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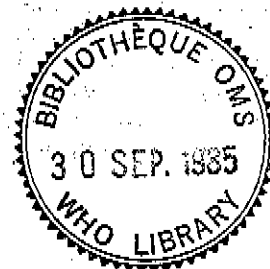
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DRUG MARKETING

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DRUG MARKETING

1. This paper outlines the various factors involved in the marketing of drugs and focuses on those most pertinent to the developing countries in their efforts to establish and maintain health care at a cost they can afford. Drug marketing is often mistakenly considered as synonymous with drug advertising. In fact it has many components, beginning with the registration of a drug and ending in its safe delivery to the end user, with many steps on the way. This paper considers the various steps.

Registration of drugs

2. Modern drugs have potent influences on the body. Their very potency, laudable in itself, is however a source of danger since it carries the risk of adverse effects either on the organ or system for which the drug is intended or on other organs or systems for which it is not intended. Control over the safety, efficacy, and quality of drugs must therefore not only be the responsibility of the manufacturer but also be the subject of regulation by the government. This principle of drug approval is fully accepted by all responsible pharmaceutical companies. Prescribers, consumers and their elected representatives, and industry all have a role to play in determining the nature of such regulation and ensuring compliance with it.

3. The assessment of efficacy, safety and quality requires sequential studies - first in the laboratory, including pharmacological and toxicological testing, then possibly in volunteers, then clinically in controlled clinical trials. Even when these have been completed, large-scale field trials accompanied by epidemiological analysis are now often required before it can be concluded with any degree of certainty that a drug is indeed effective and safe. However, at a certain stage a decision has to be taken whether to permit the use of the drug in clinical practice. This is only one episode, however, in the assessment of the drug; post-marketing surveillance, including the monitoring of adverse reactions, has to be maintained, in the course of which the drug may occasionally have to be reconsidered in the light of experience.

4. In addition to the basic problems of legislation on drugs, starting with the need to have them registered before they can be marketed, there are quite fundamental differences between countries in relation to the nature of studies required before drugs can be approved. For example, the law currently does not require studies on healthy human volunteers in France; and in the United States of America extremely rigid protocols exist for the design of clinical studies.

5. Even though each drug regulatory authority evaluates the data submitted under the same general criteria of safety, quality, and efficacy, the complexity of the criteria often leads to different results arising in different countries due to different interpretations of the data. What is important, however, is that in the developed countries approval of new drugs does take place and procedures are being used, even if these are not necessarily identical in all countries and give rise on occasion to somewhat different indications for drug use. Fundamental differences in medical practice, attitudes, and traditions may also result in different standards. Moreover, since certain conditions such as tropical diseases do not occur in certain countries, drugs to treat them are not registered there but may be exported from them to countries that do need them, thus giving the erroneous impression of double standards. A real issue of double standards would arise if a drug tested and not approved for use in one country were to be allowed to be exported from that country to other countries, or a drug withdrawn from use in one country because of its adverse effects continued to be exported to others, or

information provided for the domestic market in an exporting country were withheld when the drug is sold elsewhere, or claims not permitted in the country of origin were made in other countries.

6. To the uninitiated the process of drug approval may seem complex and often confused, although through patient and prolonged efforts between regulatory authorities, the pharmaceutical industry, and WHO a movement is beginning toward similarity rather than difference. This is particularly the case for the many well-established drugs for which there is general agreement about their indication, use, adverse reactions, manufacturing standards, formulation, etc. This being so, developing countries should perhaps in the first instance consider accepting the marketing approval of countries with well-developed regulatory mechanisms, particularly where these involve a comprehensive product data sheet or detailed labelling and package insert requirements. Moreover, they have at their disposal the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, which currently is the only umbrella scheme that attempts to provide the relevant technical data in a form easily assimilated by any regulatory authority (see Working Paper 2.6). It could be complemented by additional information such as the product data sheet from the country of origin, particularly if this is designed to incorporate the indications, dosage, use, precautions, adverse effects, drug interactions, etc. The international pharmaceutical industry has stated that it will support WHO along these lines and participate in this information transfer.

Brand and generic products

7. Newly discovered products in market economy countries are usually sold by their proprietary or brand name. However, after the expiry of the patent, other companies may manufacture an identical product either under the international (or a national) nonproprietary name, a generic name, or another brand name (so-called "branded generics"). The sale of drugs by their brand name on the one hand or generic name on the other usually affects their price, as is explained below.

Labelling and packaging

8. The labelling of pharmaceutical products depends on the registration requirements of a country and the end user, who may be professionally qualified or a member of the public. The method of end use must be clearly indicated, e.g. prescription, pharmacy only, or general sale. Simple clear instructions are required regarding the indications, dosage, contraindications, precautions, side-effects, interaction with other drugs, action to be taken for overdosage, storage conditions, expiry date, etc. They should be specifically addressed, as appropriate, to the prescriber or the consumer, and may require simple illustrations for example, of the method of administration. Incomplete information, or inadequate emphasis on certain information, for example side-effects or interaction with other drugs, can lead to improper use of the drug; hence the importance of complete and unbiased information in package inserts. Packaging components must match the environmental storage and transport conditions that the formulation will be subjected to, and the unit pack size must be appropriate to the final user. Moreover, the name and other essential information must be clearly printed on the package to avoid mistakes in dispensing or consuming.

Pricing

9. Many factors affect drug prices. Since the pharmaceutical industry is divided broadly into two sectors, the first carrying out research and developing new drugs, the second not carrying out research but supplying already existing drugs, the marketing of a drug from either of these two sectors will obviously affect its price. The calculation of the real price of a drug also has to be considered, in relation for example to its cost/benefit and proper utilization or otherwise. Moreover, pricing normally takes into account the market size and potential and the competition from other drugs in the same therapeutic class.

10. To discover and develop drugs requires large-scale research and development. For each new drug as many as 10 000 compounds may have to be tested. Screening these requires laboratory studies and clinical trials as outlined in paragraph 3 above. All this may require a time-scale of 8-10 years at a reputed cost of up to US\$ 100 million. Demands for increased safety require more toxicity testing, so that an increasing proportion of projects fail. Higher standards are being demanded for quality. All these factors raise the cost of developing new drugs considerably. In market economy countries, industrial property developed at such a risk needs protection for a limited time, and this is secured through patents. Research-based industry in these countries must recoup its investment and make a profit during the patent life of the drug.

11. It should be noted that research and development, product registration, etc., are normally regarded by pharmaceutical manufacturers as part of their fixed costs as they find it extremely difficult to allocate them to specific products. The remaining costs go to production, distribution, and promotion, and additional costs are now accruing in the field of post-marketing surveillance. A breakdown of costs for each of these items is not generally available. A report by the Office of Health Economics, London, mentions a study carried out in seven countries in 1982 which revealed the following expenditures on research and development as a percentage of output: Switzerland 15.2%, Federal Republic of Germany 13.1%, United Kingdom 12.1%, France 10.8%, Italy 8.4%, United States of America 7.4%, Japan 7.1%.¹ However, the authors of the report state that the figures have to be treated with caution in view of the difficulties in compiling national data that are both accurate and comparable. Costs in Switzerland have been subdivided into two parts, manufacturing and distribution, the former accounting for 55.7% of the total, the latter for 44.3%. Manufacturing costs were broken down as follows: production 40%; research, development, and licensing 15%; information to physicians 11%; sales 9%; publicity 4%; administration 11%; profits 10%. Distribution costs were broken down as follows: wholesalers 13.5%; pharmacists - auxiliary staff 36.5%, storage 9%, other operational costs 11.5%, capital expenditure and amortization 8%, basic income of pharmacists 13.5%, profits and business risk 8%.² It is difficult to discern from the above exactly what items to include under promotional expenditure. One estimate of average promotional expenditure as a percentage of sales is as follows: United States of America 22%, Federal Republic of Germany 22%, Italy 22%, Sweden 18%, France, 17% United Kingdom 15%, and India 10%.³

¹ Chew, R. Teeling Smith, G. & Wells, N. Pharmaceuticals in seven nations. London, Office of Health Economics, 1985.

² La santé publique en Suisse - prestations, coûts, prix. Bâle, Pharma information, 1984. (Available only in French and German.)

³ Blum, R. et al. Pharmaceuticals and health policy. London, Croom Helm, 1981.

12. There are great differences in the price of the same drug in different countries, sometimes by as much as tenfold. While it may be possible to explain them in part by such circumstances as retail margins or direct or indirect subsidies, many of the reasons are less apparent. The above-mentioned report of the Office of Health Economics in London quotes a study carried out in 1982 that showed the following index of pharmaceutical prices in six countries: Japan 100, Switzerland and the Federal Republic of Germany 83, United Kingdom 58, Italy 38, France 33.¹ The authors of the report observe that one of the most serious consequences of the effects of price control as shown in the above figures has been the encouragement of so-called parallel imports, that is, the practice whereby traders buy in cheap markets and then sell in competition with the original manufacturer in higher-priced markets. Another factor affecting prices may be transfer pricing, that is, the charges made within a company as a product moves from one location to another at different stages of its manufacture. Such pricing may be at the origin of high costs in countries in which there are daughter companies of a parent company in another country, the latter "selling" its products or raw material to the former at inflated prices.

13. Branded generics, which are products sold under distinctive brand names and promoted in the same way as the leading brand, can be sold at a lower price because of the minimal research and development input, that is, lower development costs. They have marketing support, technical information, and selling costs, but are usually sold at significantly lower prices than new drugs. Other products marketed under the generic name have minimal promotion and are usually sold by tender or direct sale. Such products are frequently sold at even lower prices than branded generics.

14. Distribution costs can affect the end user price remarkably. In market economy countries the manufacturer normally sells to a wholesaler, who distributes to pharmacies, naturally adding to the cost; or alternatively drugs may be purchased directly by a group, which may be a regional or national unit, and the distribution costs may not be passed on directly to the end user. This occurs, for example, with many supply contracts. On the other hand, even with supply contracts to a central body at a negotiated price, the ultimate price to the end user may be considerably higher, particularly when relatively small amounts of a drug are required urgently on a non-routine basis, as well as for a variety of other less ethical reasons.

15. The distribution system must have a feedback to each source of supply and establish lead times for order and supply. It must provide for the delivery of drugs in good condition to the patient and for proper storage conditions on the way. Such a logistic system is essential to ensure the rational use of drugs but it costs money, and if the cost has to be covered by consumers the price they have to pay will be proportionately higher than the purchase price at the source. In many government health systems the distribution cost is not transferred directly to the consumer but included in the overall cost of the health service.

16. Direct and indirect control over pricing can be exercised in many ways, for example by cutting promotional and distribution costs. Some countries have a reimbursement list and commercial success can only be achieved when a product is included. Other countries establish a price by calculating from the bottom up, i.e., beginning with the raw materials and adding the various incremental factors such as production cost, overheads, research and development, promotion, etc.

¹ Op. cit., p. 45-47.

17. Whereas in countries with centrally planned economies domestic prices are determined by governments, having regard to projected needs and costs, in market economy countries market forces affect prices depending on whether the supply arrangements are for a single purchase, a commitment for purchase over a period, a small volume, or a large volume in which economies of scale come into force. Other factors influencing prices are whether drugs are produced locally, need to be trans-shipped, are made under contract to the specifications of the buyer, or are supplied under special conditions. International procurement is affected in addition by such factors as whether the drugs are purchased free on board (f.o.b.) or cost including freight (c.i.f). One way of keeping prices down is by open tenders - national and international. Recent experience with international tenders for generic drugs in developing countries has been very encouraging; good quality drugs have been obtained at lower prices than ever before, thanks to purchasing larger quantities required for a longer period of time and thus benefiting from the economies of scale, as well as to international market forces. Moreover, research-based companies have provided generic products, sometimes through subsidiary companies, and have done well in the competition. They include their company name on the label in addition to the generic name. These factors may well have to be taken into account by developing countries when they contemplate introducing large-scale local drug production, notwithstanding their legitimate desire for self-reliance in drug production.

Rights to prescribe, distribute, and sell

18. In many countries rights to prescribe, distribute, and sell are governed by regulation and licence. Where there is a dearth of professional health personnel licensing requirements may have to differ from those of more developed countries.

19. In most countries only registered medical practitioners are entitled to prescribe allopathic drugs of the type known as prescription drugs. Registered dental practitioners may prescribe drugs specific to dentistry. However, in many countries the public health service, particularly in rural areas, is sorely lacking in doctors and it is necessary to permit other categories of health worker - including nurses, pharmacists, and in many cases nonprofessional primary health care workers - to prescribe certain drugs, following suitable training. In some countries, particularly in the large towns, the public has almost unlimited access to all forms of drugs, including prescription drugs, which they can purchase without a prescription. In many of these countries, however, the rural population, which makes up the vast majority of the population, has little or no access to a regular supply of drugs.

20. The right to distribute drugs wholesale from manufacturer to retailer also varies in different countries. Distribution entails not only physical distribution but also proper storage and handling and often involves good stock control advice to users, such as attention to shelf life, since the medical products are often held in general stores. For these reasons the wholesale distribution of drugs requires both pharmaceutical and managerial skills, whether in private or government distribution systems.

21. The right to sell prescription drugs to the end user is usually governed by licence, e.g. permitting a pharmacist to dispense them. However, in many countries such drugs are sold without prescription or as over-the-counter (OTC) commodities in non-pharmacy outlets, often as a single treatment purchased on a daily basis, sometimes even as a single dose. OTC drugs are products sold in pharmacies and, to a limited extent, other outlets without prescription. They are normally less

potent than prescription drugs and include mild analgesics, laxatives, cough and cold preparations, topical preparations, and the like. They are often sold as branded generic formulations as a means of conveying an assurance regarding their quality, safety, and efficacy. In many countries, particularly developing ones, the OTC market is an outlet for the uncontrolled supply of prescription drugs. OTC drugs are usually supported by substantial promotion directed at the general public. In some countries many such drugs are sold in food stores, masquerading as food supplements and thus avoiding the normal control exercised over drugs. Counterfeiting is an additional compounding factor.

22. In many developing countries patients have not the money to purchase the total treatment and frequently buy one dose at a time. Moreover, while some purchase drugs on the advice of health personnel, many purchase without such advice and without the minimum knowledge required to make a rational decision. In most industrialized countries, too, the right to sell most drugs to the end user is limited to qualified pharmacists, but in many developing countries this restriction is often not possible outside the main towns, and village stores, community cooperatives and the like may have to be granted permission to sell.

Promotion

23. The promotion of drugs takes many forms, such as providing information to prescribers in attractive ways, often accompanied by generous samples; advertising in professional journals as well as in the lay press, and in some countries through radio and television for OTC drugs; providing incentives to prescribers and pharmacists in proportion to the volume of drugs they prescribe and dispense; using sales representatives to sell to prescribers in much the same way as is done with other consumer goods; and sponsoring or subsidizing scientific symposia at which related drugs are promoted in diverse ways. Some of this promotion conforms to acceptable ethical standards; some does not. The proportion of drug costs devoted to promotion varies widely by product; in all cases the costs naturally fall ultimately on the consumer.

24. Advertising is one of the means of disseminating information on drugs. It usually presents information in an attractive manner and can thus be useful, on condition that it is objective and accurate. However, if this condition is not fulfilled it can be dangerously misleading because it is likely to take precedence over objective and accurate information presented in a less attractive form. This emphasizes the need for scrupulous integrity in all forms of drug advertising. It goes without saying that such integrity has to be universal, with no double standards for developed countries on the one hand and developing countries on the other.

25. Advertising of prescription drugs is restricted to health professionals through such means as medical journals, product literature, slide/tape and video presentations, exhibitions, and meetings either read about or attended by doctors and pharmacists. In some countries advertising of OTC drugs aimed at the public is permitted through the media but not by direct mailing. Governments and the pharmaceutical industry have a responsibility, particularly in developing countries, to use the media for the education and information of health workers and the public.

26. Drug advertising has been the subject of much criticism because of its alleged aggressivity and biased content. As far back as 1968, the Twenty-first World Health Assembly asserted in resolution WHA21.41 that drug advertising must adhere

to certain fundamental principles and that, if not objective, it is detrimental to the health of the public. It adopted the following ethical and scientific criteria for pharmaceutical advertising:

"All advertising on a drug should be truthful and reliable. It must not contain incorrect statements, half-truths or unverifiable assertions about the contents, effects (therapeutic as well as toxic) or indications of the drug or pharmaceutical speciality concerned.

Advertising to the Medical and Related Professions

In describing the properties of a drug and its use, stress should be laid on rendering facts and data, whereas general statements should be avoided. Statements should be supported by adequate and acceptable scientific evidence. Ambiguity must be avoided. Promotional material should not be exaggerated or misleading.

A full description, based on current scientific knowledge, should include information on the producer and sponsor of the product advertised; full designation (using generic or nonproprietary names) of the nature and content of active ingredient(s) per dose; action and uses; dosage, form of administration, and mode of application; side-effects and adverse reactions; precautions and contra-indications; treatment in case of poisoning; and references to the scientific or professional literature.

A fair balance should be maintained in presenting information on effectiveness on the one hand and adverse reactions and contra-indications on the other.

Advertising to the Public

Advertisements to the public should not be permitted for prescription drugs, for the treatment of certain diseases and conditions which can be treated only by a doctor and of which certain countries have established lists, or in a form which brings about fear or distress, or which declares specific remedies to be infallible, or suggests that they are recommended by members of the medical profession."

May 1968.

27. Sales representatives are frequently a much criticized part of the selling operations of pharmaceutical companies. Evidence shows that use of sales representatives is a highly effective way of promoting drugs since doctors often regard them as a useful source of information. If they are to be employed, however, they should be properly qualified to carry out their job. In some developed countries they need to pass an examination, the responsibility for training and ethical standards resting with the company; they are also accountable for their actions and strict rules are laid down. Thus, they are expected to give objective information about their products in an ethical way and to be willing to discuss published data from independent sources and know the maximum and minimum limits of the products. In many countries there is need for improvement in the standards; evidence shows that several companies are trying hard and that improvements have taken place over the past 10 years, but more needs to be done.

One of the problems is the custom in some countries of doctors demanding discounts and incentives before seeing representatives. This leads to competition and to abuse of medical practice.

28. Particularly when promoting new drugs, samples are used to encourage doctors to try them out. Too many samples can - and do - lead to abuse either by being used for current treatment and charged for or by becoming an exchange commodity and used as a discount. If they are to be permitted they have to be carefully controlled, for example, being supplied in limited amounts only at the request of a prescriber and their use being monitored and results recorded.

29. Symposia can be useful for exchanging information and improving medical and therapeutic education. Those sponsored by the pharmaceutical industry are best used in collaboration with organized postgraduate education with guidelines like, for example, the following:

1. Meetings sponsored by a pharmaceutical company may be allowed subject to the approval of a clinical tutor or postgraduate education committee.
2. Arrangements must be made by the same person or committee and competent staff from the pharmaceutical company invited to attend.
3. Lecture material and films should be vetted.
4. A suitably qualified independent doctor experienced in the topic must be available at such meetings.
5. Promotional material from the pharmaceutical company is allowed but must be separate from the educational content of the meeting.
6. Sponsoring should be limited to the provision of light refreshments and the printing of programmes, due acknowledgement being made.

If such guidelines are complied with, the sponsoring of symposia may be regarded as ethical and useful.

30. In many developed countries there are regulatory constraints on promotional methods, but in many developing countries governments are not yet in a position to assume that responsibility. This places even greater responsibility on the pharmaceutical industry to apply in these countries the same norms that they apply in developed countries. Examples have often been quoted of alleged flagrant breaches of promotional ethics by pharmaceutical companies. Industry has responded by initiating remedial action. Thus the International Federation of Pharmaceutical Manufacturers Associations (IFPMA) issued a voluntary Code of Pharmaceutical Marketing Practices in 1982. It includes a clause to the effect that claims for drugs should not be stronger than the scientific evidence or responsible medical opinion warrants and that every effort should be made to avoid ambiguity. The IFPMA periodically publishes reports on action taken to ensure compliance with the Code, including action taken in response to complaints about infringements, and has expressed its willingness to report to the World Health Assembly on progress made in applying the Code. Nevertheless, the IFPMA Code has been criticized as weak and ineffective.

31. In partial reply to such criticism, multinational companies have stated that even if policy decisions are taken centrally, the decisions may not be carried out by all subsidiaries. Moreover, they add, it is often erroneously assumed that the

corporate headquarters of a multinational company know all the time what is happening in every market. Experience has shown that drawing attention to misdemeanours will help to elicit positive action from responsible management; consumer groups have been active in that respect, the governments concerned less so.

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