicines Policy and Standards, Avenue Appia, 1211 Geneva 27, Switzerland.

2. Rational use of medicines

Medicines are used rationally when they are the appropriate treatment for a condition, are used in the right dose, at the right time(s) and for the right duration. Clearly, irrational prescribing, and use of irrational medicines can harm people's health, cause problems in health systems (such as antibiotic resistance) and also waste money.

Although the ideals of rational prescribing appear relatively simple, they are hard to achieve. This chapter explores the reasons why making rational choices about medicines can be problematical. It also describes how the special characteristics of drug bulletins help practitioners make rational decisions, and also make them a fundamental tool for promoting rational use.

Healthcare reforms began in Kyrgyzstan in the mid 1990s, primarily in the pharmaceutical sector. Irrational use of drugs remains a major problem in Kyrgyzstan. Polypharmacy, incorrect use of effective drugs, use of wrong or ineffective drugs and irrational prescribing are the major patterns of inappropriate use of drugs in Kyrgyzstan. Unnecessary injections are used to treat non-specific symptoms such as mild diarrhoea, colds and fatigue. About 50% of the population lacks basic information on the proper use of drugs to combat diseases.

An underlying factor in many aspects of irrational drug use is the lack of access to independent drug information.

Contributed by Saliya Karymbaeva, Drug Bulletin, Kyrgyzstan.

2.1 The relationship between evidence and rational use

Conventionally, the best evidence for an intervention is that for which there is scientific support, which means that evidence of its efficacy and safety is derived from well-controlled clinical trials. Using such evidence as the basis for making rational decisions about medicine use is logical and seems straightforward. Yet, there are several problems with relying on formal evidence alone.

Problems with evidence as a basis for rational use

- Evidence may not be available. In reality, much of what is done in medicine is not based on evidence, simply because it is not available. This is often the case for cheaper non-drug interventions. Most clinical trial 'evidence' relates to drugs and is mainly generated by pharmaceutical companies (e.g. there are thousands of published clinical trials of nonsteroidal anti-inflammatory drugs (NSAIDs) in osteoarthritis but hardly any on the use of walking sticks).
- Clinical trials are often focused on proving efficacy for drug registration instead of drug effectiveness for actual 'real life' use (see Chapter 8).
- There may be poor access to evidence and a lack of openness from regulatory authorities and pharmaceutical companies who hold such information.

- Promotion of medicines to health professionals and consumers by pharmaceutical companies is often misleading.
- Patients included in trials that make up the evidence may not be representative of 'real' patients, for example, because the trials were carried out in a different country, or the patients in the trial had no co-morbidities.
- Health professionals and patients do not necessarily behave like those involved in the trials. For example, they might be less likely to give patients detailed and motivating instructions, or to perform the specified regular checks on whether the treatment is being effective (e.g. blood pressure measurements) or causing adverse effects (e.g. liver function tests).

2.2 Other influences on the choice of medicines

Many other factors affect the choice of treatments. They include a lack of access to independent information, availability of medicines, cost, culture and politics. For example, even if a practitioner could be aware of all the 'scientific' data, a particular treatment option may be inappropriate in a local community if the product is not locally available, is too expensive, or its use clashes with local practice or customs. In deciding on a particular treatment, practitioners need to consider the alternative approaches available (including no treatment), and the evidence on the comparative benefit/harm balance of the alternatives, together with local customs, costs and resources.

2.3 Sources of information for prescribers

Prescribers have many sources of information to help them prescribe rationally. Although useful, they all have limitations (Box 2.1).

Box 2.1 Different types of sources of information for prescribers

Source	Limitations
Textbooks	Take years to produce and are therefore liable to be out of date.
Medical journals	Difficult to get an overall view of the treatment options and a variable degree of influence on the content from biased sources.
Local or national formularies	Formularies vary in quality between different countries. They show the range of drugs that can be used for a practical purpose. Some explain how to make good choices from this range, but rarely have space for much background or comparative information.
Guidelines	Conclusions depend on the terms of reference of the organization producing the guidelines (see text below).
Official prescribing information prepared by drug companies and approved by regulatory authorities (e.g. data sheet, summary of product characteristics)	These are legal documents which vary a lot between countries and are much influenced by the power or the weaknesses of the national regulatory authority in regulating commercial promotion adequately. The information is often hard to use, partly because companies and regulatory agencies regard the documents as a protection against liability claims.
Promotional information	Primarily advocates the use and sale of a drug.

The conclusions in most of the traditional resource materials will have some bias that may well distort the message. Early trials of new medicines are designed and reported almost exclusively by drug companies and the conclusions published are likely to favour the company's product. Furthermore journals tend to prefer to publish papers with 'positive' results, a tendency that again favours the pharmaceutical industry. The advice given by secondary reviewing bodies, such as the UK's National Institute for Clinical Excellence (NICE), or the Cochrane Collaboration, depends on the terms of reference of the reviewing group. For example, NICE deals with efficacy and cost and essentially ignores safety; reviews by the Cochrane Collaboration tend to deal with efficacy and so far pay much less attention to safety or cost. The documents produced by national regulatory agencies and by the European Medicines Agency (EMEA) consider efficacy and safety but not a product's cost, relative efficacy ("added therapeutic value") or ease of use.

2.4 The special role of drug bulletins

The policies of drug bulletins mean they can offer advice that differs from that available from other sources. Bulletins are published frequently and so can be up to date. Transparent working and editorial independence, which are key features of drug bulletins, allow them to present impartial and unbiased evaluations and discuss controversial topics which the industry or an official government publication avoids. Bulletins can criticise individual advertising claims, therapeutic recommendations and official licensing decisions.

Being independent allows bulletins to determine their own terms of reference. Most bulletins base their recommendations about treatments on assessments of relative efficacy, relative safety, relative quality, relative cost and relative ease-of-use when compared to other medicines that are already available or, where appropriate, to other types of therapy (e.g. surgery, physiotherapy, psychotherapy).

Bulletin editors understand the full context of their local health care system (laws, customs, politics, practice), and have a practical knowledge of the system's culture and history. The special skills of the editorial team members enable them to integrate the principles of rational use of medicines with the real world of medical practice. They can clarify and resolve differences in technical, political and commercial pressures, offer advice in the absence of relevant evidence, and so can produce practical conclusions that incorporate epidemiological and socio-economic data on which readers can act with confidence.

2.5 Specific ways in which bulletins can help

1. Giving priority to problems/diseases

Rather than just focussing on the features of a particular drug or treatment, bulletins can present the available evidence on the drug in the context of the epidemiological background and the reality of medical practice. They can discuss the practicality of the treatment in real life, and offer practical suggestions on managing the disease. Being independent, they can discuss and compare the different treatments available for managing the disease.

2. Dealing with uncertainty

Prescribers face problems, for example, when treating patients (and populations) whose characteristics do not match those of the published knowledge base (e.g. the trial participants may have been males aged 25–45). In these circumstances, slavishly adhering to the published data would not be consistent with the principles of rational use of medicines. Bulletins can help clinicians deal with this difficulty because they can present and discuss problems of uncertainty. The text must make clear which statements are evidence-based and which have weaker support. The section of an article dealing with uncertainty may well need to be longer than that devoted to discussing evidence. The text should offer clear recommendations, and these need to be based on an intelligent search for a rational approach. The reasons for uncertainty, and the need to discuss it with prescribers, are likely to differ from country to country. For example, it might be useful to recommend strategies for management when diagnostic resources are scarce.

3. Encouraging and facilitating audit and monitoring

There are often gaps between the principles of rational use of medicines and what happens in practice. Bulletins should recognise these gaps and suggest practical remedies in a positive way. For example, advice may include suggestions on methods for monitoring the problem and then auditing practice later in order to see if practice or outcomes have improved. The focus should be on offering explanations and suggesting possible solutions. It will help readers' perception of bulletins if editors can be seen as people who can, and wish to, help resolve issues at a practical level, rather than just being seen as having expertise only on principles. In addition, readers should be told when data from well-controlled trials are needed and what questions these should address. By identifying what is not known bulletins can encourage and facilitate research, monitoring and audit.

4. Communicating with patients and the public

In areas where the gap between evidence and actual practice threatens the principles of rational drug use, it is important to help prescribers enter into a dialogue and alliance with patients (and also more broadly with the public). Even if a bulletin is aimed at health professionals, to give them technical information, it needs to give space to non-drug centred discussion, addressing the cultural determinants of drug use (perceptions, acceptability, expectations). Using published evidence whenever possible, the challenge is to address the 'everyday' issues of management, offering solutions where possible. For example, bulletins can deal with the problems parents face when dealing with minor symptoms in their children, the handling of forgetfulness or dementia in the elderly, the integration of medicines with traditional or complementary strategies, and can offer advice on helpful non-drug measures for managing conditions.

Bulletins directed expressly at a lay (non-healthcare) audience include *Worst Pills, Best Pills* (USA) [**http://www.citizen.org/hrg/**] and *Kusuri-no-Check* (Japan) [**http://npojip.org**]. In other arrangements 'lay' bulletins are published as 'sister' pamphlets based on a 'healthcare' bulletin but 'translated' for a lay readership; an example of this is *Drug and Therapeutics Bulletin's Treatment Notes* (UK) [**http://www.dtb.org.uk/dtb/tnotes/**]. Other bulletins produce press releases about the topics of each issue which might be of interest to the public, and allow the lay press to reproduce them (e.g. *la revue Prescrire*: its press releases are disseminated in different francophone countries, and this create links with lay-press journalists).

The growing literature on the more patient-orientated issues is one with which bulletin editors need to become familiar. To do this they may need the help of people outside the core editorial staff. Often the task is to translate successful approaches across cultural and socio-economic settings.

2.6 Bulletins as part of wider initiatives for promoting rational use of medicines

Producing a bulletin is unlikely to be enough to affect prescribing practices. Drug bulletins can and have been used in medical education (e.g. *Boletin AIS-COIME*, Nicaragua; *Therapeutics Letter*, Canada; *Australian Prescriber*, Australia) and also to complement the work of drug information centres (e.g. *Drug Bulletin*, Pokhara, Nepal; *Drug Bulletin*, Kyrgyzstan).

To have influence in the broader dialogue on rational use of medicines in a country, bulletin staff may relate to and form loose partnerships with other leaders in the field (professional bodies, clinicians/prescribers, drug policy experts, regulators etc.) when they have developed credibility (see also Chapter 12). This does not mean that there should be formal alliances, but rather the aim is to engender a sense of mutual respect and understanding. In keeping with this, when preparing articles, bulletins should work with external referees/consultants from across national professional and consumer networks. While on occasion the position taken by a bulletin will be at odds with the general view, ideally articles should be seen as the product of wide consultation and so the consensus position of the health community at large. There is also a role for responding to questions, of being seen as a respected local resource to which the media, for instance, can turn as an impartial authority. Such a role can

be time-consuming, and requires expertise, but is well worth cultivating if a bulletin wishes to be an established part of the national healthcare environment.

Case study: *Drug Bulletin*, Kyrgyzstan

Drug information centres have an important role in responding to the need for independent drug information. Our Drug Information Centre (DIC) was established and is maintained in collaboration with the Government of the Kyrgyz Republic and the WHO Regional Office for Europe, Essential Drug Unit, and is coordinated by the Special Pharmaceutical Project for Newly Independent States. The DIC is a unit of the Department of Drug Provision and Medical Equipment under the Ministry of Health.

We work closely with the National Drug Committee and regularly take part in the revision of the Essential Drugs List and the development of a National Formulary for Kyrgyzstan. The DIC facilitates working groups designed to introduce clinical protocols with recommendations on evidence-based medicine, collects and circulates adverse drug reaction reports (as a member of the WHO International Monitoring Programme) and gives recommendations on the rational use of drugs. It is involved in monitoring implementation of national drug reform.

The Centre publishes a quarterly *Drug Bulletin,* which covers news about national drug policy, aspects of clinical pharmacology, pharmaceutical treatment and prevention guidelines, adverse drug reactions, etc. It is distributed free of charge to doctors, pharmacist and policy-makers throughout Kyrgyzstan. Normally we distribute 3000 copies of the bulletin. Ideas for bulletin articles come from participation in the meetings of the Ministry of Health and Drug Department, requests from health professionals and the public, and from monitoring implementation of drug reform. Recent topics included: features of pharmacotherapy in paediatrics, drug interactions, medical errors related to the names of drugs, and modified–release preparations of drugs. Every year the DIC receives about 500 enquiries and teaches around 200–250 doctors and pharmacists. But there are 15,000 healthcare practitioners in Kyrgyzstan and most of them have no opportunity to contact us for drug information. Given our shortage of resources, the *Drug Bulletin* is the most accessible tool that reaches as many health practitioners as possible and disseminates unbiased and updated drug information and promotes rational drug use and aspects of health reform.

Contributed by Saliya Karymbaeva, Drug Bulletin, Kyrgyzstan.

2.7 Summary

Drug bulletins have the task of providing independent advice on the best use of medicines, making sure that readers know the strength of the basis for that advice and suggesting how that advice might be further strengthened. In addition to being clearly written, the advice should be reliable, unambiguous, independent, and understandable. Also, it needs to be relevant to, and implementable in, the local health environment. Through their writing, bulletins should work to become a source of advice that is trusted and needed by health workers and the public alike.

3. What are drug bulletins?

3.1 Definition

Drug bulletins are specialised periodicals providing comparative information and advice on the prescribing and use of medicines. Doctors and pharmacists are the primary audience for most drug bulletins. Some bulletins, however, are read by a broader range of health professionals, including nurses and community health workers, and a few reach the general public. The aim is to provide practical, reliable information about medicines and promote more rational, informed decisions about their use. Although the main focus of most bulletins is on improving individual prescribing decisions, many also deal with broader policy issues.

3.2 The history of drug bulletins

Drug bulletins began to appear around 1960, at a time when pharmaceutical research leading to the introduction of new drugs had begun to revolutionise the practice of medicine. This was also the time of the thalidomide disaster, which forced the world to pay serious attention to the harm that drugs might cause.

Medical, pharmacy, nursing and other health journals for health professionals have always published articles about drugs and other medical treatments, but such articles have to compete with a mass of other material. The result remains a rather haphazard coverage of therapeutics in both general and specialist journals. Through their practical orientation, drug bulletins fill a special need: to provide information in a way that helps practitioners make informed decisions about the use of pharmaceuticals.

The growth in importance of the pharmaceutical industry during the 1950s and 1960s was accompanied by a large increase in drug advertising. An increasing number of thoughtful and critical doctors wanted to be better informed about drugs, especially new drugs, and needed independent assessments of manufacturers' claims. The 1960s also marked a time in which a growing consumer rights movement became increasingly active in health policy. The earliest drug bulletins were published by consumer organizations although their readers were almost all doctors. This is still the case for several large, successful, national bulletins and no doubt reflects a recognition by consumer groups that independent prescribing information for doctors can help to contribute to better health services.

The first drug bulletin, *The Medical Letter on Drugs and Therapeutics*, was started in the USA in 1959 by Harold Aaron, a physician who had been medical adviser of Consumers' Union (CU), itself the world's oldest consumer organization, and Arthur Kallet who had been the director of CU. In 1962 it was adapted for prescribers in the United Kingdom (UK) as the UK edition of the *Medical Letter*, published by the Consumers' Association, and a year later this became the separate *Drug and Therapeutics Bulletin*. At the same time the Ministry of Health in the UK began to publish *Prescribers' Notes* for doctors working in the National Health Service, which later became *Prescribers' Journal* (no longer published).

One can guess why this activity started in the USA and in the UK. At that time American pharmaceutical companies were producing more new drugs, were marketing them more aggressively, and had a larger domestic market than companies elsewhere, so a critical mass of doctors perceived a need for independent information earlier than in other countries. Britain was unique in having a National Health Service that paid for all medicines. The Government thus had a strong reason for wanting to improve the quality of prescribing, to get better value for the large expenditure on drugs.

In the next 30 years many more drug bulletins were started in various European countries and also in Australasia, Asia, Africa and Latin America. Now between 50 and 100 bulletins are published worldwide – the exact number depends on the definition used. These bulletins differ greatly in their target groups and circulation, their scope, size and frequency, the method of production and style of presentation, the teams producing them, their links to institutions and organizations, and how they are funded. One perhaps unexpected aspect of this diversity is that in some countries (e.g. Germany, Italy, Spain) several bulletins exist side by side, addressing different though sometimes overlapping readerships and sometimes specialising in different topic areas.

3.3 What makes an 'independent' drug bulletin independent?

An independent bulletin's focus on practical comparative information about medicines is one aspect of what defines it. An essential aspect is its financial and editorial independence from pharmaceutical companies and from pharmaceutical industry associations. This independence is a fundamental basis for the work of drug bulletins, whether they focus mainly on providing comparative treatment advice for a specific health condition, assessing the benefits and harms of a new medicine, or discussing national drug and regulatory policies. ISDB defines independence as consisting of two main components[1]:

- being run by an independent editorial team, working within an organizational structure capable of guaranteeing editorial independence;
- financial resources that guarantee independence, such as public financing through a national or local government, financing by a non-governmental organization, or self-financing through reader subscriptions or membership fees.

Most bulletins are funded either by the organization that publishes them or by subscribers. Readers may pay individually (e.g. *la revue Prescrire*, France; *Drugs Bulletin*, India; *Pharma Kritik*, Switzerland). Bulletins that are published or supported by a government are generally distributed to readers free of charge (e.g. *Cito!*, Latvia), as are some bulletins published by non-governmental organizations (e.g. *Boletin AIS-COIME*, Nicaragua).

Drug bulletins do not rely on pharmaceutical advertising, unlike most medical journals. Journals that carry advertising from drug companies are vulnerable to conflicts of interest and often cannot publish openly critical comments when this would be in the interest of patients and prescribers.

Drug bulletins differ in many ways. These include:

- who reads them: is it doctors, pharmacists, rural health workers, the public?
- the main focus of their articles: is it drug policy, adverse effects, new drugs, treatment guidelines?
- the size and presentation of the bulletin, from a two-sided single sheet to an 80-page magazine; from simple black on white printing to glossy paper and full colour illustrations;
- the size of the editorial team and staff;
- how much they rely on unpaid volunteers;
- their institutional base and organizational structure;
- funding sources.

Case study: *Boletin AIS-COIME*, Nicaragua

Boletin AIS-COIME is produced by AIS-Nicaragua, a national NGO, which promotes the appropriate use of drugs through information, training, research, networking and advocacy. The 12–16-page bulletin is distributed free of charge to all doctors working in hospitals and primary health care units of the Ministry of Health, to pharmacy and medical students and teachers, NGOs and some private pharmacies.

AIS-COIME focuses on rational use of standard drugs and on treatment guidelines. But it also includes articles about drug policy, information about some relevant new drugs introduced to the national market, adverse drug reactions, critical appraisal of advertising and results of monitoring of the WHO Ethical Criteria for Medicinal Drug Promotion, and tests of knowledge about topics published in previous bulletins.

The bulletin is produced by a small editorial team of three or four people and a group of volunteers who revise the articles. The bulletin has been financed mainly by international NGOs and some of the issues by the Pan American Health Organization (PAHO). One of the objectives of the bulletin is to be useful as a support for continuing education activities in the primary health care unit of the Ministry of Health. *La revue Prescrire* and WHO *Essential Drugs Monitor* have been important references.

Contributed by Benoit Marchand, Boletin AIS-COIME, Nicaragua.

3.4 Types of editorial content

Many bulletins publish articles with information on individual drugs or classes of drugs. This may include an overview of benefits and harms of drugs and the conditions for their appropriate use, and information on how new drugs compare with existing treatment options. The focus of a bulletin article may also be on how best to manage a medical problem. Many bulletins try to include a balance between articles that focus primarily on specific drugs and others that focus primarily on treatment of specific diseases or problems. The emphasis of a bulletin's content often reflects the target audience: for example, bulletins distributed mainly to pharmacists tend to be more drug-oriented, those mainly for doctors often focus on treatment of a specific disease or health condition. Some, which have a mixed audience, are actively promoting good collaboration among health professionals in the best interest of patients.

In many countries, up-to-date information on adverse drug reactions (ADRs) is especially hard to get and health professionals are largely unaware of what types of harm to watch out for or how to report suspected adverse effects. Some bulletins, such as Spain's *Butlleti Groc* [**http://www.icf.uab.es/informacion/boletines/bg/asp/bg_e.asp**] and *Prescriber Update* from New Zealand [**http://www.medsafe.govt.nz/Profs/PUarticles.htm**], focus entirely on ADRs and are produced by organizations concerned with pharmacovigilance. The aim is to get the information on ADRs collected by a pharmacovigilance centre back out to doctors and pharmacists, and to stimulate more awareness of the need to report ADRs.

Another specialised type of bulletin deals with clinical toxicology and the management of poisoning. The National Poisons Centre in Malaysia publishes two bulletins (*PRN8099* in English and *PanawaRacun* in Malay) with information on avoidance and treatment of poisoning, as well as on the use of medicines [**http://www.prn2.usm.my/mainsite/bulletin/index.html**].

Several bulletins focus on national and international drug policies, highlighting problems in the way medicines are provided, marketed and regulated, and discussing strategies for improvement. Their focus may be on a broad range of drug policies or a specific policy issue. For example, *TheNetwork's Drug Bulletin* in Pakistan also covers news items on international measures to ban or withdraw unsafe drugs [**http://www.thenetwork.org.pk/magdb.htm**].

3.5 Styles of communicating information

Bulletins vary greatly in their styles and in the length and tone of articles. In general the most successful have developed a concise format for articles with clear subheadings. These may be standardised so that readers know where to find particular kinds of information. For example, the US Public Citizen's *Worst Pills, Best Pills*, a bulletin for consumers, ends each article with a practical advice section titled, "What you can do". Titles usually give a clear idea of the topic of the article, but occasionally catchy titles are used to attract readers' attention.

Most bulletins cite the references used as information sources (something that all bulletins should do, wherever possible). Some provide illustrations and tables, others do not. In addition to producing individual issues, many bulletins produce a yearly index. Some also publish bound collections of articles or CD-ROMs containing back issues. In countries where readers have Internet access, bulletins are increasingly published on Internet web sites as well as in print.

3.6 The institutional base

A bulletin usually needs an institutional base. Local opportunity largely determines what this is. The spectrum ranges from a bulletin housed in a Health Ministry to a health insurance organization, a consumer organization, a professional association, a university department, or a non-governmental organization. Some bulletins have their own independent institutional base and are legally incorporated as a company or a non-profit organization. A bulletin housed within a parent organization needs a structure that allows

the editors the freedom to do their job and to control editorial content. On the other hand, a parent organization can offer the advantage of taking responsibility for financial management and protecting the bulletin against legal threats. Chapter 11 discusses the pros and cons of different types of institutional and legal structures.

3.7 References

1. Constitution of the International Society of Drug Bulletins. Available at: **http://www.isdbweb.org**

4. Defining aims, target and type of bulletin

4.1 Principles

A drug bulletin can succeed only if it serves a real need and if it is planned with the target audience in mind. You probably think a drug bulletin is needed, but do your colleagues agree? There are already many sources of drug information. In some countries people complain about an "information overload", even though comparative information is not so abundant. How will your bulletin succeed against competing information? In other countries people lack information. How will your bulletin reach the people who need it?

The key to success is to involve the readers of the bulletin as much as possible. Nobody knows better what they want than they do. A bulletin that subscribers have to pay for will only succeed if it gives them something that they want and value. However, they may not realise that they lack a source of objective information until that source is actually available. When a bulletin is funded publicly, the funding body will want to be satisfied that the recipients appreciate it. You should spend time researching the market before you launch a new bulletin (see Box 4.1). Established bulletins also need to listen to their readers (through readers' mail, surveys and research) to keep them up to date with what their readers want.

Box 4.1 Finding out whether a bulletin is needed: questions that might be included in a survey of potential readers

1. What is your job?
2. Do you give advice about, or prescribe, or dispense medicines?
3. If you need information about a medicine, where do you look for it?
4. What sort of information about a medicine do you frequently look for? e.g. dosage, adverse effects, interactions, how to store the medicine, information for the patient.
5. In the past year, have you had difficulty getting information that you needed?
6. What sort of information on medicines do you have most difficulty in obtaining?
7. How do you get information about a **new** medicine?
8. How do you find out what is the current best treatment for a medical problem?
9. Can you currently get independent, unbiased information on medicines? If yes, do you get it from international sources or from national ones adapted to the local situation?
10. Do you need additional independent, unbiased information? If yes,
    - in what form (i.e. bulletin, web site, telephone information service etc.)?
    - who should provide it?
    - would you pay for it?

4.2 What is already available?

If your country has many sources of drug information, does it need a bulletin? Health workers are usually busy people, so your bulletin has to compete for their time and attention. If your bulletin offers them something different they are more likely to read it. For example, if the only other drug information available comes from pharmaceutical companies then you can offer information which is not designed to increase drug use or sales.

Consider what health workers in your country do if they want to find out something about a drug. Do they have access to:

1. Library services:

- books and journals
- computerised databases

2. Drug information services, including drug information centres

3. Industry information:

- product data sheets
- company medical departments

4. The Internet

5. Informal sources of drug information, such as advice from hospital specialists and other knowledgeable colleagues.

4.3 Information on drug utilisation helps you choose topics

Any bulletin that is intended to change prescribing must be informed by knowledge of what is being prescribed and what the problems are. These problems may range from use of a less than ideal drug because the best drug is unavailable, to overuse of expensive drugs for simple problems. The quality of data available will vary greatly. Some countries have good records of all drug prescriptions, but few collect information about the indications for prescribing.

Where prescription data are collected, it is often the trends in utilisation that are the most interesting to monitor. For example, in many countries the use of selective serotonin re-uptake inhibitors (SSRIs) for depression has increased greatly even though it remains unclear when they should be preferred to older and cheaper antidepressants. Figure 4.1 shows an example from the Italian bulletin *Dialogo sui Farmaci*, which has access to drug utilisation data, showing the growth in use of atypical antipsychotic drugs in recent years.

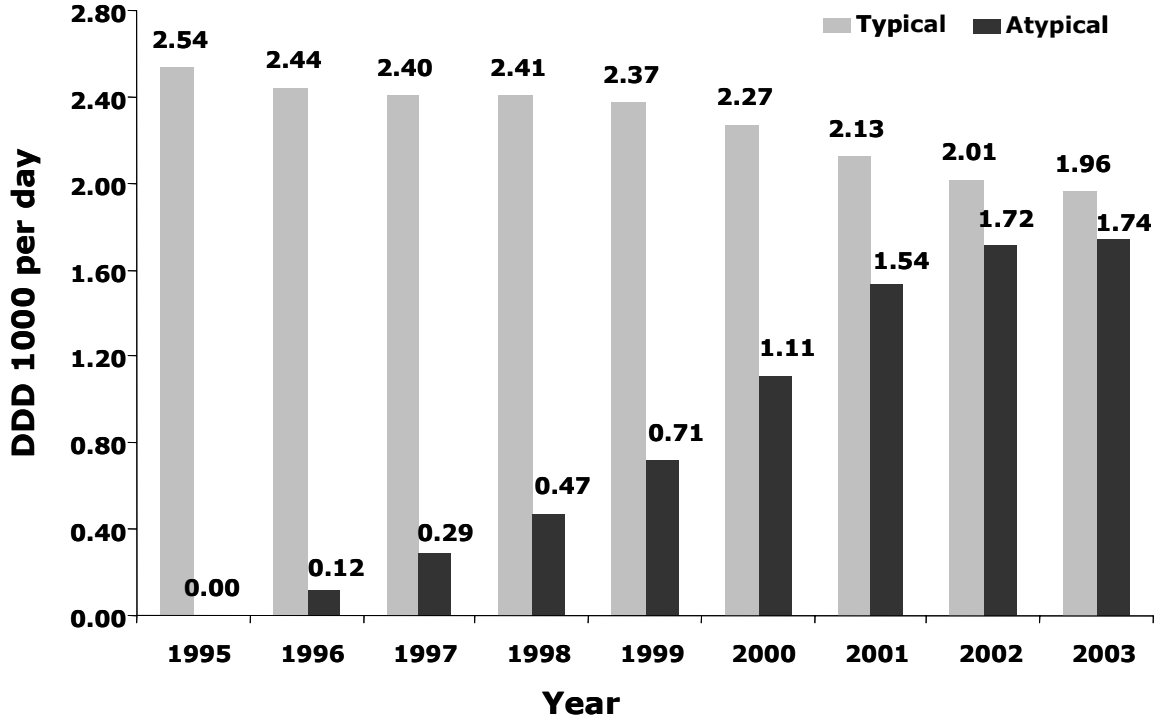
Changes in prescribing can signal problems, as may reports of adverse drug reactions or interactions. It may also be possible to discover what proportion of hospital admissions are due to problems with medication, for example overdose or failure to take necessary drugs.

Laboratory data can also be useful, for example an increase in resistant bacteria may imply the over use of broad-spectrum antibiotics.

Assuming patients have access to necessary medicines, various utilisation problems may be encountered:

- using a drug with no therapeutic effect, e.g. most tonics;
- prescribing a drug when it is not indicated (and its use is pointless, e.g. it is not effective);
- prescribing a drug which does not cure a condition that should be cured, e.g. prescribing an anti-ulcer drug instead of eradicating *Helicobacter pylori*;
- using an expensive drug when a cheaper one is equally effective;
- using a drug which is more potent than necessary;
- using drugs for longer than needed or at higher doses than necessary, e.g. non-steroidal anti-inflammatory drugs;
- not using drugs for long enough, e.g. chemotherapy of tuberculosis;
- using too low or too high a dose;
- patients misunderstanding the best way to use their medicines.

Figure 4.1. Change in use of typical and atypical antipsychotic drugs (expressed as Defined Daily Dose DDD/1000 inhabitants/day) in Italy



Source: *Dialogo sui Farmaci*, Italy.

4.4 Defining and refining the aims of the bulletin

If you have decided that you want to produce a drug bulletin, you will already have some idea of what you are trying to achieve. Review why you wanted a bulletin, then consider if others share your views. If your aims are inappropriate for the readers then the bulletin is unlikely to succeed. Several different aims are worth pursuing and most bulletins have more than one. They may include:

- improving prescribing, dispensing and use of drugs;
- warning of adverse effects;
- advising on therapeutic problems;
- reviewing new drugs, including their cost-effectiveness;
- advocating change, e.g. calling for a national drug policy, or a regulatory improvement;
- criticising activities of the pharmaceutical industry, e.g. the accuracy of advertisements;
- reporting on drug utilisation studies.

A bulletin usually combines education and information. A bulletin that is easy to read is more likely to be read. To succeed a bulletin must have credibility. It should regularly provide reliable, unbiased information that is relevant to its readers. Where possible the material should be referenced so that readers can see that it is evidence-based.

4.5 Who are the readers?

A bulletin aimed at improving prescribing will probably be read by doctors, but may also interest pharmacists and nurses. Knowing your bulletin's target audience is very important: it should determine how the bulletin is presented. A bulletin for village health workers will differ greatly from a bulletin aimed at hospital doctors, general practitioners or pharmacists.

You first need to ask who needs your drug information. You then have to consider who wants it. When starting a bulletin it is often wise to send it to people who value the information. Later, you can try and involve the people who do not understand the point of a bulletin. Often the people who think they already know everything are the ones who most need to read a drug bulletin!

In some countries, a useful strategy is to identify opinion leaders and seek their support for your bulletin. If reading a bulletin is seen to be part of being a good health professional your readership will soon grow. Professional bodies, such as medical or pharmaceutical associations, can also be important allies. Some may, for example, be able to distribute a bulletin to their members. In other countries, when these bodies and opinion leaders have no credibility, their support should be avoided. Finally, pressure from consumers can help to motivate health professionals to search for objective information, and so widen support for a bulletin.

Your readership will be determined largely by how the bulletin is distributed. Will it be distributed to all health workers, only to particular professional groups, or will it be available only by subscription?

Case study: *Folia Pharmacotherapeutica*, Belgium

Folia Pharmacotherapeutica is a monthly drug bulletin, which has been sent free of charge to all Belgian licensed physicians, pharmacists and dentists since 1975. The circulation is about 60,000. Present and past (since 1999) issues are also available on the web site. The bulletin is edited by the Belgian Centre for Pharmacotherapeutic Information (BCFI in Flemish; CBIP in French) which is an independent organization, subsidised by the Belgian Ministry of Health.

Folia Pharmacotherapeutica contains summaries of important articles about pharmacotherapy which have appeared in the international literature. Much attention is given to the evidence base of the information but the bulletin tries to reconcile the requirements of evidence with the need to be of practical use for the busy health professional, which is far from easy. In each monthly issue there is also a communication from the Belgian Centre for Pharmacovigilance. From a recent survey of the readers it appears that the Folia are well read and appreciated by health professionals.

The bulletin is put together by an editorial team (clinical pharmacologists, pharmacists, general practitioners), with the help of a network of general practitioners, specialists and practicing pharmacists. All texts are seen by the members of the editorial team, but also by specialists in the subject matter. The Belgian Centre for Pharmacotherapeutic Information is responsible for a number of other initiatives as well: an annual drug formulary, leaflets about new chemical entities appearing on the market, pharmaco-economic assessment and brochures about important therapeutic topics. It is thought that the existence of these other sources of information enhances the impact of our monthly bulletin.

Contributed by Marc Bogaert, Folia Pharmacotherapeutica, Belgium.
[**http://www.cbip.be**].

4.6 What type of information is needed?

Just as the aim of the bulletin should influence who reads it, the readers should influence the content of the bulletin. A bulletin containing articles on highly specialised hospital treatments is unlikely to attract someone working in a community dispensary. As most bulletins aim to improve prescribing, prescribers are usually a key audience. Most prescribing is done in the community, so family doctors (general practitioners) are often an important target for drug bulletins. The content of the bulletin should therefore focus on the diseases and health problems managed in that community. Often this will require articles on the best use of standard drugs rather than detailed reviews of expensive new products with limited indications.

The best way to find out what your readers want is to ask them. There are several ways to do this:

- An existing bulletin can carefully consider readers' letters (for example, *la revue Prescrire* receives around 2000 letters per year, which are an important source of information on readers' needs), or it can survey some or all of the people on its mailing list.
- It can also be useful to survey some people in your target audience who are not on the mailing list. There may be some simple reason why they are not receiving the bulletin, and if you can correct this problem you may gain more readers.
- If you are in the first stage of planning a bulletin (see also Chapters 5 and 6) you should consider surveying members of the target audience you have identified.

Readership surveys can be simple or complex. How extensive they are depends on the budget available – and on your appetite for information. You may be able to send people a questionnaire by post or attached to the bulletin. Another approach is to invite people to focus groups. A focus group is a small, informal discussion group, usually of between six and 10 people, organized around the discussion of a few open-ended questions. They are often used in market research to discuss ideas for new products. Focus groups can be held in connection with another meeting, for example a conference, to reduce the costs. It can also be useful to talk – and listen – to opinion leaders and other key people.

You will want to ask questions that identify the information readers would consider useful for their work. For example, which conditions do they find difficult to manage, which treatments are they uncomfortable about prescribing, dispensing or explaining to patients? You may also want to elicit their views on how the information would be best presented. Do they prefer a frequent one-page newsletter or a larger journal less often? Chapter 12 provides practical advice on how to develop reader surveys and other methods of feedback and evaluation.

5. Planning resources

5.1 The first steps in planning

Careful planning of human, financial and material resources is an important prerequisite to starting and maintaining a bulletin. Where resources are limited, you will need to set strict priorities. However, with adequate motivation and commitment, it may be possible to achieve a lot with limited resources.

It would be ideal to run a bulletin after gathering together all the resource materials, physical facilities and equipment recommended for a drug information service. This is often not possible, especially in developing countries. It is therefore important to be realistic about your needs and the possibilities available. An initial task is to carefully identify the resources you already have (e.g. through local organizations or institutions) and what additional resources are needed for a modest but useful beginning.

Box 5.1 Types of resources needed to start a drug bulletin

- people: editors, secretary or administrative assistant, accountant, etc.
- references: books, journal subscriptions
- an office
- computer(s) with Internet access
- office supplies
- telephone, fax
- a means of distributing the bulletin (either autonomous or 'piggyback').

5.2 Identify what is already available or accessible

First find out what is already available locally in terms of human resources, publications and offices. It may be possible to make use of these with little or no expense.

Valuable sources of information include other bulletins, local or national drug formularies, standard treatment guidelines or protocols, selected medical and pharmaceutical journals and books. It may be worth developing links with universities, medical and pharmaceutical associations, research centres, libraries, consumer organizations, government departments and non-governmental organizations, depending on their degree of independence and reliability. Duplication of expensive resources should be avoided, particularly in developing countries.

You may want to get to know the people who are in charge of these different organizations and seek their cooperation. They could help you with their experience and materials and may also provide some financial support. Try to explore areas that could be of mutual interest and strive for cooperation instead of seeking competition with others in the same field (see Chapter 13). Being linked with established organizations, such as teaching institutions, hospitals or drug information centres, when they have credibility, can be an

advantage for bulletins in terms of human, financial, material and administrative resources. Such links can also provide moral support from ideological allies.

5.3 Make a realistic assessment of additional needs

After you have made an inventory of the resources that are already available, make a realistic assessment of your bulletin's additional needs. Where financial possibilities are limited, it is essential to set priorities. Sometimes people have exaggerated ideas about what is needed and produce huge and unrealistic plans and budgets. Usually this is neither necessary nor possible. If there is a strong and continued commitment, useful bulletins can start and survive with modest resources and very few people involved.

5.4 Human resources: who will do the work?

Production of a drug bulletin requires an editor or editors, writers, reviewers and part- or full-time office staff. Depending on the resources available, this may be mostly paid work or much of it may be done by volunteers.

It would be premature to set up a drug bulletin without a local team that is committed, determined and has a clear policy. Some ISDB bulletins have faced difficulties after starting an ambitious project too rapidly. The team may start with one or two people if they have enough time and energy to give to the bulletin and have the support of a network of interested colleagues. It is sometimes considered a handicap if only a few people are centrally involved in starting a bulletin. This is not true. A bulletin needs a critical mass of supporters of good quality drug information, but the group running the bulletin can be small. ISDB bulletins have functioned for years with editorial teams ranging from one or two people to around 25 people. This does not include technical staff, external reviewers or advisers. Wherever possible, editors should try their best to use the skill and expertise of other practicing professionals and academics for the benefit of the bulletin. Involvement of a wide range of experts, most often as advisers or reviewers, is likely to increase the standard, feeling of ownership, acceptance and credibility of the bulletin.

Many bulletins rely on two separate groups for direction and overall editorial policy:

- **the editorial team:** a local team responsible for production of articles, publication of the bulletin, and ensuring that the bulletin is meeting its editorial objectives;
- **the advisory board:** members may be local or physically distant; their role is to give guidance on the global orientation of the bulletin, its adaptation to the readers, and short- and long-term priorities.

Together, the editorial team and advisory board must:

- determine the bulletin's editorial policy;
- set priorities;
- develop rigorous but simple editorial methods;
- maintain quality in the long term;
- manage relations with readers and respond to feedback;
- evaluate the results and revise the editorial process.

5.4.1 The editorial team

Whatever the size of the editorial team, its members should:

- strongly agree with the objectives of the bulletin, which means that there should be a clear and explicit editorial policy;
- have no conflict of interest with any institution, organization or company that could impair the independence of the bulletin. Some bulletins ask editors to sign formal declarations (ISDB is developing a model conflict of interests policy. Check the web site at: **http://www.isdbweb.org**);
- clearly define how much time they can devote to the bulletin;
- have had relevant training in therapeutics and/or public health;
- be capable of critical analysis and synthesis of data;
- have a reasonably good knowledge of English, as many scientific articles are available only in English;
- include health practitioners, for example, doctors and/or pharmacists and/or nurses; ideally an editorial team should include different types of professionals;.
- include patients and lay people in the editorial team in addition to the above if the bulletin is aimed at the public and patients.

The editorial team is responsible for selecting and defining the outline of topics for articles, editorial planning, ensuring the necessary documentation, organizing the work of authors and reviewers, quality control, and analysis of feedback from readers. It has the overall editorial responsibility for the articles published in the bulletin and for the bulletin itself. Usually, one person acts as chief editor, and has ultimate responsibility for decisions about the bulletin's content.

Case study: *Sri Lanka Prescriber*

There are no full-time members of staff; we all work part-time on the bulletin. There are three editors and an editorial board comprising pharmacologists, medical specialists and a pharmacist. We do not have a separate office for producing the bulletin. The editorial board meetings are held at the Department of Pharmacology and we use departmental computers, printers and photocopiers. The editorial board meetings are convened by the secretary to the editorial board, who is responsible for taking minutes, writing to selected authors and liaising with the publishing organization.

Contributed by Gita Fernando, Sri Lanka Prescriber [**http://www.spc.lk**].

5.4.2 The advisory board

The advisory board plays an essential role, even if it has few members, providing guidance to the editorial team. For example, it can help the editorial team to identify articles that do not adequately meet their objectives, lack of independence, or useful topics that have not been covered. The advisory board can also help the editorial team to discover new information sources and opportunities for collaboration, and may assist in promoting the bulletin. It is very helpful to have an advisory board consisting of members with backgrounds in different therapeutic areas.

Experienced members of other bulletins' teams can also play this role. The advisory board may include non-health professionals and patients, as well as professionals who differ in orientation from the editorial team. For example, it is helpful for university-oriented editors to have clinically-oriented advisers, for hospital-based editors to have community-based advisers, for public sector editors to have private practice advisers, and vice-versa. The expertise of the members of the advisory board helps to broaden and complement the expertise of members of the editorial team.

Should 'opinion leaders' and 'scientific experts' be included in the advisory board? It may be useful to include them because of the help they can provide, especially if they are available and not too far removed from everyday practice, or because their involvement helps to extend the bulletin's sphere of influence. However, if they have conflicts of interest or a clear lack of independence, no title or supposed expertise justifies involving them in the advisory board.

Neither the members of the editorial team nor the advisory board members should be appointed for life. Regular evaluation is necessary to maintain and improve the bulletin's quality. Fixed-term contracts, lasting, say two–three years, may therefore be useful.

5.4.3 External reviewers

It is useful to build a database of critical reviewers. Over time, you may find that some of them are also very suited to be new members of the editorial or advisory board. It could also be helpful for strategic reasons to ask influential persons to become advisers or board members, for instance the dean of a medical faculty, the president of a professional organization of doctors or pharmacists or the drug inspector of the Ministry of Health. You will want to ensure that they have no conflicts of interest, for example, because of financial ties to the pharmaceutical industry or because they are linked in some way with the government departments that have a tendency to support any national pharmaceutical companies.

5.5 Maintaining the motivation of contributors

There are three main ways to motivate editors, authors and advisers:

- through adequate acknowledgement of their contributions;
- through remuneration;
- through attention to their values and needs (for example, by providing feedback, explanation, respect, etc.).

Bulletins that can afford it should pay their authors and editors, and sometimes also give some form of honorarium to members of the editorial or advisory board. You can also thank your reviewers in a way that is inexpensive, but still shows that you appreciate their contribution. The most important thing is to handle their comments with care and treat them with respect. They will always appreciate it if you give them some form of feedback on how you handled their comments, although this can be time-consuming. In this way you will be more likely to get their continued support. (See also Chapter 7, Sections 7.3.2 and 7.4.7).

Case study: *Drugs Bulletin* – Chandigarh, India

Drugs Bulletin is published by the Department of Pharmacology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. It is a quarterly publication, which has been published since 1976 and is funded by the Institution, a public sector organization.

The bulletin includes only review articles, and the topics are generally selected from current developments and especially those relevant to a developing country. However, topics of international interest, recent advances and pathophysiological aspects are also published. The articles are generally contributed by specialists in their respective fields and the published articles are signed by the authors. No remuneration is offered. However, a complementary copy is provided to each of the authors. This has been our policy ever since the bulletin was started.

Contributed by Promila Pandhi, Drugs Bulletin, India [**http://www.pgimer.nic.in**].

5.6 Material resources – an office, equipment and references

Chapter 7 contains a detailed discussion about books and journals that are useful to drug bulletins, as well as suggestions for key references for bulletins with limited finances. It is useful to subscribe to national and local health journals in order to keep abreast of current trends and events and develop locally relevant articles.

The Internet is another very useful resource as it provides instant worldwide access to information. The cost of Internet access may still be prohibitive in some developing countries, but this is changing fast. It provides access to many useful and sometimes free sources of information (see the appendix at the end of the manual).

Wherever possible it is a good idea to link drug bulletins with other drug information services. If a telephone, hospital or clinic-based service is providing answers to individual questions, it is a logical step to write down the answers to the most frequently asked questions and then to disseminate these in the form of written information. For example, Nepal's *Drug and Therapeutics Letter* is an integral part of the Drug Information Unit of Tribhuvan University Teaching Hospital (TUTH). The physical, material and human resources available in the Unit come in very handy while preparing or editing articles for the bulletin and also in its distribution. Moreover, the drug information service sometimes helps to identify areas of need that can be addressed in the bulletin. The bulletin has also been used to publicise the information service and to contribute new reference materials. Such an integrated approach to drug information provision gives increased credibility as well as organizational support.[1]

It is desirable to have a furnished office and a computer with printer and an e-mail connection to produce a bulletin. If possible you should try to secure these facilities, but they are not indispensable. For example, when the Drug Information Unit at TUTH was first established, it had no computer and e-mail facilities and everything was done manually.

5.7 Financial resources – the key to sustainability

Financial sustainability is vital to the success of any bulletin. Money is needed for:

- human resources: payment for administrative staff, writers and editors;
- material resources: references, equipment, rent, phone and electricity charges;
- printing and distribution of the bulletin.

Financial resources vary greatly from country to country and between different regions or centres within a country. Developing countries usually have severe budgetary constraints and sources of funding are usually limited. It is important to carefully manage finances right from the start. Decisions on the size, appearance and the extent of circulation of a bulletin should be based on a realistic assessment of the financial resources available. It is best to start modestly, at least initially, and then slowly expand as the bulletin gets established and more resources become available.

Much can be achieved with a limited budget if there is a strong commitment and motivation at both individual and organizational levels. As an example, the production cost of the Nepal *Drug and Therapeutics Letter*, described above, is very modest. Seven hundred copies of the bulletin, produced every two months, cost around US$10. This cost is borne by the university teaching hospital.

Sources of funding

There is no simple answer to the question of how to finance a bulletin. Some say that whenever possible bulletins should try to generate their own income through paid subscriptions. Having a lot of small sponsors can support a much stronger and more independent editorial base than one or more main sponsors (e.g. through a bulk subscription arrangement). Relying on the sponsorship of individual readers means relying on people who share the views of the editorial team. Bulletins that depend on subscriptions expect their readers to be interested enough to pay for their information, and subscription renewals are indeed a sign of readers' interest.

Most doctors and pharmacists are used to receiving promotional information from industry free of charge. Some bulletins who do not try to change this established custom choose a system of controlled circulation in which all or most health professionals receive their copy of the bulletin free. This may be possible with financing from the Ministry of Health, a consumer organization, a sick fund, a professional association or a non-governmental organization. Charging for a bulletin may discourage or diminish its use, especially in developing countries. It is not unusual for a bulletin that depends on subscriptions to reach only 10–20% of professionals whereas a bulletin distributed free to health professionals may reach 80–95%. Broad distribution of a free bulletin has the advantage that it may reach the 'not-yet-converted'. Readership surveys should be carried out, however, in an attempt to know to what extent a bulletin is being read (see Chapter 12). Bulk subscribers (e.g. governments, health authorities) will also need to be assured that the bulletin is worth paying for.

The choice of financing will also depend on how you can obtain funding with the maximum guarantee of maintaining your editorial independence. No interest group should be allowed to influence the choice of topics or the contents of a bulletin. Before accepting any external funding, the bulletin's editors need to assess if there are any implications for the independence of the bulletin. The following could be considered.

Government

In countries where national drug policies exist and are really implemented, it is very helpful for bulletins to try to be included and funded within the framework of such policies. Some bulletin editors might be as wary of government funding as of private industry. An important difference however is that the government normally represents the general public interest and does not promote the use of certain brand name drugs. By contrast, it might be in the interest of the government to reduce costs and therefore to promote use of the cheapest, but not necessarily the best, option. There are examples where drug bulletins published by government department have had 'sensitive' articles censored. A national government cannot be considered as one monolithic block, but as an umbrella for different sections, often with conflicting interests. Funding is best sought from a government department that is oriented towards public health and directly concerned with the aim of promoting rational drug use (for example, the department responsible for drug reimbursement or for the development of national health and drug policies); such a department is probably less likely to have conflicts of interest than, for example, the authorities in charge of industry development.

Institutions and non-governmental organizations

Depending on the local situation, funding for the bulletin could be secured from several other sources. These include local, national or international non-governmental organizations, universities, hospitals, professional organizations of doctors or pharmacists, health insurers, consumer organizations, donor agencies and charities.

The pharmaceutical industry

Pharmaceutical companies are never a good option to ask for funding. Sooner or later they will want to influence the contents of your bulletin. How will you write critically about a certain new drug if the company selling the drug is your main sponsor? Companies will often want a return on their investment, for instance by being named or by letting you print advertisements for their products. Concern about future funding can also lead to a less critical editorial policy or to silence on sensitive issues. A bulletin cannot be a member of ISDB if it receives funding from the pharmaceutical industry.

Case study: *Boletin AIS-COIME, Nicaragua**

Under the Sandinista Government (1979–1990) there had been strict control of the supply of drugs and drug information. After the change of Government in 1990, one of the first actions taken by the new Ministry of Health was to 'free' the drug market and allow the importation of drugs without any requirement for registration. As a result of these changes the number of private pharmacies increased, pharmaceutical industry representatives renewed their activities and there was widespread advertising of drugs in newspapers, on television and on street posters.

To address some of these problems we started our bulletin. The first two editions were published in 1992 and they denounced the unethical practice of advertising unnecessary, inappropriate or unsafe drugs (e.g. antidiarrhoeal drugs, strychnine and vitamin A-based sexual and brain stimulants). These articles prompted a national campaign in the mass media and, at a television press conference, the Ministry of Health was forced to publicly support the control of drug advertising. Subsequently, offending street posters were withdrawn in the capital. This episode stimulated us to produce an independent source of information for the country.

It took us four years to get to the stage of publishing our bulletin regularly three times a year. We were able to achieve this by 1996 once we got financial support to employ a young physician full time to develop the different activities of our organization (AIS-Nicaragua), including information, training, advocacy, networking and research. Now five medical practitioners are working in AIS. We work together in a very small room ($20m^2$) and have access to facilities such as a fax machine, photocopier, store, library and a meeting room, which we share with another NGO. The printing alone costs us US$1500. Most of the issues have been funded by European NGOs and some by the Pan American Health Organization office in Nicaragua. We are involved in all AIS activities, so only part of our time can be devoted to bulletin activities and the production process. However, we can call on a small group of physicians and nurses from different specialties in the Ministry of Health, NGOs or private practice to act as reviewers. We have a good working relationship and collaboration with the Ministry of Health drug information centre that provides us with information and reviews as needed, and also helps with the distribution of the bulletin. AIS is also an active member of the Interinstitutional Coordination for Access to Essential Medicines and the National Group for the Promotion of Evidence-Based Medicine. Participants from both networks take part in the article review process.

*AIS = Acción Internacional para la Salud (Health Action International)
COIME = Coordinadora Interinstitucional de Medicamentos Esenciales (Inter-institutional Coordination for Access to Essential Medicines)

Contributed by Benoit Marchand, Boletin AIS-COIME.

5.8 Long-term sustainability

Long-term sustainability is necessary for any bulletin. Ability to generate revenue for the services provided helps to assure long-term survival. Some bulletins charge higher subscription rates to international organizations or institutions in general. This helps to subsidise local distribution to individuals at a reduced rate or at no charge. Chapter 10 describes strategies to finance distribution and the use of differential subscription fees.

> *"Economic sustainability and impact assessment have been, and will be, a challenge. Publications like this – that do not accept any advertisements and keep a critical eye on the pharmaceutical industry and its backdoor relationship with the Ministry of Health – always have economic problems. Presently though, we do have funding for 3 years, but beyond that, we see a struggle again."*
>
> Zaeem-ul-Haq, *TheNetwork's Drug Bulletin, Pakistan* [**http://www.thenetwork.org.pk**].

In the long run, much depends on the quality of the work and the ability to establish the bulletin's usefulness to its audience as well as to funders. An established bulletin with credibility is likely to receive continued financial commitment and achieve sustainability. Satisfied users are also likely to continue subscribing to a bulletin and to recommend it to other potential users. Some bulletins involve subscribers in promoting the bulletin's usefulness.

It is important to formulate objectives for the bulletin (see Boxes 5.2 and 5.3 for examples of these), to establish your own style from the beginning, and to strive for continuity. Publishing timely overviews on specific issues of local importance, organizing seminars on certain themes, and creating annual awards are other ways of increasing the influence of the bulletin and its long-term survival.

Box 5.2 Objectives of *TheNetwork's Drug Bulletin*, Pakistan

- To provide independent drug information to doctors.
- To make health professionals aware of the latest therapeutics and research.
- To cover news items on international measures to ban or withdraw unsafe drugs.
- To voice consumers' concerns.
- To promote rational use of drugs and the essential drugs concept.

[**http://www.thenetwork.org.pk**].

Box 5.3 Mission statement and aims of *Australian Prescriber*

Mission statement

To promote the quality use of medicines by providing independent, reliable, readily accessible information about drugs and therapeutics.

Aim

Australian Prescriber is an independent review of therapeutics. It aims to provide short, direct and didactic reviews on a range of topics which will assist the readers in their professional duties.

[**http://www.australianprescriber.com**].

It is also wise to avoid too much dependence on any single source of funding. Then even if one source of support dries up the bulletin is likely to survive.

5.9 Cost-saving strategies

A number of strategies can help to reduce costs. Bulletins belonging to or linked with established organizations such as teaching institutions or hospitals tend to have an advantage in terms of human, financial, material and administrative resources. For example, you may be able to negotiate to use the organization's computers and other electronic facilities for desktop publishing. Reference materials that are already available can also be easily used.

It is best to clearly define the scope of the bulletin and its target audience. A focused activity helps limit spending while increasing the bulletin's expertise within a defined area.

It may be possible to reduce printing costs by using fewer colours or publishing fewer pages.

Distribution of a bulletin can be costly. This task, although as important as publication, is often neglected or carried out inefficiently. To save on distribution costs it is essential to find out which mailing services have the lowest rates. Establishing good links with other organizations can also be of assistance in distribution. It may be possible to reduce costs considerably by using a mechanism that is already in place. For example, in some cases a drug bulletin is distributed together with another journal, such as a national journal of a medical or pharmaceutical association. Bulletins which have a long experience of subscription, distribution and promotion can help less experiences ones. For example, as well as editorial training sessions, *la revue Prescrire* has organized special sessions on these topics for young bulletins.

Inexpensive electronic communication channels such as e-mail can be an economical means of achieving quick national and international dissemination. Similarly, more and more bulletins are starting to be published on the Internet.[2]

5.10 Key messages for starting a drug bulletin

- Identify the bulletin's target audience.
- Find out what is available locally and establish links with local organizations.
- Identify your additional needs.
- Assess what resources are available.
- Based on these assessments, set priorities for what you need and want to achieve.
- Be realistic and begin modestly.
- It is often possible to manage a good quality bulletin with modest resources.
- Sources of funding should not compromise the bulletin's editorial independence.
- The key to success is motivation and commitment. Identify ways of keeping a core group of people motivated and involved in the bulletin.

5.11 References

1. Joshi MP. University hospital-based drug information service in a developing country. European Journal of Clinical Pharmacology 1997;53:89-94.

2. Morris S. Getting started in electronic journal publishing. 4th ed. Available at: **http://www.inasp.info/psi/ejp/** (in English, French, Russian and Spanish).

6. Planning bulletin production: schedules and timing

6.1 Why is planning necessary?

When starting a new bulletin, an editor's main objective is to ensure the bulletin's quality and usefulness to readers. But very soon a second challenge appears: how to sustain production in the long term. Well-established bulletins have often experienced problems with planning, leading to delayed publication, the need to publish double issues to make up for lost time, or, in the worst case, to send letters of apology to readers.

Like any organization, a bulletin needs short-, medium- and long-term planning. Some basic principles and tools may help.

6.2 Start modestly and grow gradually

It is very tempting to cover too many aspects of drugs and therapeutics when starting a bulletin, especially if few alternative sources of information exist locally. For example, editors may wish to produce new drug assessments, alerts about adverse effects, guidelines or reviews of treatment options for specific health conditions. They may also wish to train their readers in pharmacoepidemiology, drug evaluation and pharmacoeconomics. None of the established drug bulletins began with such a wide scope, and many have chosen to limit their focus, even after years of experience. Each type of article or bulletin section requires specific skills and documentation. Too much diversification may stretch limited resources too far.

Producing good quality articles is also a long and time-consuming process involving a number of steps, including commissioning the article, outlining the topic, collection and analysis of references, writing and checking the first draft before circulation to reviewers, sending the article out for review, rewriting, verifying accuracy, and copy editing. Then come the steps of design, production, printing and dissemination. Time is also needed for ongoing editorial, administrative and financial planning, and fundraising or subscriptions management to keep the bulletin afloat.

Start with a few clear objectives, produce a few useful articles adapted to local needs, and then develop the bulletin very gradually as your resources grow. It is better to produce a quarterly bulletin regularly than a monthly bulletin that is always late. For the same reason, it is better to start, for instance, with a 4-page bulletin than with 8 or more pages. Readers appreciate a regular publication that they can include in their own training schedule. This is true whether or not they pay for the bulletin themselves.

Many established bulletins started by reprinting articles from other independent drug bulletins (after getting their permission). A commentary could be added to make such an article relevant locally.

Case study: *Folia Pharmacotherapeutica*, Belgium

Folia Pharmacotherapeutica is a monthly bulletin. The resources of the bulletin are not sufficient to be able to publish only original articles in each issue. So, the bulletin regularly includes interpretations of interesting papers, which are found by scanning the literature, and sometimes original articles are prepared for publication in the bulletin.

Contributed by Marc Bogaert, Folia Pharmacotherapeutica, Belgium
[**http://www.cbip.be**].

6.3 Develop a framework for producing articles

Chapters 7 and 8 give an overview of the steps needed to produce an article, from choice of topic to final quality controls. This can take less or more time according to the type of article produced. For example, it may take a few weeks to produce an adaptation, translation or summary of an article from another bulletin or journal, or to adapt treatment guidelines to a local audience. Producing a drug review may take a few months. An original review of therapeutic options in a controversial area may take a year or more. Your framework for planning articles will need to include the same steps for each type of article but the time needed for each step may vary. Box 6.1 gives a few reasons for differences in timing.

Box 6.1 A few examples of situations leading to variations in editorial timing

- The review process is generally shorter if an article is being translated or adapted to the local situation.
- It generally takes more time to outline the topic and edit the first draft with an external author than with a member of the editorial team.
- To obtain reports of unpublished clinical trials takes longer than a simple literature search on a familiar database.

When the editorial team is small, you may find that some authors or editors end up with too much work, especially if bulletin editing is not their only job! It is useful to draw up a production schedule that makes it easy to see who is responsible for what at any point in time. This makes it possible to evaluate each writer's and editor's workload and schedule.

Scheduling can be carried out with a small computerized database, a card index or by posting each person's work responsibilities along a timeline on a bulletin board. This should obviously allow for personal constraints, such as other professional activities, travel, personal holidays, etc. It should also include some space set aside to deal with editorial opportunities or necessities created by sudden important events (see examples in Box 6.2). It is important to update the schedule regularly, to incorporate any changes (e.g. information about articles being prepared, revised deadlines), and to circulate revised schedules to the editorial team, so that everyone involved knows about any changes.

Box 6.2 Topics which may deserve exceptionally fast publication

- Newly identified drug side effects (especially if there is no efficient national alert system).
- Serious adverse drug reactions.
- Drug withdrawals for safety reasons.
- Misleading promotional campaigns on a specific drug.
- Direct-to-consumer advertising of a new drug, not yet well-known by health professionals.
- Important regulatory decisions that change everyday practice or patients' daily lives.
- Implementation of new government policies on medicines.
- Local epidemics.
- Interpretation of important new studies.
- Letters to the Editor, controversies.

Setting aside time to discuss plans for a bulletin's editorial content helps to stimulate authors and editors and can prompt them to reconsider priorities. Box 6.3 shows an example of a production schedule. See also Section 7.2.5 in Chapter 7.

Box 6.3 Example of a production schedule

Week 1:	topic identified and article commissioned and outlined
Week 12:	first draft arrives (if author is on time!)
Week 14:	draft edited by bulletin editor
Weeks 16–18:	first circulation to reviewers (who are given 2 weeks to comment)
Weeks 19–22:	collation of comments and revision of article by bulletin editor
Weeks 22–24:	circulation of revised article (again 2 weeks for comments)
Weeks 25–28:	collation of comments and another revision of article by bulletin editor
Week 28:	near-final version of article ready for checks and controls
Week 29:	press day (checking page proofs)
Week 30:	publication

6.4 Flexible planning for each issue

Combine long-term planning of articles with short-term flexibility for each bulletin. A good way to avoid delays and interruptions in publication of the bulletin is to let editors plan to have a few articles on hand without having the production of a new issue constantly in mind. The aim is to build a stock of articles, ideally the equivalent of two or more bulletins, and to separate the planning of each bulletin issue from the production of articles. However, there is a danger with this, in that an article may become out of date if the publication is delayed too long. In that case, a literature search for recent references may be needed.

How long is too long to keep an article on hold? This varies, depending on the topic. In AIDS research, for example, it may be as short as several weeks. In some domains with little research activity it could be more than a year. Bulletins often have policies in place about how long to keep articles on hold or when to carry out an extra literature search to make sure they have missed no important new studies. For example, the French bulletin *la revue Prescrire* tries to publish all articles within three months of completion, but still after up-dating references when necessary. The experience of the German bulletin *arznei-telegramm* is that more articles need to be produced than will be needed. Articles not published in the month they are completed are usually published in the following two months.

With an ongoing stock of articles, the preparation of individual issues becomes easier and more flexible. You may choose to mix longer and shorter articles or more specialised or general topics to make the bulletin more readable. The articles may also be selected to reflect a main focus for each issue, such as misleading promotional campaigns, epidemiological reports, the time of year, international or local debates on treatment strategies or drug policy, etc. Specific articles or alerts can be included when they are in the news. Editorials can also act as position papers on topics of current interest.

Writing an article is only the first step. Do not underestimate the time needed to put together the articles, adapt their presentation and size, design a bulletin issue, and check over the text to verify that no mistakes have been made. A precise timetable is needed to help the printer meet publication dates and to organize distribution.

An easy approach is to develop an annual plan for these steps, to guide everybody involved in the process. Annual planning should take into account bulletin and printers' staff holiday times and public holidays. Planning varies from bulletin to bulletin according to how it is produced. For example, if the printer does the layout, time must be allowed between layout and printing to let the editor check the printer's work.

6.5 Allow time for delays in distribution

The time the bulletin takes to get to readers will depend on local circumstances. Where possible, the delay between completing the article and publication should be kept to a minimum so that the article is not out of date by the time it reaches readers. It may take from a few days to a month for mail delivery. The essential point is to produce the bulletin regularly and to allow time in your planning for likely delays in distribution. If you are unsure how long it takes for your bulletin to reach readers, you may want to ask a few subscribers who live far away to send you a message to let you know when they receive the bulletin. Knowing how long distribution takes also makes it easier to coordinate your editorial content with promotional activities. For example, if you decide to publish an announcement praising a review published in the last issue, you want to be sure that readers have already received the bulletin containing the review.

When the distribution of paper copies is problematic, for example if the postal service is unreliable, electronic production might be another solution. Obviously, this will depend on how well the local telecommunication system works and whether your readers have access to the Internet.

6.6 Integrate necessary sidelines into your overall planning

Some of the editorial team's activities take time, but are often neglected in overall planning. These may include, for example, acknowledgements and follow-up letters to reviewers, follow-up of letters to the editors, which sometimes require a correction or erratum in the next issue and resolution of conflicts with pharmaceutical companies (or their opinion leaders) or other institutions. The team may also prepare an annual index of drugs and topics covered in each bulletin (this work can be made easier by building the index over time by adding new entries each time a new issue is prepared).

Some of these activities can be planned for in advance, for example the preparation of the index and follow-up with reviewers. Others are unpredictable, but time needs to be set aside for them. If a bulletin is produced by a small editorial team, the editors may also be in charge of subscriptions, promotion or accounting. A realistic amount of time must of course be allowed for these time-consuming activities. There is no need to point out that financial planning and management – discussed in Chapter 5 – are also crucial.

6.7 A few principles for planning the production of a bulletin

- Start modestly and grow gradually.
- Develop a comprehensive framework for the production of articles.
- Use flexible short-term planning to produce individual issues.
- Draw up a production schedule.
- Allow time for delays in distribution.
- Integrate some flexibility into your overall planning.

7. The editorial process

7.1 Outline of the editorial process

The editors of a drug bulletin aim to produce scientifically valid information, to clarify current scientific consensus, and to help readers to optimise their therapeutic activities in the best interest of the patient.[1]

Drug bulletin editing therefore differs from producing a research paper on a scientific experiment. An article for a drug bulletin should be edited to be:

- accurate, providing a counterweight to misleading or incomplete information;
- comparative, helping the reader to choose and decide;
- transparent, showing clearly how and why conclusions are drawn;
- adapted to the needs of potential readers;
- locally relevant;
- easy to read and to retrieve in everyday practice.

Writing is not the central part of this process. It is more important to define objectives clearly, to develop a conceptual framework for an article, to search for scientific evidence and to set up an efficient quality control system. The essential tool in such a process is not the computer or the printer, but the editors' brains and their ability to take readers' needs into account, whether or not those needs are explicitly expressed.

7.2 Editing a drug bulletin

The need for independence in order to be able to produce reliable comparative information on drugs and therapeutics has already been underlined in the earlier chapters of this manual. Coming to everyday editorial practice, one has to ensure and maintain the independence of the bulletin.

7.2.1 Editorial independence

Producing good quality articles implies:

- the ability to choose useful topics with total freedom according to the readers' needs, keeping in mind that these needs may differ at times from an editor's wishes, and;
- the freedom to put patients' interests first, and not to follow a political, industrial or any other agenda that is unrelated to patients' interests;
- access to all useful scientific data, and the freedom to fight for access if necessary;
- the freedom to tell the truth, without any political, economic, commercial or administrative pressure;
- the freedom to respond to criticism and to denounce false claims or statements.

This can be achieved only by people who have total editorial independence. The international WHO meeting on drug information, held in Madrid in 1985 defined independent editors as "having no commercial or other interest in the promotion of particular patterns of drug treatment, their sole aim being to optimise such treatment in the interests of the patient and society at large".[1] The organizational structure and financial resources of the bulletin should be capable of guaranteeing the editorial team's independence.[2]

Financial independence also creates sustainability, as discussed in Chapter 5. The editorial team and bulletin may become fragile if they are too dependent on sponsors who may decide at any time to end their support. However, if a bulletin has the support of a strong network of contacts, this may prevent sudden interruption of sponsorship.

7.2.2 Strong and sustained editorial policy and a committed team

It is obviously essential to choose the appropriate authors for specific articles, but it is even more important to put together a committed bulletin team, even if this team is small and its members may change.

Many bulletins rely on two separate groups for direction and overall editorial policy:

- **the editorial team:** a local team responsible for production of articles, publication of the bulletin, and ensuring that the bulletin is meeting its editorial objectives (see Chapter 5);
- **the advisory board:** members may be local or physically distant; their role is to provide guidance on the global orientation of the bulletin, its adaptation to the readers, and short- and long-term priorities and developments (see Chapter 5).

External reviewers do not necessarily fully share the same views as the editorial team and the advisory board. They are chosen for different types of reasons (see the paragraph on reviewing below, and also Chapter 5).

7.2.3 Selecting topics for articles

The type of article produced by a bulletin will vary greatly according to circumstances, the medical and social context in which the bulletin is operating, therapeutic areas addressed, and national or local drug policy. The aim of an article may be to:

- produce a critical review of what has already been published about a therapeutic question;
- inform readers about recent events, such as an alert on a new drug side effect or a regulatory decision;
- publish results of original research, such as a local drug utilisation survey or comparisons of drug prices;
- express an opinion or campaign on a specific health problem, usually in an editorial, or a letter to the editor and its response;
- be locally relevant, by quoting local practices, brand names, regulations etc.

Because the type of article varies, the methods used to search for documentation will also vary. However, the four basic criteria outlined at the beginning of this chapter remain central: the article should be reliable, transparent, adapted to local needs and easy to use.

The selection of topics depends on the bulletin's main target audience, on the availability of other information sources, on the availability of potential competent editors and on public health priorities.

Articles that identify essential medicines or other essential therapies may be especially important if there is no good quality national formulary or guide to appropriate drug therapy, or if the basic essential drugs concept has been forgotten, as in some industrialised countries. As an example, *la revue Prescrire* of France referred to the methods used in developing countries to prevent diarrhoea because they have been almost forgotten in France. (Prévenir la diarrhée chez les jeunes enfants. Tenir compte de l'expérience des pays pauvres. *Rev Prescr* 1997;18:527-9). (Preventing diarrhoea in young children. Draw on the experience of poor countries).

In the face of excessive drug promotion, a key task may be to identify non-essential drugs. Bulletins often provide comparative information on new drugs and therapies to help readers to distinguish between real therapeutic innovations and new drugs that provide no real treatment advantage (see Chapter 8 for more detail on this). Some ISDB bulletins consider all (or nearly all) new therapeutic entities and publish a critical analysis (e.g. *Dialogo sui Farmaci*, Italy; *Information sui Farmaci*, Italy; *Pharmaca*, Croatia; *Pharma Kritik*, Switzerland; *Geneesmiddelenbulletin*, Netherlands; *la revue Prescrire*, France). Others select drugs that they consider innovative or controversial (e.g. *Drug and Therapeutics Bulletin*, UK; *Boletín Terapéutico Andaluz*, Spain; *Pharmainformation*, Austria).

As mentioned above, many countries have no pharmacovigilance system in place or have a system that does not produce enough information. In this case a major role of the bulletin is to warn readers of adverse drug reactions. See Box 7.1 for examples of actions by drug bulletins.

Box 7.1 Examples of actions by bulletins on pharmacovigilance

- In 1998, the drug bulletin of Burkina Faso, *La Lettre du Cedim*, developed the concept of pharmacovigilance in its country and called for reporting of adverse reactions.[3]
- The German bulletin *arznei-telegramm* is an example of a drug bulletin that has encouraged reporting of side effects by its own readers, developed an important data-base, and which publishes alerts or raises questions when needed.
- Some bulletins publish a regular section on drug side effects (e.g. *Dialogo sui Farmaci*, Italy; *Pharmaca*, Croatia; *la revue Prescrire*, France); a few have created a sister bulletin focused only on pharmacovigilance, like *Alerta* created by the *Boletín Terapéutico Andaluz* of Spain.

Sometimes specific topics may be especially relevant locally because reliable information is not available. For example, the former *Datis Bulletin* of Zimbabwe published original articles on intoxications with local plants, mushrooms or pesticides; *La Lettre du Cedim*, Burkina Faso, has published articles on snake bites; the Indian bulletin BODHI has published critical reviews on Indian traditional medicines; and the French bulletin *la revue Prescrire* has published critical articles and a book on homeopathic drugs.

Some bulletins also include a specific section on drug regulation to highlight relevant or irrelevant regulatory decisions and matters of regulatory policy. For example, *Drug and Therapeutics Bulletin*'s articles on how drugs get to the market (*Drug and Therapeutics Bulletin* 1990;28:101-4) or on the European licensing system (European Medicines Agency and the new licensing arrangements. *Drug and Therapeutics Bulletin* 1994;32:89-90), or the work of *la revue Prescrire* (**http://www.prescrire.org**) together with the Medicines in Europe Forum on the new European legislative framework for medicines (2004) are good examples of articles explaining regulations. Ideas for article topics can be prompted by warnings from regulatory agencies (such as "Dear Doctor" letters), or the published recommendations of institutions such as the UK National Institute for Clinical Excellence and WHO.

The choice of topics also depends on the evolution of international knowledge about medical treatments and therapeutic strategies. It is useful to screen international information sources, such as the latest editions of textbooks, the web sites of evaluation agencies in health care, the Cochrane Library, and messages on electronic forums (such as E-drug), to find areas where new, relevant consensuses or guidelines have emerged as a result of new research evidence. The appendix at the end of the manual provides a list of useful web sites and information sources.

You can also use local epidemiological data to set priorities for topics for articles. What are the most common or the most serious diseases? Collaboration with editors of epidemiological reports, centres for tropical diseases and international organizations can be helpful.

No matter what country you are in, you are likely to find it necessary to publish articles denouncing misleading promotional campaigns or warning health professionals and patients about therapeutic or pharmacoeconomic problems (e.g. the articles on prices and therapeutic value of drugs in *Worst Pills, Best Pills Newsletter* (USA) ("Cutting your drug bill while reducing your risk of avoidable adverse drug reactions: six examples" *Worst Pills, Best Pills Newsletter* February 2005) or *Butletti Groc* (Spain), "Gasto en medicamentos e innovación terapéutica" (Cost in medicine and therapeutic innovation). *Butlleti Groc* 2004;17 (4-5): 3-18 (in Catalan; French version available at *la revue Prescrire*), or the special issue of *la revue Prescrire* (France) on drug prices. Prescrire Rédaction,"Prix des médicaments: la folle envolée" (Medicine prices: shooting out of control. *Rev Prescrire* 2004; 24 (256 - Supplément):881-45). Bulletin articles may also be a means to disclose important information on drug safety, efficacy or policy that has not been published. For examples, see the articles of *BODHI* (India) on Essentiale, *TheNetwork's Drug Bulletin* (Pakistan) on chlormezanone or fluoxetine, and of *Pharmaca* (Croatia) on drug donations.

As resources are generally scarce and the supply of authors is limited, you may want to avoid some topics even if they seem interesting, for example, because:

- good quality information sources on these topics are already available locally, in which case it is better to refer to these;
- the diseases concerned are both rare and minor;
- little evidence is available; except if risky irrational therapies are being used, or the aim of an article is to highlight the lack of evidence and call for review of licensing decisions.

Do not hesitate to write articles again and again about key issues. This serves both as a reminder and to inform new readers.

7.2.4 Using and adapting existing material

Editing a good quality original article for a drug bulletin takes time. To save time, energy and resources, the exchange and adaptation of good-quality articles among bulletins may be very useful for topics that are common to different countries with similar health care conditions.

Before beginning to write an original article, it is worth checking to see whether another bulletin has already produced an article on the same topic. An article may be reproduced, translated, summarised or adapted. This avoids unnecessary waste of resources, especially for new bulletins or bulletins with few people involved. It also allows editors to concentrate their energy on local topics requiring original work. Using existing material can also help well-established bulletins to show their readers that health professionals in one country can benefit from outside experience. An article from another country or an external source may also add weight to a controversial position (see Box 7.2).

Box 7.2 Mutual support among bulletins

Many examples from ISDB show how bulletins can support each other:

- During one of the first misleading public promotional campaigns in France (the campaign on *sumatriptan*), *la revue Prescrire* contributed to a more objective appraisal of the evidence not only through its own articles, but also by publishing summaries of articles on the drug from *Geneesmiddelenbulletin*, *Drug and Therapeutics Bulletin*, *Informazioni sui Farmaci*, and *Pharma Selecta*.
- *TheNetwork* in Pakistan was able to raise questions about why *chlormezanone* was still on the market in Pakistan when other countries had withdrawn the drug, referring to articles in bulletins of countries that had taken regulatory action.
- The bulletin of the Swedish Medical Products Agency, *Information fran Läkemedelsverket*, and *la revue Prescrire* have produced a collaborative study comparing their judgement on the added therapeutic value of newly marketed drugs. The fact that these very different bulletins often reach the same conclusions gives weight to their assessments.[4]

It is sometimes possible to collaborate with local or national institutions and to reproduce their materials if the information supports rational drug use. **If foreign material is used, careful adaptation is obviously essential.** In some cases this may not be possible, for example, if the health care systems of the two countries are too different.

Specific rules govern the reproduction of existing materials (see also Section 11.5 of Chapter 11):

- Copyright rules governing periodicals, textbooks, formularies, recommendations and guidelines, as well as the publications of organizations such as WHO, non-governmental organizations, scientific societies, etc. may vary. To avoid unpleasant surprises, it is important to contact the publisher and ask about conditions for reproduction.
- Always state the source of any reprinted material, including tables, drawings and any other graphic material.

Most organizations allow reproduction of their materials and are often pleased to be able to help bulletins.

7.2.5 Planning a bulletin issue

The amount of work needed to produce a bulletin differs according to how often it is published, how many pages and sections it contains, etc. However, some basic principles generally apply:

- You need to plan the content of an issue as much in advance as possible, and especially plan lead articles well ahead of time (see Chapter 6).
- In choosing articles for different sections of the same bulletin, aim for a balanced result. For example, you can include a complex article in one section, simpler articles in another. Including a diversity of topics makes a bulletin easier and more interesting to read, but you may occasionally also want to publish a special issue on one important topic.
- Set some space aside for last minute news or brief reports, which will make the bulletin livelier and help to establish it as a source of relevant current information on drugs.
- Clearly distinguish between writing and editorial work. Authors should be given enough time to work and not have the stress of planning bulletin issues. This is the editor's task. If bulletin editors are also acting as authors, as is often the case, they will have to get used to a schizophrenic work-style!
- Editors need to have a sufficient number of good quality articles available as replacements in case an author is late or if new controversial information or evidence becomes available (see Chapter 6).
- The appearance of the bulletin, its layout, titles and sub-titles, and illustrations, lend value to the contents and are obviously of great importance. There is no universal recipe for a bulletin's style and tone. The local team, who knows the readers and cultural context, must determine this (see Chapter 9).

7.3 Writing bulletin articles

This chapter deals with general items applicable to any type of article in an independent drug bulletin. Chapter 8 focuses in more detail on a particular type of article that bulletins frequently produce: the appraisal of a newly marketed drug. As was pointed out in Chapter 6, a detailed outline of the steps involved in producing a bulletin article will help you to realistically plan its timing. This planning can either be geared to specific bulletin issues or to creating a stock of available articles to provide flexibility in the planning of each

issue. Similarly, the work of an editor of a bulletin may be more or less separate from the work of an author. Some bulletins' editorial teams also write most articles. Other bulletins maintain a separation between the tasks of authors and editors.

7.3.1 Finding and motivating authors

The ideal author, is a 'rare bird', who:

- is available;
- is a clear and rigorous thinker;
- is knowledgeable about the topic;
- can analyse data critically;
- writes clearly and concisely;
- knows and understands the audience;
- is willing to change a text after it has been reviewed;
- has time to write articles and respond to editorial queries.

All of these qualities rarely exist in one person. Collective work is unavoidable even if the team is small. Both editors and external reviewers can help to improve an author's work.

Many drug bulletins have found it difficult to identify external authors, for a variety of reasons. Specialists in a field may be out of touch with the everyday work of a clinician. They may not be able to set aside enough time to produce a good quality article. Some may have the title of 'expert' or 'specialist' but have not taken the time to update their knowledge. Others do not bother to thoroughly read and analyse the literature, even when the bulletin provides the references. They do not necessarily have experience in systematic appraisal of the evidence from clinical trials. An expert may not be used to accepting the criticisms of a rigorous review board. Finally, many have ties to the pharmaceutical industry, which may be using them as 'opinion leaders'.

It is better to select a few reliable external authors than many who will produce inadequate articles generating difficult re-editing and possible conflicts. Many editors of ISDB bulletins prefer to write draft articles themselves in-house. Instead of asking external specialists to write the articles, they ask them to act as reviewers. Once an author who is skilled and available has been chosen, it is important to provide support and direction, especially if you would like the author to finish the article and to write for the bulletin again.

- When you commission the article provide clear and concise instructions for authors. Simple general guidelines can be found in the Healthlink Worldwide publication "How to produce a newsletter".[5] But specific instructions adapted to your bulletin will be even more useful.
- Provide the author with complete documentation for the article, explaining in detail how and when the literature searches were carried out, and what other strategies were used to search for extra references. It can be risky to leave an author to search for references as s/he may be too confident in their own knowledge and less thorough in seeking other sources.
- Junior authors should be helped by support from a more experienced editor when needed.

- When an article has been accepted and published, the authors should receive acknowledgement, and payment or other rewards (see below).

7.3.2 Rewarding authors

There are many ways a bulletin's editorial team may thank authors, even if resources are scarce. As was discussed in Chapter 5, a bulletin's sustainability requires the continued motivation of contributors. Adequate acknowledgement of contributions is a key factor in keeping people involved.

You can acknowledge the author's contribution by publishing signed articles if this is your bulletin's policy. An editorial team may also choose a policy of publishing anonymous articles, either to protect authors from pressure or to acknowledge the collective nature of the work leading to a finished article. In this case, the names of all contributors can be published together at the beginning or end of each bulletin. Some bulletins, including the UK's *Drug and Therapeutics Bulletin*, prefer to publish an annual list of contributors at the end of the year.

You can pay authors for their work or give them a present, such as a reference book (guide, textbook etc.) or provide them with training sessions. Training is an especially valuable and well-appreciated reward for junior authors. However, many ISDB bulletins have found that purely voluntary writing and/or editing is rarely sustainable. Asking a valued author repeatedly to work for nothing is also embarrassing. Funds need to be found to pay authors and editors.

It is also important to keep the author informed of readers' responses. These may be enthusiastic or negative. Either way, feedback from readers can be valuable and stimulating if it is analysed collectively.

7.3.3 Writing an article

This chapter deals with general items applicable to any type of article in an independent drug bulletin. Chapter 8 focuses in more detail on a particular type of article that bulletins frequently produce: the appraisal of a newly marketed drug.

Several existing drug bulletins and other organizations have guidelines for writing articles, which you can consult for more detailed information; for example *Drug and Therapeutics Bulletin* (contact the editorial team at dtb@which.co.uk to see a copy); *la revue Prescrire* (see its web site: **http://www.prescrire.org/**).

7.3.4 Outlining the topic

This is one of the longest steps. When feasible it is helpful to organize a meeting of editors and advisers to discuss this collectively. These are the aims of the topic outline:

- to set limits for the article and agree on what **not** to include;
- to raise the questions likely to interest clinicians and patients that need to be answered;
- to determine what kind of information is needed to write the article.

You will need to distinguish clearly between what is and is not known about the topic. Box 7.3 outlines the importance of clearly separating out different types of information in an article.

Box 7.3 Avoiding a confusing mixture

A reliable and useful article should clearly separate:

Facts	from	hypothesis or extrapolation
Area of knowledge	from	area of belief
Scientific evidence	from	opinions
Clinically relevant endpoints	from	surrogate endpoints
Therapeutics	from	clinical pharmacology
Results of controlled experimental trials	from	descriptive, non-experimental data

It is also useful to think about negative influences on readers:

- false and preconceived ideas;
- traditional concepts;
- vulnerability to drug promotion;
- the force of habit.

7.3.5 Searching for documentation

The author, an editor, or a technical staff member, depending on the bulletin's resources and situation, can carry out a literature search. The aim is to gather the most reliable information needed to answer the questions raised during the previous step.

The following is an overview of the main types of sources that can be consulted, depending on the type of article being prepared, with a few examples in each category (see the appendix at the end of the manual for links to electronic sources):

- **Basic textbooks and formularies** – the most recent edition, either in print or an electronic version – remain an essential information source. Examples are *Martindale*, the *British National Formulary*, *Meyler's Side Effects of Drugs*, some WHO publications, such as the *WHO Model Formulary* etc.
- **Systematic reviews** produced by independent sources, for example, those available from the Cochrane Library, or from Clinical Evidence, or the Database of Abstracts of Reviews of Effects (DARE);
- **Guidelines issued by medico-economic evaluation bodies** like the National Institute for Clinical Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), the Canadian Centre of Health Technology Assessment (CCOHTA), the National Guidelines Clearinghouse (NGC), USA, etc.
- **Health care evaluation agencies' recommendations**, such as those of the International Network of Health Technology Assessment Agencies (INAHTA), or of national agencies.
- **Published articles in scientific and medical journals**. These are now easily retrievable from computerised international databases such as Medline or Embase. It is important to distinguish between original publications of randomised clinical trials, meta-analyses, reviews, etc. and to look carefully at the methods, study design and editorial procedures used by authors. It is often difficult for beginners to evaluate the reliability of results of published studies. It may be helpful to attend a training session in critical appraisal of journal articles, for example at an ISDB summer school or workshop. Some bulletins have

published methodology articles like "Reading Between the Lines of Clinical Trials".[6] The book How to Read a Paper by Trisha Greenhalgh is also extremely useful.[7] See also Chapter 8 for a discussion of analysis of published clinical trial results.

- **Unpublished reports of clinical trial results**. These may be obtained from the industry (through the on-line register of some companies, even if incomplete or biased, or on request), through regulatory agencies or from clinical experts. It is important to distinguish between full trial reports and abstracts, as the latter are generally of much lower quality. There is some controversy among bulletins over the use of unpublished data. Some avoid them because the reports of results have not been peer reviewed, because they may not be easily accessible to readers, or because they give too little information on the methodology to enable one to interpret the results (this is particularly true with abstracts and congress communications). Others have no systematic confidence in peer reviews. They use unpublished reports because in certain areas few or no published reports exist. This is the case for some new drugs or suspected side effects. It is also useful to make unpublished data visible in order to clarify the existing state of knowledge or underline inconsistencies.
- **Databases dealing specifically with drug side effects** such as Reactions, Current Problems, etc. Even if some are not independent, most databases of adverse drug reactions are worth looking at: the evidence is often scarce and cross-checking to verify the reliability of reports is important.
- **Databases on patients' experience,** such as the Database of Personal Experiences of Health and Illness (DIPEx).
- **Promotional material and other unreliable information**. It is very useful to find out what types of misleading claims are being made about a topic or a specific drug, in order to address these claims in the article.
- **Evaluation reports published by drug regulatory agencies,** like those provided by the U.S. Food and Drug Administration (FDA) or other national agencies, or the European Medicines Agency (EMEA). Although they may not be complete and much of their content comes from pharmaceutical companies, they are useful if cross-checked.
- **National drug utilisation data, or consumption or reimbursement data**, when available.
- **Drug prices.**

Internet literature searches and the use of computerised databases are efficient means to search for documentation, provided of course that Internet access is available, and that the person carrying out a search has the necessary training to select relevant and appropriate references. It is easy to carry out a search, but selection of references requires more editorial and clinical experience.

If you are starting a new bulletin, it is essential to know that good quality, successful articles can be based on a few well-selected information sources and that **quantity does not mean quality**. The credibility of a drug bulletin does not depend on the length of the bibliographies at the end of its articles. The references should be valid, relevant and up-to-date, avoiding speculation and opinions not based on evidence.

In some cases you may face a lack of evidence even after a thorough search for documentation. Do not hide this from the reader. You can explain what questions remain unanswered and the degree of uncertainty remaining. The article can conclude with recommendations for the most reasonable therapeutic attitude, given what is and is not currently known, and express a willingness to change if new evidence becomes available.

7.3.6 The first draft

The first draft should be developed around the central questions identified when an outline was prepared for the topic, using the results of the literature search to see if you have the information you need. Constantly keep the reader and target audience in mind and aim to produce a draft that is as concise and clear as possible, avoiding ambiguity. The Healthlink Worldwide guide to good writing[5] is a useful reference on wording, length of sentences and priorities for information presentation. Aim to build the article logically and make it easy for the reader to understand how and why you have drawn your conclusions.

The ISDB experience in training sessions is that an article should not be too long if it is to be easily understood by readers. You may be able to split a long article in to two parts. Box 7.4 presents a few tricks drug bulletin editors use to simplify technical explanations.

As an author, during the writing phase you are on your own. The first step in quality control is up to you. Reread and check the draft carefully before sending it out for review. The cleaner the draft, the more relevant reviewers' comments will be.

Box 7.4 A few ways to simplify complex articles

- Include less important facts as footnotes.
- Use boxes for practical tips, information aimed at specific readers, or to highlight a risk for patients.
- Use titles and subtitles to summarise information and provide clear conclusions. This allows readers to skim an article for key messages.
- Be obsessive about cutting and shortening sentences, especially on very technical topics such as analysis of clinical trials.
- Avoid superlatives. A therapy is rarely THE absolute best choice in any circumstance. Instead, provide clear therapeutic strategies and facilitate choice.
- Separate clear description of facts from editorial comments.
- Use the right verb tense to distinguish between things that are already known and things that should still be tested.
- Ban words that are too technical and avoid unnecessary use of abbreviations.
- If you use tables or graphs, make sure that labelling and headings are simple and clear.

7.3.7 Discuss the draft with an editor

Before circulating a draft of an article to a group of reviewers, you may want to first go through it with the bulletin's editor (if there are several, one of them, or the one who dealt with the outline) and revise it. When this is not feasible, you can act as your own editor after two or three nights of good sleep. The aim is to check the article carefully:

- how well does it correspond to the intended outline?
- do the documentation, analysis and the arguments used seem correct?
- does the article seem to be adapted to readers' needs?
- is it well presented and not too difficult to read?

This first step avoids hostile reactions from external reviewers caused by circulating inadequate drafts. Reviewers may be distracted or irritated by mistakes or simple errors that could have been corrected beforehand.

7.4 Reviewing the article

The review process varies greatly among drug bulletins according to context, resources and the type of article, but the aims are similar:

- making sure that the information contained in the article is accurate and its conclusions are valid;
- ensuring its relevance to readers' needs and its transparency;
- checking for clarity and readability.

7.4.1 How many people should review an article?

Here again quantity does not mean quality. A large reviewing board of skilled persons from different scientific and non-scientific areas (doctors, pharmacists, nurses, working in hospital and in the community, etc.) is certainly helpful, but a team of two people including a motivated, well-trained physician and a patient with experience in critical analysis may already be effective. Large review boards require management skills and a lot of follow up. Some types of articles and some uncontroversial topics require fewer reviewers than others and fewer cycles of review.

7.4.2 Should a bulletin set up a permanent review board?

The risk with a permanent board, such as an advisory board whose members review each new article, is that reviewers may have too much to do and become less critical over time, or give up from exhaustion. If the review board is selected specifically for each article, it may be better suited to the topic, for example including specialists and non-specialists interested in the topic. However, these people have less training in critical appraisal or in judging a text.

Most ISDB bulletins use a mixture of permanent reviewers, including methodologists, clinical pharmacologists and health professionals, and occasional reviewers who have a special interest or expertise in the topic. This is the recommended approach.

7.4.3 Should readers be included in the review board?

The comments of readers are very useful. Many bulletins ask readers to review articles, either as individuals or groups of clinicians. Some change their panels of readers regularly in order to get 'naïve' comments. However, this requires management staff and some resources.

7.4.4 Should patients or lay people be included?

The comments of concerned patients, contacted, for example, via patients' associations, or of lay people may be useful for drug bulletins, even if the bulletins are aimed at health professionals. If an article does not answer patients' questions adequately, it will be less useful for the clinicians who provide them with care. The opinions of patients or lay people can also be useful in selecting and outlining topics for articles.

When a bulletin is written for a consumer audience, having experienced patients review the articles can be very useful.

Family members of editors sometimes act as reviewers when resources are scarce. Their input on readability, coherence and relevance of the article can be very valuable.

7.4.5 Should the pharmaceutical industry review drafts?

ISDB bulletins have different policies on this (see Box 7.5). The selection of reviewers, as well as the selection of authors, raises the problem of conflicts of interest. It is easy to ensure that a few authors or a close editorial team have no conflicts of interest. It becomes more difficult with external reviewers especially when their number increases. Some bulletins ask reviewers to inform them in confidence of any conflicts of interest, or anything which may influence or bias their comments (e.g. *Drug and Therapeutics Bulletin*). In some cases known conflicts of interest do not prevent a bulletin from sending a draft to a reviewer. A biased opinion can be helpful. If there are weaknesses in a critical argument or if important information has been left out, a biased reviewer will be quick to notice this and point it out.

Box 7.5 Should the pharmaceutical industry see articles before publication?

Some bulletins send articles to pharmaceutical companies, before publication, preferring to get any legitimate corrections or comments before, rather than after, publication. Other bulletins choose not to, in order to avoid wasting time going back and forth with comments and counter-comments before publication. If articles are well-referenced and care is taken to present correct, unbiased information, complaints after publication are rare. If a company does send a complaint, it can easily be published in the bulletin (or put on its web site) with an editorial comment.

Whether or not an article should be sent to the pharmaceutical industry also depends on the topic. Some bulletins do this when the evidence is scarce or hidden, as on some side effects. The time between review and publication needs to be short to prevent the company from organizing a counter campaign at publication time.

If you choose to ask industry to review drafts, as with other reviewers it is important to remember your primary goals: presenting the evidence in a fair, unbiased manner, and keeping patients' best interests in mind. New bulletins should also remember that even if you do not send a draft to companies directly, they might get it from an expert who has received the draft for review.

7.4.6 Tips for reviewing articles

Whatever the size of the review board, these are some recommendations for the review process:

- circulate anonymous drafts. This greatly facilitates criticism. Some bulletins also do not name the editor and some inform reviewers that their comments will be kept confidential;
- try to get people with different therapeutic opinions to review a draft. It is always useful to find out why people may disagree with your conclusions;
- use the review process to involve specialists or health professionals in the bulletin's development and to identify future editors or authors;
- reinforce links with readers by involving them as reviewers;
- provide guidelines to reviewers explaining what you expect of them and how to present their comments (e.g. you can ask them to back their comments on scientific evidence with specific references);
- monitor the performance of reviewers.

The more effective reviewers you involve, the more difficult management becomes if you want them to receive feedback in order to maintain motivation. Electronic reviewing (e-mail) is, for example, used by the Dutch bulletin *Geneesmiddelenbulletin* to help simplify this process. However, the same amount of time and competence are needed to produce a careful evaluation of reviewers' comments whether they arrive in the post or electronically.

7.4.7 Rewarding reviewers

An important task for bulletins is to find ways to reward reviewers. This may be by mentioning their names in the bulletin and/or paying them and/or sending them a present. Many ISDB bulletins send them reference books or cheques to buy books, or offer a free subscription to the bulletin or perhaps a special issue or guide produced by the bulletin. It is useful to send feedback to reviewers on their comments. Some bulletins send personal letters, others send circular letters summarising the comments of reviewers and how they were incorporated into the article. Occasionally reviewers may ask for certificates acknowledging their role.

Some bulletins have systems in place to evaluate the quality of reviewers' work. Even without such a system, it is a good idea to check regularly if reviewers are not too overbooked, or less critical, or if some change in their professional life has affected their ability to review.

7.5. Rewriting the article

Management of reviewers' comments is not always easy and the skills of experienced editors are helpful. These are the main steps used by ISDB bulletins in rewriting articles:

- before looking at the comments some bulletins suggest that the author or the editor re-reads the article and makes his or her own comments on it;
- first consider comments from reviewers that are easy to integrate: style, wording, length of sentences, technical points with simple and clear references, etc.;

- deal with technically complex and/or controversial comments at the end, in some cases through personal contacts with the reviewers;
- in some cases, you may want to re-circulate very controversial articles to a smaller group for final consensus. Some bulletins, such as the *Drug and Therapeutics Bulletin* (UK), do this systematically.

7.6 Final checks

Few bulletins have a staff member who is specifically responsible for the final quality control of articles because of the extra cost involved. However, even small bulletins need to carry out a final step to carefully verify the accuracy of the article. Preferably someone who has not seen the article recently should do this.

These are the steps in a final quality check of an article:

- check that each time a reference is cited, the information in the article corresponds to the information in the reference (figures, dates, doses, quotations, claims, etc.);
- check that the content of tables, figures and graphs corresponds to what is stated in the text;
- make sure that editing of complicated sentences has not changed their meaning or introduced errors;
- check the article's coherence and how well it hangs together as a whole;
- make a final check of the conclusion – check that it still reflects the content of the text.

This final stage is crucial. If you omit it, the quality of articles is likely to suffer and it will be easier for critics to find flaws in the bulletin.

7.7 Follow-up after publication

The follow-up work after publication is sometimes neglected during planning for a new bulletin, yet this requires a fair bit of time and energy.

7.7.1 Indexing

A good quality, easy-to-use index makes the bulletin's contents much more accessible to readers. You will need to update the index immediately after the publication of each issue and to review regularly the use of some words, or introduce new key words. Some bulletins employ a professional indexer, but the person who selects key words must be familiar with the readers' needs.

7.7.2 Authors' certificates

Many drug bulletins publish anonymous articles. However, authors may need certificates as proof of their collaboration, for example for use in curriculum vitae. Reviewers sometimes also ask for such certificates. It is useful to have a policy concerning certificates and develop a set format for each type of certificate.

7.7.3 Post-publication correspondence

Readers often write to a bulletin, either to express their opinion or discuss technical issues. A bulletin may include a regular section with letters to the editor. Readers often welcome this approach. Even if you do not publish readers' letters, for example, if your bulletin is too short to have the available space, you will need to reply to readers' letters.

You may also receive letters of protest, for example from the drug industry and from opinion leaders close to the industry. Some bulletins make these letters public, together with the answers of the editorial team (e.g. *la revue Prescrire* on its web site: **http://www.prescrire.org/**) in order to stress the importance of transparency in scientific matters. Sometimes regulatory authorities also write when their decisions have been discussed in articles. In rare cases, bulletins have had legal action started against them (see Chapter 11). The editorial team should be prepared for these sorts of situations.

7.7.4 Corrections

A section devoted to errata, corrections or clarifications, is a good criterion for quality. Mistakes are bound to occur from time to time, and scientific matters often require supplementary information. Quality control mechanisms should be in place to avoid them as far as possible. However hard one tries to avoid making mistakes, they do arise. If the bulletin is to remain trusted, it must publish a 'correction' as soon as possible. It might feel awkward to make a correction, but it is more important to correct errors and possibly save lives, than to remain quiet in the hope that the bulletin's reputation will remain intact. The prompt publication of a correction is a way of allowing readers to see that you are honest and trustworthy.

The UK's *Drug and Therapeutics Bulletin* was the first bulletin to include a section for errata, followed by many other ISDB bulletins. Since bulletins often have a faithful readership, readers are likely to see corrections or clarifications published in the following issue. Readers should be encouraged to point out errors they notice in the bulletin or statements that are ambiguous or too vague. The corrections or clarifications need to be included in the index.

7.7.5 Requests for reproduction

When a bulletin becomes well known nationally or internationally, it begins to receive requests for reproduction of its articles. These may come from other bulletins or other periodicals, patients' associations or organizations for continuing education, in which case they cause little or no difficulty. However, they may also come from the pharmaceutical industry or industry-sponsored institutions. This requires more caution. The editorial team needs to know how a reprint will be used, for example, whether it will be used to promote a drug, or to attack a competitor's product.

The bulletin needs a clear policy on how to deal with such situations. Some ISDB bulletins have a written policy for reproduction of their articles (e.g. *Drug and Therapeutics Bulletin*, UK; *la revue Prescrire*, France). You need to make sure that the article will not be shortened, or a section reproduced out of context, and that the source will be mentioned. One concern is whether a reprint by a pharmaceutical company gives the impression of a link between this firm and the bulletin. One way used by bulletins to deal with this risk is that the bulletin produces reprints, sells them at cost to the company (i.e. without profit) and puts a stamp on the reprint saying: *"Reprinted and sold at cost by [name of the bulletin]"*.

7.7.6 Keeping track of how bulletin articles are quoted and used

In addition to official requests for reprints, bulletin articles may be quoted or reproduced without permission. In some cases this is welcome and desirable, in others not. Misleading or ambiguous use of a bulletin's content may come to the attention of the editorial team, with the help of reviewers, advisers and readers. Strong and visible written reactions can help to prevent recurrences.

7.8 References

1. WHO Regional Office for Europe. Definition of independent drug information. In: *Independent drug bulletins*. Report of an international WHO meeting on drug information, Madrid 1985:
2. International Society of Drug Bulletins Constitution. Articles of the Society. 31 March 1987.
3. Comment établir l'imputabilité des effets indésirables des médicaments? (How can we determine the causes of adverse effects of drugs?) *La Lettre du Cedim* 1998;3(1).
4. Ahlquist-Rastad J, et al. Judging the therapeutic value of drugs: a comparison between la revue Prescrire and Information fran Läkemedelsverket, the bulletin of the Swedish Medical Products Agency. *International Journal of Risk & Safety in Medicines* 2004;16:83-90.
5. Commissioning and writing. In: *How to produce a newsletter*. Rev. ed. London: Healthlink Worldwide; 1998. (Out of print, but a scanned version is available at: **http://mednet2.who.int/DrugBulletinProject/**).
6. Reading between the lines of clinical trials-I: design. *Drug and Therapeutics Bulletin* 1985;23:1-4 and "II: analysis" *Drug and Therapeutics Bulletin* 1985;23:5-8.
7. Greenhalgh T. *How to read a paper. The basics of evidence based medicine.* London: BMJ Publishing Group; 1997.

8. Reviewing a new drug: is it a therapeutic advance?

8.1 Introduction

Of the many new drug treatments that appear on the market each year (including new chemical entities, new licensed uses for existing drugs, and new formulations or methods of administration of existing drugs), only a few offer a real benefit to patients over existing treatments.[1,2] Promotional claims for these new products can make it difficult for health professionals to distinguish those that offer real benefits from those that are no better, or sometimes worse, than what is already available. By publishing reviews of new drugs, bulletins have an important role in helping their readers recognise the products that really are an advance and which deserve to be included in the list of drugs they use.

This chapter outlines the principles of how to evaluate a new drug. It is mainly for editors from established bulletins looking to develop their working practices on evaluating drugs that are new in their country. See Chapter 7 for the more general aspects of planning, writing and editing an article.

Many independent bulletins publish their own evaluation of new medicines. It is a task that demands significant and specialised resources, including the ability to access relevant data, and editors skilled in critically appraising the data. Because of the time and energy involved in reviewing a new drug, bulletin editors could think of collaborating with each other or sharing information, rather than different groups repeating the same work again and again. Even if a bulletin reuses the evaluation of another, there is still a need to take account of local circumstances (e.g. local spectrum of morbidity and mortality, inter-racial variation in the activity of metabolising enzymes, availability of services, local cost, etc.) in making a recommendation about the value of a drug (see Section 8.5.1 of this chapter for more about this).

Some bulletins have become experienced and expert at certain aspects of evaluation. For example, the group producing the Japanese bulletins *Informed Prescriber* and *Kusuri-no-Check* routinely appraise preclinical and animal data in their evaluations, in particular looking for signals of harm associated with long-term use of drugs. This particular aspect is dealt with in the annexe to this chapter.

8.2 When is a new treatment a therapeutic advance?

Before substituting an existing standard treatment with a new drug, prescribers need to be sure that the new treatment has advantages over what is already available. To be considered an advance when compared with existing treatment(s),[2] a new treatment should have:

- better efficacy, and/or
- fewer or less severe adverse effects, and/or
- safer or more convenient administration.

Therapeutic advance should not be seen in isolation. When reviewing a new drug, cost is obviously an important consideration, although it has no bearing on whether a drug is a therapeutic advance. Section 8.6 of this chapter discusses how cost is considered in the evaluation.

Questions to ask about the new drug

At the start of a review of a new treatment, there are three main questions to consider:

1. Is treatment really necessary for the patient? That is, does the drug improve the appropriate outcome(s) in the targeted population, and is it relevant to the health of your country's population? There is usually little or no available evidence from randomised controlled trials that have used appropriate outcome measures with which to answer the question (see Boxes 8.1 and 8.2 and Section 8.4 for a discussion of hierarchy of outcome measures and evidence). However, non-randomised studies, such as observational follow-up studies, with mortality as the outcome measure may be available and can be useful. For example, serum cholesterol concentrations of 6.21-6.71 mmol/L, which are considered high in western countries, occur in the healthiest people with the lowest mortality and living a normal life in Japan, and so it follows that in Japan such people should never be regarded as 'patients' with hyperlipidaemia needing treatment.[3]
2. If a treatment is necessary, is there an effective non-drug treatment?
3. If drug treatment is needed, what are the standard, or already available, drug treatments?

The next step will be to examine whether the new treatment is more effective, safer or more convenient to administer than what is already available.

8.3 Collecting evidence about the drug

8.3.1 Where to find evidence on new drugs?

The main sources of information about new drugs are:

- **ISDB member bulletins.** It is worth finding out if an independent drug bulletin has reviewed the drug already. This may save you some work. You can do this by asking bulletin editors via the ISDB electronic network (see **http://www.isdbweb.org**).

- **The pharmaceutical company.** Write to the medical director of the company that markets the product to ask for all the preclinical and clinical trial data. You may not get what you requested, but among the information supplied you may find important data indicating negative aspects of the product, such as no efficacy and/or potential or substantial evidence of harm.

  It can be interesting to see how the medicine is being promoted. If asked, the company might send copies of adverts and other promotional material (such as detail aids, mailers). You can also find evidence on how the drug is being promoted in adverts published in professional journals, in the lay press, on the company's web site, and by collecting material sent directly to health professionals. You should critically appraise the evidence on efficacy and harm, compare the results with what the company is claiming and discuss your findings in your article. (Examples of how bulletins can deal with misleading promotional claims include ▼ Is Yasmin a truly different pill? *Drug and Therapeutics Bulletin* 2002:40:57-9; ▼ Yasmin advert withdrawn – why and how. *Drug and Therapeutics Bulletin* 2003;41:17-18).

- **Regulatory authority web sites**, including the U.S. Food and Drug Administration (FDA), Japanese Pharmaceutical and Medical Device Agency (PMDA), and European Medicines Agency web sites (see the appendix at the end of the manual for addresses). Although useful, materials on these sites are usually summaries of the original full data submitted to the regulatory authority by the company that may exclude (perhaps intentionally) important findings: for example tacrolimus ointment (see Section 8An-3.5 in the annexe at the end of this chapter).

- **Web sites of authoritative drug evaluation organizations**, including the UK Committee on Safety of Medicines, UK National Institute for Clinical Excellence, etc. (see the appendix at the end of the manual for addresses).

- **Databases of published information**, e.g. PubMed. You should always do your own search to check for missing data (see Chapter 7 for a list of general sources to search).

8.3.2 What about using unpublished information?

There may be little or no published clinical trial data available when a drug is new. There is a variation in opinion among drug bulletin editors on the use of unpublished information, such as company data on file, and incomplete information, such as that published only as abstracts. Reasons for avoiding unpublished information are that it has not been peer-reviewed, and cannot be independently assessed by the bulletin's readers. However, this approach may miss important parts of the picture, because studies with positive results are more likely to be published than those with negative results (i.e. no efficacy and/or with more serious adverse effects).[4] Whatever the policy of your bulletin, it is important that it is transparent so that your readers know the basis of the advice. Some bulletins give a precise description of the documents they used in preparing an article and how they obtained them. This is useful for the bulletin's readers, and also to show those who may disagree with the recommendations of the article that the article is robust.

8.4 Evaluation in terms of efficacy, harm and convenience

8.4.1 Efficacy

Efficacy describes to what extent a drug achieves its intended effect (e.g. longer survival, reduced morbidity, pain relief, contraception).

1. Strength of the evidence

The strength of the evidence must be assessed by looking at the primary outcome measures used in the trials and at other aspects of the design of the study. The outcome measures and the design and conduct of randomised controlled trials are often inadequate, and lead to unreliable or irrelevant conclusions. Therefore careful appraisal of trial reports is needed to assess the reliability of the trial results.

When evaluating a treatment for a disease from which patients die, the most obvious and measurable outcome is whether the treatment improves survival. However, even when 'survival' is the most appropriate primary endpoint, very often in clinical trials a surrogate endpoint, such as transient symptomatic relief and/or improvement of certain laboratory tests, is used instead. The reason for this is that it allows trials to be shorter or to require the inclusion of fewer patients.

Another problem is the use of combined endpoints (e.g. definite myocardial infarction (MI) and death from MI (cause-specific morbidity and mortality)). A combined endpoint may miss important effects of treatment that actually shorten overall survival and/or lead to other serious complications.[5] The primary endpoint of real interest for patients is death from all causes, with all serious events, such as cancer, included in the endpoint. Box 8.1 shows a hierarchy of endpoints. The hierarchy is from the US National Cancer Institute and relates to evaluation of treatments for cancer, but it can be adapted to other therapeutic areas too. Box 8.2 shows a hierarchy of study design.

These hierarchies do not include non-clinical evidence, which should also be considered in an evaluation – e.g. pharmacokinetic studies, dose-ranging studies, studies in healthy volunteers, toxicology (see Box 8.1 and the annexe at the end of this chapter).

Box 8.1 Strength of endpoints (ranked in descending order)

A. Total mortality (or overall survival from a defined point in time)
Comment: This outcome is arguably the most important one to patients and is also the most easily defined and least subject to investigator bias.

B-1. Cause-specific mortality (or cause-specific mortality from a defined point in time)
Comment: Although this may be the most biologically important in a disease-specific intervention, it is a more subjective endpoint than total mortality and more subject to investigator bias in its determination. It may also miss important effects of therapy that actually shorten overall survival. For example, oestrogens in the treatment of prostate cancer.

B-2 Cause-specific morbidity alone or in combination with B-1 (*a)
Comment: It is also a more subjective endpoint than total mortality and more subject to investigator bias in its determination. It may also miss important harm induced by therapy that may actually shorten overall survival and/or quality of life.

C. Carefully assessed quality of life (i.e. assessed independently of other indicators of activity in daily life) (*b).

D. Indirect surrogates

1) Disease-free survival
2) Progression-free survival
3) Tumour response rate
4) Scales and other measures that are not clinically validated in the specific clinical condition or population (*a).

Source: Based on a hierarchy from the US National Cancer Institute web site at:
(http://www.cancer.gov/cancertopics/pdq/levels-evidence-adult-treatment/)
*a: Added by the manual's editors, to make more applicable to other diseases and interventions.
*b: If "carefully assessed quality of life" is combined with overall survival, the combined endpoint could be classified as A-2.

Box 8.2 Hierarchy of study design

1a. Systematic review (with homogeneity) of randomised controlled trials or single large-scale randomised controlled trial (mega-trial).

1b. At least a single randomised controlled trial.

2. Systematic review of cohort studies or non-randomised controlled trials.

3. Systematic review of case-control studies.

4. Case series (includes poor quality cohort and case-control studies) (*a).

5. Expert opinion without explicit critical appraisal.

Source: Based on a hierarchy from Levels of Evidence and Grades of Recommendation by Centre for Evidence-Based Medicine, Institute of Health Sciences, Oxford, UK.
[http://www.cebm.net/levels_of_evidence.asp#notes]
*a: All or none case-series (i.e. when all patients died before the treatment became available, but some now survive on it; or when some patients died before treatment became available, but none now die on it, are classified as 1c).

2. How reliable is the evidence?

It is helpful to use a checklist of strength of endpoints (e.g. as in Box 8.1) and of other design features to look out for when appraising a clinical trial. A simple validated scale such as the JADAD[6] scale is very easy for beginners to use for assessing quality of clinical trials (note: this was originally developed as an instrument for assessing a large number of clinical trials for systematic reviews and/or surveys, such as time trends of quality of clinical trials). It involves asking five questions when assessing a clinical trial:

1. Is the study randomised?
2. Is the study double blinded?
3. Is there a description of withdrawals?
4. Is the randomisation adequately described?
5. Is the blindness adequately described?

A positive answer to any question scores 1 point. Good quality randomised controlled trials score 3 points or more.

Other tools are the CONSORT statement[7] (for clinical trials) and QUORUM statement[8] (for systematic reviews), which set out standards for the reporting of clinical trials and systematic reviews. The UK "Critical Appraisal Skills Programme" (CASP) has tools for appraising various types of study on its web site [**http://www.phru.nhs.uk/casp/casp.htm**].

3. Are other key aspects of the design of the trial appropriate and relevant?

Is the test treatment and/or comparator appropriate?
Occasionally, wrong comparators are used. Examples include comparing the new drug with a non-standard treatment, with a standard treatment at suboptimal dose or at too high a dose inducing more adverse effects, or with placebo when an established treatment already exists. Another important consideration is whether the new drug used in the trials is exactly the same as the one finally marketed: i.e. the same pharmaceutical form, with the same excipients, same administration route, etc. This might have an influence on adherence to treatment, or on adverse effects, etc.

Is the study population and/or context appropriate?
Study populations and/or contexts often do not represent those where the new treatment would be applied. For example, evidence of efficacy of oseltamivir for influenza prevention is very limited in people at high risk (e.g. because of old age, chronic obstructive respiratory disease, cardiovascular disease and diabetes).[9] Nevertheless, it is licensed for influenza prevention in these populations in many countries.

Is the trial duration appropriate?
Therapies for chronic conditions need long-term studies. Check the appropriateness of the trial duration according to the purpose of the trial. Studies lasting two or three months are not sufficient to draw reliable conclusions about the benefit or harm from drugs used for life-long therapy (e.g. antihypertensive or lipid-lowering drugs). For example, it may be many years before it becomes apparent that a drug causes cancer.

Is the statistical test appropriate for the purpose of the study?
Comparative trials are often designed to prove only that the new drug is no less or only as effective as a standard treatment (non-inferiority or equivalence trials). These do not help in determining if the new drug is an advance over existing therapy. Sadly, these represent a large proportion of industry-sponsored clinical trials. A superiority test is usually reserved for trials in which the new drug is tested against placebo.

4. Could there be bias in the trial?

Consider carefully whether bias could have been introduced. It is fairly easy to check for bias:

- **at the start of the trial,** by looking for differences between the baseline characteristics of the groups. But be careful, because the p values for differences in key baseline data are sometimes close to or even less than 0.05, but authors may still claim "no difference in baseline characteristics" and make no adjustment in analysing the results.
- **during the trial** the most important thing to check is whether the trial report takes account of patients who have dropped out of the trial due to adverse reactions. This influences both the comparability of groups and the results.
- **at the end of the trial** the most important check on bias occurring is whether measurement of outcome has been manipulated, particularly when subjective outcome measures are used.[10]

5. Interpretation of results

You should look carefully at the authors' interpretation of the result. Authors often misinterpret results especially when they have conflicting interests. Look at the statistical tests, the level of significance, confidence intervals, p value and statistical power for the efficacy analysis. When analysing harm, look carefully for signs of harm from adverse events, including whether any adverse reaction is misclassified as a non-drug related adverse event (see Section 8.4.2 and the annexe at the end of this chapter for a further discussion of evaluation of harm). Secondary outcome measures of cause-specific morbidity may only be listed as adverse events when the intervention induced more morbidities.

Be aware that authors might present interpretations of results without giving the reason or a citation to validate their conclusions. For instance, the authors of the VIGOR study of rofecoxib (two employees and 11 paid consultants of the sponsor) wrote that the comparator naproxen was cardioprotective.[11] By claiming this they tried to hide the cardiotoxicity of rofecoxib.[12] Headings and abstracts which are routinely reproduced in databases like PubMed may be misleading and not supported by the data of the article.[13] **So never draw any conclusion without having read the complete original article.**

6. Do the investigators have any conflicting interests?

You should look at the declaration of interests. Is the publication written by employees of a pharmaceutical company and/or by paid consultants or by authors who declare that there are no conflicting interests? Conflicts of interests of the authors

could be the reason for interpretations of the results which cannot (completely) be understood from the data presented.

Box 8.3 summarises the areas that need to be checked when appraising the evidence. You should write about the deficiencies in the trials in your article, for example, if you find no data on overall survival related to the intervention, you should state this clearly in your assessment. However, be aware that with increasingly sophisticated manipulation of data (especially in trials sponsored by pharmaceutical companies), it may not be possible to uncover all the faults in a clinical trial.[14]

Box 8.3 Summary of what to check when appraising a clinical trial

1. What was the purpose of the study?

- Is treatment necessary? (See Section 8.2.1 and Box 8.1).
- Is the outcome measure appropriate and relevant? (See Box 8.1).
- Is an effective treatment already available?

2. How strong is the study design? (see Box 8.2)

3. Are the other key design elements of the trial appropriate and relevant?

- Is the test treatment and/or comparator appropriate?
- Is the study population and/or context appropriate?
- Is the trial duration appropriate?
- Which is appropriate: superiority, equivalence, or non-inferiority test?

4. Is bias in the study possible?

- **at start of trial:** method of randomisation; comparability of groups (difference in baseline data)
- **during and at the end of trial:** masking (blinding); patients who withdrew from the study, e.g. as a result of adverse reactions?
- **at the end of trial:** measurement of outcome – consider whether it could have been manipulated, e.g. particularly when subjective outcome measures are used.

5. Are there factors that might lead to misinterpretation of results?

- intention-to-treat analysis (ITT): was an ITT analysis planned at the outset and were the results analysed on the basis of ITT?
- efficacy analysis: statistical test, level of significance, confidence intervals, p value, statistical power,
- harm analysis: have any adverse effects been misclassified as adverse events (i.e. as unrelated to the drug treatment)?

6. Do the investigators have any conflicting interests?

8.4.2 Adverse effects/harms

New drugs are generally approved on the basis of efficacy studies with adverse outcomes considered as a secondary issue. However, adverse effects/harms are just as important a consideration as efficacy. See Section 8An-1 in the annexe at the end of this chapter for a discussion of the use of the word harm in preference to risk.

It should be remembered that much of the data mentioned in Box 8.4 will not be publicly available when the drug is new. You should ask the pharmaceutical company to provide them.

Trials of efficacy usually involve hundreds of patients, and so a rare serious adverse effect, affecting say 1 in 500 patients taking a drug, is unlikely to show up in the initial trials. Ideally, information from as many of the sources listed in Box 8.4 as possible is needed to ascertain the full risk of harm from a drug. However, much important information will not be known when a drug is new, so it is reasonable to be cautious, and make an allowance for unknown harms.

Remember, the safety of a new drug cannot be known with certainty until it has been on the market for many years.[15,16] For this reason new drugs need to be re-evaluated from time to time. As more information becomes available over time it becomes possible to use data from the various sources to ascertain the risk of harm. Watch out for any signals suggesting harm, by analysing as many data as possible, (even single case reports) from the sources listed in Box 8.4. To read more about assessing the risk of harm, including assessing causation and using animal data, and examples of the experience of the Japanese bulletins, *The Informed Prescriber* and *Kusuri-no-Check* [**http://npojip.org**], see the annexe at the end of this chapter.

Box 8.4: Data needed for full evaluation of risk of harm

1) Preclinical data (see Section 8An-3)
   - chemical characteristics, including similarities in structure to drugs that have caused serious harm (see Section 8An-3.2)
   - pharmacological tests (general, efficacy, safety)
   - toxicity tests (acute/single, subacute-chronic/repeat, carcinogenicity, genotoxicity, reproduction toxicity)
   - pharmacokinetic data on absorption, distribution, metabolism and elimination (ADME), especially on area under the curve (AUC), Cmax, t½ of the active ingredients and metabolites. Is the drug eliminated via the liver or kidney or other routes?

2) Clinical data
   - pharmacokinetic data on ADME, especially on AUC, Cmax, t½ of the active ingredients in humans and metabolites if necessary: Phase I studies
   - dose-response data
   - Phase II studies (small, preliminary efficacy and safety and dose finding or bridging trials)
   - Phase III studies (larger, randomised controlled trials).

3) Post-marketing large-scale randomised controlled trials or comparative study for long-term efficacy and safety (Phase IV).

4) Post-marketing pharmacovigilance data (post-marketing surveillance).

5) Large scale long-term epidemiological observational mortality data.

6) Epidemiological studies (ecological, case-control, cohort studies), to provide a clear picture of safety profiles, including interactions and safety in at-risk groups (such as elderly people, children, pregnant women and patients with renal failure).

7) Systematic reviews or meta-analysis of those studies above.

8) Case report(s) including legal cases (law reports, evidence given in court) and reports sent to adverse drug reaction monitoring centres.

8.4.3 Convenience

A product that is easier to use can have a benefit for patients. For example, smaller tablets, fewer daily doses, oral instead of subcutaneous administration, or shorter treatment duration could increase the likelihood of patients adhering to the treatment regimen. There might be benefits for the health service if a new product is easier to administer (e.g. oral instead of intravenous, thus saving staff time and reducing use of equipment) or safer (e.g. a preparation of a cytotoxic drug that does not need reconstituting before administration). Other aspects to consider are storage requirements (especially in warmer climates), the quality, safety and ease of handling of the packaging, and risk of errors due to similar packaging for different drugs or dosages. For examples of packaging evaluation, see the French bulletin *la revue Prescrire* and the English language edition, *Prescrire International* (Prescrire Editorial Staff. Drug packaging quality: neglected by regulatory agencies. *Prescrire Int* 2005;14(77):114. Also Prescrire Editorial Staff " 2004 Packaging awards" *Prescrire Int* 2005;14(76):66.), and patient information leaflets (risk of medication errors due to inadequate, non-understandable, non-updated information).

However, bear in mind that easier use may come at a price: fewer daily doses mean long absorption and/or elimination half-life. Consequently in some patients the blood concentration of the drug may increase due to accumulation, and high levels may persist even after the drug is stopped – leading to serious adverse reactions. For example, toxic epidermal necrolysis can be caused by various drugs; seizures can be induced by slow-release theophylline. In general, easier use can be a net disadvantage if the harm/benefit ratio of the medicine for patients increases.

8.5 Judging the overall value of the drug

Each of the three criteria above cannot be considered in isolation. You will need to make a judgement about the net benefit from the new drug in the context of existing treatments. For example, a small increase in efficacy compared with the standard treatment may not be acceptable if the new drug also has a worse adverse effect profile; a new drug might seem safer, but only because there is less experience with it or perhaps because it is being used at a lower (and so less effective dose) than alternatives (see Box 8.5 for examples); the new drug might have a different safety profile (e.g. because it is excreted by the kidney rather the liver, or is involved in different kinds of interactions), and so it might be considered useful in certain well-defined circumstances.

Box 8.5. Judging the net benefit from a new drug

Example 1. Apparently safer, but also less effective
In a short-term clinical trial, etodolac (a nonsteroidal anti-inflammatory drug first marketed in 1986 in the UK), was reported to cause less damage to the stomach than naproxen. But later the UK Drug Safety Research Unit (DSRU), using a Prescription-Event Monitoring system, rated etodolac effective in only 56% of 9109 patients. The DSRU concluded that the average daily dose of etodolac (400mg) was too low to be effective.[17]

Example 2. Trading in one type of adverse effect for another
Coxibs seem possibly less likely than conventional nonsteroidal anti-inflammatory drugs (NSAIDs) to cause dyspeptic-type symptoms and are associated with fewer endoscopically visible gastroduodenal ulcers or erosions. Epidemiological data also suggest a lower likelihood of upper gastrointestinal bleeding with celecoxib than with conventional NSAIDs. However, long-term outcome studies have not demonstrated a significant reduction in major ulcer complications (such as bleeding or perforation) with celecoxib compared with commonly used NSAIDs. An important unexpected finding of the VIGOR study was a significantly higher incidence of myocardial infarction with rofecoxib than with naproxen. Also, as experience with the recently withdrawn rofecoxib has demonstrated, there may be a 'trade-off' between better gastrointestinal tolerability with coxibs and a possible increase in the risk of serious cardiovascular events.

Source: Taking stock of coxibs. *Drug and Therapeutics Bulletin* 2005;43:1-6.

8.5.1 Considering the new drug in the local and individual context

Randomised controlled trials usually assess efficacy, i.e. the effects of a treatment when used under controlled conditions (e.g. in a precisely defined population of patients who are closely monitored). Therefore, care is needed in extrapolating research results to countries where cultures, races, etc. may differ. It is crucial to consider the value of the new drug in terms of the population and health system of your own country. For example, the effectiveness of a specific intervention may vary, depending on factors such as age, co-morbidities, pregnancy, culture, race, and also on economic and other factors (e.g. facilities for diagnosis, storage etc.).

The following are factors to consider:

- **The width of the safety margin** (i.e. the difference between toxic range and therapeutic range) of the drug. For example, the safety margins of digoxin and theophylline are both narrow, and the toxic effects are sometimes serious and can result in death. Use of these drugs (e.g. aminophylline for severe asthma) requires close monitoring, including perhaps measurement of the serum concentration of the drug. But if therapeutic drug monitoring cannot be easily done in your country because of the costs or lack of resources, these drugs cannot be safely used, especially in infants aged less than one year, even in status asthmaticus.
- **Inter-racial variation in the activity of metabolizing enzymes.** The isoenzyme cytochrome P450 (CYP) 2D6 is involved in the metabolism of several important groups of drugs, including antiarrhythmics, antidepressants and neuroleptics. Some people have CYP 2D6 isoenzymes with decreased or absent activity and so have reduced capacity to

metabolise drugs that are substrates for this enzyme, leading to their accumulation during therapy and an increased risk of unwanted effects. For example, around 7% of Caucasians, but only 1% of Asians are poor metabolisers of the antihypertensive drug debrisoquine.[18]

- **Inter-racial variation in the spectrum of susceptibility to diseases and responsiveness to treatment.** Between 20-25% of Caucasian people die from ischaemic heart disease (IHD), compared with only 7% of Japanese people. Consequently, even if the efficacy of some statins were proven in Caucasian people, the evidence may not be relevant to Japanese people and this may be the same for people living in developing countries.
- **Inter-individual variation in response to the drug.** The activities of the cytochrome P450 enzymes can also differ between individuals: e.g. the activity of isoenzyme CYP3A4 can vary up to 40-fold between individuals. As many drugs are metabolised mainly by this enzyme, the enzyme's activity can affect an individual's response to a drug.
- **Whether the development of serious adverse reactions can be predicted, prevented or detected.** The optimal dose of a drug which is eliminated entirely through the kidneys can be calculated according to the patient's renal function and monitored by therapeutic drug monitoring if possible and if necessary. However, poor metabolisers of major cytochrome P450 enzyme subtypes, who are therefore at risk of high plasma concentrations of the drugs, cannot be identified before the drug is started.
- **Whether developed serious adverse reactions should be controlled or treated.** Many adverse reactions are difficult to control once they occur, e.g. torsade de pointes, cerebral or intra-meningeal haemorrhage, stroke, pulmonary embolism, neuropathy and/or nerve injuries. These adverse reactions must be considered serious even though they are relatively uncommon. In this context, if a drug induces some mild adverse reactions preceding these serious and irreversible reactions, such a drug should be preferred. Although extrapyramidal symptoms such as dystonia, akathisia and parkinsonism are not trivial effects, they are less serious and easier to control than torsade de pointes. Sedation is an inconvenient adverse effect accompanying the treatment of urticaria or allergic rhinitis. But contrast this with the use of high doses of the non-sedating antihistamine terfenadine to avoid sleepiness which incurs a risk of hazardous cardiac arrhythmias.

8.5.2 Overall rating scales

Some bulletins use a rating scale, with a picture or shorthand phrase to indicate the overall judgement on a new drug. See Boxes 8.6 and 8.7 for examples.

Box 8.6 Rating scale for new products used by *la revue Prescrire*, France

Bravo
A real advance
Offers an advantage
Possibly helpful
Nothing new
Not acceptable
Judgement reserved

[http://www.prescrire.org]

Box 8.7 Rating scale used by *Worst Pills, Best Pills*, USA

Do not use
Limited use
Do not use until five years after release

Note that there is no "Use" category per se.

[http://www.worstpills.org/]

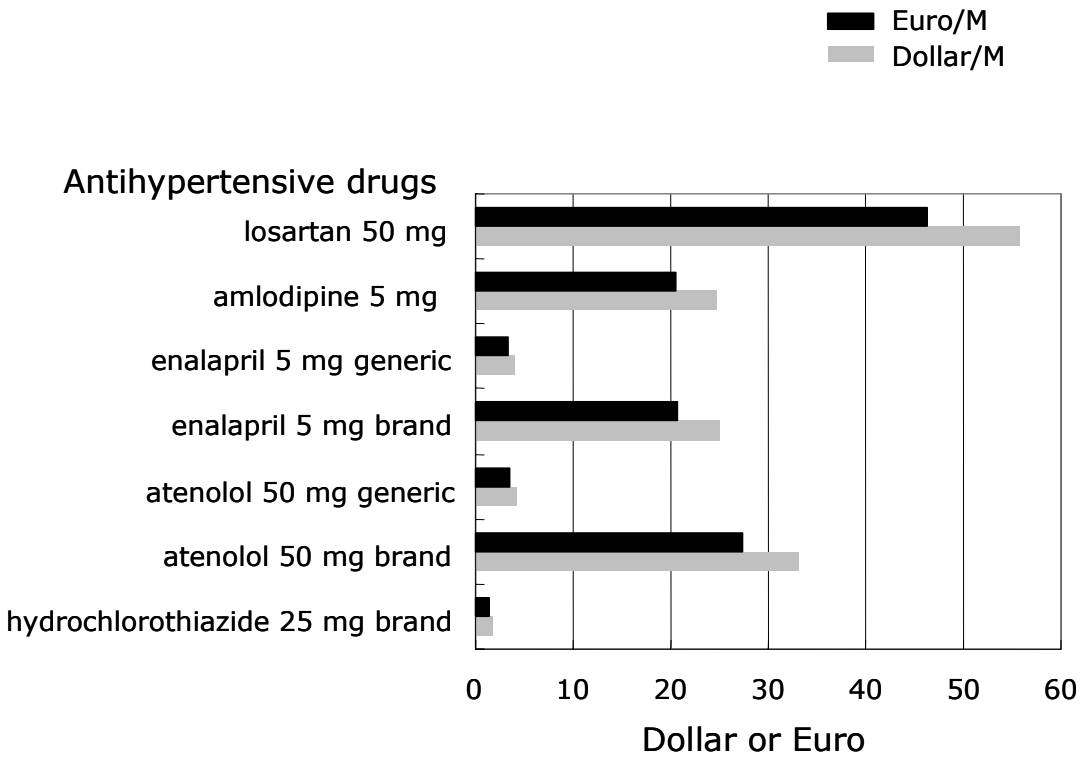
8.6 Cost

8.6.1 Compare costs in the light of true therapeutic value

Cost is obviously an important consideration in deciding whether to use a drug. So each evaluation should routinely include a price comparison for the new product and the existing alternatives. However, the influence on the choice of drug should come only when the clinical value (efficacy, safety and convenience) of the product has been established relative to standard therapies.

In general, new classes of drugs are far more expensive than the standard classical drugs. There are many examples of this: antihistamines (sedative versus less sedative); anti-depressants (tricyclic versus SSRI), anti-allergics (inhaled steroid versus leukotriene receptor antagonist), antihypertensives (diuretics versus angiotensin receptor inhibitors). But very often, the higher cost is not accompanied by any significant advantage in terms of therapeutic value. And there is always the possibility that a new drug is harmful and less effective but only more expensive than the standard drugs.

Figure 8.1 Comparative price per month of antihypertensive drugs (in Japan)



When several new drugs from the same class (e.g. less-sedative antihistamines, statins, leukotriene receptor antagonists, angiotensin receptor inhibitors) become available (so-called 'me-toos'), it is often the case that there is little difference between the drugs in the same chemical group.

Costs comparisons can be shown in various ways. Illustrated below are examples of the use of bar charts (Figures 8.1, 8.2 and 8.3) and a table (Table 8.1).

8.6.2 Comparisons should be appropriate and practical

Price comparisons should be based on the usual daily dose (or other appropriate dose), the appropriate pack size and should include at least one comparator drug (standard therapy, if available, and/or the drug(s) which has been compared with the new drug in the clinical trials. The price comparison should also cover an appropriate period of time – for instance one month for drugs which are taken long term. Antibiotics can be compared on the basis of the usual lengths of a course of treatment. Comparisons on a price-per-day basis may be misleading.

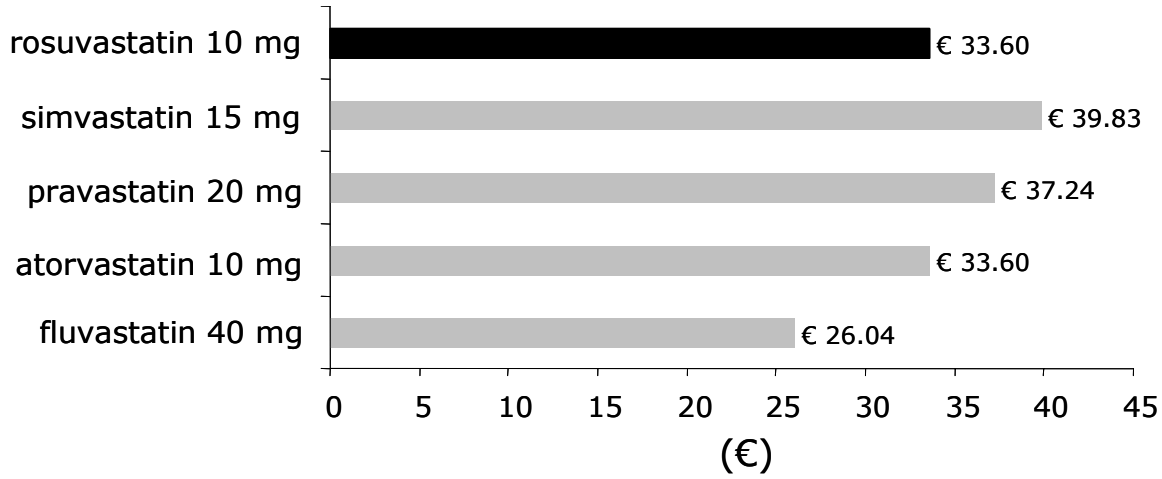
Case study: *Dialogo sui Farmaci,* Italy

When a new drug is launched that is a 'me-too' drug, the Italian bulletin *Dialogo sui Farmaci* compares the cost of the drug with other drugs in the same class, e.g. rosuvastatin versus other statins (see Figure 8.2). If instead, the new drug belongs to a new class (e.g. teriparatide for osteoporosis), the cost is compared with that of the drugs and doses used in the clinical trials of efficacy (see Figure 8.3). If the drug has been only tested against placebo, the reference drugs are those considered as first-line or standard therapy for such a condition.

Contributed by Maria Font, Dialogo sui Farmaci, Italy [**http://www.dialogosuifarmaci.it**].

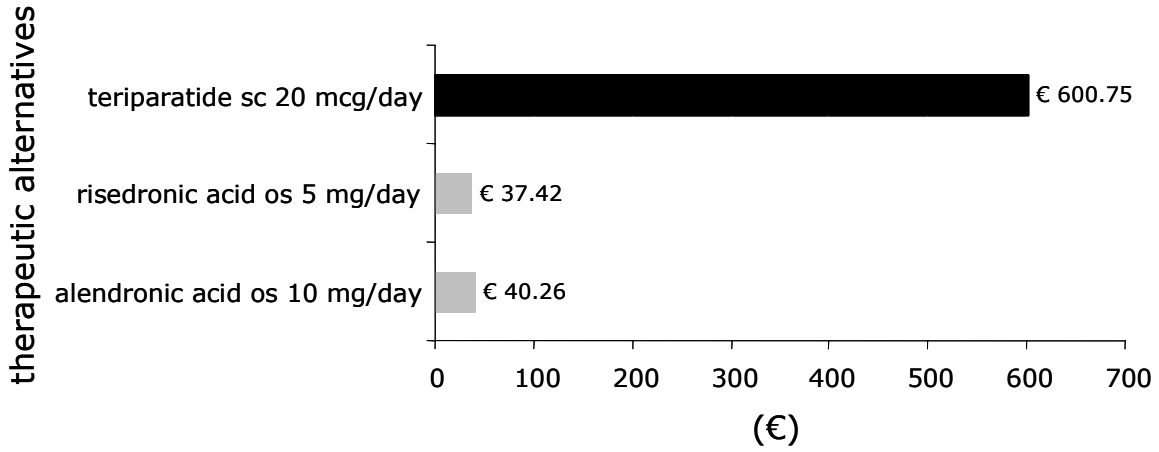
Source: *Dialogo sui Farmaci,* Italy.

Figure 8.2 Cost comparison among "me-too" drugs statins: 28 day treatment cost



Source: *Dialogo sui Farmaci,* Italy.

Figure 8.3 Cost comparison between new and standard drugs teriparatide and bisphosphonates: cost of 28 days' treatment



Source: *Dialogo sui Farmaci*, Italy.

Table 8.1 Approximate drug cost of 1 year's treatment in the UK*

Statin	Licensed daily dosage	Cost
atorvastatin	10–80 mg	£246–£613
cerivastatin**	100–400 µg	£169–£226
fluvastatin	20–80 mg	£166–£209
pravastatin	10–40 mg	£211–£387
simvastatin	10–80 mg	£235–£387

* Costs calculated from Drug Tariff and Chemist & Druggist prices, where available.
**Cerivastatin was withdrawn from the market worldwide in 2001

The drug costs of treatment for intermediate dosages of statins (e.g. atorvastatin or simvastatin) may be greater than for maximum dosages.

Source: Statin therapy – what now? *Drug and Therapeutics Bulletin* 2001; 39:17-21.

8.6.3 Bear in mind additional costs for using drugs

Bear in mind that the price charged by the company is only part of the total cost of using a drug. For instance, using the drug may involve use of equipment (e.g. for intravenous administration). Also, prescribing, dispensing, administering and monitoring of the treatment will involve the time of the doctor, pharmacist, nurse, laboratory staff and the patient. Sometimes these associated costs are considerable.

8.7 What patients need to know

Information for health professionals often only deals with what the health professional needs to know. It can be helpful to think about what the patient will want and need to know about the treatment, and to include this in a section of your article. For drug bulletins aimed at patients or the public, information for patients is essential. It might be valuable to prepare a model patient information leaflet for the drug that health professionals can give to patients. In some countries, including those in the European Union, pharmaceutical companies are required by law to include a patient information leaflet in the drug packaging. However, these are often too long and/or stereotyped, and include too much unimportant information that conceals the really important information.

Information and instructions for patients should be well balanced and explain the likely benefits and harms with short-term and long-term use of the drug. Information should be given on the individual adverse reactions (including the symptoms the patients is likely to experience as a result of the adverse reactions), when and how to stop taking the drug, or how to modify the dose according to the relief of symptoms or the development of new signs and symptoms.

Box 8.9 Examples of information for patients

Worst Pills, Best Pills (Public Citizen Health Research Group)
[**http://www.citizen.org/**]

Treatment Notes [**http://www.dtb.org.uk/dtb/tnotes/titles.htm**]

Kusuri-no-Check [**http://www.npojip.org/english/check-up1/check-up03.htm**]

United States Pharmacopeia-DI (Advice for the Patient) - searchable via Medline Plus
[**http://www.nlm.nih.gov/medlineplus/druginformation.html**]

DIPEx [**http://www.dipex.org**]

The Australian National Prescribing Service has links to consumer-friendly resources
[**http://www.nps.org.au**]

8.8 References

1. Prescrire editorial group. A review of new drugs in 2004. *Prescrire International* 2005;14:68-78. First published in French in *la revue Prescrire* 2005;25:139-48.

2. International Society of Drug Bulletins. *ISDB Declaration on Therapeutic Advance in the Use of Medicines* (in English, French, German, Italian, Portuguese, Russian, Spanish) 2001. Available at: **http://www.isdbweb.org**

3. *Kusuri-no-Check*. Available at: **http://www.npojip.org/english/sasahi/20010714.htm**

4. Melander H, Ahlqvist-Rastad J, Meijer G, Beermann B. Evidence b(i)ased medicine - selective reporting from studies sponsored by pharmaceutical industry: review of studies in new drug applications. *BMJ* 2003;326:1171-3.

5. Montori VM, Permanyer-Miralda G, Ferreira-González I, et al. Validity of composite end points in clinical trials *BMJ* 2005;330:594-6.

6. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trails: is blinding necessary? *Controlled Clinical Trials* 1996;17:1-12.

7. Begg C, Cho M, Eastwood S, Horton R, Moher D, Olkin I, Pitkin R, Rennie D, Schulz KF, Simel D, Stroup DF. Improving the quality of reporting of randomized controlled trials. The CONSORT statement. *Journal of the American Medical Association* 1996;276:637-9.

8. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of reporting of meta-analyses. *Lancet* 1999;354:1896-900.

9. Cooper NJ, Sutton AJ, Abrams KR, Wailoo A, Turner D, Nicholson KG. Effectiveness of neuraminidase inhibitors in treatment and prevention of influenza A and B: systematic review and meta-analyses of randomised controlled trials. *BMJ* 2003;326:1235-40.

10. Hayashi K and Hama R. Evaluation of oral anti-allergic drugs in Japan. *Lancet* 1996;347: 77.

11. Bombadier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. *New England Journal of Medicine* 2000; 343(21):1520-8.

12. Juni P, Nartey L, Reichenbach S, Sterchi R, Dieppe PA, Egger M. Risk of cardiovascular events and rofecoxib: cumulative meta-analysis. *Lancet* 2004;364:2021-9.

13. Kiess W, Raile K, Galler A, Kapellen T. Insulin detemir offers improved glycemic control compared with NPH insulin in people with Type 1 diabetes [letter]. *Diabetes Care* 2004;27:2567-8.

14. Sackett DL, Oxman AD. HARLOT plc.: an amalgamation of the world's two oldest professions. *BMJ* 2003;327:1442-5.

15. Lasser KE, Allen PD, Woolhandler SJ, Himmelstein DU, Wolfe S, Bor DH. Timing of new black box warnings and withdrawals for prescription medications. *JAMA* 2002;287:2215-20.

16. International Society of Drug Bulletins. ISDB EU: *Berlin Declaration on Pharmacovigilance*. 2005. (in English, French and German). Available at: **http:www.isdbweb.org**

17. Dukes G, Aronson J (eds). *Meyler's side effects of drugs*. 14th ed. Amsterdam: Elsevier; 2000.

18. Bertilsson L. Geographical/interracial differences in polymorphic drug oxidation. Current state of knowledge of cytochromes P450 (CYP) 2D6 and 2C19. *Clinical Pharmacokinetics* 1995;29:192-209.

Annexe to Chapter 8: Evaluating harm

8.An-1 Talk about harm, not risk

Health workers need to share their understanding and perceptions of benefits and harms of treatments with patients and their families as fully as possible. When doing so it is important to remember that how we personally value particular benefits and harms may well differ from how another person values them. A clinician who recommends an intervention does so believing that its benefits outweigh the harms that it can cause. In most consultations, time is too short to explain in detail what these benefits and harms are, or to find out what the patient thinks about them. Moreover, most clinicians are not practised at describing and explaining benefits and harms clearly to patients, and often they also lack important information about these aspects. Very often people use the word "risk" when they mean "harm", and this causes ambiguities and confusion. The widely used expression "benefit/risk ratio" is meaningless – no such ratio exists. Before a decision is made to use an intervention, its benefits and harms must be weighed, ideally by the clinician and the patient together. Other advantages and disadvantages, such as convenience and cost, may also be relevant. This analysis requires use of the same dimensions for considering both benefits and harms. These dimensions are obvious, but have not been generally recognised. In this context any benefit or harm has four dimensions:[1]

1. Its **nature**, described by its quality, its intensity, and its time course (onset, duration and reversibility).
2. The **probability** that it will occur.
3. Its **importance to the person experiencing it.**
4. How the benefit can be maximised or the harm **prevented** or **minimised**.

The clinician is expected to know or find out about the nature and probability of each benefit and harm, and how to maximise benefits and minimise harms. But only patients can say how they regard the hoped for benefits and the possible harms, though many need help to think clearly about them. Clinicians should identify how much the benefits matter to their patient – for example, are the benefits of taking a medicine or having an operation "worth the trouble"? – and whether a specific harm is particularly threatening or would be intolerable to that particular patient. People's fears, wishes and priorities differ greatly and unpredictably.

8.An-2 Assessment of causation of a harmful effect

A link between a harmful effect and use of a drug should be assessed according to the epidemiological method (see Box 8.10).

Box 8.10 Criteria for analysing causation

1. **Association** – any epidemiological association is observed. Bias and confounding factors should be kept in mind.
2. **Temporality** – cause should precede the effects. Was the epidemiological study properly designed so that the temporality could be proved?
3. **Consistency** – repeated observation of an association in different populations under different circumstances (different place and different time).
4. **Strength** –
   - high odds ratio
   - high significance level (low p value) or high lower limit of 95% confidence interval of odds ratio
   - dose-response relationship.
5. **Specificity** – for example, thalidomide embryopathy: association is specific.
6. **Coherence** – coherent with other evidence:
   - does not conflict with other clinical evidence
   - coherent with evidence from laboratory experiments.

Source: Based on criteria published elsewhere.[2,3]

This does not mean that you cannot assess causation from a single clinical case. If you find one or a few important cases of an adverse reaction reported in a clinical trial, search the medical literature (e.g. PubMed, Embase) for published case series and/or epidemiological analytical study reports. If only one or a few case reports can be found, these may be assessed individually with the help of an algorithm (see Box 8.11).

Box 8.11 Example of an algorithm for assessment of adverse drug reactions[4]

To assess the adverse drug reaction, answer the following questions with a pertinent score (Yes, No, Do not know)		Example
1. Are there previous conclusive reports on this reaction?	(+1, 0, 0)	0
2. Did the adverse event appear after the suspected drug was administered?	(+2, -1, 0)	2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	(+1, 0, 0)	0
4. Did the adverse reaction reappear when the drug was readministered?	(+2, -1, 0)	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	(-1, +2, 0)	-1
6. Did the reaction reappear when a placebo was given?	(-1, +1, 0)	0
7. Was the drug detected in the blood (or other fluids) in concentrations known to be toxic?	(+1, 0, 0)	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose decreased?	(+1, 0, 0)	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	(+1, 0, 0)	0
10.Was the adverse event confirmed by any objective evidence?	(+1, 0, 0)	0
	Total score*	**1**

* A total score of 9 or more suggests a definite causative link; with a score of 5–8 the link is probable; with 1–4 it is possible.

This algorithm may help when the authors of a clinical trial have concluded that an adverse event was not related to the drug under investigation. Quite often adverse events that authors have misclassified as unrelated to the treatment can be identified as suspected adverse reactions by using this algorithm. If epidemiological analytical data such as a case-control study suggest a significant relation between an adverse event and a drug, analyse the causation using the criteria listed in Box 8.11.

For example, in clinical trials of the antidiabetic agent pioglitazone, cardiovascular events such as myocardial infarction, severe palpitation necessitating hospital admission and ischaemic strokes were sometimes reported, but investigators often classified them as non-related events.[5] According to the algorithm they should be classified as 'possible' even though some cause other than the drug could have led to the reaction. Moreover, animal data for pioglitazone show dose-dependent cardiac toxicity with a similar toxicity profile to that seen in clinical trials. These findings suggest a strong link between the drug and the adverse effect and thus the cardiovascular events could be classified as 'probable' adverse reactions to pioglitazone.

Suicidal events in the clinical trials of SSRI antidepressant drugs are another notorious example.[6] They should be classified at least as 'possibly related' for the same reason.

8.An-3 Assessing coherence with preclinical data

8.An-3.1 General principles

If you want to assess whether or not any adverse events observed in the clinical trials and/or in practice are related to the treatment, not only other clinical data but also preclinical data can help greatly with assessing causality of the events.

It is important to discuss the coherence (congruence) with other evidence, especially from laboratory experiments: i.e. pharmacological tests and toxicity tests. Search for similar findings as observed in humans in the safety pharmacological tests and in the acute to chronic toxicity tests. If you find any, compare the area under the curve (AUC) values for active ingredient (preferably the unbound drug) between the animal and human. If they are close, it suggests that the adverse event observed in humans is associated with the drug. Be aware that pharmaceutical companies generally do not want to disclose critically important data for assessing risks. So ask for those important data whenever you can and search the web sites of regulatory agencies such as that of the FDA.

8.An-3.2 Chemical structure of new drugs

It may be helpful to look at the chemistry of a new drug. Comparing the chemical structure of a new drug with existing drugs may help give an impression of what kind of effects may evolve. This comparison should not be limited to drugs which are marketed for the same indication. (See Box 8.12 for examples).

Box 8.12 Examples of how a drug's chemical structure can explain its effects

Example 1. In 1990/91 torsade de pointes was reported in connection with the urinary incontinence drug terodiline.

The German bulletin *arznei-telegramm* realised that terodiline was chemically very close to the antiarrhythmic drug prenylamine which had been withdrawn from the market 10 years earlier because of fatal arrhythmias. After publication of the similarity in the drug structures and the suspicion of parallel adverse effects (*arznei-telegramm* 1991; no 8: 65) the company withdrew terodiline from the market immediately (*arznei-telegramm* 1991; no.9: 79). The manufacturer had not been aware of the chemical affinity of the two drugs before this.

Example 2. Atomoxetine is now approved for attention deficit hyperactivity disorder. It had previously been in clinical tests under the International Nonproprietary Name tomoxetine as an antidepressant drug. Atomoxetine has a lot of similarities in chemical structure with serotonin re-uptake inhibitors, like fluoxetine. This may help in understanding and assessing some of the adverse drug reactions, such as aggressive behaviour, which is seen with both drugs [*arznei-telegramm* 2005; 36: 33-4.].

Contributed by Wolfgang Becker-Brueser, arznei-telegramm, Germany [**http://www.arznei-telegramm.de**].

8.An-3.3 Considering the profile of adverse effects

The profile of pharmacological safety tests such as electrocardiogram QT interval and/or hormonal and cardiovascular effects, toxicity profile in single dose and/or repeated dose, and carcinogenicity tests can be helpful in assessing the causality of the adverse events.

8.An-3.4 Ratio of toxic and efficacy level in the same animal

The ratio of toxic and efficacy levels in the same animal is another important piece of information in assessing causality (see the example of pioglitazone below in Box 8.13).

8.An-3.5 Extrapolation of animal toxicity (safety) level to humans

a) Do not use mg/kg
b) Use Area Under the Curve (AUC)
c) If AUC is not available, then use mg/m2 (mg/kg factor 9 for mice, mg/kg factor 6 for rats).

AUC is considered the most comprehensive pharmacokinetic endpoint since it takes into account the plasma concentration of the compound and residence time in vivo (ICH-S1C[7, 8,9]). Search for AUC of the active ingredient (preferably the unbound agent) both in animals (at the maximum non-toxic dose) and humans (at the usual clinical dose). The ratio of the two is the most important safety parameter of the drug. If it is below 1 for subacute and/or chronic toxicity tests, the agent will probably be very harmful if it is used for more than three months (e.g. pioglitazone[10] [see Box 8.13] – and gefitinib[11]). If the ratio is about 1 to 3 for subacute and/or chronic toxicity test, the drug may possibly be very harmful if it is used for more than three months (e.g. the ratio for cerivastatin was almost 2).

Box 8.13 How toxicity data from animals can be used to predict clinical effects (toxicity). Example 1: pioglitazone[5, 10]

1. In rats, the dose of pioglitazone causing hypoglycaemia (3.0mg/kg/day) is about the same as that causing chronic toxicity (3.6 mg/kg/day).

2. One of the most important findings is cardiotoxicity, including
   - cardiac hypertrophy (safety level is 0.9 mg/kg/day and toxic level is 3.6 mg/kg/day)
   - cardiomyopathy with focal necrosis, cardiac/pulmonary weight increase and/or lung haemorrhage (safety level is 3.6 mg/kg/day and toxic level is 14.5 mg/kg/day).

3. These findings are important in interpreting the adverse events of pioglitazone. Myocardial infarction and/or heart failure later emerged as one of the most important adverse reactions to pioglitazone.

Contributed by Rokuro Hama, Kusuri-no-Check, Japan [**http://www.npojip.org**].

In Japan, the data cited above can be found in the New Drug Approval Package (NAP) which may be available within a few months of approval of marketing of a drug. The data are available on the Internet (Japan Pharmacists Education Center: **http://www.jpec.or.jp/**) and/or can be read as a paper document (in Japanese only). Boxes 8.14 and 8.15 show two more examples of how toxicity data in animals may predict toxic effects in humans.

Box 8.14 How toxicity data from animals can be used to predict clinical effects (toxicity). Example 2: fluticasone[12]

We received important animal toxicity data showing that inhalation of 200 micrograms of fluticasone over 52 weeks induced adrenal atrophy in dogs. Inhalation of 200 micrograms of fluticasone by a dog weighing 12 kg is equivalent to 400 micrograms/day for a human, which is within the clinical dose range.

While only 13% of prescriptions for inhaled corticosteroids were for fluticasone, 94% of the patients with adrenal crisis had used fluticasone. It was concluded that clinical doses of fluticasone may induce adrenal insufficiency, although all the reported cases used more than the recommended dose.

A paediatrician on our advisory board had a case of adrenal insufficiency associated with use of inhaled fluticasone propionate (FP). He asked how to analyse the paper reporting the epidemiological study on adrenal crisis and inhaled corticosteroids. The paper shows a very close relationship between adrenal crisis and FP. We examined the pharmacokinetics of FP in animals and in humans and also the chronic inhalation toxicity tests. These data indicated that FP has binding affinity to corticosteroid receptors that is 18 times more potent than for dexamethasone; it has an elimination half-life about 2.4 - 3 times longer (14.4 vs. 5-6 hr.) and within the usual clinical dose (400 micrograms/day) induces histologically observed adrenal atrophy in dogs. The trough level of FP rose above the detection threshold after 1 week in the phase I study. Within 6 months, several patients treated with the usual clinical dose of inhaled FP became non-responders when tested with adrenocorticotropic hormone (ACTH).

Contributed by Rokuro Hama, Kusuri-no-Check, Japan [**http://www.npojip.org**].

Box 8.15 How toxicity data from animals can be used to predict clinical effects (toxicity). Example 3: tacrolimus[13,14]

There are no definite data for carcinogenicity in humans from using tacrolimus (Protopic) ointment, because no large long-term randomised controlled trials have yet been done. But we have a 2-year mouse carcinogenicity study using 0.03% and 0.1% tacrolimus with sham and vehicle-only control, with toxicokinetic data including area under the curve (AUC), and human pharmacokinetic data including AUC.

The lower concentration (0.03%) induced more cancer (all sites) than the vehicle-only control. So it could induce malignancy in long-term clinical use. It seems reasonable to think that small infants may be more affected than adults.

On 26 June 2003, the Advisory Committee to the Japanese Ministry of Health, Labour and Welfare decided to include warnings on a potential cancer risk associated with tacrolimus ointment use, in response to the petition by *Kusuri-no-Check* and *The Informed Prescriber*[13] insisting that cancer development can be expected considering the animal carcinogenicity tests and concentration of tacrolimus in the patients treated with it.

On 10 March 2005, the U.S. Food and Drug Administration (FDA) advised health professionals to prescribe Elidel (pimecrolimus) and Protopic (tacrolimus) only as directed and only after other eczema treatments have failed to work because of a potential cancer risk associated with their use. In addition, the FDA is adding a black box warning to the health professional label for the two products and developing a medication guide for patients.

These actions follow the recommendations made by the FDA's Pediatric Advisory Committee at its 15 February 2005 meeting,[14] which reviewed findings of cancer in three different animal species. The data showed that the risk of cancer increased with the amount of the drug given, although only a few cancers had been reported in children and adults treated with Elidel or Protopic. Most of the cancers might be first apparent after several years of marketing.

On 18 May 2005, the EMEA also began to investigate the potential cancer risk of Elidel (pimecrolimus) and Protopic (tacrolimus).[15]

Contributed by Rokuro Hama, Kusuri-no-Check, Japan [**http://www.npojip.org**].

8.An-4 References

1. Herxheimer A. Communicating with patients about harms and risks. *PloS Medicine* 2005; 2 (2):e42-43. Available at: **http://medicine.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pmed.0020042**

2. Fisher FD. *An introduction to epidemiology – a programmed text.* New York: Appleton-Century-Crofts; 1975.

3. Rothman KJ, Greenland S. Causation and causal inference. In: Rothman KJ, Greenland S, editors. *Modern epidemiolog*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1998.

4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, Janecek E, Domecq C, Greenblatt DJ. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981 Aug;30(2):239-45.

5. *Pioglitazone hydrochloride, new drug approval package* (NAP). Japan Pharmacists Education Center 1999 (in Japanese). Available at: **http://www.jpec.or.jp/**

6. GlaxoSmithKline. *Study reports of paroxetine for pediatric and adolescent patients. Unipolar major depression: study 329*. Available at: **http://www.gsk.com/media/paroxetine.htm**

7. The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines. *Safety guidelines.* Available at: **http://www.ich.org/UrlGrpServer.jser?@_ID=276&@_TEMPLATE=254**

8. ICH Safety guideline S1C: *Dose selection for carcinogenicity studies of pharmaceuticals.* Available at: **http://ww.ich.org/UrlGrpServer.jser?@_ID=276&@_TEMPLATE=254**

9. *Addendum to ICH S1C:* (Addition of a limit dose and related notes). Available at: **http://www.ich.org/UrlGrpServer.jser?@_ID=276&@_TEMPLATE=254**

10. Kusuri-no-Check Editorial Team. Don't take ACTOS !!! *Kusuri-no-Check* (Check-up your Medicines) 2004;1:36-39 and 43-47. Available at: **http://www.npojip.org/english/check-up1/check-up04.htm**

11. Hama R, Sakaguchi K. Gefitinib story. *ISDB Newsletter* 2003;17(1):6-9. Available at: **http://www.npojip.org/english/The-gefitinib-story.pdf**

12. Hama R. Adrenal insufficiency induced by inhaled fluticasone propionate. *The Informed Prescriber* 2004;19:25-29. This summary will be available at the following site in a few months: **http://www.npojip.org/english/**

13. Hama R, Shimazu T. Tacrolimus (Protopic) ointment and cancer risk. *The Informed Prescriber* 2003;8:86-90. Summary is available at: **http://www.fda.gov/ohrms/dockets/ac/05/slides/20054089OPH2_09_Rokuro%20Hama%20letter.pdf** and **http://www.fda.gov/ohrms/dockets/ac/05/slides/2005-4089OPH2_10_Rokuro%20Hama%20slides_files/frame.htm**

14. U.S. Food and Drug Administration Pediatric Advisory Committee 15 February 2005. **http://www.fda.gov/ohrms/dockets/ac/05/slides/2005-4089s2.htm**

15. CHMP to look at potential cancer risk with pimecrolimus and tacrolimus. *SCRIP* No.3053, 11 May 2005: 30.

9. Design and production

The extent to which a drug bulletin is read and valued is greatly influenced by its appearance. The time and effort spent gathering information, evaluating evidence and writing articles may be wasted if the bulletin is not attractive and easy to read. This chapter explains why good design and careful production are important.

9.1 Elements of good design

To maximise the likelihood of the bulletin being read, it should be:

- **Recognisable.** Readers should recognise the bulletin when it arrives, or when they are searching for it. Having a distinctive, consistent appearance will help. This applies not only to the name of the bulletin (the masthead of the bulletin), but the overall look of the bulletin.
- **Structured**, so that readers can find their way around the bulletin. The bulletin will need 'signposts', such as contents lists and named sections to direct readers to what they want to find. These are particularly important if the bulletin contains more than 4 pages. As well as being able to see quickly what articles are in the bulletin, readers need to be able to find out easily how to respond to an article, to start a subscription, or to notify the bulletin of their new address.
- **Readable.** How clear and easy the bulletin is to read will depend in part on how the text is written (Chapter 7 discusses writing style). It will also depend on the size and style of the font (type), and width of the columns. Many font styles exist. The size depends in part on the width of the columns: the wider the column, the larger the type size needed. A font size of 10point is usually suitable for an A4 page with three columns, 11 or 12point for a two-column page, and 8 or 9point for a four-column page. The font used here is Palatino Linotype, 11point, and the heading of this section is in **Verdana 12point.**
- **Appropriate to the subject matter and target group.** You will need to judge what is acceptable to your target group. For example, readers might expect an independent drug bulletin to be quite plain in style, with little or no use of colour, as they may associate colour and glossiness with material published by the pharmaceutical industry. Too many cartoons might give the impression that the bulletin is not serious.

9.2 Creating the design

Several things must be decided when designing a bulletin:

- **Page size.** The size most commonly used by drug bulletins is A4, but a few use other sizes (e.g. the pocket-sized *Drugs Bulletin* from Chandigarh, India);

- **Number of pages.** This will depend on the type of information in the bulletin and the frequency of publication. Many independent bulletins have 2 or 4 pages and contain perhaps 2 to 4 articles, while some are around 80 pages long, and are divided into several different sections (e.g. *la revue Prescrire*, France: **http://www.prescrire.org/**; *Dialogo sui Farmaci*, Italy: **http://www.dialogosuifarmaci.it/**);
- **Choice of paper**, including colour and weight (thickness); new or recycled paper. This affects the cost of producing the bulletin;
- **Use of colour printing.** Colour can be used in many different ways. A single colour can be used to highlight boxes or headings, or to give a tinted background. Adding a single colour will probably not add much to the cost of printing. The choice of colour may be important. For example, yellow is used to colour headings in Spain's adverse drug reaction bulletin, *Butlleti Groc* ("Yellow Bulletin"): **http://www.icf.uab.es/informacion/boletines/bg/asp/bg_e.asp**.

All these features when combined and applied in a publication create its identity. Unless you have the necessary knowledge and experience to design a bulletin, it is best to work with a designer. The designer can create a template for the bulletin, defining the number of columns, the width of the columns and page margins. The designer can also develop the style and position of the permanent features, such as the name of the bulletin (the masthead), the date, issue number, page numbers, and contents list, and define the size and type of font to use for the text and for headings. A template makes it possible to know how many words fit into a page, so that the text can be edited to the right length.

There is value in reviewing the style and format of other bulletins before meeting with the designer. This helps you to communicate what you like and do not like in different designs. Readers will become familiar with the bulletin's appearance and layout, so do not be tempted to change these too often and without good reason.

Case study: *Drug Bulletin*, Eritrea

Our *Drug Bulletin* started as a 4-page publication and soon grew to 6 and then 8 pages. Until recently it was produced as a camera-ready print using Microsoft-Word. The logo was drawn using Paintbrush in an old version of Microsoft-Word, while most drawings in the subsequent bulletins were drawn using CorelDraw. The one-colour final camera-ready product was taken to the printing press on an A4 page for conversion into an A3 film. The printers were instructed to print one of the A3 faces in two colours with the remaining faces in one colour. The coloured face when folded gave the first and the last pages two colours. This minimised the production cost while giving the bulletin a better look. We always try to keep the layout of our bulletin simple and consistent in terms or fonts (types and sizes) and in two columns. We use some photos, tables and text boxes to highlight messages.

Recently we have moved to full colour using Adobe PageMaker (and InDesign), Photoshop, Illustrator for our layout. The final product is sent to printing press by CD. We use Microsoft-Word for all editing and proof reading purposes. We still believe that word processors, such as Microsoft-Word alone, can be used successfully for designing and producing a bulletin.

Contributed by Embaye Andom, Drug Bulletin, Eritrea.

9.3 Using images

Many bulletins include images in the form of photographs, drawings or cartoons. These are used to clarify the messages, to show what words cannot easily express, and can also be used to entertain the reader. Some bulletins have a picture on the front cover. For example, *TheNetwork's Drug Bulletin* (Pakistan) and *la revue Prescrire* (France) usually have drawings or cartoons on the cover and inside the bulletin; the *Sri Lanka Prescriber* includes illustrations produced by local medical students on its front covers.

Case study: *Bulletin d'Information du Médicament et de Pharmacovigilance*

Use of photography. In our article about body surface area[1], we included a photograph that was originally in the 1914 publication by Dubois and Dubois describing the derivation of the formula for body surface area (the photo was of a child born with severe hypothyroidism and the paper cast of his body). We received many congratulations from our readers for having found and published this original photography.

Use of drawings and cartoons to inform and entertain. In our article about compression stockings in the prevention of venous thromboembolism after surgery[2], many readers enjoyed the ''Giraffe model and drawings'', and the "interview" with a giraffe explaining why it didn't suffer from 'heavy legs' (an extract from a novel by Primo Levi).

1. Loewert M. Concept de surface corporelle historique et pertinence dans l'adaptation posologique ["Body surface area: historical aspects and relevance in drug dosing"]. *Bulletin d'Information du Médicament et de Pharmacovigilance* 2003; 105.
2. Rose F-X. Les bas de contention dans la prévention des thromboses veineuses profondes en chirurgie. [Compression stockings in prevention of deep vein thrombosis after surgery]. *Bulletin d'Information du Médicament et de Pharmacovigilance*. 2002; 102.

Contributed by Michel le Duff, Bulletin d'Information du Médicament et de Pharmacovigilance, France.

9.4 The production process

Once a template for the bulletin has been made, creating the layout for each issue is more straightforward. This is most commonly done using desktop publishing software (e.g. PageMaker, Quark). It involves incorporating the article text into the template to create the layout of the issue. The staff of a bulletin often includes one person (commonly called the production editor) with responsibility for production matters, including producing the layout of the bulletin issues.

It is important to be sure that the text is in as final a form as possible before it is laid out and to minimise the number of changes made after this stage. With desktop publishing it can be tempting to make lots of changes to the layout and the text, but this is also a time when mistakes can be introduced. Once the article has been laid out, its length usually needs some adjustment, and the text may have to be rearranged. For example, the headings, once imported, may be found to be too long, or the article is too long or too short, or the text falls badly, leaving a single line of a paragraph at the bottom of a page, or the layout of a table needs to be refined.

Using desktop publishing

From my practical experience, many people are scared of initiating a bulletin or newsletter because of visualising the hectic and expensive type of traditional production processes. Many printing houses are still accustomed to using traditional production processes that involve many people including the editor, a graphic designer, a typesetter, a graphic artist, and a paste-up artist etc. But with a little training on desktop publishing techniques the editor can do almost all those activities alone, and most successful publishers both in highly- and less-developed countries are now using desktop publishing.

Contributed by Embaye Andom, Drug Bulletin, Eritrea.

9.5 Developing a house style

Permanent features of the layout, such as the name of the bulletin, will already have been defined in the design of the bulletin. But style issues, such as grammar, spelling and punctuation must also be dealt with consistently in each new issue. For example, what name do you use to describe a new class of non-steroidal anti-inflammatory drugs: COX-2 inhibitors or coxibs?; do you always write out the name of an institution such as the European Medicines Agency, or is the acronym EMEA alone sufficient? Do you call clinical trials by their acronyms (e.g. VIGOR) and how do you include them in the index so that they can be retrieved easily? (See Box 9.1). The way a bulletin represents certain things needs to be consistent between the articles in an issue and between issues. To achieve this consistency, it is good practice to have a house-style guide in the form of a sheet or a booklet containing style 'rules' and to incorporate in it all new decisions about style issues when they arise. It is a good idea for a new bulletin to adopt an established bulletin's style guide while it develops its own (you could do this by contacting the editor of an ISDB member bulletin via **http://www.isdbweb.org**). Editors will need to refer to the house style during the editorial process, and it can also be used when the final checks are made during the production process.

Box 9.1 Examples of rules in a house-style guide

- Use of abbreviations, e.g. RCT, NSAID. (In general, try to avoid these).
- Drug names, e.g. beta-blockers or ß-blockers; adrenoceptors or adrenoreceptors; whether to use the generic name alone, or together with the trade name(s), whether to include the pharmaceutical company's name.
- Drug doses, e.g. whether to write units in full or abbreviated, e.g. micrograms or mg.
- Use of italics (e.g. for genus and species names for bacteria and fungi).
- Numbers: when to write out in full.
- How to cite references.

9.6 Ensuring accuracy – proof reading

Having systematic checks during the production process is crucial. For example, moving text around can result in the references being wrongly numbered. Occasionally, text can be 'lost' because of incomplete scrolling of the text using the software. After any changes have been made to the text or layout, it is important to print off and check the new version and not just read the article on the computer screen.

Before the article goes to the printer, it must be proof read. This involves checking the pages of the bulletin thoroughly: at least two or three times per page by one or more people who have not been involved in writing or editing. This should pick up spelling mistakes (computer spell checkers will not pick up typing errors such as 'for times' instead of 'four times'), the appearance and consistency of headings, subheadings, and tables, and the appearance of the text i.e. font, bold, italic and type-size (see Box 9.2).

Box 9.2 What to check before the bulletin goes to the printer

- References are correct and cited correctly (e.g. according to Vancouver Convention)
- Reference numbers are correct
- House style
- Headings
- Spellings (don't rely on the spell-checker)
- Drug doses
- Costs
- Regular parts of the bulletin that change with each issue, e.g. page numbers, headers, footers, dates.

It is worth documenting the checks (for example, by having a form or stamped box that the checker signs). This helps to ensure that no checks are missed and will also help with retracing steps to discover what went wrong in the event of a mistake (see Chapter 14 for a discussion about documentation).

Case Study: *Drug and Therapeutics Bulletin* (*DTB*), UK

DTB was started in 1962 as 4 pages every 2 weeks. In the early 1990s it changed to 8, A4-size pages once a month to save on postage costs. Each issue usually contains two or three articles. No colour is used. Articles often contain tables, but rarely illustrations.

Draft articles are prepared in Microsoft Word. During the editorial process, the article editor is responsible for critically appraising the references cited in the draft, reorganizing the draft according to house style, adding text and references if necessary, and then integrating relevant points and data arising from peer review into revised drafts. (For more information about *DTB*'s editorial process, see "How *DTB* articles are written" on the *DTB* web site: **http://www.dtb.org.uk/dtb/content/written.html**).

Checks are made at several stages. During the editorial process (while the article is being circulated to reviewers for a second time), a member of the team called the 'verifier', who is not the article's editor double checks that statements in the article are supported by the cited references. The verifier also checks house style, drug doses and any other facts. Any queries are noted and passed to the article editor to resolve. The article editor gives the final version of the draft article, at roughly the required length, to the production editor, who lays it out, using PageMaker. A copy of the formatted article is printed in the office, and any necessary adjustments to the layout are made, such as shortening headlines that are too long, or moving boxed text or tables.

Several members of the editorial team, including the article editor, then read the article carefully and discuss any errors, inconsistencies or anything that is unclear. Every time changes are made, the production editor and article editor check the changes. Just before the article goes to press, reference citations, the spelling of drug names, drug doses and costs are checked once again. Finally, the whole article is read through carefully once more.

DTB is sent to the printers as a "SEP" file by ISDN (integrated services digital network) from a MAC computer, but it could be sent by FTP (file transfer protocol – a way of telling one computer to copy files to another) also. A copy of *DTB* is faxed to the printers too, so they know what it should look like. One hundred and forty thousand copies are printed.

Contributed by Sheema Sheikh and Andrea Tarr, DTB. [**http://www.dtb.org.uk/**]

9.7 Printing

In choosing a printer, you will need to consider the quality of printing and whether printing deadlines will be met. You can find out about these by having a look at samples of materials produced by the printer, and contacting referees. Once a decision is made, it is important to monitor the printer's performance. The cost of printing depends on the number of copies needed (becoming cheaper per issue if greater numbers are printed), the quality of the paper and whether colour is used. Colour is not always much more expensive, depending on the type of printing machine used (e.g. *la revue Prescrire* was offered four colours for the same price as two colours because, for the large number of copies needed – tens of thousands – the printer had no more machines available for printing two colours, and did not want to lose the bulletin's business).

A printing schedule has to be agreed. The printer may need the bulletin files in a particular format. It may be possible to pass the desktop publishing files directly to the printer or it might be necessary to convert files into films using an image-processing house. Where an interim form is used, it is essential to check the result before taking it to the printing press. It is also necessary to know if the printer is able to deliver to the dispatch house in time for enclosing and posting out the bulletin.

Case study: *Sri Lanka Prescriber*

During the past two years we have had problems with printing. To cut down on printing costs the bulletin's publisher decided to call for tenders when selecting printers. However, such tender procedures caused delays in printing. After several discussions, the publisher agreed to use a competent printer recommended by the editorial board.

Contributed by Gita Fernando, Sri Lanka Prescriber.

9.8 Electronic publishing

The technical issues involved in electronic publishing are beyond the scope of this manual. Chapter 10 discusses some aspects of electronic distribution. Some useful information about electronic publishing in developing countries can be found on the following web sites:

- Electronic Publishing for Development [**http://www.epublishingtrust.org/**];
- International Network for the Availability of Scientific Publications (INASP) [**http://www.inasp.info/index.html**]; and
- The Association of Learned and Professional Society Publishers (ALPSP) [**http://www.alpsp.org/default.htm**].

9.9 Further reading

Albert T. Set up a newsletter. *BMJ* 1992; 305: 631-5.

How to produce a newsletter. Rev ed. London: Healthlink Worldwide; 1989. (Out of print, but a scanned version is available at: **http://mednet2.who.int/DrugBulletinProject/**).

10. Dissemination

10.1 Why dissemination is important

Bulletins are produced as a means of communication between the publisher and the readers, and such communication relies greatly on a good distribution. Nevertheless, some editors of drug bulletins may view the task of distributing the drug bulletin as an unnecessary and unwelcome burden. They may only be interested in producing good quality information and may never have learned, or even considered, how to promote or disseminate their 'message'. The importance of gaining a wide audience cannot be overestimated. In reality, planning the distribution of a bulletin should be seen as an integral part of production, in which the strategies for reaching the target audience are matched to the resources available.

Table 10.1. Financing arrangements and bulletin distribution

Source/type of financial support	Advantages	Disadvantages
Block funds provided by independent organizations such as: government departments, professional associations, consumer organizations.	• offers a means of reaching a wide readership at minimal cost or 'free of charge', for example to all doctors or pharmacists nationally.	• can affect the bulletin's independence; • vulnerable to changes in the sponsor's policies, political changes.
Funds offering indirect financial support: • bulletin included in mailings of another journal, such as medical or pharmacy journal.	• the bulletin's staff does not need to do the distribution work; • the bulletin may gain credibility among the audience from an association with a prestigious national journal.	• readers may associate the bulletin too closely with the journal, which may contain adverts or which has editorial content unrelated to the bulletin; • the bulletin has to rely on the publishing arrangements of the sponsor, and so delivery times may be delayed or schedules inconvenient.
Income from individual subscriptions.	• long-term sustainability may be better with many subscribers compared with one big sponsor; • subscription rates provide an ongoing indication of the bulletin's success; • this is efficient as only those who want to read the bulletin get it.	• much time and effort may be spent trying to find (and keep) subscribers; • in developing countries, the audience may not be able to afford the subscription fee; • those who most need the information may not subscribe.

Adequate financing is a prerequisite for good circulation (see Chapter 5). However, the wider the readership the more difficult and costly it is to distribute a bulletin. If the circulation is large the cost can sometimes be prohibitive, because, in addition to the cost of the larger print run, funding will be needed to cover such things as the cost of stamps,

envelopes and people to manage distribution (e.g. keep subscriber lists up-to-date, chase up subscribers to ensure subscription renewal, deal with subscribers' queries, run recruitment campaigns for new subscribers such as newly qualified doctors or pharmacists). All of this work needs reliable and dedicated budgetary support.

Sources of financing relate closely to distribution, in that self-financed bulletins often rely on subscriptions, while bulletins supported by a government agency or other organization are often distributed to doctors and/or pharmacists free of charge. Table 10.1 describes some key advantages and disadvantages of different financing arrangements as they relate to bulletin distribution.

10.2 Managing a subscription-based approach

Financing through subscriptions is likely to be more feasible in industrialised than in developing countries and easier for well-established bulletins. One of the advantages of subscription-based distribution is that the bulletin will not be regarded as 'unsolicited' material and so is more likely to be read by those who receive it.

To attract a critical mass of subscribers, it is helpful to have a sliding scale of fees for different types of personal and institutional subscribers, charging more to those who can afford to pay more. For example, if a bulletin is closely allied to an association of health professionals, members may pay for a bulletin as part of their membership dues, perhaps at a lower rate than non-members. Often bulletins charge only a nominal fee for students and sometimes lower fees for recently qualified health professionals. This helps to sustain future circulation, and also helps the bulletin to serve as an educational tool.

Institutions often pay a higher rate. It is normally a small item on the budget of a large institution. Public and university libraries provide a strong base for dissemination as well as a reliable source of income. The bulletin is available to many readers at once. Other institutions, such as government health agencies, may have their own specialised libraries for staff.

Bulletins frequently charge more to subscribers from developed than developing countries, more to commercial than non-commercial institutions, and more to government agencies than to non-profit groups. Still other approaches to differential pricing are, for example, reduced rates for long-term subscribers or special subscription rates for regular subscribers, or for those who automatically renew their subscription by direct transfer from their bank account. Discounted introductory rates are a way to attract new subscribers. Some bulletins differentiate by volume (single versus bulk distribution) or speed (air versus surface mail). Some charge for single issues, for example, back copies and reprints; others distribute a limited number of single issues free of charge as a way to attract subscribers. Whatever basis is used for differential pricing, the differences should be fair and not too large.

Collection of subscription fees can be time-consuming and expensive, requiring additional staff time and money. Simple tailor-made software packages are available for managing subscriptions, which can help to make the process more efficient. However, the better you know your subscribers (profession, age, etc.), with the help of in-house management, the more effectively you can promote and sell your bulletin.

Case study: *Drugs Bulletin*, India

Drugs Bulletin is published by the Department of Pharmacology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India. It is a quarterly publication, which has been published since 1976 and is funded by the Institution, a public sector organization.

The bulletin is distributed free of cost to all the medical college libraries and at a very nominal annual subscription fee of Rs.60.00 (US$1.25) for personal use. Interested readers are required to send the required subscription amount by bank drafts in the name of the Director of the Institution. Approximately 1000 copies are distributed to all corners of India. Back issues, since 1995, are available for sale. Most of the bulletin's readers are physicians working in peripheral medical/health centres. Faculty members as well as students in various medical schools are the other important categories of readers. Interestingly, although the bulletin is totally independent of the pharmaceutical industry, a substantial number of readers do in fact work in industry.

The journal is not actively marketed or advertised and most subscriptions are by word of mouth. We have now started to more actively ask for feedback from readers in order to improve the bulletin.

Contributed by Promila Pandhi, Drugs Bulletin, India
[**http://www.pgimer.nic.in/inabout.htm**].

10.3 Guidelines for effective distribution

Some suggestions for managing regular bulletin distribution:

- Prepare a detailed plan for regular distribution of the bulletin. Take into consideration the many factors that may influence the distribution processes, such as national holidays.
- Prepare alternative plans in case you encounter unexpected difficulties.
- Schedule deadlines for the timely delivery of the publication. These may involve earlier mailings for some readers, for example, those in other countries.
- Develop and maintain an up-to-date database of bulletin recipients. Information about age, educational qualifications and occupation can be useful for planning promotion of the bulletin and some aspects of content. Changes of address, new subscriptions and timing for renewal notices also need to be entered regularly. The more subscribers you have, the more important it is to maintain a well-organized database to facilitate distribution.
- You may want to prepare additional mailing lists for specific bulletin issues.
- Check the cost of using a mailing service for distribution versus mailing your bulletin in-house. If you distribute yourself, consider using self-adhesive mailing labels printed directly from your computerised database and inexpensive environmentally-friendly wrappers or envelopes for packaging.
- You may want to consider a bulk mailing arrangement, with redistribution at the point of delivery. This is often cheaper and easier than mailing directly to individual subscribers.
- Follow up to find out if your subscribers are getting their bulletins on time. You can carry out a small random survey of local and distant subscribers. If you are conducting a larger reader survey, include a question on distribution. You can also simply include a

questionnaire with the subscription renewal form: completing it at the same time as paying the subscription can prompt pertinent criticisms from subscribers, which can help the editorial team improve the bulletin.

In addition to a distribution list, you may want to reach people in your target audience who are not yet aware of the bulletin's existence. One approach is to leave copies at public places, for example reception counters and lounges, where many people tend to congregate. You can also distribute the bulletins at special events, such as meetings and exhibitions. If an event such as a conference is relevant to the bulletin's contents, you may want to mail a copy to participants or ask conference organizers to include the bulletin in their conference materials. However, if your bulletin relies on subscription, such free distribution might be risky because it can give the impression that the bulletin is regularly available free. It might be better to distribute a promotional leaflet describing the bulletin, or some extracts from the bulletin.

Case study. *Farmakoterapeutické informace*, Czech Republic

In 1995, the State Institute for Drug Control decided to launch a new independent drug bulletin *Farmakoterapeutické informace [Pharmacotherapeutic Information]*, which would deal with rational therapy, information on specific groups of drugs, and new drugs and reports of adverse drug reactions. The bulletin was to be distributed free of charge to all doctors actively practicing medicine. This publishing activity was supported by WHO, and the publishing expenses were largely borne by the Ministry of Health through the State Institute for Drug Control budget. The bulletin was published monthly in the form of 4-page issues, with a circulation of 40,000 copies, which were distributed as a no-cost appendix to the *Journal of the Czech Medical Chamber* and to the Institute´s bulletin.

Cuts in the state budget in 1997 also brought a shortage of money for our bulletin. We were pressed to make a decision about how to continue publishing. In 1998 *Farmakoterapeutické informace* became an 8-page bimonthly bulletin; 14,000 copies were distributed on subscription with physicians paying only postage, as a no-cost appendix to the Institute´s bulletin and to the Czech *JAMA* and free of charge to every hospital owned by the state (around 20 copies). In 1998 most of the expenses were paid by the Foundation of Professor Skarnitzl (a non-profit organization) cooperating with the Institute.

At the start of 1999, cooperation with the Czech Medical Chamber was resumed and the bulletin is again published monthly in the form of 4-page issues which are distributed as a no-cost appendix to the journal of the Czech Medical Chamber, the *Journal of the Czech Chamber of Pharmacists* and to the Institute´s bulletin, with a total circulation of 52,000 copies. The expenses are partially paid (a small part) by the Foundation of Professor Skarnitzl and partially by the Czech Medical Chamber and Chamber of Pharmacists.

Contributed by Blanka Pospisilova, Farmakoterapeutické informace, Czech Republic [**http://www.sukl.cz**].

Electronic distribution

Another strategy is a distribution network using electronic media. In many countries electronic communication cannot replace printed materials, especially where access to computers and the Internet is limited. Additionally, clinicians may find a well-indexed printed bulletin easier to retrieve and use in daily practice. Many editors who publish their bulletin electronically do this in addition to a printed version. INASP has several useful articles about electronic publishing on its web site [**http://www.inasp.info/index.html**].

The primary advantage of online publishing is the rapid and efficient dissemination of information. It can also be used as a marketing strategy to reach a wider audience and solicit new subscribers. For example, the entire text of a bulletin can be electronically published and sent by e-mail to a list of readers. The creation of individual Internet homepages or web sites for a bulletin is yet another way of disseminating information. If the bulletins are being distributed free of charge, publishing them on the Internet creates greater visibility to an even wider audience. If the bulletin relies on subscriptions, part of the content can be made accessible on the web site, the rest being reserved for paying subscribers.

Another form of electronic publishing is on CD-ROM. Many bulletins publish CD-ROMs containing several years' worth of back issues. This can be useful to people who do not have reliable access to the Internet, and they can provide readers with an easily accessible archive of bulletin issues.

Box 10.1 How to publish a drug bulletin electronically

There are various ways to publish a bulletin electronically. The first and simplest is to send the bulletin by e-mail as an attached file produced by a word processor. You can create an e-mail distribution list with addresses of all your subscribers. This may sound too simple, but it works well.

Another simple and straightforward system of distributing a bulletin through the Internet is by converting the contents of the publication into a web format, using HTML (Hyper Text Mark Language). This does not require highly technical and sophisticated equipment or a designer. Many word processing programmes can convert text into HTML. Examples include the latest version of Microsoft Word, Front Page and others.

Hiring a skilled designer may produce fancy results at the cost of too many graphics, leading to slower transmission, which your readers may not appreciate. Often, a simpler approach is clearer and more useful. A good example is the bulletin produced by the LANIC network (Latin American Network Information Center) of the University of Texas, called *Farmacos*.

An interesting alternative, which can – and should – be offered together with the HTML version of the bulletin is the publication of the bulletin in a PDF format. PDF is a format developed by Acrobat that permits a file to be exported, downloaded and printed locally. If you have a PostScript printer of average quality, the results will be exactly like the original but in black and white. Colour printing is also possible. To download or print PDF files you need an application called Acrobat Reader. This is available free over the Internet [**http://www.adobe.com/products/acrobat/readermain.html**]. Often, PDF file publishers include a link to the Acrobat Home Page with instructions on how to get and use Acrobat Reader. To produce PDF files from almost any desktop publisher or word processor you must use the Acrobat Printer software, which is available from Acrobat at a very reasonable price.

Apart from the advantage of letting readers print the bulletin 'as is', Acrobat Reader prevents other users from changing it. As a result, no spurious changes can be made after downloading, unlike a file produced on a word processor.

Acrobat Printer allows you to link various pages and graphics in an interactive manner, giving some life to your publication. There are several examples of bulletins distributed in this manner, including the bulletin of EURO-DURG (the Drug Utilization Research Group) [**http://www.eurodurg.com/**].

Contributed by Emilio Sanz

10.4 Communicating your bulletin's messages more widely

Traditionally, drug bulletins focus their messages on a chosen 'target' group which will usually consist of doctors or pharmacists. This group is the bulletin's constituency. It is the group which the bulletin wishes to satisfy, to which it would naturally direct any questionnaires to assess customer satisfaction, and in whose language (style, vocabulary) the material is written. There are, however, others who it is also worthwhile addressing, including the media, politicians, opinion formers, patients and consumers.

It is important to remember that, in any country, bulletins will have an unrivalled knowledge of locally appropriate treatments, because any decisions they make on the use of a treatment will have been made in the context of local knowledge about healthcare. The advice given in the bulletin will also be up-to-date, unbiased, impartial and accurate. Inevitably, and because of its work, the bulletin becomes the repository of data and sound decision-making and this resource should be widely available. Influencing groups other than the bulletin's natural target has all sorts of potential advantages (see Table 10.2), but a bulletin will need to develop a strategy if such influence is to be successful. However, it is important for the bulletin's editors to keep in mind that as bulletin representatives their areas of expertise lie within the topics that have been the subject of bulletin articles. Advising or informing on subjects outside one's area of expertise is a recipe for disaster!

Table 10.2. Advantages of influencing two non-target groups*

Group	Advantage
Media	• Exposure in the media will broaden understanding of therapeutic issues by the population at large, and may make patients and consumers more receptive to new ideas. • Because stories in the media will also be read by the bulletin's normal target group, they will remind them to read the bulletin. • Stories can provide a public health warning. If an article raises concerns about the dangers of particular treatments, affected patients may specifically consult their doctors and have the problem resolved. • When the media are approached with stories from others (industry, government), bulletins can offer an independent informed view of the issues and so minimise the publication of biased or groundless claims.
Politicians	• Politicians normally influence health policy and the better informed they are the more reliable the policy. • Politicians should respond to public demand and to respond well they need information that is reliable, accurate and impartial, and which they can trust. • Politicians may have to decide on a bulletin's funding or comment on its perceived place in society. The more they know about the bulletin the easier it will be for them to identify with (and support) your cause.

*Assuming the target groups are health professionals

Of course, there are potential disadvantages in having a policy involving addressing new and broader audiences (see Box 10.2), and these need to be taken into account before embarking upon such a policy.

Box 10.2 Potential disadvantages of involving a wider audience

- Takes extra time.
- Requires 'media' training.
- Needs senior members of staff who are prepared to be exposed to the media or other public arenas.
- Requires planning.
- May backfire if the bulletin is misquoted or the relationship 'goes wrong'.
- Exposes the bulletin to criticism.
- May anger some of the bulletin's primary target readership.
- May concern a body involved in the funding of the bulletin.

Introducing a policy of communicating with a wider audience requires the agreement of all of the bulletin's senior staff. Once this has been decided, the steps listed in Box 10.3 are worth considering. If closer working with politicians is part of the strategy, arrangements will need to be made to meet identified persons (e.g. member of parliament) and the occasion should be carefully scheduled. At the end of the session, the politician should know exactly what you do and how you do it, what your aims are, the areas in which you have expertise and can offer advice, and how s/he could contact you for advice (phone, fax and e-mail details are essential). The meeting should probably take place at your office so that the politician has a clear picture of you in your own setting.

Box 10.3 Some steps when considering working more closely with the media

- Ensure all the senior staff agree with the policy.
- Identify those who will act as communicators. They may need media training.
- Identify articles that you feel would benefit from being highlighted in the media.
- Provide a press release on the article, drawing attention to the important issues. The press release should be sent in plenty of time for the media article to be written. It should include some short quotes from the editor, a copy of the original article, an embargo date, and also the contact details of the bulletin's trained spokesperson.
- Journalists should be made aware that they can call on the bulletin at any time if they want impartial, accurate and independent advice about medical interventions.

Journalists

It is worth identifying potentially interested and capable journalists (for example, newspaper health correspondents, writers for consumer columns/publications, magazines for women, parents and elderly people, financial pages, TV and radio reporters and editors, journalists from the medical and pharmaceutical press). You should encourage those who want to get the information right and avoid those who are more interested in communicating a distorted message. It can take years to get to know and trust journalists. By sending regular press releases on selected topics, you may attract their attention so that they gradually come to consider your bulletin as a reliable source of information. In the longer term, being known as a reliable source of information can bring about a new problem, in that it can be difficult to

manage the number of journalists calling for information (for example, as many bulletins experienced because of the media interest in the Vioxx affair). If your bulletin is seen to produce articles that have clear messages for the public, you may be invited to write a regular column for a lay publication (as occurred for a Japanese bulletin). Do not miss a good chance to communicate with the public or with patients.

10.5 Key messages

In planning distribution of your bulletin, there are five key things to consider:

- the type and number of people you want to read the bulletin;
- how large a physical area your bulletin serves;
- the frequency of bulletin publication;
- alternative distribution channels available; and
- the comparative costs of various types of distribution as well as the financial resources available.

There is no single ideal way to disseminate a bulletin. What will work best for you depends on your own situation and the context in which you are working. Producing good quality information is only the first step. An effective distribution plan gets it to the people who need it.

11. Organizational and legal issues

11.1 Introduction

As soon as a group of people get together and decide to jointly establish a drug bulletin they will need some kind of organizational structure. Without an organizational structure it is difficult to agree on the mission of the group, make decisions, determine working procedures, manage finances and establish legal and contractual relationships with others. The credibility of a drug bulletin depends on a number of factors, including the quality of the information provided, the independence of the editorial board, good editorial procedures and financial independence. A sound economic and organizational base helps to provide for these.

A new bulletin may find it difficult to form its own organization at first. Many bulletins start with two or three doctors or pharmacists working from an office or their clinical practice. If the bulletin remains a small initiative its editors may feel no immediate need to create an organization. However, some of the principles regarding legal responsibility discussed in this chapter may still be relevant. Many new bulletins benefit from the hospitality of another organization. In some cases that organization becomes the bulletin's permanent home. For example, many drug bulletins are part of a medical or public health school, a health ministry, a hospital or a drug information centre. Being part of another organization has helped bulletins to become established.

Several bulletins have published notes describing the way they work and their organizational structure. This can be very helpful because it makes it clear to readers where the bulletin is from and how the work of the bulletin is undertaken. For examples see *DTB* [**http://www.dtb.org.uk/dtb/content/index.html**]; *Geneesmiddelenbulletin* [**http://www.geneesmiddelenbulletin.nl/**]; *la revue Prescrire*, [**http://www.prescrire.org/signature/qui/index.php**].

11.2 Why does a drug bulletin need a structure?

There are a several reasons why a drug bulletin needs an organizational and legal structure, either through a formal relationship with an existing organization, such as a hospital or a university, or by establishing a separate legal entity. When a non-profit organization is incorporated, it becomes a separate and distinct legal entity, possessing virtually the same powers as an individual. Thus, it acquires rights and obligations, and may own and control assets, enter into contracts, incur debts, sue and be sued. A corporation, unlike individuals, can only act through agents, namely its directors and officers.

It safeguards and maintains independence

A legal and organizational structure protects the independence of the drug bulletin. The independence of the organization is crucial for a drug bulletin and forms one of the criteria for membership of the ISDB. An organizational structure provides a means to develop formal criteria for independence and a democratic process for discussing and further developing such policies.

It can provide legal protection

An organizational and legal structure can provide the editors of a drug bulletin with protection from legal actions taken against them individually. Generally speaking, members and directors of a corporation are not liable for the defaults of the corporation (although any group planning to become a non-profit corporation should consult a legal expert in their own country about this). Individual persons become responsible for those debts and obligations only if another legal principle applies – for example, they give personal guarantees, participate in a fraudulent transaction or something of that sort. In order to tap into this limited liability concept, it is necessary for the organization to disclose its limited liability status on contracts, invoices and other similar documents. This involves making sure that the proper legal name of the organization appears on all those documents, including the "Inc." or "Incorporated" or "Ltd.", or "S.A." portion of the name, depending on the country. Directors and officers of a corporation can, however, become personally liable to third parties if they breach the duties and obligations imposed on them by law. A legal expert in your own country should be consulted about these issues, including the issues of the corporation and individuals obtaining liability insurance.

It provides financial protection and makes fundraising possible

An organizational and legal structure provides protection against financial risks for the individuals involved. The financial risks of the organization should not rest on the shoulders of individuals. Financial risk should be carried by the organization as a whole. The organization would be responsible for financial management, budgeting, bookkeeping and reporting.

Many drug bulletins raise money from government, foundations, sponsors or from individuals, for example through subscription fees. These donors will be reluctant to trust their money to a bulletin that does not have a proper organizational basis and responsible financial management. Most funding agencies and governments will not provide funding to an initiative without a formal legal structure.

It allows the bulletin to enter into contracts

In order to be able to enter into contracts with others, for example, to rent an office, hire staff, or make arrangements with a printer, the organization will need to have a separate legal identity. An informal group or a committee cannot normally make such agreements.

It facilitates the decision-making process

An organizational structure is necessary to make responsibilities clear, to facilitate decision-making processes and to help to solve problems. Most organizations establish a basis for the way they work in a set of governing rules (often referred to as a constitution or statute). A very good starting point for writing your own constitution is to collect examples from other related organizations. A lawyer can help to adapt the text to the specific needs and situation of the new bulletin and the legal requirements of the country.

11.3 Different kind of structures

The choice of structure partly depends on what the main activities of the organization will be, on how those involved with the bulletin want to regulate decision-making, and on national laws and regulations. Many ISDB drug bulletins have chosen a structure that expresses their non-profit status, such as a foundation or association. Being a non-profit organization does not necessarily mean that the bulletin makes no profits. It means that any profits made by the organization go back towards fulfilling its aims and are not paid out to members or shareholders. As discussed above, a foundation or association may be incorporated, but this is not a requirement in many countries.

11.3.1 An association

An association is a membership organization. It aims to achieve its goal through collaboration. The members therefore play an important role. An association usually has two governing bodies: the general assembly (a regular meeting of the membership), and a board. The general assembly elects the board and the board appoints the staff. The governing rules of the association state the name of the organization, the aims, the obligations of members, how meetings are called and how board members are appointed and dismissed. An association needs to have membership meetings and ways to communicate regularly with members. This may be more cumbersome to manage than an organizational structure without membership meetings, such as a foundation (see below). The advantage of an association may be that more people feel committed to the goals and dissemination of the bulletin. Membership demands organizational time and effort but in return members provide support and cooperation. A membership structure may also encourage the involvement of people who are in a position to help promote the bulletin. For example, a bulletin with members from all regions of a country may obtain national recognition. Membership of an association may be unlimited or may be restricted to certain groups.

Generally, one major benefit of unincorporated associations is the lack of strict organizational, reporting and registration requirements normally imposed on non-profit corporations. Formal documentation and organizational requirements, in addition to possibly helping the organization apply for tax-exemption status, may also help to refine and focus the goals of the organization itself. In many countries, including the USA, the main differences between an unincorporated association and a non-profit corporation are that the members of an unincorporated association can be held directly liable if someone were to sue the association, and it is problematic for unincorporated associations to have paid employees. In UK law associations are the loosest legal form. But associations as such have no legal personality in their own right. Legal form is given through the governing rules of the association. Legal liability, however, rests with the members individually and collectively, (thus any transactions, such as property purchases, are the responsibility of all the members).

In Switzerland, association members can also be held personally responsible if the association has debts that it cannot pay. However, it is possible to limit the risk for members by limiting their responsibility in the association's statutes. It may also be possible to take out a company style "legal liability" insurance policy. A legal expert from the country concerned should always be consulted.

11.3.2 A foundation

A foundation does not have members. In general a foundation is more focused on the aims it wants to achieve than on the process. A foundation has only one obligatory body namely the board with, minimally, a chairperson, secretary and treasurer. The board of the foundation is responsible for the daily running of the organization, legal representation and financial management.

A foundation also has governing rules. These may include the aims, the way board members are appointed and dismissed, and how the organization is financed. Requirements for what should be included in the statutes differ per country.

Case study: Mieux Prescrire – an association

The "Association Mieux Prescrire" is the publisher of the French drug bulletin *la revue Prescrire* and its English edition *Prescrire International*. "Mieux Prescrire" means "Better Prescribing". The aim of the association as described in the statutes is: *"to contribute, fully independently, to quality of health care, in the patients interest, by dissemination of knowledge and training of care givers (…)"*. It is a non profit association.

The founders of the bulletin chose to set up an association with a maximum of 70 members forming the General Assembly. Since 2005, all members sign a pledge for independence called "Charte Non merci" (like "No thank you" in the same spirit as "No free lunch", USA and "No grazie, pago io," (No thank you I'll pay) Italy). The membership is made up of four groups, which are called 'collèges' elected by the General Assembly. Each collège makes up a set percentage of the membership:

The founders. This group consists of people who have contributed considerably to the creation and development of the organization. The founders make up 20% of the membership.

The permanent advisory group. This group consists mainly of people from the scientific community (from France and other countries) who support the work of the association. This group makes up 20% of the membership.

The editors. This group is made up of editors of the bulletin who have been with *la revue Prescrire* for more than one year. They are elected by the other editors and make up 35% of the membership.

The readers. This group consists of readers of the bulletin, in total 25% of the membership.

The administrative council, the board of the association (20 members), is elected by the general assembly and consists of representatives of the four groups mentioned above. Members of the administrative council, of the directorate general and of the editorial team must have no conflict of interest, and sign a declaration confirming this point.

A bulletin for exchange of news among the members of the association is published for internal use and called *Les Nouvelles du Moment.*

Contributed by Danielle Bardelay, la revue Prescrire **[http://www.prescrire.org].**

Both associations and foundations can have working groups, committees, an advisory board, etc. Most countries require registration of the association or foundation with the appropriate authorities. Payment of a fee is usually required to register an association or foundation. Different countries have different registration requirements. In Finland, for instance, certain members of a foundation can be held liable for their actions.

11.3.3 Other legal entities

Depending on national laws and regulations, other non-profit organizational structures are possible. A new bulletin will benefit from consulting a legal adviser to make sure that it chooses a structure that fits the way the bulletin wants to carry out the work and the circumstances in which editors need to work. A legal adviser to a health ministry or university with which you have links can often give good advice on the best legal form to adopt when the time comes. In many countries it is not necessary to establish a venture, such as a bulletin, as a company. This may also be costly.

Case study: Therapeutic Guidelines Limited, Australia

Therapeutic Guidelines Limited (TGL) was registered on 15 July 1996 as a public not-for-profit company limited by guarantee. The objective of the organization is to improve health outcomes by producing comprehensive and independent disease-based treatment information, based on the best available evidence integrated with clinical experience. The information is designed to support health professionals in their management of patients to improve health outcomes across the community.

The company has nine directors who are appointed for 2-year terms. Because TGL arose out of activities undertaken by two other structures (the Victorian Drug Usage Advisory Committee and the Victorian Medical Postgraduate Foundation) the constitution allows for these bodies to nominate two of the directors. The Board consists of:

- one appointee of the Victorian Medical Postgraduate Foundation;
- one appointee of the relevant Commonwealth Department;
- one appointee of the Royal Australian College of General Practitioners; and
- five other persons elected by the membership of the company.

Because the members of the company have the authority to elect the majority of the directors (five), control of the company rests with its membership. Members of the company are appointed by the board, membership being open to persons or bodies corporate described as interested in the objects and purposes of the company. The company currently has 18 members.

Contributed by Mary Hemming, Therapeutic Guidelines Ltd. [**http://www.tg.com.au/**].

11.3.4 A bulletin within another organization

Many drug bulletins are part of another organization and do not need a separate legal structure (see also Chapter 13). This can have advantages and risks. One advantage is that the editors and bulletin team can focus on the editing of a bulletin because others are doing a lot of the organizational and administrative work. A larger organization may also provide protection against legal action. In some cases it may increase the credibility of a bulletin, for example, if it is linked with a reputable medical school, a health ministry, a drug information centre or consumer organization. The risk of being part of another organization is loss of independence and vulnerability if others have control over decisions about the existence of the bulletin. If one day the ministry decides to no longer publish the bulletin there is little you can do. This is particularly the case when the bulletin is also financially dependent on

the organization under whose umbrella it operates. Another risk is the explicit or implicit censorship and loss of independence to please the 'mother' organization.

The relationship between the editors or bulletin team and the other organization may, in some places, be thought of as an 'agent/principal' relationship. A disadvantage of this structure is that, under certain circumstances, the actions of the 'agent' (the editors) can legally bind the 'principal' organization, even though the organization may not have given permission for the 'agent' to act. A legal adviser should always be consulted when creating a drug bulletin as part of another organization.

A bulletin that is part of an existing structure does not need to draft a constitution. However, it will need to formulate a mission statement outlining its goals and how the bulletin will try to achieve them. The bulletin will also need to draw up rules for the editorial process to assure information quality and safeguard editorial independence (see Chapters 5 and 7). There needs to be a clear agreement on the working relationship between the two organizations and a set of rules that protect the independence of the bulletin.

Case study: *Australian Prescriber*

At one time *Australian Prescriber* was published by Australia's national Department of Health and Ageing. The Department of Health was cooperative and did not interfere in the editorial work of the bulletin. The content of the bulletin was determined by health professionals rather than the Department even though the editorial board was appointed by the Minister of Health. The editorial board was advised by an advisory editorial panel, which consisted of Australia's medical and pharmacy colleges and societies. This arrangement enabled *Australian Prescriber* to be sent to all doctors, dentists and pharmacists. Readership surveys showed that readers considered the journal to be reliable because it was semi-official and not promoting a particular product.

However, with this arrangement, there was always a risk of losing the funding. Many years ago this actually happened to *Australian Prescriber*, but due to protests - and an election - the bulletin was started up again.

One useful thing about being published by the national Department of Health was that it would be very difficult to take legal action against the Government unless something that was published was very wrong or defamatory.

The Department of Health and Ageing later established an organization to promote good prescribing in Australia: the National Prescribing Service has been set up as a private company funded by the Australian Government. As the National Prescribing Service is at 'arm's length' from government it can act independently. *Australian Prescriber* is now published by the National Prescribing Service under this new corporate structure.

Contributed by John Dowden, Australian Prescriber
[**http://www.australianprescriber.com**].

11.4 How to deal with legal action

The first rule in dealing with legal action is to avoid it. A bulletin should make sure that the information published is correct, carefully worded, based on reliable sources and that the conclusions can be defended. Appropriate editorial processes, quality control and peer review procedures help to ensure the accuracy of the information that is published (see Chapters 7 and 9). Some bulletins routinely ask a legal adviser to check the content before publication.

Even if the published information is accurate a bulletin may still encounter pressure from others, such as pharmaceutical firms that are not pleased with what is written about their product. These pressures sometimes include legal threats, but in practice legal action from the pharmaceutical industry against ISDB member bulletins has been rare.

Although legal action is rarely taken against a drug bulletin, if a firm objects to an article (or the draft of a proposed article), they may well send a letter signed by their legal department or by an independent lawyer threatening to take legal action if the piece is not amended or withdrawn. As a rule this is little more than sabre-rattling. Ask your own lawyer to look at it, but don't be afraid of empty threats. It may be sensible to modify words that have given particular offence, but if you have told the truth and told it well there will be very little risk of legal action. In some countries, including the USA, under some circumstances there is no liability for good faith publication of even a defamatory falsehood, although the truth is the "perfect defence" to a lawsuit for defamation (i.e. the legal doctrine that allows a person to sue in court and recover damages from someone making false statements that harm the plaintiff's reputation). Each country may have different legal rules.

Box 11.1 Legal aspects of electronic publication

As more and more human conduct appears online, questions often arise concerning whether and how to apply to the Internet the legal principles developed for the offline world. What rules apply when allegedly defamatory statements are made online? Generally, allegedly libellous (i.e. written) statements made online are usually evaluated by the same standards as statements made offline, with some countries adopting by legislation special rules defining the liability of various online service providers. A legal expert should be consulted.

In case of legal threats or strong objections to the content of your bulletin by a pharmaceutical company, it may be helpful to offer to meet with company representatives at your office. This may help to settle the criticism. Some bulletins offer the pharmaceutical industry an opportunity to comment on the text before publication. This can be done as part of the review process. It may however lead to unnecessary delays in publication and extra work for the editors when a company is dissatisfied with the content of an article. If you publish letters to the editor in your bulletin, this may be a better place to deal with criticism and comments from companies.

Box 11.2 Disclaimers

Some publications contain a 'disclaimer' in every issue in order to avert legal action. The following text is from *Meyler's Side Effects of Drugs*:

"No responsibility is assumed by the Publisher for any injury and/or damage to persons or property as a matter of product liability, negligence or otherwise, or from any use or operation of any methods, products, instructions or ideas contained in the material herein. Because of the rapid advances in the medical sciences, the Publisher recommends that independent verification of diagnoses and drug dosages should be made."

The legal value of a disclaimer is dubious. A law court may well feel that it is rather like a company trying to escape from giving a guarantee, but having a disclaimer may keep the publisher happy.

Many drug bulletins receive letters from companies (or from opinion leaders defending companies that pay them) complaining about the content of an article. Most bulletins deal with such complaints by responding to the company or the opinion leader directly. Take time to respond to threatening letters, and make sure you have had a chance to calm down before drafting a reply. Certain bulletins deal with complaints by publishing the complaint and a reply in their 'letters to the editor' section and/or on their web site to make the whole exchange visible. There are important advantages to publishing the letter and the editor's response in the bulletin. The bulletin shows that it takes criticism seriously and it will be more difficult for the company to publicise their criticism – for example, through sales representatives – without taking the response of the bulletin into account.

Should your bulletin come under pressure do not hesitate to ask for help from other bulletins. It may help to contact ISDB or individual drug bulletins in other countries to ask for support, for example, by confirming certain scientific statements in case of a disagreement on the content of an article. The simple fact that it is becoming known internationally that a third party is pressuring your bulletin may ward off the pressure as verified on several occasions by member bulletins.

11.5 Copyright

Copyright is the law that gives an author or artist ownership of his or her work. It protects against unauthorised use of their work and ensures a share of any earnings from the use of the work. It applies to all types of original expression including art, sculpture, literature, music, songs, choreography, crafts, poetry, flow charts, software, photography, movies, CD-ROMs, video games and graphic designs. It does not apply to ideas as such. For example, a plan for an article on a certain subject cannot be subject to copyright. It is the article itself that is subject to copyright not the idea behind it.

'Moral rights' in copyright law, are rights relating to a creator's reputation in connection with his or her work. They are additional to, and separate from, the 'economic' rights associated with the work, such as the right to reproduce the work. The moral rights protect creators if:

- they are not attributed or credited for their work;
- their work is falsely attributed to someone else; or
- their work is treated in a derogatory way, e.g. by distorting it.

Unlike 'economic rights', a creator is not able to assign his or her moral rights. Even if the creator assigns all his or her economic rights in a work, s/he would retain the moral rights.

Spanish drug editor wins case brought by Merck, Sharp & Dohme

A victory for all independent drug bulletins was declared last week when Professor Joan-Ramon Laporte, the editor of Spain's *Butlletí Groc*, won a district court case brought against it by the pharmaceutical company Merck, Sharp & Dohme.

The multinational firm had sued the editor and the publisher of the bulletin, the Catalan Institute of Pharmacology, over an article that the bulletin had published in 2002. The company said that the article had contained false and inaccurate information about the trial of one of its drugs, the Vioxx gastrointestinal outcomes research (VIGOR) trial, which looked at the safety of its arthritis drug, rofecoxib.

The company had wanted a statement—which it had prepared—to be published in the bulletin and on the Institute's web site under Spain's 1984 "rectification" legislation, which allows anybody the right to rectify any information they consider to be incorrect and whose distribution could cause them harm.

However, the judge, Maria Victoria Salcedo, rejected the demands of the company, absolved Professor Laporte and the Institute, and demanded that the company pay the court costs.

In her judgment on 27 January, she said the contents of the bulletin were accurate as they were based on a series of articles published in journals such as the *Lancet* and the *BMJ*, which had mentioned the irregularities surrounding the publication of the VIGOR trial, including a commentary that had said the company knew of the cardiovascular risks in relation to rofecoxib and suggested a bias in the selection process of the trial.

However, one aspect of the bulletin's article was found to be not correct. Judge Salcedo said the institute had not supplied enough evidence to show that distorted information on rofecoxib had been submitted to the EU regulator, the European Agency for the Evaluation of Medicinal Products, unlike that presented to the US Food and Drug Administration. But she said this had taken up only a few lines in the bulletin's article, while the company's rectification text was twice as long as the article, making this disproportionate.

The judge also said the company's text did not limit itself to the contents of the article, and its coverage exceeded what it wanted rectified. The text said, for example, that rofecoxib had better gastrointestinal safety compared with other drugs, but the bulletin had looked only at cardiovascular risk; it had also claimed that Merck, Sharp & Dohme had an ethical tradition, but this too had not been questioned in the bulletin.

Professor Laporte said the judgment "echoes the international debate which took place (in the literature) regarding the irregularities in the VIGOR trial and the omission of cardiovascular adverse effects in Merck, Sharp & Dohme's promotional materials."

The Catalan Institute of Pharmacology said the judgment was a "victory for all those involved in independent information on medicines and therapeutics."

A spokesman for Merck, Sharp & Dohme said after the ruling, which the company is reviewing, that the bulletin's article was almost completely based on a commentary that appeared in the *Lancet* in 2002 (360:100-1) on the design and conduct of the VIGOR trial. It claims that there were several inaccuracies in the commentary, but a letter to the *Lancet*'s editor spelling these out was not published.

Source: *BMJ* 2004;328:307 (7 February).

11.5.1 Limits to copyright

Copyright law also limits the granting of copyright protection for social policy reasons, such as the need to have access to certain knowledge and news about events in the world. For example, the news of the day published, broadcast or publicly communicated is not protected. Other unauthorised use of copyright material is generally accepted under the notion of 'fair use' (see below).

Copyright rules are fairly similar worldwide because of international treaties. The most important treaty is the Berne Convention, which was signed by 100 member countries. In general, copyright protection lasts for at least the author's lifetime plus 50 years.

For drug bulletins copyright is important because it provides a way to protect their work against unauthorised reproduction by others. For example, a bulletin can prevent drug companies from photocopying or reprinting their articles for promotional use. Drug bulletins also need to be aware of the copyright of others.

11.5.2 How is copyright created?

Copyright is created the very moment a work assumes a tangible form. As soon as the article is written and it is an original creation – not a copy of someone else's work – copyright exists. This includes the draft of an article.

Copyright is automatic. The creator or author becomes the owner. Exceptions to this rule are when an employee in the course of his or her employment creates a work, if the work is commissioned and the commissioning party owns the copyright, and if the copyright is sold to another party. Some countries only allow human beings who created the work to establish copyrights because only real persons can create. A legal entity has to acquire or buy the rights and cannot be seen as the original author. Drug bulletins need to ask outside authors to assign the copyright of an article they have written to the bulletin, for example by buying the copyright. It is a good idea to do this as soon as the draft is received to prevent the author from withdrawing the text. For example, the letter to an author who has agreed to write the first draft of an article for the UK *Drug and Therapeutics Bulletin* states *"We will circulate the draft to various specialists in the field, to our Advisory Council and Editorial Board and to the manufacturers of any drugs named. The draft will be edited and probably changed a lot in the light of all the comments. All our articles are the result of such collaboration and are therefore published unsigned. For this reason, Consumers' Association will have copyright in the article from the 'circulation draft' stage to publication".*

To strengthen the right, the author or bulletin can mark the publication with a copyright notice: © followed by the name of the copyright owner and the year of first publication. This is the international notice of claim, which was established by the Universal Copyright Convention of 1952 administered by UNESCO. If a publication carries the copyright notice, an infringing party can never claim not to have been aware of the copyright. In some countries copyright laws require this notice to inform the public that a copyright is claimed. In some countries it is also possible to register work with a national copyright office. There is usually a fee.

11.5.3 How to use copyrighted material

New bulletins often use other bulletins' articles, in which case they need to obtain permission. (See also Chapter 7 on using existing materials). Make sure that you are asking permission from the person or organization that has the copyright. In most cases bulletins will find that other publishers are generous in granting permission for articles to be copied provided that the source is mentioned. Copyright also applies to tables, graphs and illustrations, such as photographs and cartoons. If a bulletin wants to copy an illustration, they will need to get permission from the copyright holder.

11.5.4 Fair use and quotes

Some uses of a copyrighted work are considered 'fair use'. The use is not legally considered to be an infringement if its use is non-commercial or incidental in nature. There is no single definition of fair use but courts have interpreted it depending on the purpose and character of the use. For example, they may look at whether it was a non-profit use versus commercial use, how much text was copied in relation to the entire work, and the potential market or value of the copyrighted work. Fair use is often legitimate when a work is being used for teaching, research, scholarship, criticism or journalism. You can also quote within reasonable limits from other work without prior agreement, provided that the source is given and the text is not presented out of context.

11.6 Further reading

How to write a constitution. Doing it ourselves. A resource kit for consumer organizations. The Hague: International Organization of Consumers Unions; 1988.

The ABC of copyright. Paris: United Nations Educational, Scientific and Cultural Organization; 1986. This booklet provides an overall view of the function of copyright with respect to educational, scientific, cultural and information policies. For details of how to get a copy, see: **http://portal.unesco/**

Copyright law: overview, see: **http://www.nolo.com**. The web site aims to explain law in simple terms. It contains a section on copyright and has several interesting links to copyright resources.

12. Evaluating quality and usefulness

12.1 Introduction

Evaluation is an essential component of establishing and maintaining the quality and usefulness of a drug bulletin. Evaluations should, therefore, be an integral part of any plans to start or improve a drug bulletin. This chapter outlines the benefits and difficulties of undertaking an evaluation and describes the different types of evaluation: audit of bulletin processes, feedback from readers and impact assessments.

12.2 Evaluation brings many benefits

When planning a new bulletin, an assessment of readers' needs will increase the likelihood of providing useful information (e.g. what type and depth of information is needed, whether local or overseas authors are preferred – see Chapter 4). From this initial assessment, clear objectives for the bulletin can be formulated. Future evaluations can then measure to what extent the objectives are being met and help guide ongoing work planning.

An evaluation of an **established** bulletin can tell you whether the information published is useful and relevant, and what is needed to improve quality and effectiveness, such as using a new format, providing abstracts, improving indexing, etc. An evaluation can also sometimes establish whether a behavioural change (e.g. a change in prescribing behaviour) has occurred in response to information in the bulletin, and can be used to measure the degree of change. Evaluation can be used to determine if the bulletin is actually being read.

An evaluation can positively reinforce the editorial team's efforts and give assurance that resources, particularly time and money, are being used effectively. It can also demonstrate the value of the bulletin when seeking increased or continued funding. It may be the only way to counter funders who prefer to put their money into activities with more obvious immediate outcomes.

Evaluations are often perceived as difficult, costly and time-consuming. This may be true for large impact assessments (see below), but any bulletin can successfully carry out simple audit and obtain feedback from readers, even if experience and funding are limited. Starting with smaller, simpler tasks will also build the knowledge and confidence needed to undertake more complex evaluations.

12.3 Three approaches: audit, feedback and impact assessment

Evaluating a drug bulletin involves finding out whether it is meeting certain objectives. These objectives could relate to quality, level of readership, usefulness of articles, or influence on the reader's knowledge, attitude or actual prescribing behaviour.

There is no single correct way to evaluate a drug bulletin. Research involving quantitative data collection (direct measurements of what is happening) is not necessarily better than research involving qualitative data (measurements of attitudes, beliefs etc. showing why something is happening). What is important is that research, whatever type is chosen, is carried out rigorously so that there can be confidence in the validity of the results.

The choice of evaluation depends primarily on the intended objective. You may want to start with a self-evaluation of the quality of the bulletin, and then move on to evaluate the usefulness of the information to the reader. When your bulletin is well established, has a committed readership and has been running smoothly for a period of time, you may want to undertake an impact evaluation.

12.4 Start with your own evaluation of the bulletin

A logical starting place is to audit the bulletin's production process as this type of evaluation does not involve readers, is inexpensive, and once the method of data collection is established, it can easily be repeated for each bulletin issue.

First, decide what aspects of production it is most important to monitor and set an acceptable quality standard for each. For example, an editor may decide to take specific action if the number of typographical errors exceeds three per 10 pages, or if more than 10 business days elapse between the expected and actual publication dates. See Box 12.1 for further examples.

Box 12.1 Examples of areas to audit

- Grammatical and formatting errors.
- Paper and printing quality.
- Review process, e.g. what proportion of reviewers send comments back within the specified period, or at all?
- Timeliness of the information, e.g. how soon after a new drug is marketed is an article on the drug published in the bulletin.
- Coverage of significant issues e.g. including information on a serious adverse reaction.
- Editorial process, e.g. whether authors follow guidelines on writing an article, how well editorial procedures are followed.
- How long it takes to respond to readers' letters.
- Whether the mailing list is up to date.

Next, establish who will collect the data, and how. For routinely collected data on the production process, an audit should be completed after each edition of the bulletin is distributed and action taken, if necessary, to improve quality. Also consider monitoring indicators of the bulletin's perceived value, such as subscription rates, citations in other publications, comments on feedback forms etc.

12.5 Assessing readers' opinions of the bulletin

12.5.1 Methods of assessing readers' opinions

Regular assessments of readers' opinions on the quality and usefulness of articles are not difficult and should be undertaken by all bulletins. At the simplest level, information about subscribers and their opinion of the bulletin can be collected from the subscription renewal form, by analysing spontaneous mail from readers and by asking questions about why people stop subscribing. Bulletins that receive a large number of letters (several thousands per year) can retrieve much relevant information from this mail, with the quality of the letters' content increasing with the development of the bulletin. The richer the content of the bulletin is, the more varied and interesting the exchanges with readers are.

Simple readership surveys can be carried out annually and more in-depth surveys, focus group discussions, etc. every few years. It may involve surveying everyone on the mailing list, a random sample of the mailing list or a specific professional group (e.g. primary care doctors). This type of evaluation is useful for finding out if a bulletin is read, easily understood, kept for future reference, and how readers value the information in it.

This can be done through:

- a readership survey;
- focus group discussion;
- discussions involving 'spontaneous' groups of readers (for example, groups of readers with common practices, such as refusing visits from pharmaceutical company representatives, or generic prescribers, or readers' clubs simply meeting together to critically discuss each issue of the bulletin);
- in-depth interviews with individuals (in person or by telephone);
- 'target audience' contact. You sometimes want to study the views of non-readers in your target audience as well as the views of your loyal readers.

Sometimes two or more separate, but complementary, methods are used, such as a postal questionnaire and interviews. A telephone survey can be used to validate the postal survey because it can be done without identifying who the survey is being conducted for; this can eliminate some of the response bias which occurs when it is obvious which publication the survey is about. For bulletins that are available electronically, surveys by e-mail may be feasible.

Using one of these methods it is possible to find out what readers think of a bulletin and how it can be improved. They are relatively easy and inexpensive to conduct, especially simple surveys, and do not require an external infrastructure, such as one that collects prescription data or adverse drug reaction reports. In addition, a single assessment can cover a range of issues. For example, a *Prescriber Update* survey[1] included questions about how well the bulletin was read, usefulness of various types of articles, perceived influences on prescribing,

readability, preferred authors, design improvements and whether electronic distribution was an acceptable alternative to paper copies. However, when designing survey questions, it is important to maintain a balance between how much is asked and the likelihood of the respondents completing the survey.

12.5.2 Potential problems

One of the problems with carrying out assessments is getting enough readers, and a representative cross-section of readers, to respond. Another is to make sure that the information they provide is accurate.

Reader feedback poses other potential problems including recall bias, because of people's selective memory, and non-representative results, because people who bother to fill in a questionnaire and send it back may have different opinions from those who do not reply. In addition, the quality of the data may be poor due to incomplete responses to surveys, inconsistent interview technique or a poorly designed survey. The likelihood of poor quality data can be minimised through validating questions and using standardised interview techniques. The references on survey design listed at the end of this chapter provide additional information.

Assessments of readers' opinions measure how people think the bulletin has influenced their behaviour, not actual behavioural changes. Despite these limitations, canvassing the views of readers through surveys, discussions or interviews provides invaluable feedback and should be a regular part of the activity of all drug bulletins. Letters to the Editor and other feedback (e.g. letters to other publications) can also give an indication about what readers are thinking.

When designing a readership survey, it is useful to include questions relating to the bulletin's impact. For example, a survey of doctors might ask whether articles have influenced prescribing practices, helped them to recognise an adverse drug reaction or interaction in a patient, or changed the advice given to patients. These types of questions cannot measure true behavioural change. People's reports of changes in their own behaviour are often much more optimistic than reality. However, they do provide an indication of the value readers place on the information in the bulletin. If they are suspicious or critical of the bulletin's advice, they are less likely to report a behavioural change.

12.5.3 Selecting the data collection method

The data collection method used (survey on paper or by e-mail, focus group discussions or interviews) depends on the type and depth of information needed, and on available resources. For example, if the aim is to find out if the bulletin is read and about the usefulness of various sections, then a survey would be preferable as it can canvass the opinion of many readers quite inexpensively. If you require more qualitative information on complex issues, such as what depth is required in adverse reaction articles or what format is preferred, then focus group discussions or interviews may be preferable. A face-to-face or telephone interview can allow you to explore the responses. However, these can be costly, both in terms of money and time, and possibly non-representative because of the non-random selection of a sample or because only interested readers agree to participate. If you want to know whether the quality of the bulletin's information is high and consistent, then external review by experts is needed. To find out if articles change prescribing behaviour, an impact evaluation is needed.

Next consider who will conduct the assessment. The best way to avoid bias is to ask an independent external researcher to carry it out. However, this is likely to be more costly than carrying out the assessment yourself.

12.5.4 Planning the survey

The next step is to plan all aspects of the survey. Studies often fail simply because they were poorly planned. Box 12.2 lists questions and hints that may be useful as a checklist of the issues that need to be considered when planning and conducting a readership survey. In addition to these pointers, you will have to operate to your country's data protection legislation AND any professional standards for confidential survey research. Check the Esomar Code of Conduct for market research at: **http://www.esomar.org/** as a starting point.

12.5.5 How many replies are enough?

Sample size and selection of respondents need careful consideration. The simplest option is to send the survey to everyone on the mailing list. A response rate of no more than 20–25% is a realistic expectation. Where the mailing list is large, resources may not permit analysis of thousands of responses. Alternatively, you can select and send the survey to a representative sample of those on the mailing list.

In constructing a representative sample, you may want to consider demographic factors such as age, sex, individual or group practice, medical specialty, rural or urban location. This will help to make sure that you are reaching a range of different types of readers. The variables used depend on what you know about your readers. For example, if you know the location and specialty of those on the mailing list, select the sample by first grouping men and women separately, then subgroup by primary care doctor and specialist, then further subgroup by rural and urban location. If your mailing list is large, you can divide it into many subgroups. If it is small you may want to stick to larger groups of different types of readers. You can then randomly select names from each group. Most computerised statistical programmes include a random number generator. Consult a statistician on the number of individuals to be selected from each group.

Strategies for increasing the response rate include:

- A follow-up telephone call/letter to non-responders. Contacting non-responders is good if you know who they are. (This needs to be taken into consideration if the survey is confidential i.e. you have to be able to identify who has responded without knowing their name); or
- Replacing non-responders with another group of readers who meet the same randomisation criteria;
- Always assume you will get a poor response and send out more questionnaires than you think you need.

Box 12.2 Readership survey checklist

Purpose of the survey

- What are the bulletin's aims? E.g. convey current drug information, advocate changes in regulation, etc.
- What readers are you targeting? E.g. all, or a subgroup such as primary care doctors, hospital doctors, pharmacists, the public.
- What sort of information do you need from this survey? e.g. extent bulletin is read, usefulness of the articles, suitability of electronic publishing.
- Whose opinion do you want? E.g. all on mailing list, or a particular subgroup.
- What will the survey achieve? E.g. ideas for improving the format, evidence to support continued funding.

Literature review

- Have similar surveys been done? Review the literature for published reports.
- Ask editors for survey reports and sample questionnaires via the ISDB network [**http://www.isdbweb.org**].
- What errors were made and what problems were encountered in other similar studies? Talk to other editors and ask for a copy of their survey.
- Who could give advice? Ask an experienced editor or researcher.

Methodology

- Will you let participants know who the research is being conducted for? This has potential advantages and disadvantages.
- What questions need to be asked?
- How many readers should be sent the survey?
- How will they be selected?
- What demographic variables (profession, location, etc.) should be considered?
- Should respondents be anonymous? This is usually recommended to encourage a full and honest response.
- What is the likely response rate? Remember you may be working with busy medical professionals so this may not be as high as for other types of survey.
- Will non-responders be followed-up; if so, how will they be contacted?
- Is an inducement needed/appropriate to ensure a good response rate?
- Is it necessary to include a stamped self-addressed envelope?
- If the service is available, consider reply-paid envelopes – you only pay the postage for those returned.
- What is the cut-off date for processing responses?
- Is it sufficient for a few readers to review the questionnaire before full distribution or is a pilot study needed?
- How will the data be collected, processed and analysed?

Continued on next page

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Administration, workplan and budget

- Who has overall responsibility for the survey?
- Who will monitor activities/progress?
- Who will process and analyse the results?
- How long will it take? Is the estimated length of time realistic?
- What resources are needed (staff/money/data processing software etc.)?
- Do you have the appropriate analysis tool?
- Do you have the necessary expertise or access to expertise?
- Who could provide funding and equipment?

Data analysis

- Was the response rate adequate?
- Can valid conclusions be drawn from the results?

Publication and use of results

- Who needs to see the final report? Who is interested in your results? You may want to publish a summary of the results in the bulletin. This is a way of showing respect for respondents and valuing their contribution, as well as allowing readers to compare their attitudes to the overall trend.
- What actions are needed in response to the survey results? Who will do this?
- Who else could benefit from this research? You may want to submit an article on your survey and what you learned from it to the ISDB Newsletter.
- How could you have improved the survey?
- When should you next undertake an evaluation?

If you have divided people into subgroups using demographic variables, such as whether they are male or female, a primary care doctor or specialist, etc., include a question on these variables in the survey. This will help to show you whether a representative sample of people from each of these groups responded to your survey. Also, bear in mind that, in order to draw valid conclusions from the survey findings, you may need to be able to identify respondents (e.g. which responses are from general practitioners) so build this into the survey design.

12.5.6 Drafting the questions

Once planning is complete, develop the questions. Consider what questions to ask, how they will be asked, and the order (see Box 12.3).

Box 12.3 General rules for drafting survey questions[2]

1. Avoid asking two questions at once e.g. 'Do you consider articles are accurate and unbiased?' These two points need to be divided into two questions.
2. Word questions so that all respondents understand the same meaning.
3. Be as precise as possible in the framing of questions e.g. 'Have you recently changed the advice you gave a patient because of an article?' would be clearer if worded as 'In the last six months, have you changed the advice you gave to a patient because of an article?'
4. Tell respondents when a question can have more than one response, e.g. 'You can tick more than one box'.
5. Design the survey to make the task of reading questions, following instructions and recording answers as easy as possible.
6. Word questions so that clear, unambiguous answers are more likely to be given.
7. Simple tick/check boxes work well for answer options, along with providing space for respondents to write additional comments.
8. Consider using questions with similar scales to one another so that respondents can become familiar with the task they are undertaking.
9. If using agree/disagree statements, try to ensure a mix of positive and negative statements.
10. Remember to allow for all possibilities in your responses: this may include having a 'don't know' or 'none of these' for some questions.

The questions asked will depend on the information being sought. Here are some ideas from which to develop questions:

- The extent to which the bulletin is read.
- What happens to each issue?
- Factors preventing more articles being read.
- General readability of the bulletin.
- Preferred authors (national/international, specialists/primary care doctors etc.).
- Level of detail required in articles.
- Usefulness of various articles or sections.

- Content of articles (e.g. should clinical advice be given? If it is already, is the level of advice adequate?).
- Perceived influence of the articles (on prescribing practice, advice given to patients etc.).
- Acceptability of format, suggestions for improving design.
- Frequency of bulletin editions.
- Comparison with other journals.
- Suggestions for future articles.

Many questions merely require a yes or no response, or a comment. Those that measure degrees of frequency, satisfaction or other such parameters require presentation of a scale from which the respondent can select.[3] Appropriate options have to be provided. Where there may be interpretation problems, consider using scales respondents are familiar with. It is always helpful to design your survey form with enough space for people to enter comments about the bulletin, which could be unrelated to the questions you asked them.

Measuring frequency

One approach is to ask the respondent to estimate the frequency of a certain action e.g. 'In the last six months, how many times did you refer back to previously published articles?' However, respondents may not remember how often they did something so providing a response scale with a rough quantification may be useful e.g. 'How often do you refer back to a previously published article?'

Every few weeks
Every few months
Less often than every six months
Never

Avoid using a response scale of ‘often’, ‘sometimes’, ‘occasionally’, ‘rarely’ etc. as they are difficult to interpret.

Asking evaluative questions

Questions asking respondents to say how they rate specific aspects of a bulletin are common in readership surveys, e.g. what do you think of the standard of the book reviews? A numerical scale from 0 to 5, where 5 is excellent and 0 is poor, could be used or a scale such as:

Excellent
Very good
Good
Fair
Poor

To encourage accurate and full completion of the survey, keep scales simple (i.e. restrict the number of different answer options) and ensure there is a clear distinction between scale levels. If the differences are too subtle, this will affect the quality and accuracy of the survey results.

Measuring feelings

The following scale is often used to rate how respondents feel about something:

Very positive
Generally positive
Mixed: about equally positive and negative
Generally negative
Very negative

A numerical scale can also be used to measure feeling, for example, 'Do you feel the bulletin improves your ability to recognise an adverse reaction in a patient?' (on a scale of -2 to +2, with 0 being the midpoint). Note: while every point on the continuum does not need to be defined, there should be a midpoint where positive feelings turn to negative.

Rating agreement

Often readership surveys ask how much the respondent agrees with certain statements e.g. 'Some readers have suggested including a summary at the beginning of each adverse reaction article. How do you rate this suggestion?' An appropriate scale may be:

Strongly agree
Agree
Disagree
Strongly disagree

While it may be appealing to offer a middle category (neither agree or disagree) it may be more useful to make the respondents commit themselves.

Ranking the bulletin

If, for example, you want respondents to prioritise your bulletin against three others publications for usefulness, list the publications and ask the respondent to rank them from 1 to 4, where 1 is the publication they find most useful, and 4 is the publication they find least useful.

Data processing and analysis

While data from simple readership surveys can be processed manually, a software package may be needed to process more complex survey responses. There are many data processing software packages available – ask a local researcher for advice about which to use.

Unlike clinical studies or full impact evaluations, statistical analysis of readership surveys is not usually necessary. If statistical analysis is required, ask a statistician for advice when planning the research.

At the end of this chapter there is an example of a readership survey questionnaire together with the results, from the French bulletin *Bulletin d'Information du Médicament et de Pharmacovigilance.*

12.6 Evaluating the impact of the bulletin

Once you have conducted some assessments and gained confidence, and your bulletin is well established, with production running smoothly and a fairly stable readership, you may want to look for opportunities to evaluate the impact of the bulletin. Impact evaluations are usually undertaken to find out what effect a particular bulletin article has had on its audience, i.e. whether a behavioural change actually occurred following publication of the article, and to establish a cause-effect relationship. All drug bulletins strive for long-term change in the culture and discipline of prescribing, dispensing, and explaining drug use, and thereby improving patients' health. Even a small change in prescribing behaviour could have a big effect if the bulletin has a large readership or if the drug is prescribed frequently. For example if a drug bulletin in a developed country achieved a 0.5% improvement in the prescribing of statins it would benefit many people. A carefully designed impact study is needed if you want to know whether your bulletin is having a direct effect on the behaviour of readers. Following the publication of an article you may wish to assess readers' actual:

- prescribing of a particular medicine;
- communication with patients on a specific topic; or
- knowledge about a particular therapy.

Although it is desirable to assess whether the bulletin has caused readers to change their behaviour, this requires a high level of research skill and is time-consuming and costly. It is, therefore, useful to build up experience and skill on simpler evaluations before attempting an impact evaluation. Crucially, it depends on the required data being available. For example, few regions or countries have databases of prescribing statistics. Even if they are available, the data may not be reliable or they may not be able to reveal the trends of interest. When using data that have been collected for another purpose, you cannot be sure that the bulletin caused the change that you observed, as other influences cannot be excluded. For example, if an unnecessarily hazardous drug is used less often than previously, it may be because of your bulletin article, it may be because doctors received similar information from other sources, or it may be for other reasons, such as lack of availability, higher price, etc.

Box 12.4 Can a bulletin change practice on its own?

There is a fair bit of controversy in the scientific literature over whether providing health professionals with written information on its own is enough to bring about changes in prescribing. A US study found that articles can significantly change behaviour.[4] However, a Cochrane review of 11 studies concluded that the impact is at best small and of uncertain significance,[5] while a Dutch study found the effectiveness of information in changing behaviour was variable.[6]

More recently a Canadian study looked at this question with particular regard to a series of regular and expected printed educational bulletins, *Therapeutics Letter.*[7] The study sought to measure the impact on prescribing to newly treated patients. A paired, cluster randomised community design was used. The study population included 499 physicians and 12 issues of the bulletin, *Therapeutics Letter* were followed-up. Physicians in the control group (n = 241) received the letters 3-8 months after physicians in the intervention group (n = 258). The impact on prescribing to newly treated patients (defined as patients who had not previously made a claim for any medication from the class of drugs profiled in the letter) was analysed. The probability of prescribing a drug recommended in the *Therapeutics Letter* rather than another drug in the same class increased by 30% in the three months after the mailing of the letter relative to the preceding three months, adjusted for any before-after changes in the control group (relative risk 1.30; 95% confidence interval 1.13-1.52). No letter achieved statistical significance on its own. However, 11 of the 12 letters produced prescribing changes in the predicted direction such that the overall result was significant when their effect was combined. The researchers concluded that the combined effect of an ongoing series of printed letters distributed from a credible and trusted source can have a clinically significant effect on prescribing to newly treated patients.

Types of impact studies include:

- Testing reader knowledge on a topic before and after the publication of an article.
- Reviewing prescriptions for a particular medicine or therapeutic group. This could be used to see whether a newly recommended dosing regimen has been adopted by prescribers.
- Simulated patient surveys, where an 'actor' consults a number of doctors and acts out a set scenario on each occasion. The doctor's response is carefully recorded by the simulated patient(s). Each doctor is consulted by a simulated patient before and after publication of a particular article and the pre- and post-publication responses compared to see whether there has been a change in actual behaviour; however, there are potential practical and ethical problems with this kind of research.

When designing an impact study consider:

- Potential confounders – factors unrelated to your bulletin that can also cause the same result. For example, an editorial published during the study period potentially distorted the outcome of the Dutch impact study.[6] Choose issues where it is possible to eliminate some confounders and control the impact of others on the study results.
- The length of the study. An impact study should be repeated after some time to see whether the behavioural change was sustained.
- Use of controls. Controls are essential to enhance the detection of differences and confounders. In the British Columbian Ministry of Health's study to ascertain the influence of educational interventions and adverse media publicity on the prescribing rate for calcium-channel blockers,[8] inadequate controls limited the ability to infer

causation. A large control group will be needed if you are trying to detect a small behavioural change. Ask a statistician for advice on the size of control and study groups.

Large robust impact studies are unlikely to be achievable for all bulletins. More targeted impact studies can, however, provide valuable information about a particular aspect of a bulletin. For example, the independent evaluation of the impact of the readers' test of *la revue Prescrire* showed physicians who used the test were more knowledgeable than those who did not.[9]

12.7 Feedback is achievable and invaluable

In summary, it is important to evaluate your drug bulletin regularly to ensure that the information it contains is of high quality and is useful. Start by monitoring the production process and conducting a readership survey. Both activities are achievable and will provide invaluable data. Always plan well. Once you become more skilled at research, seek opportunities to evaluate the impact of the bulletin, but be realistic about what can be achieved.

12.8 Simple observations can tell a lot

Changing prescription, dispensing and consumption habits is extremely difficult and it probably cannot be achieved by a bulletin alone. By simply paying attention to events such as these experienced by some bulletins, you can guess that your own bulletin has some impact:

- the complaints of companies about the “disastrous impact of the article on the launch” of their last new product;
- the complaints of the regulatory agency who felt “obliged to take a decision” because you raised the point in a particular article;
- the number of journalists asking for advice on a drug’s efficacy or side effects;
- the increase in the number of paying subscribers, or of those who ask for permanent subscription renewal, etc.

12.9 References

1. *Prescriber Update* survey results. *Prescriber Update* 1998;17:35.

2. Adapted from Fowler FJ. *Improving survey questions*. Design and evaluation. Applied Social Research Methods Series, Volume 38. London: Sage Publications; 1995. Chapter 4: Some general rules for designing good survey instruments, p.78-103.

3. Adapted from Fowler FJ. *Improving survey questions.* Design and evaluation. Applied Social Research Methods Series, Volume 38. London: Sage Publications; 1995. Appendix A: Commonly used measurement dimensions, p.156-165.

4. Fendler KJ, Gumbhir AK, Sall K. The impact of drug bulletins on physician prescribing habits in a health maintenance organization. *Drug Intell Clin Pharm* 1984;18: 627-31.

5. Freemantle N, Harvey EL, Wolf F, Grimshaw JM, Grilli R, Bero LA. Printed educational materials to improve the behaviour of health care professionals and patient outcomes. *The Cochrane Database of Systematic Reviews* 1997, Issue 2. Art. No.: CD000172. DOI: 10.1002/14651858.CD000172.

6. Denig P, Haaijer-Ruskamp FM, Zijsling DH. Impact of the Dutch drug bulletin on drug choices and prescribing. *Ann of Pharmacol* 1990;24:87-93.

7. Dormuth, C. R., M. Maclure, et al. (2004). Effect of periodic letters on evidence-based drug therapy on prescribing behaviour: a randomized trial. *CMAJ* 171(9):1057-61.

8. Maclure M, Dormuth C, Naumann T, et al. Influences of educational interventions and adverse news about calcium-channel blockers on first-line prescribing of antihypertensive drugs to elderly people in British Columbia. *Lancet* 1998;352:943-8.

9. Broclain D, Mura P, Nivet-Carre D, et al. Quasi-experimental study on the effectiveness of the readers' test in the medical journal *la revue Prescrire*. *J Cont Ed in the Health Professions* 1998;18:47-57.

Example of an assessment survey

BULLETIN D'INFORMATION du médicament et de pharmacovigilance

CHU Rennes

Assessment Survey
about issue 104 Nov-Dec 2002

Sore throat quick test - DTCA - Drug stop order before anaesthesia

Raw Results (out of 45 answers)

1. You are practicing or studying in — Medicine **18** — Pharmacy **25** — Nursing **1** — Other **1**
2. You are working in — Public hospital **37** — Private hospital **1** — Community **6** — Other **1**
3. Other persons had access to your own copy of this issue **25** yes **15** no, whether yes : how many ? **+ 88**
4. You read it
   - in full **23**
   - partially **14**
   - skipping through **4**
   - not at all **0**
5. You found it

	yes	no
• suitable sized	**44**	**1**
• attractive	**35**	**3**
• well illustrated (diagrams, algorithms)	**31**	**4**
• easy to read	**33**	**5**
• easy to understand	**34**	**3**

6. You found the information

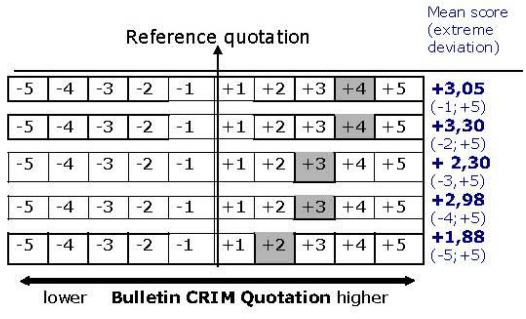
	yes	no
• new	**32**	**5**
• interesting	**39**	**0**
• good quality	**35**	**0**
• useful for your knowledge	**35**	**3**
• useful for your practice	**32**	**5**

7. You consider it possible to incorporate into your practice
   - regularly **24**
   - occasionnally **17**
   - rarely **4**
8. If so, it seems to you that this could contribute to

	yes	no
• a better therapeutic efficacy	**36**	**1**
• a better therapeutic security	Yes **38**	**1**
• a better drug funding utilisation	**25**	**7**

9. If not, why? (please, precise on the back)

10. On the whole, comparing with your usual drug information sources ("reference quotation") tick one box for each of the following aspects of the Bulletin to mark your own evaluation:



- Continuing education, knowledge updating
- Information reliability (validity, independance, actualisation...)
- Potential impact into your prescriptions or practice
- Public Health (quality, efficacy, security, usefulness...)
- Drug funding rational utilisation

(As a whole, negative quotations were ticked only 8 times out of 212 filled in boxes)

Please turn the page ⇨

If the need arises, would you be interested in getting your subscription to the Bulletin electronically ?

- **Website** yes **26** no **12**
- **Mailing list** yes **29** no **11**

2 = continue paperprinting

Thank you for sending back this questionnaire by **30 march 2003**, to

✉ **C. R. I. M. - C. H. U. Hôtel-Dieu**
35064 RENNES Cedex - France

Fax 02.99.87.34.08

✍ Free comments and suggestions

About issue Nr 104 Novembre - Decembre 2002:
✍
Sore throat quick test - DTCA - Drug stop order before anaesthesia

☺ (very) interesting, very well written and illustrated. Good review ; informative ; had only partial information from elsewhere. Better undestranding of the test.

DTCA

☺ Interesting, good review. Was totally unaware of this topic. Agree with the necessity to counter drug firms pressure. Speak about that kind of topics more frequently.

Drug stop order before anaesthesia

☺ Very interesting. Practical. Useful for practice. Simple but useful (anaesthetist).
☹ Neither detailed nor documented enough (anaesthetist).
Table of contents missing.

About this current issue Nr 105 January-February 2003 :
Body Surface Area : History and relevance in dosing adaptation
✍
☺ New. Interesting. Excellent. Very stimulating. Makes one think.
☺ Brought the Pharmacy and Therapeutic Committee to speak about BSA.
☹ Theoretical. Too technical. Hungry for more.
Academic. Poorly practical. Boring mathematical formulas.

About Bulletin d'Information du Médicament et de Pharmacovigilance, on the whole :
✍
☺ Interesting subjects usually. Well written, clear (diagrams, algorithms).
☺ Good and concise information. Good tool for CE.
☺ Bravo quality, regularity, independence. High standard reference. Bravo. Super. Keep on the way.
☺ Meet readers' expectations : practical – applicable in ordinary practice, adapted to daily problems.
Useful for hospital practice and teaching. Helps in hospital/community relationship. Useful to prevent drug adverse events.
☺ Improve practical level to improve integration into professional practice.
Extend readership. Have the Bulletin better referenced in databases.
How to generalize know-how and experience of CRIM ?
☹ Script too compact.

13. Partnership and collaboration

13.1 The importance of supportive partners

Many drug bulletins face difficult circumstances, especially when they are first starting, or when resources are limited, as in many developing countries. It may be difficult to obtain needed information, professional advice, financing and the means to assure the drug bulletin's independence. Collaboration and supportive partnerships are crucial for a new drug bulletin, and can play a key role in the future success of the organization. Every drug bulletin, regardless of the level of its development and experience, can gain strength through the support of other similar publications. This was one of the main motives for creating an international network of drug bulletins, ISDB.

An unpredictable aspect of publishing a bulletin that cannot be ignored is the possibility of legal problems arising from the publication of critical articles and reviews. The existence of reliable partners at national, regional or international levels not only lends support to a bulletin but also enables it to act more independently. Several drug bulletins, such as CITO in Latvia and *Geneesmiddelenbulletin* in the Netherlands, have faced situations where the support of other organizations enabled them to counter opposition successfully and to continue publishing their bulletin.

As in personal relationships, a prerequisite for successful partnerships and collaboration is that the different parties know each other well enough to establish a relationship that satisfies the needs of the weaker partner without making undue demands on the partners who are providing support.

13.2 Possibilities at national, regional and international levels

Cooperation is possible at national, regional and international levels. At a national level, it is important to build good relationships with the national authority dealing with drug registration, licensing and quality control. In many countries this is a separate agency or department within the Ministry of Health. These institutions can serve as a great source of information and expertise on pharmaceuticals, particularly on new drugs.

Collaboration with universities is important in that it makes use of existing technical expertise and resources. A number of drug bulletins are affiliated to universities. This enables them to convey the ideas presented in their articles to a wider readership, including students of medicine, nursing and public health. Other groups of potential partners at the national level include professional, medical and pharmacists' associations and societies. They can provide valuable advice about therapeutic approaches and treatment. Collaboration with professional societies also helps to build a bulletin's credibility among health professionals.

For drug bulletins mainly targeting health professionals, it is important to recognise partners among other groups concerned about health issues, like women's, patients' and consumers' groups. This kind of partnership is mutually beneficial because these groups can provide needed expertise on the experiences of patients and the types of treatment outcomes they consider important. Very often they also need the expertise of a drug bulletin's editorial team and associated health professionals for organizing advocacy work or campaigns, or developing information materials for the general public.

Partnership with other newsletters and journals on medicine or health issues, especially other drug bulletins published in the same country or in the same language, can help in the choice of the topics for articles and in initiating discussions about specific health issues or therapeutic practices.

At a regional level, neighbouring countries may face similar cultural, political and economic conditions. Similarities can also be found in health issues and health policy, such as common causes of morbidity and mortality, similar approaches to treatment and the use of drugs, and regional trends to harmonise the process of drug registration. All of these factors make collaboration among drug bulletins at the regional level valuable and important. Regional partnerships not only strengthen the professional capacity of bulletins, they can help increase the bulletin's influence at a national level. It is also helpful to meet colleagues regularly and discuss ways of solving problems and improving the quality of publications. Bulletins operating within smaller countries may want to rotate editorial responsibilities at a regional level.

The organization of international meetings involves a great deal of work and financing. Regional seminars and workshops serve a similar purpose, but cost less and are more manageable. Box 13.1 lists some of the meetings that have been organized by ISDB and individual bulletins over the years. Those who cannot attend such meetings can still gain much from contact with colleagues via e-mail.

International cooperation varies from partnership with other drug bulletins through ISDB, to collaboration with non-governmental organizations and networks working on health-related problems, to support from international agencies like WHO, other UN agencies and governmental development agencies. WHO's Essential Drugs and Medicines Policy Department (renamed Medicines Policy and Standards in December 2004) has supported drug bulletins in developing and developed countries for many years, encouraging the establishment of new bulletins and strengthening existing ones.

Box 13.1 Some past regional meetings for bulletins

- ISDB International seminar on strategies and efficacy of drug information - (Reggio Emilia, Italy). April 1988. Supported by Farmacie Comunali Riunite;
- ISDB Summer School (Reggio Emilia, Italy). June 1991. Organized by the Italian bulletins;
- Meeting on drug information (Madrid, Spain). October 1991. Organized by the Spanish Ministry of Health, WHO Regional Office for Europe and ISDB;
- ISDB Summer school (Algiers, Algeria). April 1992. Supported by the Algerian National Institute of Public Health, the German Development Aid Foundation, the Italian Aid Agency, Health Action International, Pharmaciens sans Frontières, *Drug and Therapeutics Bulletin* and *la revue Prescrire*;
- ISDB Summer School (Yokohama, Japan). July 1992. Organized by the Japanese bulletins, with support of the WHO Action Programme on Essential Drugs;
- Workshops of the ISDB General Assembly (Granada, Spain). September 1996. Supported by the Public Health School of Andalucia, WHO Action Programme on Essential Drugs, WHO Regional Office for Europe, Health Action International and individual bulletins;
- ISDB-European Medicines Agency (EMEA) Joint Workshop on EMEA information provision and policy and the needs of independent bulletins (London, UK). June 1998. Organized by ISDB and the EMEA and individual bulletins;
- ISDB Central and Eastern European Regional Meeting (Riga, Latvia). January 1998. Organized by Cito! and ISDB. Supported by ISDB and WHO Europe.
- ISDB European workshop on pharmacovigilance (Berlin, Germany). November 2003. Organized by ISDB and the German bulletins. Supported by WHO.
- ISDB South-East Asia Regional Meeting (Kathmandu, Nepal). February 2004. Organized by *Drug Bulletin* Nepal and ISDB. Supported by ISDB and WHO, including the WHO Regional Office for South-East Asia.

13.3 Various forms of collaboration

13.3.1 Twinning arrangements

A twinning arrangement is a one-to-one relationship of support between an established bulletin and a small or newly formed bulletin. Some drug bulletins in Western countries have more than 30 years of experience. Their knowledge of work organization, the editorial process, dissemination of the drug bulletin, financing and fundraising are valuable resources. Even if it is necessary or more appropriate to do things differently in your country, you are likely to gain a lot from this wealth of experience. Developing twinning arrangements between one of the experienced journals and a new or small drug bulletin can benefit both partners. It can also stimulate an established bulletin to learn about pharmaceutical issues new to them or to view their own national situation in a new light.

Some twinning arrangements are particularly successful between bulletins sharing the same language or close languages (e.g. *la revue Prescrire,* France and *La Lettre du Cedim*, Burkina Faso; *la revue Prescrire,* and *Dialogo sui Farmaci*, Italy). Other examples have been successful despite linguistic differences.

Such twinning arrangements can be organized directly or through ISDB. A systematic approach to this type of support helps to ensure that the arrangement benefits both partners. One type of twinning programme is on-the-job training for new editors. The steps for developing such an arrangement would be to:

- identify needs;
- identify who can provide the needed support;
- establish contact with the organizations or institution;
- reach either a formal or informal agreement about collaboration;
- review and revise the agreement periodically.

13.3.2 Sharing information and resources

One of the biggest problems that new and small bulletins face is obtaining necessary information and reference materials, which are often too expensive for them to afford. If a bulletin can share resources and references with other drug bulletins or organizations, this can alleviate many of their difficulties in becoming established.

Lack of professional capacity and the scarcity of necessary materials invariably do not allow new bulletins to prepare all the in-depth review articles or original articles that they would like to produce. It helps them if they can use materials published by other drug bulletins, having first reached an agreement about this. (See Chapter 7 for more on sharing resources, and Chapter 11 on copyright.)

Exchange of documents that are difficult to obtain (for example, in the field of pharmacovigilance) among drug bulletins is always useful. Small and new or more experienced bulletins all face the same problems of lack of transparency, and difficult access to some data.

13.3.3 Using established bulletins' expertise

There may also be situations where a new or small drug bulletin can develop its own articles, but where additional advice or the professional support of experts is needed. For example, it is useful to send drafts of articles for review to other bulletins that have recently produced articles on the same or a similar topic. An established bulletin may have contacts with medical experts in a specialised field you wish to write about. This kind of professional advice is most valuable. Some bulletins have great experience in retrieving and interpreting data from their regulatory agency and can help others to find evidence. In particular, members of staff from Public Citizen, USA, have shown other bulletin editors how to find information on the U.S. Food and Drug Administration web site.

Sometimes legal advice may be needed, especially if you expect a negative reaction from a critical article that may affect a company's sales. You may find it helpful to obtain an opinion from a legal expert associated with another bulletin even if the legal situation in your country differs somewhat.

13.3.4 Training sessions and workshops

In addition to motivation and commitment, the team starting a new bulletin needs practical training in the editorial process, production, distribution and all aspects of developing a bulletin. Training can be organized in several ways:

- A specialised training session may be organized by a more experienced drug bulletins for colleagues from a new bulletin.
- Training may be organized and supported by an international organization to promote independent drug information and to improve the quality of the drug bulletins.
- International and regional workshops and seminars organized to build partnership and improve cooperation can include practical training sessions and contribute to the professional development of drug bulletins.

13.3.5 Ongoing information exchange between bulletins

The process of information exchange is valuable in itself. It allows bulletin editors to learn about new developments, issues and concerns of colleagues working in the same field in other countries. Informal exchanges are very frequent, particularly concerning pharmacovigilance data, and on new drugs which are launched at nearly the same time throughout the world. The ISDB Newsletter also provides a forum for information exchange between bulletins. Electronic media are also useful, for example the English e-mail discussion list 'E-drug' [**http://www.essentialdrugs.org/**] (there are also essential drugs networks in French, Spanish, Russian and for India via the same web site), Healthnet [**http://www.healthnet.org/**] and INDICES [**http://www.essentialdrugs.org/indices**] and the network of editors of ISDB member bulletins (to find out about this, visit **http://www.isdbweb.org**).

13.3.6 Collaborative research among bulletins

Bulletins can collaborate for research. Box 13.2 contains examples of such collaborative work.

Box 13.2 Results of collaborative research among drug bulletins

- "Judging the therapeutic value of drugs: a comparison between *la revue Prescrire* and *Information fran Lakemedelsverket*, the bulletin of the Swedish Medical Products Agency" *International Journal of Risk & Safety in Medicine* 2004;16:83-90.
- "Prescribing information in 26 countries: a comparative study" *Eur J Clin Pharmacol* 2003; 59: 263-270. Collaborative study by WHO, Institut Català de Farmacologia, Istituto Mario Negri and ISDB.
- "An ISDB survey (23 bulletins) to assess the degree of transparency of drug regulatory agencies" *International Journal of Risk & Safety in Medicine* 1996;9:151-155.
- "An international survey of quality control procedures in independent drug bulletins" Poster 1996.
- "How informed general practitioners manage mild hypertension: a survey of readers of drug bulletins in 7 countries" *Eur J Clin Pharmacol* 1996;49:445-450.
- ISDB survey on "Which books are essential for bulletins?" by 15 bulletins, five of them in developing countries *ISDB Newsletter* July 1995.

13.3.7 Information and support for funding applications

The support of partner organizations and other drug bulletins is most helpful when a new drug bulletin or even an existing one is seeking funds to cover its operations. It may help to have a letter of support from well-established drug bulletins and/or other partner organizations, or to be able to list them as members of an advisory board when applying for funding from government or international agencies. Partner organizations may also be able to provide you with personal contacts and with information on what has helped them to obtain funding in the past.

13.4 Identifying partners and networks

A remarkable number of organizations and individuals are actively working on health issues. To identify a potential partner, it is important to understand its objectives and to recognise the driving forces of the organization. Unfortunately, many patients' organizations and associations of health professionals are sponsored by pharmaceutical companies and are therefore to an uncomfortable extent tied to the industry's goals. This is liable to cause conflicts of interest and can create pressure on the bulletin to tone down its conclusions and avoid publishing critical articles; fears about how sponsors might react can make potential partners hesitate to help a drug bulletin.

When seeking partners, it is worth asking the advice of organizations that have already proved their commitment to the promotion of rational drug use. Box 13.3 lists some international organizations that promote the rational use of drugs. Box 13.4 is a list of questions you may want to ask potential partners and networks.

Box 13.3 Some organizations promoting the rational use of drugs

- International Society of Drug Bulletins (ISDB) [**http://www.isdbweb.org**]
- Healthy Skepticism [**http://www.healthyskepticism.org/**]
- Health Action International (HAI) [**http://www.haiweb.org/**]
- The International Network for Rational Use of Drugs (INRUD) **[www.inrud.org/]**
- E-Drug: [**http://www.essentialdrugs.org/**]
- Cochrane Collaboration [**http://www.cochrane.org/index0.htm**]
- Scottish Intercollegiate Guidelines Network (SIGN) [**http://www.sign.ac.uk/**]
- WHO:Department of Medicines Policy and Standards Policy, WHO Geneva [**http://www.who.int/medicines/**]
- No free lunch [**http://www.nofreelunch.org/**]

Box 13.4 Questions to ask of potential partners and networks

- Who are the founders and/or members of the organization?
- What are its main objectives?
- If this is a network, who are the partner organizations?
- Who does the network represent?
- From what sources does the organization get funding?
- What have been the organization's recent activities? Does it have some recent examples of its work, such as publications or other written materials?

13.5 Clearly define conditions for partnership

Partnership means cooperation and support, and does not imply a donor-recipient kind of relationship between the drug bulletin and other organizations. Every newly established drug bulletin has to plan its further development to ensure self-sufficiency, sustainability and independence. Without this, unnecessary dependence on partners may develop, leading to strain between partner organizations and a crisis if partners eventually withdraw support. These are a few questions to answer before establishing a partnership:

- Who is the partner providing assistance?
- Does the new bulletin have a plan for further development, identifying the needs for assistance from other partners?
- What kind of support is required in the initial phase of work?
- For how long is this assistance required?
- What are the possibilities for mutual support?
- Is there a plan for cooperation with other partners?
- Should this partnership be formalised?

It is helpful to discuss these questions together and develop a clear understanding that the partnership cannot be perceived as a donor-recipient relationship. This not only helps to avoid future problems, it provides a solid base of understanding between partner organizations. As a new bulletin develops, ideally the initial working relationships it established for support will grow into an ongoing mutually beneficial collaboration.

Case study: *Geneesmiddelenbulletin*, The Netherlands

The monthly Dutch bulletin *Geneesmiddelenbulletin* (*Gebu* in short) was first published in 1967 under the auspices of the Directorate of Public Health at the former Ministry of Social Affairs and Public Health, and distributed free of charge to doctors and pharmacists. In 1988 Gebu was threatened with closure because of cost-cutting proposals by the Government. Combined action by many of those involved with the bulletin prevented its closure and in 1990 the bulletin was privatised with the formation of the independent Geneesmiddelenbulletin Foundation. This foundation, which consisted of a board of governors, an editorial board and an advisory council, received an annual grant from the Department of Health that covered all expenses. The mission statement of the foundation defined the independent position of the bulletin: members of the editorial and advisory board were obliged to declare relationships with pharmaceutical companies, and advertising by such companies in the bulletin was not allowed. However, in the autumn of 2003 the Minister of Health proposed to withdraw all financial support to the bulletin, but thanks to the supportive actions of the readers and colleagues from ISDB this ministerial decision was cancelled. Other problems were that the editing office was a very small organization (1.7 full-time-equivalent editors and 2.4 full-time equivalent administrative support) doing highly specialised work. The expertise of the editors was difficult to replace and in times of illness or other times when the editors' work was impaired the continuity and quality of the bulletin was seriously endangered. Furthermore, such a small organization meant limited prospects for career development.

Strategy for change
Considering these problems, the foundation board decided to approach possible future partners for cooperation, and as a first step formulated some conditions for such an alliance.

1. A possible partner should not pose a threat to the editorial independence of the bulletin.
2. Such a partner should have expertise to match that of the editors, in order to better guarantee the continuity and the quality of the bulletin.
3. The organization of the partner should be solid and financially sound.
4. The future partner should be acceptable to both pharmacists and doctors.

On the basis of these conditions a small number of possible future partners was consulted. The results of these contacts were discussed with members of the editorial and advisory boards. During this process board members of the foundation kept in contact with representatives of the Department of Health as its consent was necessary to guarantee continuation of the annual financial support to the bulletin.

After some consideration the College of Health Insurances was chosen as the future partner. This organization initiates activities that focus on quality of care by reporting on medical technology and pharmacotherapy. Among other products, it produces the *Farmacotherapeutical Compass,* a kind of national formulary. This last activity in particular provides an opportunity for cooperation and exchange of expertise.

Result
Since January 2005, the bulletin has been published by the College of Health Insurances (the foundation *Geneesmiddelenbulletin* having been liquidated), with the editorial office housed in the building of the College in Diemen. The members of the editorial office have a working contract with this College. Both parties have signed a declaration of editorial independence for the bulletin; the editorial board and advisory board will continue to function as they did within the former organization, with the title of 'external experts'.

Contributed by Jan Schuling, former Chair of the Advisory Council, Geneesmiddelenbulletin.
[http://**www.geneesmiddelenbulletin.nl/**].

14. Keeping records and creating a memory

14.1 Why keep records?

It is crucial for bulletins to keep usable records of important aspects of their activities. Good records are necessary to keep track of what has been done, so that the future activities of the bulletin can be pursued on the basis of full and accurate knowledge of what has occurred and what has been decided in the past. A bulletin that does not preserve its archives will meet problems in the future if questions are raised about the bulletin's standpoints and opinions on different questions. Good management of records and archives is necessary to ensure that information can be readily retrieved when needed.

Information accumulated in archives can be reused for a variety of purposes by the bulletin, e.g. auditing aspects of bulletin work (see Chapter 12), or perhaps used for benchmarking between drug bulletins within ISDB.

Keeping a record of certain areas of bulletin work, such as article development, is obvious and essential and is easy to integrate into the routine work of the bulletin. Not quite so obvious to do, but arguably just as important, is to keep an account of important events in the development of the bulletin. Keeping a record of these more occasional and perhaps complex events is more difficult to build in to everyday work.

14.2 What to keep and record?

Records relating to published information

Back copies of published issues. A complete set of the bulletin's past issues should be available in the editorial office. The issues should be stored in chronological order and easily accessible to members of the editorial team. It is often necessary to check what was said in the bulletin about a particular subject. The copies will be useful when deciding what topics to write about in future issues: it is helpful to look back over the years to see which articles need to be updated. Past issues can also help solve style problems when there is no house style rule, e.g. for an unusual table or graph. The problem may have been dealt with in a previous issue.

Documents relating to published articles. Records need to be kept about the articles produced by the bulletin, so that the development of an article can be traced from the start if necessary, e.g. if an error is discovered, or the article is challenged in some way. Including all the relevant documents makes it easy to understand how a subject originally came up and what evidence was available at that time, or enable the retracing of steps in the event of being challenged, or the discovery of where an error was introduced.

The archive must be organized in a way that makes retrieving information easy. It is usual to arrange archives in chronological order, the oldest at the bottom, and the most recent at the

top, so that when one looks at a record, the most recent item appears first. Care should be taken not to have different archiving orders as this may undermine the structure of the record. The same order should be used for all the articles.

You should decide upon an order for sub-sections within an archive (alphabetical, chronological, thematic, geographical), moving from the general to the particular. This will make it more searchable and easy to retrieve information.

For a bulletin that publishes many articles per issue, and has existed for many years, the volume of documents used in the preparation of articles is so large that they cannot all be kept indefinitely. For example, for *la revue Prescrire*, the complete documentation for articles is kept for three months after publication (the average time for companies and their opinion leaders to complain about an article). After this, only the references quoted in the article are kept (they remain available for readers, on request, at any time) and the rare documents which cannot be easily obtained again (e.g. unpublished material not available on any web site, clinical reports from companies).

Consider whether it would be worth keeping a microfiche or digital copy of paper documents – modern paper is acid and can destroy itself. Modern inks made from synthetic substances offer no guarantee of permanent stability. See Box 14.1 for some practical steps.

Box 14.1 Archiving article documents

- Do not use rubber bands (they dry out and break), pins or paper clips (they rust and may damage the document).
- Use folders or document bags, not binders or hanging folders.
- Use standardised boxes if possible.
- Write a label on each box. Give each box a reference number so that the files can be identified and easily found.
- Use folders and sub-folders to separate the final issue of a bulletin from the records of its development (drafts of articles, correspondence, reviewers' comments).
- Remove all duplicates and blanks.
- Decide what to keep, e.g. only cited references, or all references, including uncited background papers?
- Ensure that no important element is missing, and print out important e-mail messages.
- Check that each document is identifiable, that is to say that the three questions who? when? and where? can be answered.
- Date photographs and label press cuttings to show where they are from.
- Identify the author of manuscript notes, reports, etc.
- Check the order of the records.
- Check the title and contents.
- Complete the file title with the date on which it was closed.
- Make a list of your contents in each box, and keep the lists carefully up to date so that they are accessible for research.

A record system is only effective if it is directly relevant to the bulletin's needs. Disposing of records which are not needed is as important as creating them properly in the first place. To begin with, destroy only papers that are of no use: duplicates, rough notes and the manuscripts of published documents (unless they differ markedly from the final version).

Case study: *Farmaka i fokus*, Sweden

Farmaka i focus published an article about donepezil, and received a letter from the pharmaceutical company Pfizer: they did not consider the article well balanced. Thanks to its record-keeping systems the editorial board of the bulletin could easily retrace how the article had developed before publication and quickly respond to the company with robust reasons explaining how the conclusion of the article had been reached. This would have taken much more work if the records had not been kept, since the published article is often based on a much longer and more extensive draft.

Contributed by Malena Jirlow, Farmaka i focus, Sweden [**http://www.janusinfo.org**].

14.3 Creating an organizational memory

A young bulletin, like other new and young organizations, is preoccupied with many immediate tasks and problems, and the future seems far away and unreal. Many issues and problems recur, and as people leave the bulletin, the history and experience can be lost with them. New people joining a bulletin can benefit from knowing about and understanding earlier experiences in the development of the bulletin, including what changes were made and what effects these had as far as one could tell. It might be possible to share this information with new bulletins, perhaps in future editions of this manual.

Examples of the kind of events that are valuable to record include:

- Why various editorial procedures were introduced or modified, what went well, what had to be reconsidered.
- How relationships with other organizations developed, to what extent they met expectations/hopes. On the financial and legal sides, what difficulties occurred and how they were dealt with.
- Discovery and correction of staffing imbalances, the recognition of new needs and how they were satisfied, training of staff.
- Funding and pricing aspects.
- Relationships with readers, official bodies, industry, the media, patients' organizations and advocates.

For all of these a brief written contemporary log is likely to be of value. Ideally this could enable someone to write a biography of the bulletin after, say, 20, 30, or 50 years. The following case study shows the range of significant events that can occur in the life of a bulletin.

Recording this type of information is not quite so easy. It relies on people involved in the changes remembering to write down an account of what happened. It is probably best for one person in the team to be responsible for keeping the records, and reminding and

encouraging others to contribute. Having a regular time for reflection, e.g. every six months or year, might be effective. It will be necessary to make all of the team aware of the archive so that people add to it and make use of it.

Case study: *Drug and Therapeutics Bulletin*, UK

The UK's *Drug and Therapeutics Bulletin* (DTB) was one of the first drug bulletins in the world, having been started in the early 1960s. So its long history has seen many notable changes that could be described in an historical account.

- How *DTB* started: at the beginning it included articles from the US *Medical Letter*, modifying them, and then gradually using them less; it would be interesting to know reasons for that and how the separation happened.
- Evolution of the editorial system: from using external editors to employing permanent in-house editorial staff.
- Relationships with pharmaceutical companies, including a 1964 libel action brought by a maker of eardrops, and various later disputes and threats that faded.
- The relationship with *Prescribers' Journal*, another UK bulletin which was published by the Department of Health; it seemed to be in competition, but actually was not, because the publications differed in style and method of production.
- How the Department of Health began to buy bulk subscriptions for trainee general practitioners and medical students, and how that was extended over the years to all doctors in the National Health Service, and what that meant financially and legally. This led to the change from fortnightly to monthly publication, because that saved a lot in postage costs.
- 'Translating' articles for publication to lay readers: the development of *Treatment Notes*.

Contributed by Andrea Tarr, DTB, UK. [**http://www.dtb.org.uk**].

Keeping a record of things that help to demonstrate the impact of the bulletin is also valuable. As discussed in Chapter 12, formally measuring the impact of a bulletin's messages (e.g. in terms of effects on prescribing) is difficult. But collecting evidence that gives an indication of the influence of the bulletin can be done and could be invaluable when required to show the bulletin's funders, be they individual subscribers or organizations, the value of the bulletin. Specific items to collect include noting when other publications have cited the bulletin, press cuttings, a list of radio and television programmes in which the bulletin has participated (not always as easy to retrieve as press cuttings), photographs and correspondence. More complex events might need to be described in a written account.

14.4 How to start an archive

When starting your bulletin and its archive you should take the following steps:

- gain support for keeping an archive and the methods for creating it from the bulletin's management, editorial board and advisory board;
- prepare a list of the documents and files which are of value to save in an archive. Include in this list the different media in which these documents are preserved (paper, analogue, digital), and set up procedures for their intellectual and physical management;

- raise awareness and provide information for authors, editors and reviewers to encourage them to appreciate the archive;
- encourage them to use the archive in their work.

14.5 Further reading

1. *The Dirks methodology: a users guide.* Part 1. September 2001 (rev. July 2003). National Archives of Australia. Available at: **http://www.naa.gov.au/recordkeeping/dirks/dirksman/part1.html#bg1**

2. *The records of NGOs, memory to be shared, A practical guide in 60 questions*. International Council on Archives. Available at: **http://www.ica.org/biblio.php?pdocid=171**

3. *Information and documentation - Records management - Part 1: General*. ISO 15489-1:2001. International Organization for Standardization.

Appendix: Electronic sources of information

For general access to evidence

The TRIP database

http://www.tripdatabase.com/
Turning Research Into Practice. Provides rapid access to a wide range of reliable, clinically relevant and robust sources of evidence about medicines from around the world. Access by subscription, but non-subscribers to the TRIP database are allowed five free searches. Free to low-income countries.

Database of Essential Information on Therapeutics (in Spanish)

http://www.sietes.org (http://www.icf.uab.es)

HINARI

The Health InterNetwork Access to Research Initiative (HINARI) provides free or very low cost online access to the major journals in biomedical and related social sciences to local, non-profit institutions in developing countries.
http://www.healthinternetwork.org/

Journal articles

Medline (PubMed)

http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed
MEDLINE is the National Library of Medicines' (NLM's) premier bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the health care system, and the preclinical sciences. MEDLINE contains bibliographic citations and author abstracts from more than 4,800 biomedical journals published in the USA and 70 other countries. The database contains over 12 million citations dating back to the mid 1960s. Coverage is worldwide, but most records are from English-language sources or have English abstracts.

Free medical journals

www.freemedicaljournals.com/
A site dedicated to the promotion of free access to medical journals over the Internet.

Systematic reviews

The Cochrane Library

Database of systematic reviews.
http://www.cochrane.org

Access to The Cochrane Library is free to all in England, Wales, Ireland, Australia, Norway, Sweden, Finland and South Africa. Details of how to gain access can be found on the following web site: http://www3.interscience.wiley.com/cgibin/mrwhome/106568753/DoYouAlreadyHaveAccess.html.

The publishers of the The Cochrane Library are piloting a scheme whereby editors of selected publications, including ISDB member bulletins, can receive complementary access to The Cochrane Library. Contact Alexa Dugan at adugan@wiley.co.uk giving your name, publication details, e-mail address and full postal address.

Clinical Evidence

Describes the best available evidence from systematic reviews, randomised controlled trials and observational studies where appropriate, and if there is no good evidence it says so.
http://www.clinicalevidence.com/ceweb/conditions/index.jsp

National disease prevention and control, health promotion etc.

Centers for Disease Control and Prevention (CDC), USA

http://www.cdc.gov/

Health Protection Agency, UK

http://www.hpa.org.uk/infections/default.htm

Health technology assessment

Health technology assessment (HTA) is the process of systematically reviewing existing evidence and providing an evaluation of the effectiveness, cost-effectiveness and impact, both on patient health and on the health care system, of medical technology and its use.

INAHTA - The International Network of Agencies for Health Technology Assessment

Links to 39 HTA agencies in 21 countries
http://www.inahta.org/inahta_web/index.asp

Clinical guidelines

Guidelines International Network

An international not-for-profit association of organizations and individuals involved in clinical practice guidelines.
http://www.g-i-n.net

UK National Institute for Clinical Excellence (NICE) UK

http://www.nice.org.uk/page.aspx?o=20

Scottish Intercollegiate Guidelines Network (SIGN)

http://www.sign.ac.uk/

New Zealand Guidelines Group

http://www.nzgg.org.nz/index.cfm?screensize=1024&ScreenResSet=yes

Prodigy

http://www.prodigy.nhs.uk/ClinicalGuidance/ReleasedGuidance/GuidanceList.asp

Formularies/Essential medicines

British National Formulary

http://www.bnf.org

WHO Medicines Library

http://Mednet3.who.int/EMLib

Répertoire Commenté des Médicaments

http://www.cbip.be

WHO Model Formulary

Available in Arabic, English, Russian and Spanish
http://www.mednet3.who.int/EMLib/wmf.aspx

Available on CD-ROM

WHO Model List of Essential Medicines

http://www.who.int/medicines/organization/par/edl/expertcomm.shtml

WHO Medicines Bookshelf 2004

CD-ROM of publications related to essential medicines

Regulatory authorities

European Medicines Agency (EMEA)

http://www.emea.eu.int/home.htm

European portal of all European national agencies

http://www.heads.medagencies.org

U.S. Food and Drug Administration

http://www.fda.gov/

Japanese Pharmaceutical and Medical Device Agency (PMDA)

http://www.info.pmda.go.jp/shinyaku/shinyaku_index.html

Adverse effects

Australian Adverse Drug Reactions Bulletin

The Australian Adverse Drug Reactions Bulletin is produced six times a year by the Adverse Drug Reactions Advisory Committee (ADRAC), a subcommittee of the Australian Drug Evaluation Committee which advises the Therapeutic Goods Administration on the safety of medicines.

http://www.tga.gov.au/adr/aadrb.htm

Current problems

Articles and alerts from the UK medicines regulatory agency.

http://www.medicines.mhra.gov.uk/ourwork/monitorsafequalmed/currentproblems/currentproblems.htmCSM

Canadian Adverse Drug Reaction Newsletter

From Health Canada.

http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/adrindex_e.html

U.S. Food and Drug Administration Medwatch Safety Information and Adverse Event Reporting Program

Medwatch provides safety information on the drugs and other medical products regulated by the U.S. Food and Drug Administration.

http://www.fda.gov/medwatch/

Institute for Safe Medication Practices, USA

The Institute for Safe Medication Practices (ISMP) is a non-profit organization that works closely with healthcare practitioners and institutions, regulatory agencies, professional organizations and the pharmaceutical industry to provide education about adverse drug events and their prevention.

http://www.ismp.org/

WHO publications on pharmacovigilance

The Importance of Pharmacovigilance: safety monitoring of medicinal products, 2002, World Health Organization.
http://www.who.int/medicines/library/qsm/ip_booklet.pdf

Safety of Medicines: a guide to detecting and reporting adverse drug reactions

http://www.who.int/medicines/library/qsm/who-edm-qsm-2002-2/esd_safety.pdf

Safety Monitoring of Medicinal Products: guidelines for setting up and running a pharmacovigilance centre.

http://www.who-umc.org/pdfs/guidelines.pdf

WHO Collaborating Centre for International Drug Monitoring. Uppsala, Sweden

http://www.who-umc.org/index2.html

Information about/for patients

DIPEx

Database of Personal Experiences of Health and Illness
The growing number of modules on this site (now 20) aim to describe the fullest possible range of people's experiences with the particular disease or problem. It is based on video or audio interviews with people throughout the UK.
http://www.dipex.org/

HealthInsite, Australia

HealthInsite is an Australian Government initiative, funded by the Department of Health and Ageing. It aims to improve the health of Australians by providing easy access to quality information about human health.
http://www.healthinsite.gov.au/index.cfm

Drug promotion

No free lunch

A source of information, inspiration, and assistance for those who are trying to rid their practices, institutions and colleagues of promotional influence. It provide a forum for the exchange of ideas as well a way to connect and work together with others who are concerned about this issue. They can provide assistance to those interested in speaking on the topic, and speakers to those less interested in speaking.
http://www.nofreelunch.org/

No grazie, pago io

http://www.nograziepagoio.it/

Healthy Skepticism

Previously The Medical Lobby for Appropriate Marketing (MaLAM). An international non-profit organization for health professionals and everyone with an interest in improving health. Its main aim is to improve health by reducing harm from misleading drug promotion. Includes Adwatch – evaluations of advertising.
http://www.healthyskepticism.org/index.htm

Drug Promotion Database

Development of this database was coordinated by Health Action International and WHO under the technical responsibility of Joel Lexchin. There are currently 2178 entries on drug promotion.
http://www.drugpromo.info/

Hitting the Headlines Archive

Summarises media coverage of health topics, with indication of source of the stories. A handy web site during media frenzies.
http://www.nelh.nhs.uk/hth/archive.asp

Networks and directories

E-drug

An e-mail discussion forum on essential drugs, national drug policies and standard treatment guidelines. It is also a good source of information on future conferences and courses, new publications, recent articles, and broader political (e.g. trade, patents, pricing) aspects of medicines access. More information: **www.healthnet.org/programs/edrug.html**.
In Spanish: Acerca de E-FARMACOS
http://www.essentialdrugs.org/efarmacos/about.php

INASP-Health Directory

International Network for the Availability of Scientific Publications
A directory of international organizations and programmes working to improve access to reliable information for health professionals. Links to providers of free or low-cost information.
http://www.inasp.info/pubs/healthdir/

HIF-net

This is a joint venture between WHO and the Health Information Forum (HIF), providing a neutral focal point for finding out about useful sources of information and also for discussion of issues relating to access and use of information by health professionals in developing countries. The email list brings together the full range of stakeholders involved in the creation, provision and use of healthcare information, from over 130 countries worldwide.
http://www.inasp.info/health/hif-net.html

INDICES

An electronic discussion group for English-speaking colleagues working in the area of non-essential drug information and drug information centres. It provides a forum for discussion of issues around the organization of drug information centres including set-up, funding, management, quality and training. It also supports the promotion of objective drug information, answers technical questions on drugs that cannot be solved by standard textbooks, and responds to queries on non-essential drugs.
http://www.essentialdrugs.org/indices/about.php

INASP Health Links

The Internet Gateway to selected web sites for health professionals, medical librarians, and publishers in developing and transitional countries. **http://www.inasp.info/health/links/contents.html**

Includes section on pharmacology and prescribing:
http://www.inasp.info/health/links/drugs.html

ISDB member bulletins

For links to the web sites of member bulletins (arranged by country), visit the ISDB web site **http://www.isdbweb.org**

Feedback and evaluation form

Have you read the manual?

Which chapters are most useful?
In what way?

Which chapters were the least useful?
In what way?

Is the layout/language/format clear?

Is there anything in the manual that you disagree with, or that should be improved?

How have you used the manual in your every day practice?

Please describe how the manual has helped you in practice.

Do you have any new examples or new key lessons that could be included in the manual?

Name:
Contact details:
Address:
Telephone number:
Fax number:
E-mail address:

Please visit the ISDB web site: **http://www.isdbweb.org** for details of where to send feedback.