



WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

WHODOC 4/6

INDEXED WHO/CONRAD/WP/2.2

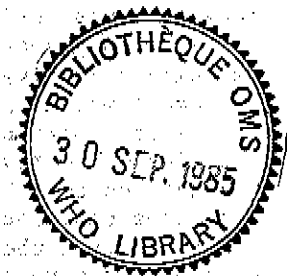
2526

10 September 1985

CONFERENCE OF EXPERTS ON THE RATIONAL USE OF DRUGS

Legis, Drug

25 - 29 November 1985, Nairobi, Kenya



REVIEW OF NATIONAL HEALTH LEGISLATION ON DRUG MARKETING¹

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¹ The Director-General acknowledges with appreciation the contribution to the preparation of this paper of Dr D. C. Jayasuriya, Attorney-at-law.

This document provides a brief review of national health legislation relating to the marketing of drugs (pharmaceuticals).^{*} A large number of countries now have legislative provisions on drugs covering a wide and varied spectrum. In preparing this review, the laws and regulations of some 80 countries were analysed. Any comprehensive review based on such a large volume of legal instruments is likely to run into several hundred pages. With a view to producing a document which enables the legal status of drug marketing to be surveyed rapidly, this review contains a synthesis of general approaches that are common to many countries. The review, therefore, does not specifically mention some or all of the 80 countries that have laws and regulations representative of the general approaches described. However, where there are significant additions to or departures from the general approach the review makes specific reference to them. The examples have been selected at random when the addition or departure occurs in more than one country. Reference in the document to any one country in relation to a particular approach does not, therefore, necessarily mean that such approach is confined only to that country.

The review is based largely on legislative texts that have appeared in the International Digest of Health Legislation (IDHL) published by WHO since 1948. A few texts to be published shortly have also been included. Most of the references in the document are to laws and regulations currently in force. Any reference to a law or regulation no longer in operation is only for the reason that such law or regulation reflected a legislative development still worthy of note. In addition to national laws and regulations, reference has been made to a few codes of conduct that contain relevant provisions. However, for the purpose of this review, no survey was made of codes of conduct and the references in the document to codes are based on published material. The review also contains references to various comparative surveys that have been published from time to time, which provide more detailed information on some of the aspects covered. They are, however, based on a survey of the laws and regulations in fewer countries than in this document. Since WHO is compiling an annotated bibliography of literature on drug marketing, this document does not contain any references to books, articles, conference proceedings, or other materials dealing with the legal status of pharmaceuticals in any individual country.

BACKGROUND

1. While this review is primarily concerned with national legal controls over the marketing of drugs, account needs to be taken of controls prior to the availability of drugs for marketing.
2. Legal controls tend to differentiate between various categories of drugs, the controls ranging from very tight to relatively loose. The categorization of drugs and the nature of the controls applicable to the different categories of drugs vary from country to country. A 1960 WHO survey of existing legislation on the classification of pharmaceutical preparations pointed out that there is a total lack of uniformity.⁽¹⁾ Some legal texts have a single list of substances, others up to five lists. In addition, some texts deal specifically with special categories of drugs, such as those liable to cause addiction. Even within this broad classification there are subclassifications reflecting, for instance, the different schedules in the international drug control treaties. In a review of

^{*} In many of the countries covered in this review there is separate legislation dealing with narcotic drugs and psychotropic substances and largely based on the principles set out in the international drug control treaties. This review does not cover such legislation, nor does it deal with the special legislation on poisons and vaccines and allied products.

this nature, covering a large number of legal and health care systems, it is not possible to make generalizations regarding the different levels of controls applicable to various categories and subcategories of drugs. All that can be attempted is an enumeration of certain common categories of drugs as a background to a discussion on specific aspects. It is important to note that, since there is no uniformity in terminology, the use of the identical concept in two or more legal texts does not necessarily mean that identical controls are applicable.

3. The basic categorization of drugs into prescription drugs and non-prescription or over-the-counter (OTC) drugs is important for the reason that controls and requirements relating to advertising and labelling often tend to be based on such categorization. Prescription drugs are generally subject to stringent controls. For registration purposes laws generally tend to use general terms such as "pharmaceutical speciality" or "medicinal product" to cover a wide and varied range of drugs. Exclusions from such a classification are limited to a few categories such as drugs prepared in hospitals and pharmacies. For registration purposes general terms such as "new drugs" are also used, often in relation to the availability of a drug in relation to a specific period of time. For instance, in the new Chinese Pharmaceuticals Control Law,⁽²⁾ operative with effect from July 1985, "new pharmaceutical" means a pharmaceutical that has not yet been produced in China. Antibiotics, oral contraceptives, combination drugs, drugs that induce anaesthesia, drugs for prophylactic use, biological preparations, sera and vaccines, blood and blood products, etc. are sometimes specifically included within, or excluded from, the general definition of drugs. Homoeopathic, ayurvedic, and herbal drugs are generally subject to different controls, even though a single law may cover all these substances.

4. A drug, to be available for marketing, must be either manufactured in or imported into the country, and controls at the stage of manufacture or importation need to be taken into account in determining the nature and magnitude of the marketing controls to be subsequently applied.

5. Safety, quality, and efficacy have been the general considerations governing traditional controls over manufacture. Licensing systems are of different kinds. Some countries grant licences for the manufacture of drugs generally, others for a named drug or specific categories of drugs. Registration of the drug to be manufactured is often a condition to the issue of the licence. Some laws provide for the issue of licences even for supplementary activities such as filling, packing, and labelling. In addition to licensing, compliance with good manufacturing practices,⁽³⁾ regular inspection of manufacturing premises, quality verification of manufactured products, compliance with pharmacopoeial standards, etc. are features of the controls over manufacture generally applied through appropriate legal instruments. In this context note may be taken of the role of WHO in the formulation of good manufacturing practices⁽⁴⁾ and in the compilation of the International pharmacopoeia, both designed to promote the safety, quality, and efficacy of manufactured products. Many countries have accorded legal or administrative recognition to requirements of good manufacturing practices and the standards in the International pharmacopoeia. Through bilateral and other arrangements⁽⁵⁾ importing countries accept inspection of manufacture by exporting countries as equivalent to their own.

6. The vast majority of countries in the world, particularly the developing countries, obtain their drug requirements through imports. Controls over imports have taken different forms, ranging from liberal import policies as part of general trade policy permitting the import of any drug (with the exception perhaps of those which are banned or are spurious, counterfeit, misbranded, adulterated, substandard, etc.) to those which restrict imports to specific categories of drugs

(such as essential drugs, registered drugs, licensed drugs, or drugs listed in a pharmacopoeia or national formulary).

7. The system of issuing import licences enables the regulatory authority responsible for drugs to determine what drugs should be permitted to be imported, by whom,⁽⁶⁾ and subject to what conditions. Naturally, therefore, countries have recourse to a licensing system to regulate the inflow of drugs. Considerations of safety, quality, and efficacy are among the main factors taken into account in determining what drugs should be permitted to be imported. Additional considerations are registration⁽⁷⁾ of the drug as a pre-condition, restrictions on the quantity to be imported (for a single consignment or over a period of time), medical need, price, etc. The requirement that the drug to be imported has been manufactured by an establishment or plant adhering to good manufacturing practices and the place and process of manufacture have been subject to regular inspection is an additional safeguard. The submission of documentation relating to quality, safety, efficacy, registration, and pricing and provision for quality verification at the time of import is a general condition of import licences.

8. National laws provide for a variety of situations in which imports or import licences can be cancelled or suspended, the commonest being those relating to unsatisfactory quality, safety, or efficacy of the drug. Drugs not of the accepted quality, safety, or efficacy and spurious, counterfeit, or adulterated drugs cannot be imported and, if imported, are liable to confiscation. Some countries have provided additional grounds for prohibiting, suspending, or cancelling imports. In Bahrain, for instance, imports can be suspended if the price exceeds the limits accepted in neighbouring Arab countries.⁽⁸⁾ Australia prohibits the importation of drugs that do not comply with stipulated labelling and packaging requirements.⁽⁹⁾

9. The WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce⁽¹⁰⁾ is designed to facilitate the efforts of importing countries to obtain assurance regarding the quality, safety, and efficacy of imported drugs. This Scheme, in which more than 100 Member States now participate, provides an administrative mechanism:

(1) to provide assurance that the product has been authorized to be placed on the market in the exporting country (if not, the reason why such authorization has not been granted, as, for example, that the drug is meant mainly for tropical diseases);

(2) to provide assurance that the manufacturing plant conforms to requirements for good practices in the manufacture and quality control of drugs as recommended by WHO and that the plant is subject to inspection at suitable intervals;

(3) to exchange information on inspection and controls exercised by the authorities in the exporting country (including dealing with inquiries about serious quality defects in the importing or exporting country).

10. Countries without adequate technical resources to conduct clinical trials and quality verification stand to benefit from this scheme. By appropriate legal or administrative measures the principles underlying the scheme can be made applicable to import licences and other import arrangements and the monitoring of adverse reactions to drugs. Many importing countries, for instance, before issuing a licence require documentation relating to registration in the country of manufacture or origin.

Strategies for the rationalization of drug manufacture/importation

11. The concept of essential drugs was developed by WHO in response to the need for the optimal utilization of limited financial resources to purchase and distribute those basic drugs necessary to the health needs of the population.⁽¹¹⁾ Based on considerations of quality, safety, efficacy, and reasonable price, lists of essential drugs have been compiled in a large number of countries. These lists are followed in purchasing drugs and distributing them to various outlets in the health care structure.⁽¹²⁾

12. Recognition has been accorded to lists of essential drugs both administratively and legally. In China a national list of essential drugs was issued in 1981,⁽¹³⁾ containing 278 commonly used drugs intended to meet the general medical care needs of the population. Manufacturing establishments are required to accord priority to the production of essential drugs, medical units to ensure that such drugs are used rationally and there is no wastage or abuse. While the Chinese approach exemplifies the administrative measures possible, in countries like Niger legislative measures have been taken to accord recognition to essential drug lists; in 1980 an order⁽¹⁴⁾ was made listing some 80 medicaments that district medical services and dispensaries are entitled to order. By another order⁽¹⁵⁾ the number of drugs for hospitals was restricted to 210. Prior sanction is necessary to obtain drugs other than those listed in the orders. Effect has also been given to the concept of essential drugs by listing drugs in a national formulary and restricting the use of drugs to those listed. In Peru the Ministry of Health, the Peruvian Social Insurance Scheme, public welfare agencies, the National Institute for the Care and Promotion of Minors and the Family, local authorities, public agencies, etc. are required by a decree⁽¹⁶⁾ to prescribe or use only the basic medicaments listed in the Official Formulary of Basic Medicaments in the Health Sector. Similarly, in Guatemala, by an order⁽¹⁷⁾ enacted in 1979, the National Therapeutic Formulary has been declared to be the definitive text listing drugs to be used in national hospitals, health centres, and health posts. In Bolivia there is a prohibition on the importation of products similar to those produced by the national pharmaceutical industry.⁽¹⁸⁾

13. A recent publication of the Pan American Health Organization⁽¹⁹⁾ deals with the development and implementation of drug formularies. It defined a formulary as "a compilation of pharmaceutical products approved for use in a given health care system".⁽²⁰⁾ Formularies are of different kinds, depending on their intent, nature and scope. Some are mainly for local use, for instance within a hospital or group of hospitals. As far back as 1959 Sri Lanka, for example, had a hospital formulary and all state-sponsored medical institutions were obliged to use the drugs listed in it and no others.⁽²¹⁾ This was achieved through administrative procedures and the formulary had no legal base. Whether a law is needed to accord sanction to a limited formulary depends on the organic structure of the health-care institutions that would be bound by it; autonomous institutions may not feel obliged to give effect to administrative schemes. Moreover, procurement procedures may have to be changed and in some countries this may necessitate a legal instrument that will have an overriding effect. As against local or limited formularies, a few countries have adopted national formularies. In Bolivia, for instance, legislation⁽²²⁾ has described the National Therapeutic Formulary as "the authoritative instrument which alone is binding on centralized and decentralized public agencies of the State with regard to the following matters: (a) the application of therapeutic criteria prescribed in accordance with the advances in and principles of pharmacology; and (b) the rational use of drugs in health administration, including planning, acquisition, preservation, distribution and supervision".⁽²³⁾ The National Therapeutic Formulary is required to contain the information essential to ensure a proper regard for the principal requirements concerning medicaments, including concentration and therapeutic guidelines such as

indications, contraindications, precautions and adverse effects. It must also include the basic list of medicaments, comprising the details required for administrative purposes such as the generic or permitted description, the level of use, the form of presentation, and the unit of measurement.

14. Countries that have adopted formularies have established mechanisms to review and update their contents and ensure the administrative, fiscal, and other measures needed to facilitate the availability of the basic medicaments. In Costa Rica the Technical Committee on the Formulary is required to undertake cost-benefit and drug utilization studies.⁽²⁴⁾ The National Medicaments Council in Bolivia has to collaborate in drawing up standards for industrial production and technological development.

15. The manufacture and importation of drugs can be rationalized by a mix of strategies instead of a single strategy, as exemplified by the Bangladesh drug law reforms of 1982. The drugs available on the market were curtailed by five measures. Firstly, no medicine of any kind could be manufactured for sale or be imported, distributed, or sold unless it was registered with the licensing authority.²⁵ The authority had to act on the recommendations of the Drug Control Committee. Secondly, certain medicines listed in three schedules were subject to special restrictions that were to become operative within a stipulated time-limit. Medicines specified in the first schedule had to be destroyed, medicines in the second to be registered after changes in their formulation as directed by the licensing authority. Non-registration meant that it was not possible either to manufacture or to sell these medicines. Drugs listed in the third schedule were prohibited from being manufactured or imported, thus resulting in a complete withdrawal of such drugs from the market. A fourth schedule was introduced subsequently by way of an amendment⁽²⁶⁾ to the principal legislation. Unless the medicines listed in this schedule were registered it was not possible to manufacture, distribute, or sell them. Thirdly, the legislation did not permit a drug to be locally manufactured under licence granted by a foreign company that had no manufacturing plant in Bangladesh, if such drug or its substitute was already being produced in Bangladesh. Fourthly, the prior approval of the licensing authority was required for the importation of pharmaceutical raw material. Fifthly, the Government was empowered to review any licensing agreement between a Bangladeshi concern and a foreign concern for the manufacture of any drug in Bangladesh and to give directions for modifying the agreement. In the event of non-compliance with any direction, the manufacturing licence was liable to be cancelled.

16. The rationalization of drug manufacture in relation to the concept of essential drugs has taken the form of requiring manufacturing establishments to manufacture such drugs. Reference has been made to the Chinese requirement. In Ecuador a decree⁽²⁷⁾ was enacted in 1977 requiring companies manufacturing medicaments to produce at least two medicaments for the basic social medicaments programme of the Ministry of Public Health in accordance with the list of medicaments issued by the Ministry.

Export

17. Restrictions on exports are designed primarily to give importing countries assurance regarding the quality, safety and efficacy of drugs they import. On the basis of available information it would appear that most countries do not have specific legal provisions regulating the export of drugs that have not been approved for domestic use.

18. Controls over exports at the national level take different forms. The Canadian approach has been to exclude the application of the drug legislation⁽²⁸⁾

to drugs meant exclusively for export, provided: (a) the package is distinctly overprinted with the word "Export" and (b) a certificate has been issued that the package and its contents do not contravene any known requirement of the law of the country to which it is to be consigned. In the United States of America, under federal legislation⁽²⁹⁾ no new drug can be exported until it has been approved or licensed by the Food and Drug Administration for use in the United States. However, antibiotic drugs can be exported to other countries even though such drugs are not approved for domestic use, provided that they meet the specifications of the foreign purchaser and do not conflict with the laws of the country of import. Under French legislation⁽³⁰⁾ every drug prepared in advance with a view to export and presented in a ready-for-use form is subject to prior licensing by the Minister of Health. A licence is granted only on the condition that the manufacturer provides justificatory evidence as to quality and inspection as required for drugs marketed in France. In Guatemala there is a requirement that only drugs duly registered and licensed by the General Directorate of Health Services can be exported.⁽³¹⁾ In Bahrain the law⁽³²⁾ prohibits any export unless the sanction of the Minister has been obtained.

19. In the Medicines Act⁽³³⁾ of the United Kingdom there are several restrictions relating to the export of drugs, but the imposition of these restrictions has been postponed until an Order is made to impose them. No such Order has yet been made though the Act has been in operation since 1968. However, the Act does provide for certificates to be issued in respect of drugs to be exported as envisaged by the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce, in which the United Kingdom participates. On the application of an exporter of medicinal products of any description the licensing authority can issue to him a certificate containing any such statement relating to medicinal products of that description as the licensing authority may consider appropriate having regard (a) to any requirements (whether having the force of law or not) which have effect in the country to which the products are to be exported, and (b) to the provisions of the Medicines Act and to any licence granted or other thing done by virtue of this Act. In addition to the United Kingdom there are countries such as Austria which participate in the Scheme and issue certificates even though national laws⁽³⁴⁾ exempt drugs meant for export from registration.

20. The export of drugs not authorized to be marketed in the country of manufacture either because they do not meet domestic regulatory standards or for other reasons has generated a fair amount of discussion in recent times. The laws of exporting countries generally do not specifically address that issue. Some drugs are manufactured primarily for diseases endemic in other parts of the world and there may never be an occasion for their use in the country of manufacture. According to the drug and antibiotic regulations⁽³⁵⁾ of the United States Food and Drug Administration that became operative with effect from 23 May 1985, an antibiotic drug product or drug substance subject to certification under the Federal Food, Drug, and Cosmetic Act but not certified or released may be exported provided that (a) it meets the specifications of the foreign purchaser, (b) it is not in conflict with the laws of the country to which it is intended for export, (c) the outside of the shipping package carries the label that it is intended for export and is not sold or offered for sale in the United States.

21. In considering the statutory framework relating to exports, it is important to note that some importing countries have legal provisions that have a bearing on this matter. Under a 1959 decree⁽³⁶⁾ of El Salvador, pharmaceutical specialities are not allowed to be imported into the country unless their use in the country of origin has been authorized. In Chad, under a decree⁽³⁷⁾ of 1966, a licence can be issued in respect of specialities manufactured and packed abroad only if they are effectively and legally marketed in the country of origin.

22. As well as national controls, various arrangements at the international level are designed to offer some measure of assurance regarding the quality, safety, and efficacy of drugs subject to international commerce. The WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce requires Member States participating in the Scheme that export drugs to take certain measures designed to ensure the quality of the drugs. WHO issues a monthly communication regarding regulatory decisions on drugs and a bulletin entitled Drug information dealing with policy and other issues of interest to regulatory authorities. WHO also disseminates information on the toxic effects of drugs as part of its monitoring programme on adverse reactions to drugs, in which 27 national collaborating centres participate.

23. The United Nations has been given a mandate⁽³⁸⁾ to prepare lists of products, including pharmaceuticals, that are banned, withdrawn, restricted, or not approved by various governments.

24. Finally, international and regional forums such as the biennial conferences of national drug registration authorities and various geopolitical groups on pharmaceuticals provide opportunities for the exchange of information and data and for the establishment of informal communication networks.

LEGAL DIMENSIONS OF MARKETING REGULATIONS

Registration of drugs

25. More and more countries now provide for the registration of drugs. A registration system, when fully operational, facilitates the regulation of what is marketed. Non-registration normally means that the drug cannot be marketed except perhaps with prior approval for limited purposes.

26. Registration systems and licensing systems often cause confusion. Some countries do not have a system for registering drugs but have a licensing system enabling drugs to be marketed. In countries with both registration and licensing systems, licences are normally granted for marketing registered products only. What is important in this context is the existence of a system that provides for pre-screening of drugs intended to be marketed. The pre-screening has to be on the basis of scientific and other criteria and procedures such as clinical trials designed to assure the quality, safety and efficacy of the drugs.

27. Different countries have different authorities and agencies entrusted with the responsibility of reviewing applications for registration and for registering drugs that have received favourable consideration.⁽³⁹⁾ In Pakistan registration is effected by the Registration Board, headed by the Director-General of Health. Registration is a responsibility of the Federal Government. Once a drug has been registered by the Board it must notify all the provincial governments. The Pakistan legislation⁽⁴⁰⁾ requires provincial governments to take all such steps as may be necessary to ensure compliance with the conditions subject to which a drug is registered and to prevent the manufacture or sale of a drug that has not been registered or the registration of which has been suspended or cancelled.

28. Registration requirements generally apply to all drugs. The information most countries require can be classified into two broad categories: administrative data and pharmaceutical, pharmacological, toxicological, therapeutic, and clinical data. Within the first category is information relating to matters such as the name of the product and details of the manufacturer, the status of the product in the country of origin and other countries, and the content of labelling and

advertising material. The second category comprises detailed information of a technical nature supported by scientific facts and figures.

29. Countries differ in their criteria for registration. In the application of criteria the three common denominators are quality, safety, and efficacy. Countries apply other criteria as well. The following table provides a representative sample of such criteria, with one or two national examples selected at random.

CRITERIA	COUNTRIES
Economic value Price	Kenya, ⁽⁴¹⁾ Pakistan ⁽⁴²⁾
Need	Norway, ⁽⁴³⁾ Gambia ⁽⁴⁴⁾
Medical justification	Norway ⁽⁴⁵⁾
Availability of speciality with identical or similar formula	Mali ⁽⁴⁶⁾
Production techniques	Indonesia ⁽⁴⁷⁾
False or misleading labelling	United States of America ⁽⁴⁸⁾
Combination product	Czechoslovakia ⁽⁴⁹⁾
Harmlessness	Sweden ⁽⁵⁰⁾
Of real benefit to the country	Mexico ⁽⁵¹⁾
Whether imported product can be manufactured locally	Bolivia ⁽⁵²⁾
More than five products with the same active ingredients already on the market	Rep. of South Korea ⁽⁵³⁾
Brand name or trade name misleading	Switzerland ⁽⁵⁴⁾

30. Registration of the drug in the country of export is generally regarded as being sufficient to warrant registration. Documentation is usually required on the preregistration clinical and related investigations and on other matters relevant to the quality, safety, and efficacy of the drug. Some countries have a different procedure. In Kenya the Pharmacy and Poisons Board is required to consider the results of investigations and clinical trials under local conditions before it registers a new drug.⁽⁵⁵⁾ However, in certain circumstances the Board can register such a drug and require the investigations and clinical trials to be conducted after registration. It may be noted that the WHO Certification Scheme

provides for information regarding the status of the product in the country of export to be furnished, if requested by the importing country. Clinical trials and the evaluation of scientific and other data require qualified manpower, time, and financial resources. For that reason several countries attach considerable weight to the registration decisions of other countries.

31. One approach that has been followed in Bermuda is to permit the import of a drug provided the country of origin is a designated country and it is lawful to use that drug in that country.⁽⁵⁶⁾ This approach is based on the premise that the designated countries have good regulatory systems, including supervision of manufacturing practices. The requirement that at the time of exportation it was lawful to use the drug in the country of export can give rise to problems, especially in respect of drugs meant for diseases endemic in the country of import but not in the country of export, e.g., drugs for tropical diseases manufactured in non-tropical countries.

32. In operating a registration system certain guidelines need to be formulated to enable applications to be systematically as well as speedily processed. Many countries have devised administrative procedures for this purpose, a few legislative provisions. In Spain the registration system is structured on a threefold classification basis.⁽⁵⁷⁾ The drugs in respect of which applications for registration are considered are divided into three groups. In group 1 are drugs where no speciality having similar therapeutic indications has been registered, or the mode of action or chemical composition of the speciality is completely different from that of specialities already licensed and the speciality represents a far-reaching therapeutic innovation. In group 2 are drugs that by reason of the composition, dosage form, or combination of or new therapeutic indications for known active principles represent a substantial therapeutic advance on similar existing specialities. Group 3 consists of drugs that do not fall within group 1 or group 2. Priority is given to drugs in group 1. For drugs in this group and in group 2 there is no annual quota or limit on the number of applications to be approved. Drugs in group 3 are subject to a quota. However, applications proposing a price significantly lower than that of similar specialities already on the market are accorded priority.

33. The period for which a drug is registered varies from country to country. Some countries have a mandatory period within which the registered product should be marketed. Renewal of the registration can also be conditional on the product being marketed. Fees levied for the first registration as well as for renewals can be the same for all drugs or vary with the category of the drugs. In Kenya, for instance, the fee for drugs manufactured locally is one-fifth of that applicable to drugs manufactured abroad.⁽⁵⁸⁾ Sometimes such fees are utilized to cover the whole or part of the expenses of the regulatory agency.

34. In registering a drug various conditions can be imposed, if the legislative instrument in terms of which registration is effected provides for the imposition of such conditions. For instance, there can be a mandatory requirement to report side-effects, withdrawal of the product in other countries, etc. Changes in the package insert and text of the advertisement can be subject to prior screening. Changes in trade marks can be accepted subject to the registration being amended or an altogether new application being made.

35. Several countries have specified different grounds on which the registration of a drug or the licence for marketing can be withdrawn. In Kenya⁽⁵⁹⁾ a certificate can be suspended or revoked if the premises on which, or on part of which, drugs are manufactured, assembled, or stored by or on behalf of the holder of the certificate of registration are unsuitable for the manufacturing, assembling, or storage of drugs, or if new information has been discovered by the

Pharmacy and Poisons Board showing that the drug is unsafe or dangerous. Other grounds are procurement of the registration by fraud or misrepresentation, violation of the conditions subject to which the drug was registered, public interest, contraventions of the provisions of the legislation, and misleading or exaggerated advertising.

36. In Saudi Arabia⁽⁶⁰⁾ registration of a new drug can be cancelled if it is not imported within one year following registration or if it is unobtainable from the agent for a six-month period. It can also be cancelled if the technical committees of the Ministry of Health or WHO have reported that it is toxic, or if it has been prohibited in the country of origin. In Sweden⁽⁶¹⁾ one of the grounds for the cancellation of the registration of a drug is that it has been the subject of publicity containing erroneous, greatly exaggerated, or fallacious information as to its action or its properties.

37. One of the reasons often advanced against registration is delay in processing applications. In Mali the National Commission on Marketing Licences is under a legal duty⁽⁶²⁾ to finalize its view on an application within four months. The time-limit is suspended if the manufacturer is requested by the Commission to supply additional information or carry out additional tests. If the Commission is inclined to reject an application, the applicant must be notified so that within a period of one month he may make further representations. Such representations, if any, must be considered by the Commission when it transmits its views to the Minister responsible for Public Health. The Minister is required to substantiate any decision to reject an application.

Marketing outlets and the sale of drugs

38. Countries differ widely in the requirements relating to who can prescribe and dispense drugs and under what conditions. In some countries these matters are governed not by laws and regulations on pharmaceuticals but by those relating to professionals such as medical practitioners and pharmacists. Since this review is primarily concerned with the marketing of drugs, no attempt is made to review in detail the different categories of prescribers.

39. In relation to the right to prescribe and dispense, national laws fall into two broad categories, the first permitting prescribers to dispense drugs as well, the second prohibiting prescribers from dispensing drugs, pharmacists being the sole persons authorized to dispense prescriptions issued by prescribers. However, even within those two broad categories there are various conditions, requirements, and limitations. For instance, countries that permit medical practitioners to dispense drugs may have a requirement that such practitioners should employ a qualified pharmacist for the purpose. In addition to requirements and conditions there are limitations, as in Rwanda, where private practitioners are authorized to keep and supply drugs only if there is no pharmacy open to the public within a radius of 10 km⁽⁶³⁾.

40. Besides specifying who can exercise the right to dispense, national laws and regulations deal with a variety of aspects such as the establishment and location of outlets, storage requirements, and conditions of sale. Apart from the requirement that to establish a pharmacy a licence must be obtained, some countries have requirements regarding the premises, the qualifications and experience of the persons to be employed at pharmacies, etc. In addition to pharmacies some countries have authorized the establishment of other outlets such as medicament stores and drug stores. In Bahrain legislation⁽⁶⁴⁾ has empowered the Minister to suspend the further issue of licences for medicament stores as soon as there are a sufficient number of pharmacies in the country.

41. To ensure that priority is accorded to the establishment of pharmacies, some countries, especially in the developing world, have assigned this responsibility to a specific institutional mechanism. In Algeria⁽⁶⁵⁾ the legislation in terms of which the central pharmacy was established requires it to establish pharmaceutical agencies in all communes to give patients access to basic pharmaceutical products. The Ethiopian Pharmaceuticals and Medical Supplies Corporation is required by legislation⁽⁶⁶⁾ to organize and operate pharmacies and medicament stores. In Bahrain⁽⁶⁷⁾ the Minister of Health is empowered to decide on the number of pharmaceutical centres that may operate in each town or village. In Benin⁽⁶⁸⁾ the National Pharmaceutical Office is required to establish a supply point (depot) in each provincial capital to facilitate the procurement of drugs by certain institutions and sales outlets such as private pharmacies.

42. Besides a statutory responsibility to promote the establishment of pharmacies, legislation in some countries provides for regulation of the location of pharmacies and distribution outlets, so as to ensure a fair geographical distribution. In Senegal a decree⁽⁶⁹⁾ in 1981 set out the criteria for the establishment and distribution of pharmaceutical dispensaries. While each regional or departmental administrative centre and each commune must have a pharmaceutical dispensary irrespective of the population it serves, no dispensary can be established in the Cape Verde region (the region surrounding Dakar) unless the minimum number of inhabitants to be served is 15 000. The minimum population target in respect of other regions is 30 000 inhabitants. These criteria come up for revision every five years.

43. Some countries have requirements additional to the general requirement that drugs must be stored in places or premises that are physically and hygienically suitable for the purpose. In Bahrain⁽⁷⁰⁾ pharmaceutical centres must be air-conditioned. Such requirements, of course, depend on the country's infrastructure and resources.

44. Marketing outlets are of different kinds. Some engage in wholesale as well as retail trade. Others cater only for individual consumers and medical practitioners who may need certain quantities of drugs in connection with their practice. Licensing systems and record systems generally differ depending on the nature of the trade carried out. Within the retail trade too there is a distinction depending on whether the drugs can be dispensed with or without a prescription. Depending on whether drugs are subject to a prescription system or not, different marketing and record systems operate. In many countries the marketing of OTC drugs is relatively free from controls. Depending on the nature of the health infrastructure and the health manpower situation, many countries, especially in the developing world, permit a large variety of personnel to prescribe as well as dispense OTC drugs. Such drugs are often subject to special advertising and labelling requirements.

45. The sale of drugs is regulated basically in two broad ways, by total prohibition and by the operation of various conditions. The sale of a drug can be totally prohibited by listing the drug in the main legislative text or in the regulations, as in the case of thalidomide in Canada⁽⁷¹⁾ and Sri Lanka,⁽⁷²⁾ or by not issuing a licence for its manufacture or importation where a licence is a condition precedent to its manufacture or import. Enforcement is facilitated by listing in the legislative text or in the regulations the drugs that cannot be sold, the availability of such drugs in the market then being prima facie proof of a contravention of the law. Provision is often made to enable the list to be updated whenever the sale of a drug has to be prohibited. Information on the adverse reactions of drugs disseminated by WHO and various organizations and countries may require that such lists should be reconsidered from time to time. Licensing authorities need such information to make timely and well-informed

decisions on whether the manufacture, import, or sale of a particular drug should be permitted or not.

46. The sale of certain drugs and certain categories of drugs (e.g. antibiotics and psychotropic substances) is regulated by law by way of the requirement of a prescription. Prescription requirements vary from country to country. In Norway⁽⁷³⁾ there is a requirement that a register should be maintained in pharmacies for prescriptions given by telephone. The register must be preserved for a period of three years from the date of the last entry. In Mauritius⁽⁷⁴⁾ no person can dispense a prescription unless he recognizes the signature of the prescriber and is satisfied that it is genuine. In Trinidad and Tobago⁽⁷⁵⁾ prescriptions in respect of certain scheduled drugs cannot be dispensed unless the signature of the prescriber is known to the dispenser or, if not known, he has first certified it. Several countries such as Uganda⁽⁷⁶⁾ and Trinidad and Tobago⁽⁷⁷⁾ require prescriptions to be preserved for a two-year period.

47. Some countries have built into their legislation safeguards additional to the requirement of a prescription. In Uganda⁽⁷⁸⁾ the Code of Ethics for the Practice of Pharmacy stipulates that drugs should not be supplied to any person when there is reason to believe that they are destined for illicit channels or will be misused. In Zimbabwe⁽⁷⁹⁾ certain restricted drugs (psychotropic substances) can be supplied only from the pharmacies of the hospitals listed in the regulations, and the prescription issued by any medical practitioner for a restricted drug must be countersigned by the medical superintendent or his deputy at such hospital. In Malta⁽⁸⁰⁾ no medical practitioner can issue a prescription for any preparation consisting of certain substances such as amphetamines or methaqualone unless he has had the prior written authorization of the Superintendent of Public Health. Furthermore, the Superintendent has to be notified when such a prescription is dispensed.

48. The mode of sale has been regulated in some countries. In Uganda⁽⁸¹⁾ there is a prohibition on the supply of drugs by means of an automatic vending machine. Exemptions have been made in respect of the use of automatic or vending machines in hospitals, for instance in the State of Nebraska⁽⁸²⁾ in the United States of America. Such exemptions are designed to facilitate access to certain categories of drugs when pharmacies are not open. However, such machines can generally be operated only by special cards or coded devices. In the Netherlands⁽⁸³⁾ sales through self-service systems are prohibited. Belgium⁽⁸⁴⁾ has prohibited the offer of gifts or benefits when pharmaceutical preparations are supplied. The solicitation or acceptance of such gifts is also prohibited.

49. National laws contain a variety of requirements regarding the maintenance of registers and other records regarding the sale of drugs. Laws generally contain a requirement that such registers and records must be made available for inspection if drug inspectors or other law enforcement personnel need them.

Advertising of drugs

50. The laws and regulations applicable to the advertising of drugs and the dissemination of information through the medium of advertising are generally different from those applicable to labels, package inserts, and warnings. This section considers the regulation of advertising only, though there are instances where identical provisions apply in respect of both advertising and labelling, package inserts, etc.

51. In many countries legislation on drugs contains provisions governing advertising. However, some countries, such as India⁽⁸⁵⁾ and Malaysia,⁽⁸⁶⁾ have enacted separate laws dealing specifically with the advertising of drugs. There

are also countries such as Portugal⁽⁸⁷⁾ where a general law on advertising also covers drugs.

52. Advertising restrictions fall into three broad categories: those applicable to specific drugs or categories of drugs; those of a general nature; and those in respect of certain audiences or target groups. Each of these categories needs to be dealt with separately, though there is a certain overlap.

53. With regard to the restrictions applicable to specific drugs or categories of drugs, many countries do not permit drugs available only on prescription to be advertised. According to a 1980 survey of about 50 countries, nearly 40 had a restriction of this nature.⁽⁸⁸⁾ A few countries permit such advertisements with prior approval. Some countries permit such advertisements if they are intended only for medical practitioners or appear only in medical journals. In Israel, registered new drug products cannot be marketed until the manufacturer has advertised the approved indications in a medical journal.⁽⁸⁹⁾ Norway does not permit advertisements of unregistered specialities or of medicaments prepared in a pharmacy and not included in an approved formulary.⁽⁹⁰⁾

54. Restrictions of a general nature are generally those applicable to drugs in general and to drugs for specific diseases. In Pakistan no drug can be advertised in a manner that encourages self-medication or use to the extent that it endangers health.⁽⁹¹⁾ In Belgium the Higher Council of Public Health can specify the diseases or ailments in respect of which no drugs can be advertised.⁽⁹²⁾

55. With regard to restrictions in respect of target groups, in some countries prescription drugs cannot be advertised to the general public and medical practitioners alike, but in others advertisements meant for the latter are permitted. In the United Kingdom there is a requirement⁽⁹³⁾ that before an advertisement is sent to a medical practitioner he should have, within the preceding 15 months, been sent a data sheet containing prescribed particulars. Among the required particulars are the name of the product, the presentation (description of appearance and pharmaceutical form), the uses, the dosage and administration, contraindications and warnings, pharmaceutical precautions (storage, etc.), the legal category, and package quantities.

56. The mode of advertising has been restricted in some countries. In Denmark drugs cannot be advertised in films, on radio or television, outdoors by means of signboards, posters, illuminated signs and the like, in vehicles used for transport, or in premises accessible to the public (other than the premises of pharmacies).⁽⁹⁴⁾ The regulatory provisions in Singapore prohibit door-to-door advertising.⁽⁹⁵⁾ In Thailand, there is a prohibition on advertising by song, by showing the suffering of a patient, by offering premiums or awarding lottery prizes, or in an impolite manner.⁽⁹⁶⁾

57. Several countries have established institutional mechanisms for screening advertisements. In Malaysia the Medicine Advertisement Board is headed by the Director-General of the Ministry of Health.⁽⁹⁷⁾ In France the Commission for the Control of Advertising has over 20 members, including pharmacists from the industry and representatives of consumer organizations.⁽⁹⁸⁾ In some countries there are statutory functionaries or institutional mechanisms with whom or which advertisements have to be registered prior to publication.

58. In some countries laws and regulations on advertising have special provisions. Three examples may be cited here to illustrate the range of matters that lend themselves to regulation. In Pakistan no person is entitled to spend more than 5% of his turnover on advertisements, sampling, or other promotional activities.⁽⁹⁹⁾ In Guatemala advertising agencies are required to ensure that

the drugs they have been requested to advertise have been duly registered with the Directorate General of Health Services.⁽¹⁰⁰⁾ In New Zealand, for the purpose of protecting the health of the public, the Director-General of Health can publish a statement relating to any matter contained or implied in an advertisement.⁽¹⁰¹⁾ Any statement so published is protected by qualified privilege - a legal defence in the event of an action based on such a statement.

Labelling, packaging, package inserts, and warnings

59. Requirements relating to labels and printed packaging materials vary from country to country. Different countries require different items of information to appear on either or both of them. The following list indicates the range of items from which different countries have specified those required to be set out in printed packaging materials or labels:

- Name of product (trade mark; approved name; generic name; international nonproprietary name)
- Dosage form (strength)
- Content of active ingredients (quantity/proportion of each)
- Inactive ingredients
- Indications and contraindications
- Directions for use
- Recommended dosage
- Whether for free sale or only on prescription
- Route of administration (or for external use)
- Warnings and cautions
- Storage precautions
- Type of packaging
- Contents of package (weight, volume, units)
- Name of manufacturer (or of local representative)
- Name of importer (and/or person responsible for marketing)
- Date of manufacture
- Expiry date (shelf-life)
- Price
- Batch number
- Registration number

60. Some countries require additional information. In Nepal the manufacturer must indicate on the label whether the drug is produced for the allopathic,

homoeopathic, ayurvedic, or Unani system.⁽¹⁰²⁾ The New Zealand Medicines Regulations of 1984⁽¹⁰³⁾ require labels of drugs available for sale without a medical prescription to contain certain items of information in a special panel on the label, the "CONSUMER INFORMATION PANEL". The information must include a statement of the purpose for which the drug is recommended. This panel has to be conspicuously placed in relation to other information included on the label and be clearly differentiated from all other promotional material or illustrations.

61 National requirements relating to labelling cover even such aspects as language, colour, and symbols. Some countries require that the labelling of imported drugs should be in the national or official language. Requirements for colours and symbols apply to a wide range of matters. In the United Kingdom⁽¹⁰⁴⁾ labels of drugs for sale only in pharmacies are required to have a capital letter "P" in a rectangle containing no other matter. The container and package of prescription drugs must be labelled "POM" in capital letters within a rectangle. In Bahrain⁽¹⁰⁵⁾ labels of different colours must be used depending on whether the medicament is for internal or external use. In Colombia⁽¹⁰⁶⁾ the labels, containers, and packaging of drugs liable to cause dependence must have a purple stripe. In the Netherlands⁽¹⁰⁷⁾ preparations intended for oral administration must carry a white label. For other methods of administration the upper part of the labels must have a pale blue strip bearing the words: "Do not swallow" or else a strip of coloured paper with the method of administration printed thereon.

62. Some countries have a system of screening labels. Screening takes place at various stages, when registration is under consideration or later, as in Poland, where the granting of a marketing licence is conditional on approval of the text of the labelling and of the printed information regarding the drug.⁽¹⁰⁸⁾ Some laws provide for the inspection of labels when a drug is imported. In Guyana a drug with a label that does not conform to local labelling requirements is permitted to be imported for the limited purpose of relabelling, and if not properly relabelled within the stipulated time-limit must be exported.⁽¹⁰⁹⁾ If the consignment is not so exported it is liable to be confiscated.

63. The variations in national approaches to labelling can be best illustrated by one or two national case studies selected at random. In Ecuador⁽¹¹⁰⁾ labels must be submitted for approval within three months of registration of the product. The label must indicate the name of the product, the pharmaceutical form, the net contents of the package, the qualitative and quantitative formulae, the active principles, the routes of administration, the batch number, the contraindications, the warnings, paediatric use (if appropriate), the storage temperature (if appropriate), whether a prescription is required, the name and address of the manufacturer, the name of the pharmacist responsible for the preparation (if appropriate), the date of preparation and expiry date, and the registration number. If the packaging size is small only the name of the product, the name of the manufacturer, the batch number, the concentration of the active principle, the expiry date, and warnings, if any, need appear on the label. The Directorate General of Health may require warnings such as: "To be sold only on medical prescription", "May be habit-forming", etc., to appear on the label. In addition to other warnings, if any, the label of every OTC medicament must state that if the symptoms persist the physician should be consulted. The labels of medicaments intended for promotional purposes must state that they are samples not intended for sale. No drawings or figures suggestive of the therapeutic value of the product or inciting the public to use it are allowed to be printed on any label, packaging, or package insert. Names that suggest improper use or the presence of active principles that are in fact not present or that exaggerate the therapeutic properties of the product are not permitted. Official names using formulae that are not exactly those officially prescribed are also not permitted.

64. The Ecuadorian approach can be compared with that of Sri Lanka. Under the Cosmetics, Devices and Drugs Act⁽¹¹¹⁾ there is no provision for prior screening of labels. The control mechanisms are based on negative stipulations, contraventions of which have penal consequences. The term "label" has been defined in the Act as any tag, brand, mark, pictorial or other descriptive matter, written, printed, stencilled, marked, embossed, impressed on, or attached to a container of a drug. In terms of the Act there is a prohibition on any person labelling any drug in a manner that is false, misleading, deceptive, or likely to create an erroneous impression regarding its character, value, potency, quality, composition, merit, or safety. For purposes of penal liability this prohibition is deemed to apply to a drug that is not labelled as required by regulations made under the Act. Where a standard has been prescribed for any drug, no person is entitled to label any drug that does not conform to such standard in such a manner that it is likely to be mistaken for the drug for which a standard has been prescribed. Where a standard has not been prescribed for any drug but a standard for that drug is contained in the International Pharmacopoeia, the British Pharmacopoeia, the Pharmacopoeia of the United States of America, the British Pharmaceutical Codex, the British Veterinary Codex, the Japanese Pharmacopoeia, or the European Pharmacopoeia, no person is entitled to label any drug that does not conform to the standard contained in those publications in such a manner that it is likely to be mistaken for the drug for which the standard is contained in those publications. If a standard has not been prescribed for any drug or a standard for that drug is not contained in any of the pharmacopoeias listed above, no person is entitled to sell, offer for sale, or distribute such a drug: (a) unless it is in conformity with the standard set out in the label accompanying the drug, or (b) in such a manner that the drug is likely to be mistaken for a drug for which a standard has been prescribed or for which a standard is contained in any of the above pharmacopoeias.

65. The legal provisions on packaging in most countries deal with labelling requirements. Argentine legislation⁽¹¹²⁾ requires laboratories to produce medicaments not only in packages intended for direct sale to the public but also in economic packages, the contents and packaging of which make possible the sale by pharmacies of the number of individual units (tablets, coated tablets, capsules, pills, etc.) prescribed by the physician by means of simple subdivision of the contents.

66. In certain countries package inserts are compulsory.⁽¹¹³⁾ In respect of specified categories of drugs it is sometimes mandatory that the package inserts should be addressed to both prescribers and patients. Some countries require separate leaflets. Inserts in OTC drugs are normally required to be addressed only to patients. Package inserts generally cover most of the items listed above. Where some of the information has appeared on the label the inserts may contain more elaborate or detailed information, especially in relation to contraindications and warnings. Some countries require advance clearance of package inserts as part of the registration procedure or independently. In Italy⁽¹¹⁴⁾ there is a requirement for a translation of the package inserts or instructions used in the country where the drug was first manufactured. Failure to comply with this requirement entails the withdrawal of registration.

67. In relation to requirements for product monographs, package inserts, and other information to health professionals, a 1968 WHO survey on pharmaceutical advertising noted that

"... it is quite rare to find, in the legislation, any precise or detailed specification of the requirements applicable to medical advertising, the greater part of the legislation, as in the case of the countries dealt with in this survey, being concerned with advertising to the public."⁽¹¹⁵⁾

68. A monograph has been defined in some countries, such as Chile,⁽¹¹⁶⁾ as the technical and scientific description of a product. The monograph must be submitted when application is made for the registration of the product. It is a form of record to which reference can be made for information on the formula and the properties of the product, etc. Some countries require scientific and technical information to be furnished to medical practitioners. The 1984 Crown Order of Belgium,⁽¹¹⁷⁾ dealing with information and advertising concerning medicaments, requires that all medicaments be provided with two information notices, one scientific for persons entitled to prescribe or supply medicaments, the other for the public, containing such information as is considered necessary for it. It may be noted that in Belgium only persons entitled to practise as physicians, pharmacists, or veterinarians are eligible to be licensed as persons responsible for pharmaceutical information. In Denmark the National Board of Health may require manufacturers and importers to circulate alterations and additions to the information contained in their advertisements addressed to physicians, pharmacists, etc.⁽¹¹⁸⁾ The form and content of such alterations and additions can be prescribed by the Board. A 1982 Council of Europe resolution⁽¹¹⁹⁾ on information concerning medicines to persons qualified to prescribe or supply them states that the information should include particulars on the legal provisions governing the prescribing and supply of the medicine. Under the heading of inducements, there is a prohibition on giving persons qualified to prescribe or supply medicines rewards, pecuniary advantages, or other inducements, with the exception of objects of negligible intrinsic value. However, this does not affect normal trade discounts. A 1984 Council of Europe resolution⁽¹²⁰⁾ on packaging leaflets requires a distinction to be made between the information supplied with medicines available only on a medical prescription and that supplied with medicines that can be sold without a prescription. The distinction is reflected in the nature and scope of the information to be furnished.

69. Under some national laws there is a requirement that various cautionary phrases should appear on labels and in advertisements and package inserts. In some countries the requirements apply to most drugs. "Keep out of the reach of children", for instance, is a warning that most countries require in respect of many drugs. In addition, special warnings are required for certain drugs. There are drugs that affect specific categories of patients such as pregnant women and patients with cardiac conditions. There are also drugs that affect psychomotor skills such as driving or working with machines. In respect of such drugs many countries require that the patient be warned in advance. In Brazil⁽¹²¹⁾ labels of all new drugs in use for less than five years must carry a warning that in the case of unforeseen suspected adverse reactions the prescribing physician must be notified.

Drug sales representatives and samples of drugs

70. The primary task of a drug sales representative, known also in some countries as medical representative, pharmaceutical consultant, or medical detailman, is to promote the sales of pharmaceutical products manufactured or imported by the company that employs him. No global statistics are available as yet of the ratio of drug sales representatives to the number of doctors or to the range of products available for marketing. The scope for the introduction of new products into the market, the availability of opportunities for advertising and other promotional activities, etc. are factors that determine the number of drug sales representatives employed by a particular company or group of companies.

71. Drug sales representatives often give samples of drugs they are promoting to doctors as well as to the health administrators who decide which drugs are to be ordered for a hospital or other institution.

72. National legal controls and voluntary codes in relation to drug sales representatives and the distribution of samples may relate to one or the other or to both. Only a few countries around the world have regulatory measures relating to drug sales representatives and the distribution of samples of drugs. These measures can be best considered in relation to national examples under the headings of qualifications for employment as drug sales representatives, permissible activities and circumstances under which samples can be distributed, and mandatory duties of drug sales representatives.

(a) Qualifications

73. A 1976 law of the Federal Republic of Germany⁽¹²²⁾ on medicaments includes provisions on pharmaceutical advisers. In terms of this law pharmaceutical dealers can appoint only such persons as have the requisite specialized knowledge. Persons who are deemed to have such specialized knowledge are: pharmacists or persons holding a certificate certifying that they have passed an examination after completing university studies in pharmacy, chemistry, biology, medicine, or veterinary medicine; pharmacy assistants and persons who have completed a course of training as technical assistants in pharmacy, chemistry, biology, medicine, or veterinary science; and persons whose training or further training has been recognized as sufficient by statutory ordinance. An ordinance enacted in 1978⁽¹²³⁾ provided that the competent authority should organize or arrange for the organization of courses of further training leading to the examination of pharmaceutical consultants. The examination is designed to determine whether candidates have the necessary knowledge, skills, and experience to provide members of the health professions with comprehensive and critical technical information concerning medicaments, and to record and make available to their employer reports from the members of the health professions regarding side effects, contraindications, and other hazards associated with medicaments. The course of training for pharmaceutical consultants lasts for 1000 hours and is spread over a period of 12 months.

(b) Permissible activities

74. On the general premise that what is not expressly prohibited by law is permissible, drug sales representatives engage in promotional and educational activities, including giving samples. A few countries⁽¹²⁴⁾ such as Czechoslovakia, Hungary, and Yugoslavia have expressly prohibited the distribution of samples. Some countries such as Argentina⁽¹²⁵⁾ do not permit samples of certain categories of drugs, e.g. psychotropic drugs, to be distributed. In Mexico it is an offence to keep samples in pharmacies.⁽¹²⁶⁾ In Morocco samples can be given only on request.⁽¹²⁷⁾ Under the French Public Health Code⁽¹²⁸⁾ samples cannot be given within premises that are accessible to the public during medical and pharmaceutical congresses.

75. Samples of drugs are primarily intended to enable medical practitioners to become familiar with them. National laws, therefore, generally require that labels of packets containing samples should indicate that they are not intended for sale. There are restrictions in some countries on the size of sample packages, the quantity of the drug, and the frequency of the distribution of samples (e.g. a specified number of years⁽¹²⁹⁾ from the first date of marketing of the drug and thereafter only on request). Since samples are intended to familiarize medical practitioners with the particular drug which is promoted, sample packages must comply with the usual labelling requirements (including those relating to package inserts).

76. In Singapore regulations⁽¹³⁰⁾ have been made under the Medicines Act, 1975,⁽¹³¹⁾ to regulate drug sales promotion. For the purpose of the regulations,

sales promotion means any sales campaign (including door-to-door sales), exhibition, competition, or other activity for the purpose of introducing, publicizing, or promoting the sale or use of any medical product. In terms of the regulations no one can carry out sales promotion without first obtaining a permit from the licensing authority. Licences are valid for a three-year period and may be granted subject to various terms and conditions. In conducting any sales promotion, gifts or prizes cannot be offered.

(c) Mandatory duties of drug sales representatives

77. In the Federal Republic of Germany⁽¹³²⁾ pharmaceutical advisers are required to keep a record of the recipients of samples and the nature, amount, and date of their supply. Such records must be presented to the competent authority on request.

78. The Pharmaceuticals and Poisons Act,⁽¹³³⁾ 1978, of the United Republic of Tanzania provides that the competent Minister, after consultation with the Pharmacy Board, should make regulations regarding the activities of medical representatives. Regulations⁽¹³⁴⁾ made under the Act require that if any pharmaceuticals or pharmaceutical products supplied contain certain specified poisons, the medical representative must, within 24 hours of having so supplied them, enter in a book details such as the name and quantity of the poison supplied and the person to whom it was supplied.

79. The activities of drug sales representatives have not been viewed solely as a matter of promotional interest to drug companies. In the Federal Republic of Germany legislation⁽¹³⁵⁾ requires them to record and forward in writing to their employers reports from members of the health professions concerning side effects and contraindications or other risks due to medicaments.

(d) Regulation through codes of conduct

80. Besides legislative interventions of the various types enumerated above, the pharmaceutical industry in certain countries has formulated its own rules relating to drug sales representatives. In Sweden the rules⁽¹³⁶⁾ have been widely publicized and have come to be recognized officially as the applicable norms. According to these rules medical representatives must have received a basic medical education in accordance with the standards laid down by the Association of the Swedish Pharmaceutical Industry and the Association of Representatives of Foreign Pharmaceutical Industries and should have been specially trained for this work by the pharmaceutical companies employing them. Examinations are conducted by a five-member training council consisting of three physicians and two representatives of the pharmaceutical industry. Field training for six months under the supervision of the employing firm is obligatory. As well as rules relating to qualifications for medical representatives, there are rules dealing with ethical conduct. Drug information conveyed by the medical representative must be based on factual data that can be assumed to be of value to the doctors concerned. Visits of a reminder character are not allowed. The representative must ascertain from the doctor his experience with the drug and his opinion regarding its use and transmit this information to the pharmaceutical company.

Brand names, generic names, and generic drugs

81. The question of generic versus brand names has loomed large in recent discussions in relation to a variety of issues such as the cost of medicines to the consumer, the transfer of technology, the capacity of national infrastructures to verify the quality of drugs, and incentives to drug innovation⁽¹³⁷⁾ some of those issues need to be considered in the context of patent and trademark legislation. However, this review is concerned primarily with the extent to which national drug

laws treat generic names and generic drugs rather than with the broad framework of intellectual property laws and industrial policies.

82. A generic name usually contains an informative stem reflecting the pharmacological class to which the drug belongs. Generic drugs are products that are marketed under their nonproprietary⁽¹³⁷⁾ or approved names rather than their proprietary or brand names. A generic name, unlike a brand or trade name, being nonproprietary in character, cannot be the subject of legal protection in favour of individual persons or corporate bodies. Generic drugs or drugs marketed under their generic names are usually cheaper.

83. Legislative measures to promote generic nomenclature are of relatively recent origin. The most widely cited example is the Drugs (Generic Names) Act, 1972, of Pakistan,⁽¹³⁸⁾ which banned any drug prescribed, dispensed, sold, or distributed under any brand, patent, or proprietary name. The scientific or official names - the generic names - of the drugs were set out in the National Formulary. The Act, however, had a relatively short life-span, mainly because of the infiltration of drugs of doubtful quality into the market.

84. Legislative trends in relation to brand names and generic names cover requirements relating to the use of names for registration and in advertisements and labels, and generic substitution by pharmacists when prescriptions are dispensed. In relation to the former, a few national examples will suffice to illustrate the range of national approaches. Pakistan generally requires single-ingredient drugs to be registered by their generic names, compound drugs by their proprietary names.⁽¹³⁹⁾ Norway requires the generic names to be included in drug advertisements for the general public.⁽¹⁴⁰⁾ Greek legislation requires the generic names of the active principles of all pharmaceutical specialities to appear on the inner and outer packaging.⁽¹⁴¹⁾

85. With regard to generic substitution, the substitution of a product, especially a cheaper one with the same active ingredients, for the product prescribed by the medical practitioner has received legislative sanction in only a few countries. In the developing world, Barbados has a law⁽¹⁴²⁾ that authorizes the pharmacist, unless the prescriber has otherwise specifically directed, to select and dispense an interchangeable product that is cheaper than what has been prescribed; no liability attaches to the pharmacist or to the person prescribing the drug by reason only of the fact that the pharmacist has dispensed such a product. The pharmacist has to exercise his discretion as to whether a cheaper substitute should be dispensed or not. In the developed world, generic substitution has been the subject of legislation in a number of states in the United States of America. Since generic substitution or drug product selection, as the process is sometimes called, is regulated not by federal legislation⁽¹⁴³⁾ but by state legislation, the United States provides a range of approaches containing different modalities, conditions, and requirements. Two examples suffice to demonstrate the legislative strategies available. In the State of Maryland, the law⁽¹⁴⁴⁾ authorizes the pharmacist to dispense a different cheaper drug product of the same dosage and strength as the brand-name drug product prescribed. The different product must be one that is generically equivalent. The pharmacist is required to pass on any savings in cost to the consumer. In the State of Massachusetts every prescription must contain two different lines for the practitioner's signature.⁽¹⁴⁵⁾ A signature on one line means that interchange is permitted, on the other that the product should be dispensed as directed. A prescription becomes invalid if the practitioner has not affixed his signature on one of the two designated lines. If the practitioner has indicated his preference for interchanging, the pharmacist is required to dispense a less expensive reasonably available interchangeable drug product as listed in the most current formulary or supplement thereof. The fact of interchange has to be reflected on the label. In the event of noncompliance by a

pharmacist the drug purchaser is entitled to lodge a complaint with the secretary of the executive office of consumer affairs, who will refer the complaint to the board of registration in pharmacy for appropriate action.

Pricing of drugs

86. In most countries prices of drugs are regulated when there is a system to regulate the prices of other products as well. Price fixation and the monitoring of price changes of drugs therefore need to be viewed in the context of national trade and consumer policies. Decisions as to whether there should be price control and, if so, the products to be controlled and the nature of the controls are often based on such policies. The mechanics of controlling the prices of drugs are sometimes to be found in statutes dealing with price control in general and not with pharmaceuticals in particular.

87. Different countries have different authorities or officials vested with functions relating to price control or the monitoring of the prices, or both. In Denmark there is a Monopolies Control Authority with jurisdiction over drugs as well as other products.⁽¹⁴⁶⁾ On the other hand, in Nepal the jurisdiction of the Department of Drugs Administration is confined to drugs.⁽¹⁴⁷⁾

88. Drug prices are relevant as a criterion in the registration of drugs, in the fixation of the sale price, in the regulation of price increases after registration, and in labelling and advertising requirements.

89. In some countries the price of the drug is one of the criteria on which registration can be refused. According to a 1980 survey⁽¹⁴⁸⁾ of registration requirements in approximately 50 countries, it was a criterion in Argentina, Egypt, Finland, Hungary, India, Mexico, Morocco, Pakistan, Spain, and Tunisia. In Austria, Greece, the Islamic Republic of Iran, Peru, Portugal, Switzerland, and Turkey, if the price is excessive registration is not granted.⁽¹⁴⁹⁾ In some of those countries as well as in a few others the price of the drug in the country of export must be furnished when an application is made for its registration.

90. The price is sometimes determined in relation to both retail and wholesale sales, and different minimum and maximum price scales are sometimes applied. Price fixation involves the consideration of various factors and items of information, as is exemplified by Norwegian legislation,⁽¹⁵⁰⁾ in terms of which no pharmaceutical speciality can be placed on the market in Norway unless its price has been approved. Such approval is conditional on the price not being exaggerated in relation to the actual value of the product, account being taken of the price of equivalent preparations manufactured by other establishments and information supplied on production costs, etc.

91. Some countries permit price changes to be effected after registration only with prior approval. In Austria prior approval is necessary, while in other countries such as Bolivia the authorities must be notified of changes in price⁽¹⁵¹⁾.

92. The requirement that the price of the product must be stated on the label and in advertisements, etc. is often to be found in legislation dealing with prices or consumer protection. In countries such as Lebanon⁽¹⁵²⁾ and the German Democratic Republic⁽¹⁵³⁾ the relevant pharmaceutical laws contain a requirement that the selling price must be indicated on the label.

93. During the past two decades there has been a great deal of discussion regarding the factors that have resulted in the high price of drugs that perhaps could otherwise be supplied at lower prices. In this context, there is a ceiling

on promotional expenditure in Pakistan.⁽¹⁵⁴⁾ The law does not permit any person to spend more than 5% of his turnover on drug advertisements, sampling, or other promotional activities.

94. Price fixation has often taken place only with regard to drugs. Recent Bangladeshi legislation,⁽¹⁵⁵⁾ however, has empowered the Government to determine the maximum price at which any pharmaceutical raw material may be imported or sold.

Sponsorship of medical symposia

95. The sponsorship of medical symposia, congresses, seminars, and similar activities by pharmaceutical companies or associations representative of the interests of such companies has been the subject of regulation in a few countries. They have adopted different approaches. An Italian ministerial decree⁽¹⁵⁶⁾ requires scientific congresses and conferences on drugs to comply with strictly technical criteria; the topics discussed at such congresses and conferences must be free from promotional or advertising interest, and pharmaceutical companies and other institutions responsible for organizing such meetings must submit in advance to the Ministry of Health details concerning the congresses and conferences. A recent Greek law⁽¹⁵⁷⁾ has made the organization and financing of congresses, seminars, and other means of disseminating information by pharmaceutical manufacturers or commercial undertakings or by advertising agencies or other service companies subject to the prior approval of the National Organization for Medicaments. Approval may be granted subject to certain conditions. In Spain cash contributions for purely scientific activities such as conferences, lectures, talks, film shows, and publications are subject to certain conditions.⁽¹⁵⁸⁾ Under the French Public Health Code⁽¹⁵⁹⁾ the supply of samples is prohibited within premises that are accessible to the public during medical and pharmaceutical congresses.

Financial interests

96. The 1983 Pharmacy Act⁽¹⁶⁰⁾ of Mauritius has a provision dealing with what is described as "illegal arrangements". In terms of the Act no manufacturer, licensee of a wholesale pharmacy, or pharmacist can enter into any arrangement with an authorized person (a medical practitioner, dentist, or veterinary surgeon) under which such person is to receive any gain or benefit in return for the custom he brings to the manufacturer, licensee of the wholesale pharmacy, or pharmacist. Furthermore, no authorized person can have any share, participation, or other financial interest in the manufacture or sale, whether wholesale or retail, of pharmaceutical products.

Enforcement of laws and regulations on marketing

97. The responsibility for enforcing pharmaceutical legislation is generally entrusted to specifically designated personnel such as inspectors, who are authorized to inspect manufacturing, processing, and packaging establishments and wholesale and retail outlets. The inspection of books and records and the taking of samples are some of the important functions they perform. Interference with the exercise of the powers of an inspector or obstructing him in the course of duties are generally the subject of penal sanctions.

98. Facilities for the analysis of drugs provide one of the best forms of ensuring the quality and safety of the drugs available in the market. Analysts have to be specifically designated and their functions and powers clearly set out. Legal provision permitting their reports and certificates to be accepted as prima facie evidence of the matters stated therein is generally sufficient to dispense analysts from being summoned to court to give oral testimony on matters of routine. Their

oral testimony is, however, required in the event of any of their findings being challenged or if further clarification is needed on the methods followed for the analysis of drugs or the rationale underlying their findings or conclusions.

99. The establishment of the administrative infrastructure for enforcement has taken different forms. In Uganda⁽¹⁶¹⁾ legislation provides for the establishment of a Drugs Bureau under the Office of the Inspector of Drugs. The Bureau maintains a register of all registered drugs as well as a list of all toxic substances, their composition, toxicity, and antidotes. Information regarding drugs is transmitted to medical practitioners. In Pakistan⁽¹⁶²⁾ legislation requires provincial governments to set up provincial quality control boards and provincial drug-testing laboratories.

100. Besides general provisions relating to inspection and the analysis of samples, some countries have specific legal provisions. In the Australian state of Victoria⁽¹⁶³⁾ there is a statutory requirement that every municipal council must submit for analysis during each year not less than three samples of drugs for each thousand persons of the population of the municipality.

101. Laboratories have many roles, ranging from the establishment of standards to the examination of samples. They have been established both by administrative and by legal measures. When laboratories are the subject-matter of legislation it is usual to assign specific statutory duties to be performed by them and to specify in the statute the powers they can exercise. The Medicaments Laboratory of Finland has been legally⁽¹⁶⁴⁾ empowered to obtain samples, without charge, from manufacturers, importers, suppliers, vendors, and other persons dealing in drugs.

102. To facilitate monitoring the movement of drugs, countries require various kinds of recording systems to be maintained. In Chile there is a requirement⁽¹⁶⁵⁾ that each batch or series of a pharmaceutical product must have a code or key permitting its identification at any stage in its production, storage, distribution, or marketing. The key must be registered with the Public Health Institute and appear on the labels and boxes or wrappings of each unit of the finished pharmaceutical product. In the Philippines⁽¹⁶⁶⁾ complete records must be maintained of the distribution of each batch of drugs in a manner that will facilitate its recall if the need arises. Records must be maintained for a two-year period. The name and address of the consignee, the date and quantity sold, and the lot or control number identifying the batch sold must be included in the records.

POST-MARKETING SURVEILLANCE

103. The view that drugs, by their very nature, need to be constantly monitored even after they have entered the market has now gained wide currency; more and more countries now accord priority to the establishment of appropriate procedures for post-marketing surveillance. For the effective operation of a post-marketing surveillance system there are two basic requirements, namely, procedures to obtain information on defective drugs and procedures to take appropriate action in respect of such defective drugs.

104. National approaches towards obtaining information on defective drugs are two. One is by legislation to require manufacturers, physicians, and other personnel (e.g. drug sales representatives) to notify the competent health authorities regarding defective drugs. The other is to obtain such information voluntarily.

105. A variety of different measures can be taken when a defective drug has been identified in the market. Among them are: recall of the drug from the market; prohibition of further sales; suspension or cancellation of the registration and marketing licence; destruction of defective stocks; warnings to pharmacists, physicians, and consumers; further investigation; legal action against those responsible for contravening laws and regulations; and inspection of production and quality control facilities.

106. The national approaches can be illustrated by way of a few examples. In Yugoslavia⁽¹⁶⁷⁾ health organizations using approved medicaments must notify the competent federal administrative agency of any adverse side-effects occurring in clinical practice that are not indicated on the label or in the package insert. The agency is required to take appropriate action on receipt of information of adverse side-effects detected in the country or elsewhere. Under the compulsory notification system in Austria⁽¹⁶⁸⁾ physicians, pharmacists, and persons engaged in trade are obliged to transmit to the Federal Ministry of Health and Environmental Protection information in relation to the safety of medicaments, including their abuse potential. In Italy⁽¹⁶⁹⁾ pharmaceutical companies that manufacture or market drugs are required to submit periodic reports concerning toxic or other side-effects associated with their drugs that have come to their knowledge. In New Zealand⁽¹⁷⁰⁾ a fine of \$ 1000 can be imposed on an importer or manufacturer who, having reason to believe that any substantial untoward effects have arisen from the use of the medicine, whether in New Zealand or elsewhere, fails to notify the Director-General of Health of the nature of those effects and the circumstances in which they have arisen. Under the legislation the licence of a licensee who is convicted of an offence can be cancelled. In Guyana⁽¹⁷¹⁾ there is a requirement that, when a manufacturer receives any report of any unexpected side-effect, injury, toxicity, or sensitivity reaction associated with clinical use, studies, investigations, and tests respecting a drug manufactured in Guyana, he should immediately inform the Government Analyst. In the case of new drugs (used in Guyana after 1 January 1977) the duty to inform is not only incumbent on the manufacturer but also on any person who receives such a report. In Nepal legislation⁽¹⁷²⁾ provides for the recall of drugs that are not safe, effective, or of the requisite standard. Furthermore, in the event of death or injury caused to any person by such drugs the manufacturer is liable to pay compensation to the successor of the deceased person or to the person who has suffered injury. In most countries the civil or criminal law or both provide various forms of remedies to an aggrieved patient.

107. Several countries have established separate institutional mechanisms for drug monitoring. Two of the more recent examples may be noted here to illustrate such mechanisms. In 1982 France established a National Commission on Drug Monitoring,⁽¹⁷³⁾ whose functions are: (a) to compile and evaluate information on the unexpected or toxic effects of medicaments subsequent to the issue of the marketing authorization; (b) to advise the Minister of Health on the measures to be taken in order to stop incidents and accidents found to be associated with the use of a medicament or the simultaneous use of several medicaments; and (c) to propose to the Minister such investigations and studies as it considers of value in conducting drug monitoring. The legislation also provided for the establishment of regional centres to collect information from hospitals, physicians, pharmacists, etc. and to transmit them to the Commission.

108. In 1983 Greece established a National Organization for Medicaments with provision for the establishment of an adverse reactions committee.⁽¹⁷⁴⁾ The committee has the responsibility of collecting, processing, evaluating, and registering all data and information concerning indications, contraindications, adverse reactions, precautions in use, and the interaction of pharmaceutical substances or combinations of them.

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4. World Health Assembly resolution WHA28.65.
5. It is of significance that as at present 110 out of the 164 WHO Member States have agreed to participate in the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce (resolution WHA28.65). Exporting countries issuing certificates have to certify that (a) the manufacturing plant in which the product is produced is subject to inspection at suitable intervals, and (b) the manufacturer conforms to requirements for good practices in the manufacture and quality control, as recommended by WHO. See also the Convention for the Mutual Recognition of Inspections in respect of the Manufacture of Pharmaceutical Products (also commonly referred to as the Pharmaceutical Inspection Convention).
6. While private individuals and corporate bodies wishing to import drugs are usually required to obtain an import licence covering the drugs to be imported, in some countries the right to import drugs is vested in an agency or authority to the exclusion of other importers unless specially authorized by such agency or authority. Examples of such import monopolies are the Algerian Central Pharmacy (Ordinance No. 69-14 of 25 March 1969 establishing rights of importation for pharmaceutical products (IDHL, 21: 667 (1970)); Ordinance No. 76-79 of 23 October 1976 promulgating the Public Health Code (IDHL, 29: 261 (1978)); and Decree No. 82-161 of 24 April 1982 amending Decree No. 77-6 of 23 January 1977 approving the statutes of the socialist undertaking known as the Algerian Central Pharmacy (IDHL, 35: 108 (1984)) and the Norwegian Medical Supplies Centre in Norway (Crown Decision of 19 February 1965 embodying provisions as to the powers granted solely to the Norwegian Medical Supplies Centre and its right to engage in trade in pharmaceutical products and poisons (IDHL, 17: 138 (1966)).
7. See page 8, Registration of Drugs. Countries differ in their registration requirements. Generally, it is a requirement that the drug should be registered in both the importing country and the exporting country. Importing countries that do not have a registration system, however, normally consider it adequate that the drug is registered in the country of export or, as in some cases, at least in a designated country or countries.
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9. The Therapeutic Goods Act 1966. IDHL, 21: 3 (1970).
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