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 SOURCES, TYPES AND AVAILABILITY OF INFORMATION CONCERNING  
 THE USE OF DRUGS 147

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SOURCES, TYPES AND AVAILABILITY OF INFORMATION CONCERNING  
THE USE OF DRUGS

THE NEED FOR OBJECTIVE GUIDANCE ON PRESCRIBING PRACTICES

1. Whereas the cumulative rate of expansion of the scientific medical literature is prodigious and much of this is related to drug therapy, little of this output directly influences the prescribing practices of doctors. The original literature is largely inaccessible to the busy generalist and over the past two decades an appreciation has developed that greater efforts are needed to provide prescribers with readily assimilated, independent and objective information that will keep them adequately informed of changes in therapeutic practice throughout their professional careers.

2. The problem is evident in both developed and developing countries. It is a product of the current and unparalleled rate of therapeutic innovation, and it is exacerbated in market economy countries by the consequential promotional activities of competing pharmaceutical manufacturers. This, in turn, has resulted in varying measures of governmental and self-imposed control over the content and presentation of advertising material by pharmaceutical manufacturers. It has also stimulated governments and the medical profession to take a variety of initiatives in the supply of independent prescribing information.

3. An account of the available sources and channels of information on drugs is given perspective by a short account of the manner and sequence in which technical data are generated on a new product before and after its registration for marketing.

THE GENERATION OF DATA ON THE SAFETY AND EFFICACY OF DRUGS

National drug regulatory authorities as assessors of information

4. To an important extent the prescriber's need for information on drug products has been alleviated by the institution of national drug regulatory authorities, particularly in those industrialized countries where drug innovation is largely concentrated, since their influence has resulted in the elaboration of independent and authoritative standards of quality, safety and efficacy in marketed products. It is beyond the capacity and the competence of prescribers to assess at first hand the potential risks and benefits of the drugs that they use. Thus, the necessity of creating independent multidisciplinary bodies at national level to adjudge the acceptability of new products for general marketing, and to subject existing products to systematic review, would ultimately have become apparent without the emotive stimulus of the thalidomide tragedy.

5. Regulatory authorities in market economy countries are not, however, constituted to develop as primary sources of drug information. Although several authorities are becoming more active in this regard their terms of reference typically invest the licence holder - usually the drug manufacturer - with the prerogative and responsibility of informing and advising prescribers on the use of the relevant product. The informational role of the regulatory authority is limited, in these circumstances, to ensuring that the product is advertised in a manner that is consonant with the terms of the product licence.

6. Whereas such control is readily instituted for new products, the control of those available before registration requirements were introduced demands a comprehensive national review of all products. In many cases it also demands the generation of new data to allow their assessment according to contemporary

standards. This is a task that many national regulatory authorities have yet to complete, but it is not applicable, of course, to countries where drug requirements are centrally planned, and where manufacture, advertising and provision of prescribing information are, largely or totally, dependent upon the government's own commitment to support health programmes.

#### Exchange of information between regulatory authorities

7. Countries that have yet to introduce comprehensive provisions for drug regulation can draw from a diversity of national systems in determining their own requirements. Nonetheless, problems in establishing drug control in developing countries have, too often, resulted from the adoption of legislative provisions successful elsewhere, but of a complexity that precludes their effective implementation on the available resources.
8. As an alternative to adopting regulatory systems devised for countries with different economic, commercial and social circumstances, scope exists for developing countries to consider whether statutory recognition might be accorded to existing international systems for exchange of information. The full implementation of an essential drugs policy, for instance, as embodied in the various WHO reports on the Model List of Essential Drugs,<sup>1</sup> is dependent upon the translation of an analogous list into national policy through an appropriate system of drug registration. Similarly, the regulatory capacity of a drug-importing country is enhanced if it takes advantage of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce<sup>2</sup> and the WHO sponsored network of formally designated national drug information officers<sup>3</sup> to establish the status and labelling of imported products in their countries of origin.
9. More extensive exchange of technical information between regulatory authorities could result, not only in more effective use of available data, but also in a basic reorientation of drug regulation in countries that are primarily dependent upon importation of pharmaceutical products. A regulatory authority that is relieved of the necessity of undertaking an independent technical review of every product to establish its acceptability for marketing, and which may not have the financial or technical resources to undertake such assessments in depth, has greater opportunity to consider how each drug will be used within the domestic context and to ensure that appropriate information is available to prescribers at every level.
10. Whereas many national regulatory authorities still regard the technical data included in manufacturers' marketing applications as confidential, commercially-sensitive information, important initiatives resulting in freer exchange of this information have been taken over the past five years within the USA. The United States Food and Drug Administration now routinely issues summarized details of the biological information on which the approval of important

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<sup>1</sup> WHO Technical Report Series, No. 772, WHO, Geneva, 1985. The use of essential drugs: report of a WHO Expert Committee.

<sup>2</sup> WHO Official Records, No. 226, 1975. Offprint - Good Practices in the Manufacture and Quality Control of Drugs and Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce.

<sup>3</sup> Director-General's Circular Letter 30 December 1981. (C.L.27. 1981).

new drugs is based.<sup>1</sup> It also publishes lists of generic products deemed to be therapeutically equivalent to other marketed formulations of the same preparation on the basis of standardized criteria, including an appropriate demonstration of bioequivalence where this is considered necessary.<sup>2</sup> Newly proposed US statutory provisions, if adopted, will further extend the opportunity for public disclosure of such data. It is important, if standards of preclinical and clinical drug development are to evolve and improve, that over-zealous protection of this information should be discouraged.

#### Information generated before drug registration

11. Drugs are currently authorized for use by regulatory authorities on the basis of their performance in biological models and in controlled, but limited clinical studies. The results of the preclinical experiments undertaken by the manufacturer establish the pharmacological profile of the compound in animal models (and of its antimicrobial or antiparasitic activity, where this is relevant); its immediate and delayed toxicity; its mutagenic and carcinogenic properties; its teratogenic potential; and its pharmacokinetic characteristics both in animals and man. The tests are conducted in animal species chosen, not with regard to their evolutionary proximity to man, but because of their adaptability to laboratory conditions and the large body of information that is available on their vital functions and on their responses to chemical exposure. They provide fair but fallible indicators of the potential effects and hazards of pharmacologically active substances in man.

12. Comparative toxicology remains a young and often empirical science. Its fundamental methodology is still evolving; demonstration and quantification of acute toxic effects based on statistically validated estimates of the lethal dose have recently been discarded; the necessary period of exposure used for demonstration of long-term toxicity remains in contention; the selection and interpretation of mutagenicity tests remain open to debate; and the relevance of traditional long-term, high-dosage carcinogenicity testing to clinical use remains in doubt. In what may well be a unique comparative toxicological study commissioned by a national regulatory authority, the Committee on Safety of Medicines in the United Kingdom in 1972 exposed the vagary of assessing the carcinogenicity of steroid contraceptive compounds in rodents.<sup>3</sup> The fortuitous use of animals from more than one breeding colony demonstrated the existence of important strain-dependent variations in response.

13. This incident alone establishes an impressive case for further comparative analyses of toxicological data generated by pharmaceutical companies. Indeed, a data bank containing comprehensive animal toxicological data from pharmaceutical companies operating in the United Kingdom has been set up under the auspices of the industry to provide for this need and to enable a more rational approach to animal studies to be developed.<sup>4</sup> Similar initiatives have been taken in other countries. These will operate most effectively to the advantage of public health - and, possibly, to the commercial interests involved - if both the data and the conclusions are made generally available.

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<sup>1</sup> Summary basis for approval. United States Food and Drug Administration.

<sup>2</sup> Approved prescription drug products with therapeutic equivalence evaluations. Fifth edition, 1984. United States Department of Health and Human Services.

<sup>3</sup> Carcinogenicity tests of oral contraceptives. Committee on Safety of Medicines. HMSO, London, 1972.

<sup>4</sup> A toxicology databank based on animal safety evaluation studies of pharmaceutical compounds. Human Toxicology, 1985, 4: 447-460.

14. The case for increased accessibility to pre-marketing safety and efficacy data applies, with the same validity, to the results of clinical studies. New drugs are typically registered for marketing on the basis of their performance in a small number of time-limited, controlled, comparative clinical trials. Even in the case of indisputably innovative products intended for prolonged use in man, therapeutic potential will rarely be assessed in more than a thousand patients, few of whom are likely to have received the product for more than a year.

15. Because these studies are limited in time they provide no more than inferential information on the long-term effects of drugs that palliate the signs and symptoms of chronic disease: the determination of long-term efficacy and risk demands experience of long-term usage. Similarly, studies limited in size, are not designed to detect - nor are they likely to generate information on - infrequent adverse reactions to treatment.

16. Moreover, sound design of a comparative trial based upon randomized allocation of the various treatment groups demands a measure of homogeneity among the patients admitted to the study. This implies that such studies are often undertaken only on a defined subsection of the ultimate target population for the drug. This being so, many new drugs enter into routine use before direct experience is gained of their performance in individuals liable to react anomalously, including the fetus, the very young, the elderly, the severely debilitated, and patients taking other drugs concomitantly for other conditions.

17. Prescribers disposed to use a new drug would have an opportunity to gain a deeper insight into its properties if, in addition to the information carried on the labelling concerning indications, contraindications, precautions and warnings, they were informed of the clinical data on which the marketing approval is based and of any hypothetical risks identified by the results of toxicological testing.

#### Information generated after registration

18. The implications of these deficiencies in information at the stage of registration are readily apparent. That they exist is an inevitable consequence of new drug development as it is now perceived, and it is for society to judge at what point or in what circumstances risk of the unknown and unpredictable outstrips anticipated benefit. Certainly risk can never be totally excluded and the clinical investigation of a drug that is unlikely to offer clinical advantage over existing therapy raises ethical considerations for manufacturers and clinicians alike.

19. Unanticipated and unacceptable hazards are occasionally detected after a drug enters into routine use and there is increasing awareness that the performance of marketed drugs should be collated and analysed as effectively as is feasible. Only through systematic observation is it possible to obtain more precise insights into benefits, risks and relative performance of different drugs within the same therapeutic class. Relevant information is generated in a variety of ways. These include:

- prospective post-registration surveys required, on occasion, by national drug regulatory authorities as a condition of granting or renewing a product licence, normally to resolve specific concerns about potential adverse effects;
- prospective trials comparing different products, or different treatment regimens, under controlled conditions. Such studies may be conducted either in a hospital setting or in outpatient practice, often on a multicentre basis and, typically, with the financial support of an interested manufacturer;

- rare serendipitous observations by individual clinicians that result in the unanticipated discovery of a new therapeutic application for a marketed product;
- spontaneous reports of presumptive adverse reactions notified by practising clinicians to a national monitoring centre or to the manufacturer. At present some 26 countries pool the notifications they receive in a data base maintained by the WHO Collaborating Centre on International Drug Monitoring in Uppsala, Sweden with a view to generating early signals of unanticipated reactions. In addition, at least two countries, France<sup>1</sup> and the USA,<sup>2</sup> have recently imposed a statutory responsibility on pharmaceutical manufacturers to disclose details of all presumed serious adverse reactions to products registered under their jurisdiction regardless of the country in which they are reported;
- epidemiologically-based studies, both prospective and retrospective, that attempt to provide a representative and statistically defined estimate of specific indicators of benefit and risk. These activities range from small retrospective case-control studies to large, prospective nationally-based or international surveys. Since the costs and organizational problems presented by the latter studies are formidable, they have hitherto been directed to issues of outstanding public health significance such as the value of treating mild hypertension and the long-term effects of systemically-administered steroid contraceptives. Although a statistically powerful methodology has been developed to address such problems, the vulnerability of even the most carefully designed studies to random and systematic error is now well appreciated and the possibility of confounding bias distorting apparent drug-induced effects raises complex problems in the analysis of results. There can be no doubt that the application of these methods to therapeutic investigation adds a new and vital dimension to drug assessment. The concomitant rapid development of computer technology creates a complementary potential for monitoring the health records of large samples of patients exposed to specific drugs by means of record linkage techniques that, in principle, have virtually limitless applications. The danger is that superficial and casual investigation will create problems of interpretation and that fact may become blurred by aberration and artefact.

#### PRESENTATION OF INFORMATION TO PRESCRIBERS AND THE PUBLIC

20. There is no stereotyped national pattern by which information from these various sources is presented to the end user of drugs. In many market economy countries the manufacturers, the government, representative professional bodies, technical journals, the media and, to a growing extent, consumerist organizations, have each assumed a role. In centrally-planned economies, in contrast, where industry is an arm of government, domestic drug advertising is designed to provide factual information rather than to promote sales. In these circumstances information flows primarily from governmental and professional sources.

21. A composite listing of the mechanisms by which information is regulated and conveyed around the world would include the following:

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<sup>1</sup> Pharmacovigilance: Organisation et Déclaration. Journal Officiel du 30 mai 1984 (No. 126).

<sup>2</sup> Adverse Drug Experience Reporting. Food and Drug Administration. Federal Register, 1985, 50: 11478-11484.

#### The product licence

22. This is the instrument issued by the national licencing authority (a national drug regulatory authority, where such exists) to the licence holder authorizing the distribution and sale of a specific pharmaceutical product within the jurisdiction of the authority. It typically contains:

- a precise description of the product including the brand name (if any), the structural formulae of the active ingredients, their approved non-proprietary names, the source of starting materials, the route of synthesis, a comprehensive list of excipients, physical details of the dosage form, bioavailability data, quality control procedures and a requirement that no substantive change may be introduced into the method of manufacture without the approval of the licencing authority;
- details of packaging and labelling to make provision, in particular, for the approved non-proprietary name, the strength of the dosage form, a batch number and an expiry date;
- the category of the product to indicate any restrictions to be applied to distribution and sale, whether it is a prescription item, a pharmacy item or a general sale item, and whether additional restrictions to prevent abuse or to limit the drug to hospital or other specialized use are required;
- a document, or data sheet, with which all subsequent advertising and promotional material must comply.

23. With the exception of the data sheet and labelling material, the product licence in this context is a confidential document that contains commercially-sensitive information considered to be essential for precise registration and effective control of the product.

#### The data sheet

24. In a few countries it is considered mandatory that all doctors should receive objective, officially-approved information about the properties and use of each new prescription medicine before it is launched on the market. The data sheet, which also provides the basis of the package insert, serves this purpose and it must be posted individually to all registered medical practitioners within a specified period before marketing. It sets out the approved indications for the product, recommended dosage regimens, contraindications, precautions, warnings, details of packaging, pack size and optimal storage conditions.

#### Summary basis for approval

25. Although a data sheet defines the usage of the product in terms acceptable to the licencing authority, it provides no description of the preclinical or clinical data on which these conclusions were founded. To provide prescribers with an account of the nature and quality of these data the US Food and Drug Administration now publishes summaries of the pharmacological, toxicological and clinical studies on which the marketing authorization was based. References to animal data are similarly included in product monographs that are updated from time to time by the Canadian Health Protection Branch, and in drug profiles produced by the Australian National Drug Information Service.

Pharmacopoeial monographs

26. Having regard to the potent biological activity of drugs and to the serious clinical situations in which they are often required, users need every reasonable assurance that their quality conforms to specification not only at the time of manufacture but throughout their shelf-life. Publicly accessible monographs defining these specifications are published both by national pharmacopoeial commissions and by WHO. The International Pharmacopoeia produced by WHO is intended particularly to subserve the needs of developing countries.<sup>1</sup> It is now complemented by a series of basic tests of identity of drugs included in the WHO Model List of Essential Drugs, simple tests of gross degradation and a compendium of stability data on these drugs under tropical climatic conditions. The objective is to provide peripheral health workers with some ability to test the quality of their stocks without recourse to laboratory facilities, and to be able to refer doubtful material for further analysis.

Manufacturers' promotional activities

27. The basic right to promote the products of private enterprise is conferred by statutory or even constitutional provisions in some countries. The advertising of pharmaceutical products is, nonetheless, extensively controlled in developed market economy countries both by regulation and by voluntary codes of practice, and some regulatory authorities routinely monitor advertising material. These restrictions place constraints on the format and presentation of advertising copy, the types of products that can be advertised direct to the public, and the use of the evanescent images of film and television. Particularly in countries where access to journals is limited, company representatives are widely deployed to promote products. Some of these representatives are highly trained, and they are in a position to offer constructive and practical advice. Their mission, however, is to promote the products of the company for which they work and it is not feasible to subject their activities to effective monitoring. At international level, the Twenty-first World Health Assembly, in 1968, adopted a series of ethical and scientific criteria for pharmaceutical advertising<sup>2</sup> (set out in extenso in paper 2.1), and in 1982 the International Federation of Pharmaceutical Manufacturers Associations produced its own Code of Marketing Practices.<sup>3</sup>

28. Notwithstanding the existence of these constraints, reservations are still expressed about the basic premise of treating drugs as normal commercial entities and soliciting their use through competitive advertising rather than objective evidence. New products, in particular, are intensively promoted when they are introduced to the market. At this time they have been subjected to limited clinical use. Their advantages and disadvantages with respect to alternative drugs are, at best, incompletely defined, and no secure judgement can be offered as to whether they will ultimately become established in routine practice. Moreover, with the exception of those authorities that are required to assess whether a proposed new product satisfies a medical need, national drug regulatory authorities are not empowered to undertake comparative assessments of products. In the latter case, no test is applied at the time of registration as to whether a new product is more or less efficacious than others already available.

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<sup>1</sup> The International Pharmacopoeia, Third Edition, Volume 1, 1979; Volume 2, 1981; WHO, Geneva.

<sup>2</sup> Ethical and scientific criteria for pharmaceutical advertising. World Health Assembly Resolution WHA21.41, May 1968.

<sup>3</sup> IFPMA Code of Pharmaceutical Marketing Practices. International Federation of Pharmaceutical Manufacturers Associations, 1982.



29. It is important, however, to consider promotion in a broader and more neutral context. Doctors themselves have a valid promotional role, whether by publishing results of trials or other clinical studies sponsored by companies, by organizing symposia on new drugs or, not least, by the example of their own prescribing practices.

#### Lists of reimbursable products

30. Because of large price differentials that commonly exist between competing products and particularly the high cost of sophisticated dosage forms, such as slow-release preparations, several national administrations notify doctors and pharmacists that the charges for specific products are excluded from permitted reimbursements to patients participating in national social security systems.

#### Officially-sponsored prescribing advice

31. To further advise doctors on efficient and cost-effective drug use some national health authorities also provide tables or bar charts indicating the comparative costs of interchangeable products as well as authoritative prescribing advice issued on a regular or intermittent basis. The content and format of officially sponsored national formularies is also being changed in some countries to accord with the same general objective: entries are selective rather than comprehensive and they are prefaced and accompanied by didactic prescribing advice.

#### Drug compendia

32. In order to provide doctors with a comprehensive collection of data sheets in a convenient format, regularly updated drug compendia are published in many countries. Some of these are published as private ventures and others are compiled by national associations of pharmaceutical manufacturers. In some cases, however, entries are included that have not been approved by national authorities. Whereas these are readily distinguishable in some publications, this is not invariably the case. In the case of some compendia sustained on advertising revenues - and issued gratis to doctors in many countries - there is no assurance that any of the entries conform to authorized texts, for the controls applied to information issued by manufacturers may not apply to information issued by independent publishers.

33. Other compendia, such as those produced by the American Hospital Formulary Service, the American Medical Association, the British Medical Association and the Pharmaceutical Society of Great Britain, are clearly independent, authoritative and encyclopaedic in their coverage. Such information, however, rapidly becomes dated and new editions of some of these works can only be produced at 3-5 yearly intervals. The development of computerized data bases offers the prospect that some of these compendia may soon be published more frequently. Meanwhile, on-line access to Martindale's Extra Pharmacopoeia, which is already available, offers an effective but costly means of obtaining updated information on selected topics.

#### Medical journals

34. Referred technical journals provide the ultimate, original source of much information on the properties and uses of drugs. Articles relevant to any one topic are so widely dispersed, however, that an extensive library with specialized search facilities is essential for adequate access to the literature. In any case, clinicians with onerous general clinical responsibilities rarely have the opportunity to undertake systematic literature surveys of the drugs that they use.

35. Several professional abstracting services now provide weekly or monthly updates on articles relating to a given specialized field that are published in major technical journals. Such information is available either in facsimile on microfiche or, in summarized form, in news-sheets. The preparation of this information, however, is a labour-intensive task; the output is directed to a relatively small, specialized readership and, in consequence, it is often prohibitively expensive for individual subscribers, even in highly affluent countries.

36. Faced with this situation, editors of many national and international medical journals now assume more responsibility for educating - as opposed to informing - their readers. Authoritative basic reviews of clinical and scientific topics, question and answer features, reports of the activities of professional governmental committees, and expanding correspondence columns challenge the traditional dominance of the original research paper, and leading articles have become concerned more with practical medicine and less with erudition.

#### Textbooks

37. Textbooks of repute, particularly those that are the product of a single author or editor, hold attraction for the undergraduate student because they are cohesive, comprehensive, yet concise. They possess these advantages because they offer a viewpoint rather than a dispassionate analysis of counter-arguments.

38. The viewpoint offered, however, has typically been that of the hospital-based consultant. The admittance of general practice as an entity in undergraduate curricula in recent years has yet significantly to influence this situation. Yet more striking is the lack of textbooks written from within the perspective of the developing world. Even standard texts of tropical medicine remain dominantly a product of specialized institutions in developed countries. In large measure, this situation reflects economic constraints. Textbooks are not commercially viable unless high volume sales can be guaranteed. This is not the case in smaller developing countries which are left no option but to resort to importation of books at prices that are now virtually prohibitive.

39. The domain of therapeutics presents an exceptional challenge to authors. Postgraduate textbooks, particularly if they are frequently updated, should offer a reliable distillate of existing knowledge on a given topic. It is becoming an overwhelming task, however, for a small editorial group, no matter how highly motivated, to keep abreast of current therapeutic information in an authoritative and comprehensive manner.

#### Review journals and drug bulletins

40. New types of publication have consequently emerged to provide both oversights and updates on important therapeutic topics. Journals have been created that present either detailed and comprehensive review material, or notes on recent therapeutic research presented in the mould of newspaper journalism. Independent, weekly or monthly bulletins published by academic groups, consumer groups and other bodies have exerted a notable influence on the assessment of marketed products and, in some cases, on the decisions of national drug regulatory authorities. Their authority is varied, being as strong as the consultative procedures and the editorial and advisory groups involved in their production.

41. A particularly encouraging feature of the past five years is the number of such bulletins that have appeared and sometimes become established in developing countries. The information, however, is often drawn largely from international sources and, as such, this is sometimes of questionable priority - or even relevance - to local needs.

### The media

42. In some countries public television time has been accorded in off-peak hours to post-graduate education for doctors and, in recent years, the media have also become more attentive to the presentation of health issues to the general public. Under the influence of consumerist groups with the active involvement of doctors, the mass media have created a greater awareness of the importance of lifestyle to health, of the values and limitations of self-medication, and of the strengths and shortcomings of the public health services. Through these activities lobbying pressures have also been exerted on drug manufacturers and governments to bring them to reappraise their performance and attitudes in the promotion and control of drugs. Undoubted successes have been achieved in obtaining or accelerating the withdrawal of several marketed products and in stemming unacceptable promotion of several drugs in countries lacking well-established regulatory systems.

43. However, bias in media reporting, even when it is unintended, can readily undermine public confidence in established practice. In the early 1970s, for example, reservations were expressed about the safety of whooping-cough vaccine and particularly about its propensity occasionally to induce encephalopathy and permanent brain damage. Subsequent controversy caused pertussis immunization to be discontinued in some countries and discouraged elsewhere; major epidemics of the disease followed resulting in many deaths. The implementation of community health programmes commonly presents governments, public health officials and pharmaceutical manufacturers with onerous ethical responsibilities including the need to make equitable provision for the rare and unfortunate victims of injuries induced by drugs or vaccines. To dramatize remote yet tragic risk when this is the inevitable price of community protection against the unacceptable burden of serious communicable disease could mean that society, particularly in developing countries, will forego potential benefits of new drugs and vaccines and it may jeopardize established programmes of health care.

### EVALUATION OF THE INFLUENCE OF DRUG INFORMATION

44. The significance of given factors on prescribing practices of doctors is not readily assessed when a variety of messages compete for their attention.

45. However, the considerable sums invested by pharmaceutical companies in advertising their products are presumably known to be cost effective. Much of this expenditure is directed to establishing and maintaining products in key markets in which companies are interlocked in commercial competition. This expenditure adds to the cost of health care without offering tangible benefit and, unconstrained, it threatens to damage the performance and even the stability of the industry itself.

46. Even in the light of authoritative objective evidence doctors are not always readily induced to alter their established prescribing habits. For example, short-term chemotherapy for pulmonary tuberculosis, which has been shown to offer important economy as well as therapeutic and social advantage in developing countries, has so far not gained wide acceptance in many developed countries despite the persuasions of committed and authoritative exponents.<sup>1,2</sup>

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<sup>1</sup> Fox, W. Compliance of patients and physicians: Experience and lessons from tuberculosis II. British Medical Journal, 287: 101-105 (1983).

<sup>2</sup> Cooke, N.J. Treatment of tuberculosis. British Medical Journal, 291: 497-498 (1985).

47. Busy doctors, with onerous clinical responsibilities, particularly when they are working outside large institutions, tend to become isolated in their work. Without the opportunity of formal in-post training or even of informal discussion with colleagues, they need to remain highly self-critical if they are to adjust effectively to the steady evolution of therapeutic practice and the pressures of competitive advertising. The failure of doctors to seek out objective information on newly introduced drugs<sup>1</sup> contrasts strikingly with the acknowledged success of local committees, particularly in hospitals, to institute and sustain efficient and cost-effective prescribing practices in both developed and developing countries. Collective discussion and decision-making among professional peers is evidently a potent stimulus to rational prescribing practices.

48. Rational prescribing devolves from sound education and not simply from access to objective information. In developing countries, the use of a limited number of essential drugs and their appropriate indications is a part of the basic information every young medical graduate and every health worker should possess. To achieve this, pervasive problems of communication have to be overcome in those countries with a multiplicity of cultures, local languages and dialects. Community health workers, no less than other prescribers within the health infrastructure, need the support of instruction and discussion to remain updated in their responsibilities. The staff of first-referral hospitals are well-placed to assume the role of educator, and arrangements could be made to outpost staff from time to time.

49. National drug regulatory authorities or associated national committees are also appropriately placed to provide independent and objective information on products registered under their aegis. They are competent to determine labelling requirements for medicines not only for doctors but for other cadres of personnel including community health workers and traditional birth attendants. They can also ensure that information on pharmaceuticals is placed in reasonable perspective with regard to the overall social, economic and educational development of the community. National authorities commonly have a large measure of assurance from regulatory decisions taken in other countries about the quality, safety and efficacy of products available in international commerce. More demanding than the decision to licence such products is the challenge of assuring, through appropriate control of labelling and distribution, that each product is used to best advantage within the national context. In the absence of a basic system of drug registration that addresses this need, a call for the rational use of drugs can never be securely founded.

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<sup>1</sup> Who receives NDIS profiles? Australian Drug Information Service. Department of Health Newsletter, September 1985.