Theme paper for Discussion

Effective Drug Regulation: what can countries do?

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<tr>
<td>ASEAN/TCDC</td>
<td>Association of South-East Asian Nations/technical cooperation among developing countries</td>
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<td>DAP</td>
<td>WHO Action Programme on Essential Drugs</td>
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<td>EMEA</td>
<td>European Medicines Evaluation Agency</td>
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<td>GMP</td>
<td>good manufacturing practice</td>
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Effective Drug Regulation: what can countries do?
Executive summary

Drug regulation is a process encompassing various activities aimed at ensuring the safety, efficacy and quality of drugs, as well as the appropriateness and accuracy of product information. Its ultimate goal is to promote and protect public health.

The special nature of drugs demands that they should not be treated as normal commercial commodities by governments or those involved in trade. In particular, governments should take responsibility for regulating the production, importation, exportation, storage, distribution, sale and supply of drugs. This process should cover the whole spectrum of drugs—from new innovative to long-established products—and should be applied to drugs from all sources, whether produced domestically or imported by the public or private sector.

For many years, various countries, the World Health Organization (WHO), and other international organizations have sought to improve drug regulation at national and international level. This has included the development of adequate norms, standards, guidelines and guides. However, despite these efforts, only a few countries operate a well-developed drug regulatory system. In many other countries such a system has been developed only partially and thus operates weakly. In yet others, a drug regulatory system is lacking entirely. Consequently, the market circulation of substandard drugs remains a concern in many countries.

This paper presents an overview of the development of drug regulation and the rationale for drug regulation. It also reviews the drug regulation situation in selected countries, examines key contributing factors to observed drug regulation weaknesses, and identifies the measures that must be taken to improve drug regulation.

Assess drug regulation performance

The reasons for drug regulation weaknesses vary from country to country. However, the most important influences on drug regulation outcomes are: the political and socioeconomic environment; drug policies and legislation; drug regulation organizational structure; enforcement and regulatory strategies; human and financial resources; and corruption. In order to take corrective action governments need to systematically assess their drug regulation performance, identify weaknesses therein and the reasons for them, and consider alternative policy options.

Identify and develop priority functions

A national drug regulatory system should reflect the level of development of the relevant country’s pharmaceutical sector. In industrialized countries where the pharmaceutical industry is highly developed, and there are no constraints on human or other resources, all the components of drug regulation need to be in
place if the safety, efficacy and quality of drugs are to be assured. In developing countries, drug regulation should be developed in phases, beginning with the most basic (but priority) and less resource-intensive functions. For instance, in countries where there is little domestic manufacturing, good manufacturing practice (GMP) inspection cannot be considered a priority, compared to inspection of distribution channels, or registration of imported drugs.

**Provide a clear mission and purpose**

Governments should make clear the rationale for regulating drugs by providing a written mission statement. The specifics of this statement will depend on the resources available and the priority objectives. Such a statement will be crucial to any assessment of whether the purpose of drug regulation has been achieved and to making known the need for drug regulation. This statement should be published and should indicate the various parties who will be involved in drug regulation, as well as its beneficiaries.

**Create a supportive environment**

Government support and commitment are essential to effective drug regulation. Policy statements are not sufficient for demonstrating this commitment. A mechanism should also be in place that guarantees public accountability and transparency. Additionally, drug regulation should be independent of political pressure, and adequate resources made available for its smooth operation. Governments should recognize the positive role that professional associations, consumer groups and other public interest groups can play in drug regulation, and create mechanisms for their participation.

**Formulate adequate drug legislation**

Drug legislation forms the basis of drug regulation. Governments should examine their drug legislation and amend it if necessary, to make it sufficiently comprehensive. They should also provide the relevant agency with adequate power to ensure that the drug regulation objectives are met. The role, responsibilities and duties of the parties involved in drug regulation should be defined clearly. Provisions for administrative measures and legal sanctions, to be taken in the event that the drug laws and regulations are violated, should be made.

**Create appropriate organizational structure**

Governments should provide appropriate organizational structure for effective drug regulation. Responsibilities, duties and functions should be distributed appropriately between the various bodies responsible. Structural and functional linkages should be defined clearly and a system of accountability should operate. The structure should provide independence in decision-making, as well as financial and administrative autonomy.

**Allocate adequate human and financial resources**

Drug regulation requires appropriately trained and highly qualified individuals of high integrity. Governments must therefore pay salaries that are commensurate with level of responsibility. Accordingly, they should allocate specific financial resources for drug regulation. A realistic fee system to ensure financial sustainability should be imposed for services rendered, and the
agencies responsible for drug regulation should have the power to collect and use them. A national plan to develop the needed human resources, including recruitment and retraining, should be established.

Minimize corruption and conflict of interest

A number of actions can be undertaken that will contribute significantly to reducing corruption in drug regulation. For example, drug regulation rules and procedures should be clear and transparent. Additionally, drug regulation enforcement should be based on written rules, and the discretionary power of regulators should be limited in order to prevent abuse. Governments should also establish a pay structure that rewards regulators for honest work, and personnel such as inspectors who have frequent contact with regulatees should be rotated regularly. A mechanism for public complaints should be established, and public interest groups encouraged to participate in regulatory and enforcement activities.

Apply most appropriate strategy

As well as traditional command-and-control government regulation, governments should consider encouraging the pharmaceutical industry and trade associations to practise self-regulation, particularly if government resources and infrastructure are limited. They can also consider encouraging public interest groups to participate in certain regulatory activities. Such an approach should be based on written terms of reference or laws, and a mechanism should be instituted to ensure accountability. Governments should also seek to improve compliance with drug legislation—for instance, by designing escalating enforcement strategies, including persuasion, warnings and fines.

The way forward

At present, drug regulation is weak or non-existent in many developing countries. Consequently, the problem of substandard and counterfeit drugs, as well as the existence of large numbers of drugs that are of no therapeutic significance, continue to be of serious concern. The pressure on countries to open their markets, including that of the pharmaceutical sector, will exacerbate these problems unless governments strengthen drug regulation. This paper highlights some of issues that countries should consider when designing drug regulation policy.
Effective Drug Regulation: what can countries do?
"Drugs are the key to modern medicine. Surgery, radiotherapy, and diagnostic tests are all important, but the ability of health care providers to alter health outcomes depends primarily on drugs. Our age has been given many names—atomic, electronic, space, and the like—but measured by impact on people’s lives it might just as well be called the "drug age"."¹

1. Drug regulation: an early concern

1.1 Historical perspective

Since time immemorial humanity has been concerned with the quality of drugs, and throughout all this time societies have undertaken some kind of regulation of the use of medicines, and of those who prescribe and dispense them. For instance, in ancient Egypt in the first century BC physicians were required to administer their drugs in accordance with written laws. If they failed to do so in any respect and the patient died, they were tried and punished.² Methods were also laid down as far back as the first century AD to counteract the problem of adulteration.³ During medieval times in Muslim countries, the muhtasib made frequent inspections and supervised the preparation of medicines.⁴⁵⁶

In Europe, between the eleventh and twelfth centuries, several laws relating to medicine and apothecaries were passed. Doctors were forbidden to keep apothecaries or to enter into business with apothecaries, and apothecaries were strictly controlled and obliged to prepare reliable drugs of good quality.⁷

Later, in the United Kingdom, the Apothecary Wares, Drugs and Stuffs Act, passed in 1540, empowered physicians to inspect the premises of apothecaries for drugs that were:

"...defective, corrupted and not meet nor convenient to be ministered in any medicines for the health of man’s body...".¹³

Later still, in the nineteenth century, during a period of rapid industrialization, the role of apothecaries was taken over by industry. This increased the number of drugs on the market, as well as trade in drugs. At the same time, gross adulteration of drugs occurred, and ultimately led to social pressure for drug quality control. Many countries responded by introducing laws establishing standards for drugs and prohibiting adulteration.⁵⁷

Thereafter, research to develop new drugs increased tremendously and made many major advances. Concurrently, pharmaceutical production and supply systems worldwide underwent major changes, resulting in a proliferation of products as well as of manufacturers and suppliers, and contributing to the increasingly serious problem of counterfeit and substandard pharmaceutical products on the international market. Additionally, drugs with serious side-effects started to appear on the international market and a number of incidents associated with their consumption occurred.⁵⁵⁶ These circumstances catalysed the revision of drug legislation and the strengthening of drug control in many countries. For example, in the early 1960s, an outbreak of phocomelia, involving
gross fetal deformities, was linked to the use in pregnancy of the new drug thalidomide. The realization of the injury that it had caused provided the greatest single impulse to the development of new drug legislation in Europe and elsewhere.³

Today, although the structure, scope and practices of drug regulation may differ from country to country, the development, production, storage, distribution, supply and sale of drugs are subject to government intervention in every industrialized country, and in much of the developing world.

1.2 National drug regulation

Drug incidents such as thalidomide in the 1960s led to the revision of national drug legislation, and the strengthening of drug regulation in developed countries and some developing countries. These countries began to make stringent demands for substantial evidence of safety and efficacy. They also started to impose controls on advertising and promotion and on labelling, and required firms to adhere to good manufacturing practice (GMP). Thus in the United States, the 1962 Kefauver-Harris amendments of the Food, Drug and Cosmetic Act required firms to provide evidence of efficacy for new drugs based on adequate and controlled trials. For new drugs, results of animal tests and research protocols for human tests now had to be provided before any test on human subjects could be initiated.³

Similarly, in the United Kingdom, the Medicines Act came into force in 1971 and required the Licensing Authority to take account of the safety, efficacy and quality of medicinal products when granting licences. The Act also gave the Authority legislative power to monitor for adverse reactions, control promotion and advertising, and inspect pharmaceutical manufacturing facilities.²⁹

Attempts were also made in many other countries to regulate drug production and sales by introducing new laws and regulatory mechanisms.

1.3 Global initiatives

International trade in pharmaceuticals increased to the extent that the dangers posed by poor quality drugs in international commerce, particularly those destined for markets in developing countries, became a concern, particularly among consumers. Following the establishment of WHO in 1948, this concern received international recognition.

WHO undertook a number of initiatives to improve drug quality in its Member States and to promote global mechanisms for regulating the quality of pharmaceutical products in international markets. These included:

- selection of international nonproprietary names for pharmaceutical substances;
- publication of the International Pharmacopoeia;
- establishment of WHO GMP guidelines for pharmaceutical products;
• creation of WHO Certification Scheme to ensure the quality of pharmaceutical products sold on international markets;
• creation of national and regional quality control laboratories.

These and other global norms, standards and guidelines developed by the Organization contributed to the improvement of drug regulation at country and global levels. With the establishment of the WHO Action Programme on Essential Drugs (DAP) in 1981, the need for providing guidance to developing countries to improve their regulatory system received more attention. At the same time, many more standards and guidelines dealing with regulatory and quality assurance issues were developed by WHO and made available to countries.

The Conference of Experts on the Rational Use of Drugs, held in Nairobi in 1985, underlined the need for developing countries to strengthen their drug regulatory system based on sound drug legislation.10 This was further emphasized in WHO’s revised drug strategy in 1986.11

Post-Nairobi developments reinforced the need for WHO to continue its activities to sensitize countries to revise and update national drug legislation and to provide assistance within its mandate and competence to strengthen national drug regulation.

With respect to developing countries, WHO has been providing support in the setting up and strengthening of drug regulatory and quality assurance systems. For instance, between 1983 and 1997, it helped around 70 countries to either enact new drug legislation, or to amend existing drug legislation.12

In the past two decades, efforts have also been made to foster closer cooperation between the drug regulatory authorities of developing countries. In 1982, WHO catalysed technical cooperation among the developing South-East Asian countries (ASEAN/TCDC), together with the United Nations Development Programme, in the area of quality assurance. The cooperation has served as a vehicle for developing regulatory standards, norms and guidelines, as well as for the transfer of knowledge and skills in drug regulation between Member States. The creation of drug regulatory authority networks, such as the International Conference of Drug Regulatory Authorities, the Eastern Mediterranean Countries Drug Regulatory Agencies Conference and the African Drug Regulatory Authorities Network, has also been instrumental in promoting closer cooperation between national drug regulatory authorities to discuss issues of mutual interest and facilitate timely exchange of technical information.

At the same time, geopolitical groups in Asia, Europe and Latin America have promoted the harmonization and mutual recognition of drug regulation at regional, subregional and global level, facilitating technology transfer and trade in pharmaceuticals.
2. Rationale for regulating drugs

Drugs are unlike other consumer goods in that they are crucial to meeting the important objective of improving public health. So they should not be treated in the same way as ordinary commodities. Their development, manufacture, importation, subsequent handling within the distribution chain and use require specialized knowledge and skills. Consequently, they should conform to prescribed standards and their quality should be controlled rigorously.

The sale of drugs in particular illustrates how drugs differ from ordinary commodities. In order for the competitive market process to work, the consumer must be fully informed about the attributes of the commodity being purchased. Thus if a seller knows more about the commodity in question than a buyer, market transaction will be characterized by incomplete or asymmetric information, and will be disadvantageous for buyers. This is precisely the situation when drugs are sold, since manufacturers, prescribers and dispensers know more than consumers about the safety, efficacy and quality of drugs they manufacture, prescribe or sell. Clearly, unlike other commodity markets, the drug market should not be allowed to and indeed cannot regulate itself.

Further justification concerning why drug sales must be regulated is given below.

Numerous interested intermediaries

In its simplest, ancient form, the provision of medicines involved only two actors: the healer (who also produced the medicines) and the patient or consumer. Interaction was between the patient and the healer. As a result, the treatment outcome depended largely on the healer’s competence. Today, a number of intermediary or third-party actors, such as researchers, manufacturers, distributors, promoters and medical sales representatives, private insurers and drug dispensers have entered into the transactions between prescriber and patient, and a variety of interactions occurs. These interactions can affect treatment outcomes.

Studies have shown, for example, that the prescribing practices of physicians can be affected negatively by their interactions with pharmaceutical industries or sales representatives, or by the gifts they receive from pharmaceutical companies.\(^7\)\(^,\)\(^13\)\(^,\)\(^16\) Similarly, interaction between researchers and pharmaceutical industries can influence research outcomes negatively.\(^7\)\(^,\)\(^18\) Drug regulation is required in order to minimize such influence.

Information

Patients and consumers generally do not select their drugs themselves. Rather, drugs are prescribed by a physician or health worker. Physicians and health workers depend largely on the information that the manufacturer or seller provides about its (new) drugs. Yet in most cases, the manufacturer or seller has not supplied them with sufficient information for fully assessing the quality,
efficacy and safety of the drugs they prescribe. Moreover, in an unregulated free market, the quality of the information provided by the pharmaceutical supplier can be influenced by profit motives, which can in turn negatively influence the prescribing practices of physicians and health workers. Thus in an unregulated market, exposure to hazardous drugs is potentially greater. Moreover, when consumers themselves select drugs, as in the case of over-the-counter drugs, they may lack not only the information but also the specialized knowledge necessary for making a critical comparison, in terms of safety, efficacy and quality, of the various products available.

In some instances, consumers are led to believe that certain drugs will cure their illness, even though those drugs are of no therapeutic effect or even toxic. In their desire to be cured of their illness consumers may then create demand for such drugs. However, government intervention in the form of regulation and public education can prevent such situations from occurring.

**Financial considerations**

If a physician or health worker acts both as the prescriber and the dispenser or seller, potential conflict of interest can occur between the financial gain to be made from the sale of more drugs and the professional obligation to advise what is best for the patient. Profit margins are a case in point. If profit margins are linked to the cost of the drug rather than to the number of prescriptions filled, dispensers will tend to stock and sell expensive brand preparations.

Additionally, if the prescriber lacks the incentive to minimize treatment costs or to choose what is most cost-effective for the patient, consumption of drugs may be unnecessarily high and resources wasted. This situation can occur in health systems where private insurers or the government cover treatment costs and the patient is insulated from the impacts of price.

**Drug testing and outcomes**

Drug manufacturers are required to carry out various tests on animals and people to establish the therapeutic benefits and risks of new products. In the unregulated free market, decisions about how much testing to undertake on new products are sometimes influenced by profit incentives. (Limited testing obviously reduces test costs). As a result, drug products, the risks of which are excessive when compared to the benefits obtained, may be introduced to the market. And in some cases, the positive results of pre-marketing safety and efficacy studies have been called into question after the relevant drug has been used by a large number of people over a long period.

**Misuse of drugs and drug shortages**

Misuse of drugs and drug shortages can have serious effects on the health of individual patients or consumers, as well as widespread impacts on the health of a country's entire population. For instance, if an individual misuses an antibiotic, or is unable to complete an antibiotic course due to shortage of supply, microbial resistance to that drug can develop, reducing its value to others, and ultimately putting more lives at risk. Conversely, curing individuals of communicable diseases such as tuberculosis prevents further transmission.
Storage

Pharmaceutical products have limited shelf-life even when stored under specified storage conditions. Thus if they are stored under adverse or improper conditions they can deteriorate very rapidly, losing their therapeutic value. Such changes may even result in the formation of toxic substances that can damage the patient’s health or cause death.
Effective Drug Regulation: what can countries do?
3. Where are we today?

Despite the efforts made nationally and globally during the last few decades to improve drug regulation at national and international levels, it is currently estimated that less than one in six WHO Member States have well-developed drug regulation. Those that do are usually industrialized countries. Of the remaining Member States, about three in six implement drug regulation of varying levels of development and operational capacity. The remaining two in six countries either have no drug regulatory authority in place or a very limited capacity that hardly functions.

Generally, in most developing countries (particularly in the least developed countries), drug regulation is very weak and the quality, safety and efficacy of imported or locally manufactured drugs cannot be assured. Very few developing countries have an operational licensing system for premises and persons engaged in the production, importation, wholesale and retail distribution of drugs, as well as for the assessment and registration of products. Operational drug inspectorates are generally non-existent and access to quality control laboratories is often lacking. Where quality control laboratories do exist, the necessary materials, trained personnel and funds to sustain them are commonly in short supply. (The boxes in Annex 1 illustrate the status of drug regulation and drug quality assurance in the WHO African Region and a number of countries.)

To make matters worse, in industrialized countries, where drug regulation is said to be well developed, drugs for export are not regulated to the same standard as those used for local consumption. \(^5\) Drugs exported to developing countries via free trade zones in developed countries are relabelled to avoid providing details of their provenance. \(^6\) Studies have also shown that the promotional material provided to developing countries differs significantly from that given to physicians and the public in developed countries. \(^{11,22,23,24,25}\) Even in some developed countries, drugs that have not been assessed for safety and efficacy—as in the case of “grandfather drugs” in Germany—are not only exported to developing countries without any restrictions or assurance of efficacy and safety, but continue to be sold in their originating countries. \(^{26}\)

The reasons for the observed weaknesses of national drug regulation vary from country to country, but according to a recent working group sponsored by the World Bank, and attended by representatives of WHO, the United Nations Children’s Fund and other organizations, the main barriers to effective drug regulation are: \(^7\)

- absence of policy, and weak legislation and regulation;
- lack of political support/will;
- insufficient human resources;

\(^{a}\) In Germany, at the end of 1996, approximately 28 000 of the more than 50 000 drugs on the German market were these so-called grandfather drugs — that is, drugs which had not gone through a regulatory procedure.
lack of financing;
- absence of transparent procedures;
- corruption;
- flawed information flow;
- poor attention to cultural constraints;
- weak or non-existent consumer and professional associations;
- absence of priorities.
4. How can drug regulation be made effective?

The scope, nature and practices of drug regulation, including the priorities, standards and norms, the enforcement strategies, resources available and the rigour of enforcement, vary from country to country. However, the goals are generally the same: promotion and protection of public health by ensuring the safety, efficacy and quality of drugs, and the appropriateness and accuracy of product information. Drug regulation encompasses several processes, as shown in Figure 1.

**Figure 1. Dimensions of drug regulation**

There is no benchmark or standard for drug regulation. What is effective varies from country to country. But an effective drug regulatory body is one that demonstrates results in accordance with the objectives and targets set for it. This in turn requires that it has a clear written mission and goals.

A drug regulatory body should:

- base its decisions on scientific evidence and facts;
- provide efficient and timely services;
- have the capacity to develop practicable regulatory and enforcement strategies (i.e. is dynamic);
- apply sound management principles;
Effect of Drug Regulation: what can countries do?

- reach its objectives cost-effectively;
- be accountable;
- operate a safeguard against corruption and conflict of interest.

The process of drug regulation should be transparent.

Countries desiring to make their drug regulation effective need to take at least the measures described below.

4.1 Assess drug regulation performance

Many countries, especially developing countries, are now being pushed to liberalize their economy. This is often reflected in reorganization of the health sector in the form of privatization of pharmaceutical production, import and distribution, decentralization of decision-making and diminution of the state’s role as regulator. In the pharmaceutical sector such changes create further opportunities for more manufacture and trade in drugs, while at the same time weakening regulation.

Experience has shown that poor regulation of drugs can lead to the prevalence of substandard, counterfeit, harmful and ineffective drugs on national markets and in international commerce. This can result in serious harm to the health of individual consumers and even to the health of a wider population. Therefore, when domestic production, and import and distribution networks expand, countries must strengthen key drug regulatory responsibilities so as to ensure the safety, quality and efficacy of drugs, and the accuracy of product information.

Responding to these changing situations will demand that countries assess their drug regulation performance, using indicators that focus on structures and inputs, processes and outcomes (Figure 2). Also, they must identify strengths and weaknesses and the reasons for them, and consider alternative regulatory options, making the most appropriate and practicable choices. Development of a framework to help organize discussion of the elements of drug regulation, to raise questions relating to those elements that require examination, and to stimulate broader thinking in policy design, is therefore recommended. An example of a framework for evaluating the structure, processes and outcome of drug regulation is given in Annex 2. It is based on work WHO is carrying out as part of a multi-country study of drug regulation.

Figure 2. Framework for the assessment of drug regulation
4.2 Identify and develop priority functions

Experience in developed countries has shown that development of regulatory capacity occurs in phases, over a long period of time. Factors such as the level of development of the pharmaceutical sector and the availability of trained human resources, infrastructure and financial resources, influence the types of regulatory functions that can be carried out, as well as the size and sophistication of the regulatory agency.

Developing countries that are totally dependent on imported drugs and which have limited qualified human and other resources will thus need to start with limited priority activities, expanding these gradually as their pharmaceutical sectors develop and resources become available. Priority-setting is particularly important in circumstances where the need for drug regulation is not acknowledged by decision-makers and political support accordingly not as strong as is desirable. In such situations, any attempt to introduce all regulatory measures and a complete regulatory process all at once will lead to failure and frustration.

In setting priorities, a regulatory agency must first decide what exactly it wants to regulate, what activities it wants regulates to perform, and how it can ensure they perform them. This requires the formation of a policy group on drug regulation, to bring together persons from different fields and disciplines so that drug regulation can be dealt with in an integrated manner. The issues to be discussed will include: the regulatory processes, strategies, and organization and management of drug regulation. Once the scope of operations has been defined, the next step will be to create the necessary procedures and practices for making regulatory decisions. Along with these, the agency must also consider monitoring and enforcement procedures. Annex 3 presents different levels of drug regulatory activity, corresponding to the financial and human resources available to a country, and the level of development of its pharmaceutical industry.

4.3 Provide a clear mission and purpose

A clear written mission, based on priorities and functions, should be provided for drug regulation, indicating what it intends to achieve. Clear definition of the mission will facilitate assessment of the degree to which drug regulation has met its central goals, and of whether the perceived objective has changed between inception and implementation. Identifying the beneficiaries and stakeholders of drug regulation is also important since this helps ensure that an appropriate implementation strategy is designed.

Although the core mission of drug regulation for all countries is to promote public health by ensuring the quality, safety and efficacy of drugs, and appropriate and accurate product information, the mission may also include:
• providing unbiased information and promoting rational use of drugs;
• ensuring timely availability of drugs (through, for example, prompt registration of new products);
• ensuring geographical access to drugs (through decisions on location of retail outlets);
• encouraging domestic production of drug products.

Some examples of mission statements concerning drug regulation are given in Annex 4.

4.4 Create a supportive environment

A country’s constitution will define its system of government (unitary or federal), the distribution of power between the different levels of government (central or local), and the rights and freedoms of citizens. It will also determine the areas to be regulated, the type of legal control to be exercised and the nature of restrictions that can be imposed.

Ideally, the power to register drugs will be centralized since decentralization of this function can create confusion. For example, if more than one body is allowed to regulate drugs the situation can arise whereby some drugs are available in certain parts of the country but not in others since there they are considered to be unauthorized or illegal products. The same consideration applies to the setting of quality standards. At the very least, the division of responsibilities for drug regulation should be clear and subject to a certain degree of harmonization at the highest level.

Effective drug regulation is also promoted if the political system in question assures basic democratic rights, for example, by allowing freedom of association and expression, enabling professional associations, consumer unions, public interest groups and consumer watchdogs to flourish, and giving citizens the means to express any concern or dissatisfaction relating to drug regulation. (The measures taken by the Punjab State of Pakistan, described in Box 1, provide one such example.) Creating such conditions helps fight mismanagement, corruption and abuse of power, and promotes transparency, accountability and good governance. Experience has shown that those countries with strong consumer unions, public interest groups and consumer watchdogs generally have stronger consumer protection. The history of drug regulation in developed countries also shows that improvements in the quality of drug regulation have often occurred in response to drug incidents and the resulting pressure exerted by public groups on decision-makers.
Box 1. Punjab Province, Pakistan

In May 1998, the Punjab State of Pakistan formed the Task Force on Spurious and Substandard Medicines. The Task Force is headed by the Punjab Minister of Health and includes representatives of all stakeholders—health and law department officials, doctors and pharmaceutical manufacturers, sellers, a citizens’ representative (a retired lawyer), and a national consumer protection group (The Network Association for Rational Use of Medicines). The Task Force was entrusted with reviewing the Drugs Act 1976 and the Punjab State Drug Rules 1988. It has a mandate to propose changes to the Act and Rules, to inspect and screen existing pharmaceutical units and medical stores, and to take appropriate action against those who violate the state’s drug laws and regulations. It also has power to review existing licensing policy and propose changes, and to examine the issue of quackery and suggest measures to control it.

Under the new policy, the government has made it incumbent on those selling drugs to produce a bill of warranty in the event of a “raid” by government inspectors on their stores.

Since the creation of the Task Force, the government has taken measures, including:

- suspension of all drug inspectors and recruitment of new ones;
- freezing of issuing of drug sale licences from 9 May 1998;
- an extensive media campaign to educate people about drug regulation.

These steps demonstrate the Punjab Government’s commitment to breaking the chain of officials, sellers and manufacturers who put people’s health at risk. It is also trying to strengthen the capacity of medicine sellers by arranging training programmes for them.

Sources: 29, 30.

A country’s social conditions, particularly its educational levels, also influence drug regulation. National policies that expand educational opportunities thus have a positive influence on drug regulation since they raise the general level of awareness of ordinary citizens by increasing their access to information and their ability to make good use of it. Expanded educational opportunities will also increase the ability of technical staff to acquire and apply new scientific knowledge and skills. In principle, disseminating drug information is easier in countries where the level of education is high and access to mass media such as radio, television and newspapers is easy and cheap.

Economic conditions also influence implementation of drug regulation. The drug supply is likely to be inadequate or erratic in countries with a poorly developed economy or whose economy is in crisis. Smuggling, illegal importation of drugs, and counterfeit and substandard drugs, then tend to be common problems. Also, if the income derived from pharmaceutical products is a government priority, commitment to drug regulation implementation will be correspondingly lower.

4.5 Formulate adequate drug legislation

Drug legislation forms the basis of drug regulation. It must be comprehensive and enforceable if it is to be effective. Countries should therefore update their drug legislation if it is obsolete or inadequate. Important determining factors of the effectiveness of drug legislation include the extent to which the legislative framework is in accord with national policies, the degree of regulation which the government considers desirable and practicable to exercise, and the situation in its country’s pharmaceutical sector.
In particular, drug legislation should be sufficiently comprehensive and flexible to meet the objectives of drug regulation. Flexibility can be achieved by adopting a basic drug law and giving the executive branch of the government the authority to formulate the detailed requirements of drug regulations. In general, drug legislation must:

- define the areas and activities to be regulated;
- state the roles, responsibilities, rights and functions of all parties involved with drug regulation, including those of the regulators and regulatees;
- create the administrative bodies necessary for implementation of drug regulation, and define their structural and functional relationships;
- set the qualifications and standards required for those handling drugs;
- create mechanisms to ensure that all responsible parties are licensed and inspected to ensure compliance with the provisions of drug legislation, as well as with the standards and specifications set for persons, premises and practices;
- define the norms, standards and specifications necessary for ensuring the safety, efficacy and quality of drug products, as well as the appropriateness and accuracy of drug information;
- state the terms and conditions under which licences to import, manufacture, distribute, sell, supply and promote drugs will be suspended, revoked or cancelled;
- establish the administrative measures and legal sanctions that will apply when provisions of drug legislation are violated.

4.6 Create appropriate organizational structure

In almost all countries, the responsibility for regulating drugs belongs to government. However, depending on national circumstances, the government may delegate certain regulatory activities to the private sector, such as consumer groups, expert or interested groups, professional associations or industry associations.

Within government, the division of drug regulation responsibilities will vary from country to country, depending on national conditions. Some examples are given in Box 2.
Box 2. Assignment of Drug Regulation Responsibilities in Three Countries

Zimbabwe

The Medicines Control Authority of Zimbabwe is an independent body with the capacity to sue and be sued. The Authority is accountable to the Minister of Health and Child Welfare but managed by an executive committee that has legal powers and which is independent in its decision-making. Drug regulatory decision-making is centralized and is the responsibility of the Authority. The Authority has the power to collect and use fees, or to raise other money and assets. It can also employ its own staff.

Tunisia

In Tunisia, the authority responsible for drug regulatory affairs (Direction de la Pharmacie et du Médicament (DPM)) is organized as a department of the Ministry of Health, under the supervision of the Director-General of Health. Other semi-autonomous units supervised by the Director-General of Health, and that are involved in drug regulatory affairs, include the Laboratoire National de Controle de Médicament, the Institute Pasteur, the Direction de l’Inspection Pharmaceutique, the Laboratoire Nationale de Controle and the National Pharmacovigilance Centre. DPM supervises the administrative work and coordinates the activities of all the units involved in drug regulation.

India

In India, responsibility for drug regulation is divided between the federal government and the country’s 31 states. Each state has its own drug control organization (responsible for quality control of drugs) and a licensing system covering the manufacture, sale and distribution of drugs. Each state employs drug inspectors as the first line of enforcement and the state authorities issue WHO-type certificates. Federal authorities are responsible for developing standards for drugs, quality control of imported drugs, coordination of state activities, provision of expert advice to ensure consistency in enforcement, and control of manufacture of vaccines, sera and blood products. Four port offices under the federal authority regulate imports.

The examples in Box 2 show that no standard formula exists for organizing drug regulation. Rather, when planning drug regulation, countries should consider all options open to them, and choose the most appropriate structure. Such a structure should provide: independence in decision-making, financial and administrative autonomy (including in appointment of staff) and, accountability to the highest government body responsible for health and the general public. In countries where the government is also the owner of pharmaceutical industries and import–export companies, drug regulation responsibilities must be separated from management of those companies, if conflict of interest is to be avoided.

If several agencies or divisions or departments are involved in drug regulation, care should also be taken to ensure appropriate distribution of responsibilities, duties, functions and powers between the different bodies. This should be done in accordance with the drug legislation or written terms of reference. There should also be written terms of reference that describe the linkages between the various bodies. Also, as far as possible, related activities should be grouped together since they will require a high degree of coordination and will need to be carried out by personnel of similar training and experience. Tasks should be divided so that no supervisor carries an excessively heavy load. Functions that need to be centralized should be carried out at central level and a mandatory reporting system between the different levels should be operated. A planning, monitoring, evaluation and reporting system should be built into the regulatory
hierarchy so that implementation of drug regulation can be assessed, shortcomings and the reasons for them identified, and timely decisions to correct them taken.

Agencies, such as consumer unions, professional associations and industry associations, that are involved in drug regulation but who do not form part of government drug regulation, should also be required to operate in accordance with written terms of reference or an established code of practice, in line with national drug legislation. Their role, responsibilities, and powers with respect to drug regulation must be clearly defined.

4.7 Allocate adequate human and financial resources

Governments must employ people with specialized knowledge and skills if they wish to promote effective drug regulation. Moreover, they must employ individuals of great integrity and pay them well, particularly since drug regulation involves various stakeholders with commercial interests who will often exert pressure to secure favourable decisions.

In promoting effective drug regulation, adequate budgeting is therefore essential to providing:

- salaries that will attract personnel with the required training and experience, and that are comparable with salaries paid to their counterparts in private structures;
- the facilities and infrastructure necessary for the proper conduct of drug regulation activities.

Provision of funds must also be regular and uninterrupted to ensure smooth running of regulatory activities.

Evidently, different countries use different financing mechanisms. In Zimbabwe, for instance, the funds of the Medicines Control Authority consist of: fees collected according to the provisions of the country’s drug regulations; moneys appropriated by parliament; and moneys and assets that accrue to the Authority.31

In the case of the USA’s Food and Drug Administration, the budget is derived from user fees as well as moneys appropriated by the US Government. (For 1999, the budget approved by the US Congress was US$1,012,729,000, of which US$141,230,000 is to come from user fees, including drug user fees.)32

In Uganda, the 1993 National Drug Policy and Authority Statute authorizes the following funding sources:33

- government grants;
- grants and loans from any body, organization, or person;
- money (fees) that may accrue to the Authority in discharge of its functions;
- interest and savings made by the Authority;
- money from any other sources, as approved by the Minister of Health and Child Welfare.
How can drug regulation be made effective?

Other Member States such as Barbados, Colombia and Indonesia do not collect any fees, and are totally dependent on government funding. In such cases, the total resources available to the country, and the priority that the government assigns to drug regulation, will influence the amount of funds allocated by government.

Fees collected for drug registration in developed countries are very high. Moreover, drug regulatory authorities in developed countries have the power to control and use the funds to finance their activities. In developing countries, however, not only are the fees collected very low, but they are also transferred to the government treasury, making drug regulation exceptionally difficult to finance. (For some details of the differences in the levels of fees collected by developed and developing countries, see Annex 5.)

Experience to date tells us that government resources are unlikely to be sufficient for promoting effective drug regulation. So in order to improve their drug regulation, developing countries must revise their drug legislation and introduce a fee system for the services provided by drug regulatory authorities, as is already the case in developed countries. However, establishing a fee system may encourage authorities, particularly if they are totally dependent on such income, to facilitate regulatory processes that generate income but that are not necessarily the best means of meeting regulation requirements. Equally, low fees or the absence of fees will encourage the submission of applications for registration of products of little or no therapeutic value. When establishing a fee system, the following criteria should therefore be considered:

- total dependence on fees should be avoided and a mechanism established whereby part of the budget for the regulatory authority comes from government and only the remainder from fees;
- fees should be appropriate to providing increased revenue to the authority (so that it can carry out its work effectively) and to discouraging industry from flooding the system with applications that do not meet official requirements;
- the fee system should cover all services: licensing of premises, persons and practices; registration of products; inspection; quality control; and control of clinical trials;
- there should be a legal basis for collection of fees and empowerment of the authority to use the funds collected;
- there should be provisions for fee reduction or exemption to ensure that vital or life-saving drugs, but which have only a limited market, are reliably available. Such provisions may also be required for locally produced drugs, generic products, etc., in line with the national drug policy.

In addition to ensuring sustainability of qualified and skilled human resources, governments must create mechanisms for human resources development. There should be a system and means for updating the knowledge and skills of regulatory personnel, either locally, or by sending them abroad to centres of excellence or academic institutions.
4.8 Minimize corruption and conflict of interest

Corruption is often seen at the intersection of the public and private sectors. Moreover, it is not specific to drug regulation. In other words, it cannot be attacked effectively in isolation from other problems.

In their study of Australian business regulatory agencies, Grabosky and Braithwaite found that corruption is more likely to occur when:

- regulators regulate a small number of client companies;
- regulators regulate a single industry rather than diverse industries;
- the same inspectors are in regular contact with the same client companies;
- a high proportion of inspectors have a background in the industry that is being regulated.

They found too that corruption was more likely in agencies that maintain close cooperative relationships with the industry. Corruption is also more likely when agencies engage in regular sanctioning of the industry; for example, if an agency frequently punishes companies and individuals it will doubtless be offered bribes to deflect such punishments.

Other factors that can act as incentives for corrupt behaviour are:

- wide discretionary powers;
- little or no accountability of public officials;
- distorted or unclear government policies that are difficult to interpret, resulting in bureaucratic delay and even in bribery if there is a possibility of interpreting the policies in a way that is more favourable to the industry;
- lack of a government system, such as a court of appeal or tribunal (where decisions taken by the regulatory authority can be questioned), that deters bribery and serves as a system of checks and balances;
- failure of the salaries offered to public employees to match those given in the private sector.

There are no simple solutions to these problems. Strategies to reduce corruption vary from country to country and depend much on political and socioeconomic conditions. For Grabosky and Braithwaite, one means of counteracting the evolution of corruption is by adopting a tripartism policy. This is a process in which relevant public interest groups become the fully-fledged third player in the “game” of regulation. Such an approach requires, of course, that a democratic system be already in place.

Other approaches to minimizing corruption in drug regulation that could be considered include:

- developing an appropriate civil service code of conduct and an appropriate culture of regulation;
- creating a rule-based bureaucracy with a pay structure that rewards regulators for honest work;
- creating a merit-based recruitment and promotion system;
- reducing regulators’ discretionary power or authority;
• enhancing accountability by creating mechanisms for monitoring and punishment;
• creating mechanisms whereby citizens and consumer groups can lodge official complaints and contribute to the exposure of corruption;
• making rules and decisions transparent;
• punishing those who take or offer bribes;
• rotating regulators or assigning them in teams to reduce the frequency of contact between the same regulators and regulatees.

Corruption also arises in some developing countries when drug regulators or inspectors are permitted to run businesses in order to supplement their government salaries. This usually means that they operate their own pharmacy or work as a technical manager for a private pharmacy or company. Understandably, such a situation often leads to conflict of interest and corruption. Countries operating such a system should consider other means of increasing the salaries of their staff. One possibility is to collect fees for regulatory services rendered and to use them to supplement salaries.

4.9 Apply most appropriate strategy

Poor enforcement of drug legislation is often associated with lack of political will, inadequate legislation, lack of independence of those responsible for interpreting and applying legislation, weak infrastructure for enforcing regulation, lack of accountability and transparency, and corruption. Governments can strengthen enforcement by ensuring that courts are independent and that the rule of the law is followed, and by strengthening infrastructure, including appropriate remuneration of regulators.

For Ayres and Braithwaite, appropriate enforcement and regulatory strategies are particularly important in terms of improving regulatory compliance. They argue in favour of responsive regulation, which they define as triggering a certain type of regulatory response. They suggest that regulation be responsive to industry structure. In other words, different structures will be conducive to different degrees and forms of regulation. They argue, too, that governments must be aware of the different motivations of those regulated if they are to design effective regulation.

Thus responsive regulation is not a clearly defined programme or a set of prescriptions concerning the best way to regulate. On the contrary, the best strategy is shown to depend on context, regulatory culture and history. Responsiveness is rather an attitude that enables the blossoming of a wide variety of regulatory approaches.

The strategies that Ayres and Braithwaite advance to promote effective regulation are:

• use of a tit-for-tat strategy (i.e. the strategy of mixing punishment and persuasion that is most likely to be effective);
• pyramid strategies (hierarchical ranges of sanctions and regulatory strategies);
• tripartism (delegation of power to public interest groups).
Tit-for-tat strategy

According to Ayres and Braithwaite, regulators are not likely to be effective if they apply only punishment. They argue that punishment alone is counterproductive since it is expensive. They argue further that punishment engenders a game of regulatory cat-and-mouse whereby companies defy the spirit of the law by exploiting loopholes. Conversely, persuasion is cheap and to be preferred in situations where technological and environmental realities change very quickly and make it difficult to ensure that the detailed content of regulations is up to date. Ayres and Braithwaite further argue that business actors are not always motivated primarily by the prospect of making money. Rather, a sense of social responsibility may underlie some or much of their action. Therefore, a strategy based mostly on punishment would undermine such goodwill. Thus a tit-for-tat strategy that combines punishment and persuasion is more likely to be effective.

The tit-for-tat strategy forms the basis of tripartism (see below). Under tripartism, the regulator refrains from applying a deterrent response provided the company is complying with drug legislation. But if the company ceases to do so, the regulator then shifts from a cooperative to a deterrent response. By cooperating with companies as much as possible, regulators avoid undermining the good faith of socially responsive actors.

Pyramid strategies

Different countries use different enforcement strategies to promote compliance with drug legislation. The strategy most commonly practised by government regulatory agencies consists purely of punishment, based on the use of deterrent action. Yet according to Ayres and Braithwaite, regulatory agencies with only one deterrence option at their disposal may find enforcement difficult. For example, it is not uncommon for regulatory agencies to have the power to withdraw or suspend licences as the only effective power at their disposal. But it may be politically impossible to apply such a drastic sanction to any but the most heinous of crimes.

For Ayres and Braithwaite regulatory objectives are more likely to be achieved when agencies operate both a hierarchy of sanctions and a hierarchy of regulatory strategies of varying degrees of intervention. They contend that regulatory agencies are best able to secure compliance when they operate an explicit enforcement pyramid of the type shown in Figure 3 below.

This pyramid of sanctions applies at the level of the individual regulated company. In this model, most regulatory action occurs at the base of the pyramid where efforts to obtain compliance are made by persuasion. The next step up in enforcement consists of a warning letter, followed by imposition of civil monetary penalties if this fails, and then progressively upwards in the direction of the apex of the pyramid until compliance is achieved. Ayres and Braithwaite assert that failure to comply is much more likely when companies face only one deterrence option rather than an explicit enforcement pyramid.
How can drug regulation be made effective?

Figure 3. Pyramid of enforcement strategies

Another strategy proposed by the authors focuses on the entire industry, as illustrated by the pyramid of regulatory strategies shown in Figure 4. Using this strategy, governments are most likely to achieve their goals by communicating to industry that they have at their disposal and are willing to apply an escalating set of enforcement strategies, ranging from self-regulation all the way up to command regulation with non-discretionary punishment.

Figure 4. Pyramid of regulatory strategies

This gives incentives to both the industry and regulatory agents to make regulation work at a low level of intervention—in other words, self-regulation at the base of the pyramid. As with the pyramid of sanctions, the main argument in support of a pyramid of regulatory strategies is that most regulatory action is channelled to where it is most effective and least resource-intensive. Self-regulation can be
further strengthened if government insists that the industry be delegated to enforce self-regulation and effectively communicates application of the pyramid, including details of sanctions it has taken, to consumers, professionals, government and industry.

Ayres and Braithwaite conclude that selection of an appropriate form of delegation and appropriate escalation of (non-delegated) regulation are important if pyramid strategies are to be effective.

**Tripartism**

Ayres and Braithwaite point out that a regulatory policy that fosters cooperation between the regulator and the regulatee also encourages corruption; if relationships are ongoing and encounters are regulated by the same regulator, corrupt dealings become more tempting to both parties. They therefore propose tripartism as a substitute for the usual methods of dealing with risks of corruption, such as rotation of personnel and limiting the discretionary powers of regulators. They describe tripartism as a process in which relevant public interest groups become a fully-fledged third player in the regulatory process. This secures the advantages of cooperation while avoiding corruption.

For Ayres and Braithwaite, a tripartism policy fosters the participation of public interest groups by granting them:

- access to all the information that is available to the regulator;
- a seat at the negotiating table with the company and regulatory agency;
- the same authority to sue or prosecute under the regulatory statute as the regulator.

Ayres and Braithwaite argue that empowered public interest groups can directly punish the regulatee (company) or regulators who fail to punish non-compliance, and in so doing prevent corruption. Thus, if tripartism is to function well, public interest groups must have regulatory authority with a legal basis and be both politically and financially independent from government.

The recent moves taken by the Punjab State of Pakistan (see Box 1) may not exactly match the tripartism strategy proposed by Ayres and Braithwaite, but constitute another possible approach to third-party involvement in drug regulation. Similarly, in Canada and the United Kingdom, pharmaceutical industries are not required to enforce sanctions or to communicate them to interested parties, but are delegated to enforce self-regulation in relation to promotional and advertising activities.9

Also in the United Kingdom, the Royal Pharmaceutical Society is empowered by the Pharmacy Act of 1954, the Medicines Act of 1968 and the Poisons Act of 1972 to register both pharmacists and pharmacies. It is also delegated to safeguard the public with respect to the dispensing and distribution of medicines, and to regulate and promote the pharmacy profession. The Society can take professional disciplinary action against offenders. Legal offences are pursued through the courts and the criminal justice system.9 Proposed new disciplinary legislation incorporates escalating enforcement strategies, as shown in Box 3.19
Box 3. Proposed New Powers for United Kingdom Royal Pharmaceutical Society Tribunals

The Royal Pharmaceutical Society of the United Kingdom has put forward proposals for reforming its 40-year old disciplinary procedures. Given that the profession is playing an increasingly important role in the delivery of health care, the aim is to ensure that pharmacists provide professional services of high quality.

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<th>Three-member tribunal</th>
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<td>Under the proposed new procedures, a three-member tribunal would be able to order:</td>
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<td>• reprimand;</td>
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<td>• retraining;</td>
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<td>• restrictions on the right to act as superintendent pharmacist;</td>
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<td>• restrictions on conditions of practice, including supervised practice;</td>
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<td>• financial penalties (against bodies corporate and individuals);</td>
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<td>• costs (but only in exceptional circumstances, where the conduct of one party to the</td>
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<td>case has caused excessive delay and expense to the other party);</td>
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<td>• referral to the society's health procedures, where it is clear that the pharmacist</td>
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<td>may have a serious health problem;</td>
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<td>• deferred decision, to satisfy the tribunal that action already initiated to remedy</td>
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<td>a problem will continue;</td>
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<tr>
<td>• referral to a five-member tribunal, when it becomes apparent that a case is more</td>
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<td>serious than appeared from the allegations and might warrant a sanction not open to a</td>
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<td>three-member tribunal.</td>
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<th>Five-member tribunal</th>
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<td>Under the proposed new procedures, a five-member tribunal would be able to order:</td>
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<td>• removal of the pharmacist's name from the register for a specified or indefinite</td>
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<tr>
<td>time;</td>
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<td>• that an individual should not be entered in the register;</td>
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<td>• removal of premises from the register;</td>
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<tr>
<td>• disqualification of a person, including non-pharmacists and companies, from</td>
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<td>involvement in running a retail pharmacy business;</td>
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<tr>
<td>• immediate removal of a pharmacist from the register;</td>
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<tr>
<td>• immediate removal of premises from the register.</td>
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Effective Drug Regulation: what can countries do?
5. The way forward

Drugs are of critical value to human health and well-being and thus play a central role in any health care system. But their potential can only be realized if they are accessible, used correctly and of acceptable quality. They can be dangerous if control over their manufacture, storage, distribution, supply, sale and use does not meet required standards.

During recent decades many pharmaceutical industries and distribution channels have flourished, leading to the proliferation of products on national and international markets. This situation has strained the capacity of regulatory authorities, particularly in developing countries. Many of them find controlling not only the quality but also the promotion and use of drugs to be difficult. This inability to exercise adequate control is reflected in the prevalence of substandard and counterfeit drugs, and weaknesses in quality assurance. The latter have sometimes resulted in the deaths of hundreds of people. Additionally, scientific and technological progress, and liberalization of world trade, will also have profound effects on the manufacture, distribution and sale of drugs. Countries must take action now to strengthen their regulatory capacity and their ability to react effectively to changing conditions.

In those developing countries where drug regulation is weakest, priority should be given to assessing the existing regulatory situation, and identifying weaknesses and the reasons for them. Additionally, these countries should identify priority activities and establish a regulatory system, taking into account local conditions and the resources available.

At an international level, new trade agreements will require the application of international standards to ensure the quality of pharmaceutical and biological products. Effective control will require adequate control facilities and technically competent staff.
Annex 1: Status of drug regulation and drug quality assurance in WHO African Region and selected countries

**WHO African Region**

- A survey conducted during 1992–1993 using a questionnaire to assess the existence of quality assurance systems in the WHO African Region (AFRO) found that of the 26 countries that completed the questionnaire, 11 had a quality assurance system (including quality control laboratory), but that it was not functioning well. A further nine countries had some kind of quality assurance system without quality control laboratory and six did not have any quality assurance system. Nineteen countries mentioned illegal importation as a serious problem. Of 21 countries that had domestic pharmaceutical manufacturing, six did not have a quality control laboratory and four were without an inspectorate.

- A study carried out during 1992–1993 on the quality of drugs available in Cameroon, Chad and Madagascar showed that of 429 products tested, only 352 (82%) complied with specifications. The remaining 77 (18%) samples were found to be substandard and failed laboratory tests. Of these, 16 (3.7%) contained no active ingredient.

Sources: 40, 41.

**Lao People’s Democratic Republic**

Before 1988 there were no private manufacturers, importers or pharmacies in the Lao People’s Democratic Republic. All drugs were distributed by the public sector. At present, there are six manufacturing plants, 32 private importers and 2018 private pharmacies – eight/class I, run by pharmacists, 67/class II, run by pharmacy assistants, and 1943/class III, run by persons without pharmaceutical education (only a few are doctors/nurses).

The Food and Drug Department (FDD) under the Ministry of Health is responsible for the registration of drugs, inspection and licensing of manufacturers, importers, and class I and class II pharmacies. It is also responsible for public sector drug supply, as well as the control of narcotic drugs and psychotropic substances. It has ten inspectors at central level. All of them are both food and drug inspectors. The Food and Drug Quality Control Centre (FDQCC) which was established in 1995 undertakes chemical analysis of drugs.

Three papers, one published in 1997 and the other two (unpublished) which were written in 1997 and in 1998, reported the following:

- Drugs are repacked in plastic bags and sold without labels.
- Drugs are smuggled from neighbouring countries.
- The number of drugs on the market is estimated to be about 3000 of which only 1600 (53%) are registered.
- There are three types of product registration fee: a registration fee (US$ 1.40), a service fee (US$ 2.80), and an analysis fee (about US$ 3.60). Collected fees go to the Ministry of Finance.
- Inspection carried out in 1995 found two cases of counterfeit drugs, 23 cases of banned drugs, and 19 cases of expired drugs, eight cases of drugs without labels and eight cases of substandard drugs.
- A study initiated by the Asian Development Bank in 1993 showed that of 112 drug samples collected from five provinces and tested, 37 products (33%) were substandard. The products that failed the tests included antibiotics and antimalarials.
- A similar test carried out in 1996 on 102 samples showed that 10.2% were substandard. Similarly, a study in 1997 of 405 samples from Savannakhet Province showed that 12% were substandard and 4% did not contain any active ingredient.

Sources: 42, 43, 44.
Kenya

Kenya has one public sector drug procurement agency, over 135 private importers/wholesalers and about 40 pharmaceutical manufacturers.

The legal instruments for regulating drugs are the Pharmacy and Poisons Act of 1957, and the revisions made in 1972 and 1989. The Pharmacy and Poisons Rules of 1981 (revised in 1983) apply to the registration of drugs. The Pharmacy and Poisons Board established under the Pharmacy and Medicines Act, Chapter 244, is responsible for the registration of pharmacy professionals, market authorization of drugs, and issuing licences to manufacturers, wholesalers and retail pharmacies. The Pharmacy Department of the Ministry of Health (MoH) headed by the Chief Pharmacist, who is also the Registrar of the Pharmacy and Poisons Board, is responsible for administering the Board's day-to-day activities. The Registrar and associated personnel (a secretary, two pharmacists and a pharmacy technologist) are MoH employees. The Board has nine members and is chaired by the Director of Medical Services. Three committees, whose members are not MoH employees, support the Board: the Committee of Finance, the Committee of Pharmacy Practice and the Drug Registration Committee.

Drug registration started in 1982, and covers both human and veterinary drugs. The registration fee is US$ 1000 for foreign products and US$ 500 for domestic products. The renewal fee is US$ 500.

A National Drug Control Laboratory was established in 1995 under the Pharmacy and Poisons Board. It carries out limited pre- and post-marketing quality control of drugs.

The Inspectorate, under the Director of Medical Services/MoH, undertakes surveillance of wholesale and retail outlets. Inspection is limited to enforcement activities and carried out by individuals (ex-police officers) who have not received any pharmaceutical education.

More specifically:

- The number of drugs on the market is not known but estimated at 12 000. Of these, only 6000 (50%) are registered.
- There is no inspectorate attached to the Board: GMP inspection is not carried out and inspectors of distribution channels do not have a pharmaceutical education.
- The Registrar has limited staff for discharging his/her functions.
- Ministerial salaries are not competitive with those in the private sector and as a result staff turnover is high.
- The WHO Certification Scheme is not applied as recommended by WHO when assessing the status of imported drugs.
- Although the exact figures are not reported, the National Quality Control Laboratory has recently detected counterfeit drugs on the market;
- Drugs are smuggled into the country.
- Kenya exports drugs to other African countries by issuing “free sale” certificates even though it has no inspectorate to assess GMP compliance.

Sources: 19, 45.
Myanmar

In 1997, there was one state-owned manufacturing plant and about 60 small-scale private pharmaceutical industries, 20 importers, 275 wholesalers, 8,500 private pharmacies and 144 public sector drug outlets.

Three authorities are responsible for drug regulation: the Myanmar Food and Drug Board Authority, the Food and Drug Supervisory Committees (FDSC) at central, state/division, district and township level, and the Food and Drug Administration (FDA). The Central Food and Drug Supervisory Committee issues licences and inspects drug wholesalers and retailers. At township level, the FDSC committee consists of the Township Medical Officer, the Commander of the Police, and the representatives of the City Development Committee and the General Administration Committee. The FDA issues marketing authorization, inspects manufacturing plants and importers, and tests the quality of drugs. There is also a Drug Advisory Committee (DAC). Applications are reviewed by the staff of the registration unit which consists of the Assistant Director of the Drug Control Section and two pharmacists. There is an assessment fee of US$ 100 and a registration fee of US$ 200. According to two reports that came out in 1997 and 1998:

- Private small-scale pharmaceutical industries do not have a licence even though they are known to produce and sell drugs. Also, they do not meet GMP requirements.
- Only 50% of the drugs on the market are registered.
- No post-marketing quality surveillance is undertaken.
- Drugs are sold in booths and most distribution outlets are run by unqualified people.
- Capsule and tablet preparations in hospital packs are removed from their original containers, repacked in plastic bags and sold without a label.
- Of 212 samples collected and tested in 1997, 34 samples contained active ingredients below the limits specified in pharmacopoeia, one contained a wrong ingredient and four were counterfeit with respect to their source.

Sources: 46, 47.

Viet Nam

Viet Nam has a fairly large domestic pharmaceutical industry. In 1996 it had 138 pharmaceutical manufacturers, 265 wholesale distributors, 22,450 public drug outlets, and more than 7000 private pharmacies. Viet Nam’s Ministry of Health (MoH) has dual responsibility. It is both the drug regulatory authority, and the manager of state-owned drug manufacturers and import–export companies. Three agencies under the MoH are responsible for drug regulation. The Food and Drug Administration has a staff of about 20 and is responsible for formulating drug legislation, registering drugs, issuing import–export licences, and controlling the manufacture, importation, promotion and advertisement of drugs. It also carries out post-marketing surveillance and dissemination of drug information. In 1996, 8000 products were registered. Of those imported by the public sector, only 75% were said to be registered.

Responsibility for drug inspection is divided between the central and provincial authorities. In 1996, there were only two inspectors at national level and only one or two in each province. The total number of inspectors in the country was 61. Quality control of drugs is carried out by the National Institute of Drug Quality Control in Hanoi, the Sub-Institute of Quality Control in Ho Chi Minh City and the drug quality control laboratories of the provincial health departments. In 1995, the number of staff working in the two institutes and the provincial laboratories was estimated to be about 700 (42 with postgraduate degrees, 313 pharmacists, 212 technicians and 134 administrative personnel). Information was gathered in 1996:

- Only two of the manufacturing plants were said to comply with GMP requirements and to have GMP certification; most of the plants operate old equipment and are housed in inadequate premises.
- In 1996, investigation of samples collected from the market showed that only 51 (40.2%), of 127 samples of imported products had been registered.
- Private drug outlets were found to have been tampering with labels, and selling or dispensing counterfeit drugs and drugs imported through unauthorized channels.
- In 1995, 1350 samples were tested by the two institutes; 288 (16.9%) were found to be substandard. During the same year, 31 125 samples were tested by the provincial laboratories; 1703 (55%) of these failed to meet quality standards while a further 166 (0.5%) of the samples lacked active ingredients.
- Drugs are smuggled in and out of Viet Nam.

Sources: 46, 48, 49
Colombia

The Instituto Nacional de Vigilancia de Medicamentos y Alimentos (INVIMA), created in 1993 by article 245 of law number 100, is Colombia’s drug regulatory authority (DRA). An autonomous body, whose head is appointed directly by the president of the country, INVIMA’s most important functions include:

- Controlling the quality and safety of medicines, biological products, foods, cosmetics, medical devices and natural products;
- Issuing licences concerning the manufacture of medicines;
- Issuing marketing authorizations.

Decree No. 1290 of 1994 includes a provision for decentralizing or delegating drug registration and licensing of manufacturing plants to district or provincial agencies that have the necessary resources. The law also includes provision to delegate inspection and analysis of drugs to other public institutions such as universities that have been accredited for this purpose by the Ministry of Health. New drugs require evaluation by the Ministry’s review committee, except when they have been approved in two or more of 11 reference countries considered to have well-developed regulatory systems.

A field report was received in 1997, containing the following information:

- INVIMA’s staff currently consists of permanent employees and others who are hired on a contractual basis. INVIMA is understaffed and unable to carry out its activities fully because of budgetary restraints.
- INVIMA does not charge any fees since collection of fees has been declared unconstitutional by the Constitutional Court.
- Owing to the low salaries that the government pays to INVIMA employees, personnel turnover is high.

Sources: 45,50.

Pakistan

Pakistan’s Drug Act of 1976 assigns responsibility for the licensing of manufacturing plants, importing and exporting, and the registration of medicines to the federal government. Regulation of the sale of medicine is the responsibility of the provinces. At federal level, the Central Licensing and Registration Board—consisting of the Federal Director-General, the drugs controller, all provincial Director-Generals of Health, together with senior representatives of the Ministries of Commerce and Industry, the Central Board of Revenue, and the Justice Division, and medical and pharmaceutical experts—is responsible for regulating manufacturing, registration and imports—exports. At federal level, about eight inspectors are working to monitor compliance with GMP. At provincial level, 81 regular inspectors of drugs at various grades have been appointed as district, divisional and chief inspectors, but in some places without a formal hierarchy. In addition, the district health officers also act as ex-officio inspectors in some provinces.

The country also has five drug-testing laboratories, four of which conduct routine analysis. However, the laboratories lack the necessary qualified personnel, chemicals and equipment.

According to a recent report, there are 16,000 drug stores and 114 pharmaceutical firms in Punjab State alone. Of the country’s 327 drug manufacturing plants, 52% of them are in Punjab State, of which 70% are concentrated in Lahore. Most of the province’s drug stores are run by unqualified personnel. Moreover, the stores lack adequate storage facilities and sell unregistered drugs. The ineffective monitoring and supervision of these outlets have also encouraged the manufacture and sale of spurious and substandard drugs. The infrastructure for monitoring cannot keep up with the speed with which licences are issued. In 1997, of 13,095 samples tested by the Punjab Drug Testing Laboratory, 526 (4%) were found to be substandard and 26 (0.2%) counterfeit.

Sources: 29,30,51.
Annex 2: A model framework for assessing drug regulation

The reasons why drug regulation in many countries is ineffective and why so few countries have achieved effective drug regulation must be addressed. WHO is therefore conducting a multi-country study to analyse and document selected countries' experience in drug regulation. This will include identifying the strengths and weaknesses of drug regulatory systems. Once the study has been completed, WHO should be able to propose effective drug regulation strategies to policy-makers and those responsible for drug regulation. Expected outputs of the study include a practical study guide and a data collection guide.

In conducting its study, WHO is using the questions in the boxes that follow to gather information for assessing various aspects of drug regulation within countries. Taken together, they provide a sample framework for evaluating the structure, processes and outcome of drug regulation.
Drug Regulation Enabling Environment Assessment Guide

Review the political and socioeconomic conditions to establish whether they support drug regulation.

- Does government policy give priority consideration to the economic rather than social benefits provided by pharmaceutical products?
- Has a freedom of information act been passed?
- Is there freedom of association?
- Does the government recognize the need for accountability?
- Does the government encourage transparency?
- Does the government provide mechanisms for public complaints and oversight including in the area of drug regulation (i.e. mechanisms for provision of an ombudsman)?

Regulatory and Enforcement Strategies Assessment Guide

Regulatory strategies
- Does the agency have a written strategy for implementing drug regulation?
- Does the agency delegate regulatory activities to other public institutions, professional associations or industries?
- Do consumer groups, interested public groups, etc., participate in regulatory affairs? Do they operate on a legal basis? Do they have a code of conduct?

Enforcement strategies
- Which of the following instruments are used to enforce drug regulation?
  - Persuasion?
  - Punishments?
  - Legal sanctions?
  - Financial fines?
  - Administrative measures such as warning letters?
- Do any social pressures operate? For example, on the part of:
  - peers;
  - consumers;
  - public interest groups.
- Are any of the following strategies used to achieve objectives:
  - negative incentives for violation, such as “negative publication” (in which, for example, the name of the offending company, individual or pharmacy is published), or frequent inspection;
  - positive incentives for compliance, such as reduction of fees or letter of acknowledgement;
  - implementation of voluntary compliance or self-regulation.
Drug Regulation Structure

Analysis of drug legislation and identification of weaknesses
- What is the mission of drug regulation? Is this mission formally written down?
- Is drug legislation comprehensive?
- Are the areas to be regulated defined?
- Are functions, responsibilities and powers of all the relevant parties defined?
- Are drug regulations, norms, standards and procedures adequate?
- Are there provisions for penal sanctions and administrative measures?
- Does the legislation impose on the regulatory authority any duty to provide information to the public?

Analysis of organizational structure and identification of weaknesses
- Is the regulatory government body federal, state or local?
- Is it a quasi-governmental body?
- Does the drug regulation structure provide independence in decision-making?
- Does the structure provide autonomy, both financially and in terms of recruiting staff?
- Is the distribution of responsibilities, duties and powers in accordance with written terms of reference and drug legislation?
- Are structural and functional linkages between various bodies involved in drug regulation clearly defined?
- Do staff have job descriptions?
- Is the private sector involved in drug regulation activities? If so, is there a legal basis for this? Are the relevant parties accountable? Are they required to submit reports?
- Are planning, monitoring, evaluation and reporting mechanisms in place?
- What are the main constraints with regard to organization and structure? What are the reasons for them?

Assessment of human resources availability and quality, and identification of constraints to implementing drug regulation
- Is the number of staff adequate?
- Do staff have the required qualifications and skills to perform their jobs adequately?
- Do staff believe in the objective of drug regulation?
- Are staff motivated to do their work?
- Is there a system for human resources development?
- Are staff salaries comparable to those paid to similarly qualified individuals in the private sector?
- What are the main constraints in terms of human resources availability? What are the reasons for them?

Assessment of financing mechanisms and identification of constraints
- How is drug regulation financed?
- Is there a specific government budget for drug regulation?
- Is financial sustainability a problem?
- Is there legal provision for collection of fees?
- Are fees collected?
- Is the regulatory agency allowed to use them?
- What are the main financial constraints?

Availability of other resources
- Are resources—such as means of transport, laboratory equipment and apparatus—that are essential for regulation activities readily available? Do they function properly? Is there a maintenance system?
- Is an adequate number of rooms available?

Availability, clarity and transparency of procedures and guidelines
- Are all procedures, guidelines and guides used in drug regulation written down?
- Are they published and distributed to all interested parties?
- Are decisions made by the agency published and distributed to all interested parties? Are they sent only on request?
Drug Regulation Processes

Licensing system: critical assessment of operation and record keeping
- Is there a licensing system? Is it operated by the drug regulatory authority?
- Does the system cover both public and private sectors in the drug sector?
- What are the different types of licences issued?
- Who is authorized to issue licences?
- What conditions must be met before a licence is issued?
- What type of qualifications are required for persons practising as pharmacists, or who are manufacturing pharmaceuticals, importing pharmaceuticals, selling pharmaceuticals by wholesale or retailing pharmaceuticals?
- How is the licensing body linked with other agencies involved in drug regulation?
- Is there a fee system for issuing and renewing licences?
- How many different types of licensed drug establishments are there and how many establishments of each type are there?
- Is the list of licensed drug establishments and persons readily available?

Inspection and surveillance: critical assessment and record keeping
- Is there a drug inspectorate?
- Does the inspectorate perform good manufacturing practice (GMP) inspection and inspection of distribution channels?
- How many inspectors in the country can carry out GMP inspection? How many inspectors are available for carrying out inspection of the distribution chain?
- What is the relationship between the inspectorate and other bodies involved in drug regulation?
- Is GMP inspection activity centralized?
- Is inspection of distribution channels decentralized? Does a reporting mechanism operate between the different levels?
- Do GMP inspectors have guidelines and manuals? Do inspectors of distribution channels have guidelines and manuals?
- Are inspectors qualified professionals? Do they undergo special training in order to be able to carry out inspection?
- Is there an external and/or internal audit and review system to examine the performance of inspectors and/or the inspectorate?
- Does the inspectorate carry out any of the following types of inspection:
  - Comprehensive/routine inspection?
  - Follow-up inspection?
  - Inspection in response to complaints?
- How often is routine inspection carried out?
- Is there a fee system for inspection?
- Does the inspectorate collect samples during GMP inspection, from distribution channels, or as part of post-marketing quality monitoring?
- In each of the last five years, what percentage of the samples tested failed? What was the average failure rate?
- What actions were taken against products that failed tests?
- Are there procedures that must be followed when considering appeals against enforcement measures imposed by inspectors?
- Are inspectors rotated to prevent corruption? Do they make their visits in teams?
- Are the results of inspection accessible to interested parties and to the public?
Drug Regulation Processes

Product assessment and registration: critical assessment of operation and record keeping

- Is there an operational product assessment and registration system?
- Is there a formal standard application form?
- Does registration apply to locally produced drugs? Does registration apply to drugs imported by the public sector?
- What information and evidence must be submitted when applying for registration of products containing:
  - new active pharmaceutical ingredients?
  - generic drugs?
  - fast-track drugs? a
- Is a WHO-type Certificate of a Pharmaceutical Product used?
- Do staff working in drug registration follow standard operating procedures?
- Are criteria (i.e. reasons for approval or rejection) for drug assessment and registration written down anywhere?
- Are assessment of applications:
  - Carried out by internal staff only?
  - Carried out by external expert committee(s)?
- Are any of the assessment activities delegated or contracted out to:
  - Other public institutions?
  - Individual experts?
  - Private institutions?
- Who makes the final decision regarding registration of a product?
- For how long is registration valid?
- On average, how long does it take to register:
  - A product containing a new active pharmaceutical ingredient?
  - A generic product?
  - A fast-track product?

- Is there a time limit for processing of an application form by the registration authority?
- Is there an appellate body?
- How many appeals have been made in each of the last five years? How many decisions were reversed as a result of these appeals?
- Is the drug registration process computerized?
- Does the authority issue the list of registered drugs regularly and update it?
- Are any of the following represented in the assessment and registration process:
  - drug manufacturers?
  - consumer or patient groups?
- Are fees levied for assessment and registration of products?
- How many applications have been received and processed in each of the last five years:
  - for new registration?
  - for variation?
  - for renewal?
  - others?
- How many applications and what types of applications have been rejected in each of the last five years?
- Are WHO-type Product Certificates issued for export products? How many such certificates have been issued in each of the last five years?
- What are the main constraints to drug assessment and registration? What are the reasons for them?

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a For example, in the event of a major public health problem, the Drug Regulatory Authority may make requirements less stringent so that a drug can be made available more quickly.
Effective Drug Regulation: what can countries do?

### Adverse Drug Reaction Monitoring
- Is there an adverse drug reaction (ADR) monitoring system?
- If so, is the system obligatory or voluntary?
- How many ADR reports have been received per year in each of the last five years?
- What happens to the reports received? How and to whom are they distributed locally and/or internationally?
- Are decisions taken on the basis of ADR monitoring?
- How many decisions have been made as a result of ADR monitoring? What kind of decisions were made?
- Are manufacturers and/or importers required to monitor the ADRs of their products?

### Clinical Trials
- Does drug legislation require control of clinical trials carried out in the country?
- Who is responsible for controlling clinical trials?
- How many clinical trial applications have been received in each of the last five years?
- Are there guidelines for conducting clinical trials?
- If so, are they consistent with:
  - the Helsinki declaration?
  - WHO good clinical practice guidelines?
- Does an ethical committee oversee clinical trials?
- Is there a special procedure for approving importation of drugs for clinical trial?

### Control of Drug Promotion and Advertising
- If legislation for the control of drug promotion is in force, is it in line with WHO ethical criteria for drug promotion?
- Is drug advertising and promotion controlled?
- Is there legal provision for controlling drug promotion and advertising?
- Are any restrictions specified in the drug law in relation to control of promotion and/or advertising?
- Which body controls advertising/promotion?
- Is prior approval required for promotional and advertising materials?
- Is there a fee for prior approval?
- How is advertising and promotion monitored?
- Is a product information sheet, data sheet or a summary of product characteristics approved at the time of registration?
- Are patient information leaflets and labels subject to approval?
- Are sanctions applied when laws on product information and promotion are violated? More specifically:
  - How many violations of drug promotion laws and regulations have been registered in each of the last five years?
  - How many legal sanctions have been enforced in each of the last five years?
  - How many administrative measures have been taken in each of the last five years?
- Are there any associations of pharmaceutical manufacturers or companies that practise self-regulation?
- Does the drug regulatory authority provide independent drug information to prescribers, dispensers and the public?
- How are the public and prescribers informed about newly registered drugs?
- Is there a mechanism to prevent false medical claims being made in advertisements?
- Do private organizations and consumers groups participate in the control of drug promotion and advertising?
- If so, do they follow a code of conduct?
- Can they impose sanctions?
- What are the main constraints to controlling drug promotion and advertising? What are the reasons for them?
Output Indicators

Licensing
- For each of the last five years, how many pharmaceutical manufacturers (out of the total number of pharmaceutical manufacturers in the country) were licensed?
- For each of the last five years, how many pharmaceutical importers (out of the total number of pharmaceutical importers in the country) were licensed?
- For each of the last five years, how many pharmaceutical wholesalers (out of the total number of pharmaceutical wholesalers in the country) were licensed?
- For each of the last five years, how many drug retail outlets (out of the total number of drug retail outlets) were licensed retail outlets?

GMP inspection
- For each of the last five years, how many routine or planned inspections (out of the total number of routine or planned inspections in the country) were conducted?
- For each of the last five years, how many pharmaceutical manufacturing plants (out of the total number of licensed pharmaceutical manufacturing plants in the country) were inspected?
- For each of the last five years, how many pharmaceutical manufacturing plants (out of the total number of licensed manufacturing plants inspected) were in violation of the regulations?
- For each of the last five years, how many pharmaceutical manufacturing plants (out of the total number of licensed pharmaceutical manufacturing plants in the country) held a GMP certificate?

Inspection of distribution channels
- For each of the last five years, how many distribution channels (out of the total number of licensed distribution channels in the country) were inspected?
- For each of the last five years, how many planned inspections (out of the total number of planned inspections) were undertaken?
- For each of the last five years, how many distribution channels (out of the total number of distribution channels inspected) were in violation of the regulations?
- For each of the last five years, how many samples (out of the planned total number of samples to be collected) were collected?
- For each of the last five years, how many distribution channels (out of the total number of licensed distribution channels in the country) were in violation of the regulations?
- For each of the last five years, how many drug products (out of the total number of drug samples collected) were found to have exceeded their expiry date?

Product assessment and registration
- How many registered products (out of the total number of products that require registration in the country) are there?
- How many registered products (out of the total number of products currently registered in the country (excluding vitamins) have more than three active ingredients?
- How many applications are currently waiting to undergo the assessment and registration process?

Control of promotion and advertising
- For each of the last five years, how many advertisements and promotions (out of the total number of advertisement and promotions monitored) violated drug regulations?
- For each of the last five years, how many labels and inserts (out of the total number of inserts or labels that were monitored) (for countries with a monitoring system) were inconsistent with what was approved during registration?

Quality control
- For each of the last five years, how many samples (out of the total number of samples submitted or collected) were tested?
- For each of the last five years, how many samples (out of the total number of samples tested) failed quality testing?
<table>
<thead>
<tr>
<th>Level I*</th>
<th>Level II*</th>
<th>Level III*</th>
<th>Level IV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulate drug legislation and regulations</td>
<td>Revise and update drug legislation and regulations as required</td>
<td>Revise and update drug legislation and regulations as required</td>
<td>Revise and update existing comprehensive drug legislation and regulations as required</td>
</tr>
<tr>
<td>Establish regulatory authority</td>
<td>Strengthen regulatory authority</td>
<td>Strengthen regulatory authority</td>
<td>Maintain strong regulatory authority</td>
</tr>
<tr>
<td>Create mandatory licensing system for private and public sector drug importers, wholesalers, retail outlets and drug dispensaries of healthcare facilities</td>
<td>Develop capacity to license drug manufacturers</td>
<td>Develop capacity to license persons, premises and practices in pharmaceutical trade</td>
<td>Maintain developed capacity</td>
</tr>
</tbody>
</table>
| Create a simple product inventory or licensing system based on the submission of:  
- A WHO-type certificate of pharmaceutical product, and  
- evidence of registration in another three or five selected reference countries (countries with reliable drug regulation, including GMP inspection and product assessment) | Strengthen capacity to undertake:  
- full assessment of applications for marketing authorization of generic products based on chemistry and pharmaceutical data  
- registration of new products on the basis of:  
  - provision of information on the basis of that provided by exporting countries (summary of product characteristics/data sheet and WHO-type certificate of a pharmaceutical product);  
  - provision of evidence of registration in another three or five countries reference countries (countries with reliable drug regulation, including GMP inspection and product assessment) | Develop capacity to make full assessment of new drug applications including biological products | Maintain developed capacity to make full assessment of new drug applications, including biotechnology products |
| Control imports by:  
- defining the points of entry for pharmaceutical products;  
- issuing a permit for each consignment to be imported;  
- requesting a batch certificate for imported products | Control imports by:  
- maintaining the points of entry/custom ports for pharmaceutical products;  
- requesting a batch certificate for imported products | Control imports by:  
- maintaining the points of entry/custom ports for pharmaceutical products;  
- requesting a batch certificate for imported products | Control imports by:  
- maintaining the points of entry/custom ports for pharmaceutical products;  
- requesting a batch certificate for imported biological and biotechnology products |
<p>| Establish inspectorate for drug distribution channels | Develop capacity to perform GMP inspections | Develop capacity to perform GMP inspection | Maintain developed capacity to undertake all types of inspections |
| Test quality of drugs when needed, using in-country or external laboratory | Establish a drug quality control laboratory to perform basic physico-chemical tests and assays | Develop capacity to make complete compendial physico-chemical tests and assays, and some tests and assays on biological products | Develop quality control laboratory to perform all types of tests and assays on marketed products including biological and biotechnology products and conduct research in the area of quality |</p>
<table>
<thead>
<tr>
<th>Level I</th>
<th>Level II</th>
<th>Level III</th>
<th>Level IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate a data system for storing information about licensed establishments and drugs</td>
<td>Strengthen capacity to store information on other activities</td>
<td>Strengthen capacity to include more activities</td>
<td>Maintain developed data retrieval system for all activities</td>
</tr>
<tr>
<td></td>
<td>Start post-marketing quality monitoring activity on target products</td>
<td>Develop capacity to conduct post-marketing quality monitoring on a wider number of marketed drugs</td>
<td>Maintain developed capacity to conduct post-marketing quality monitoring of all marketed drugs</td>
</tr>
<tr>
<td></td>
<td>Initiate drug information system for the public</td>
<td>Develop capacity to provide drug information to the public and professionals</td>
<td>Ensure drug information centre is able to undertake research work</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Establish system for post-marketing surveillance of safety of drugs</td>
<td>Maintain developed capacity to conduct post-marketing surveillance for safety of drugs</td>
</tr>
<tr>
<td></td>
<td>Initiate clinical control trial of drugs</td>
<td>Maintain developed capacity to control clinical trial</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Initiate control of drug promotion and advertising</td>
<td>Maintain developed capacity to control drug promotion and advertising</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Issue WHO type-certificate of a pharmaceutical product for exported products</td>
<td>Maintain developed capacity to issue WHO-type certificates for exported products including biological and bio-tech products</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Maintain developed capacity to conduct post-marketing surveillance for efficacy of drugs</td>
<td>Develop national quality standards or collaborate with others in the development of such standards</td>
</tr>
</tbody>
</table>

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a Ideally, drug regulation should match the level of development of the country’s pharmaceutical sector, but in reality a country’s pharmaceutical sector may be more highly evolved than its regulatory capacity.

b Countries depending on imported drugs (no domestic production) and having limited human and other resources for establishing drug regulation.

c Countries with some domestic production of generic drugs and limited capacity to develop drug regulation.

d Countries with domestic production, generic and other drugs and who export to other countries (intermediate level of development).

e Countries with a developed pharmaceutical industry.

f Countries depending on imported drugs (no domestic production) and having limited human and other resources for establishing drug regulation.

g Countries with some domestic production of generic drugs and limited capacity to develop drug regulation.

h Countries with domestic production of generic and other drugs and who export to other countries (intermediate level of development).

i Countries with a developed pharmaceutical industry.
**Annex 4. Examples of mission statements concerning drug regulation**

**Netherlands**

Safe and affordable pharmaceutical care to all is the principle upon which the Dutch government's medicine policy is based. The policy takes the quality, preparation, canalization and supply of medicines as its primary focus. The second policy objective is to control the cost of medicines. Thirdly, the policy is geared towards encouraging responsible use amongst patients and stimulating a judicious and cost-effective approach to the prescription and supply of medicines.

*Source: 52.*

**Thailand**

In response to the National Health Development and Economic and Social Development plans, Thai Food and Drug Administration offers the policy on quality services, consumer's health protection and human resources development for the sake of the public health and overall development of the country.

Quality services are guaranteed with fastness, safety, clarity, unity and reliability. The policy on consumer's health protection consists of the following:

1. Control of quality, safety of the health products and services with fair sales prices through regular inspection, testing, monitoring. Surveillance and taking immediate action to offenses against regulations.
2. Efficient dissemination of information to inform, educate, and alter the public awareness on protection of their own rights.
3. Improvement of laws and organizations to cope with the increasing and changing world situations.
4. Decentralization of the authorities to provincial and regional offices for effective and coverage control, services and problem solving.
5. Development of both central and regional officers' potential through training and seminars for improving their capabilities on serving the needs and solving problems of their own areas.
6. In meeting this policy the roles and responsibilities of the FDA will be:
   a) pre-marking control of locally produced and imported health products and household hazardous substances;
   b) post marketing monitoring and surveillance;
   c) consumer education and dissemination of information;
   d) promotion of technological development, researches and manufacturing for export.

*Source: 53.*

**Uganda**

The mission of the National Drug Authority (NDA) is to ensure the availability of essential efficacious, safe and cost-effective drugs to the entire population of Uganda as a means of providing health care and safeguarding the appropriate use of medicines.

*Source: 54.*
**United Kingdom**

The mission of the Medicines Control Agency (MCA) of the United Kingdom (UK) Department of Health is to safeguard public health by ensuring that all medicines on the UK market meet appropriate standards of safety, quality and efficacy. This is achieved through a system of licensing and monitoring medicines after the licence has been granted. The MCA has separate divisions dealing with licensing, post-licensing, inspection and enforcement of medicines, executive support and finance.

*Source: 55.*

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**The Food and Drug Administration of the USA**

According to the Food and Drug Administration Modernization Act of 1997 the amended mission of the FDA reads as follows:

“The Administration shall:

1. promote public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner
2. with respect to such products, protect public health by ensuring that—
   a) foods are safe, wholesome, sanitary and properly labeled;
   b) human and veterinary drugs are safe and effective;
   c) there is reasonable assurance of the safety and effectiveness of devices intended for human use;
   d) cosmetics are safe and properly labeled; and
   e) public health and safety are protected from electronic product radiation
3. participate through appropriate process with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements; and
4. as determined to be appropriate by the Secretary, carry out paragraphs (1) through (3) in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors and retailers of regulated products”.

The amended Act requires the Secretary, after consultation with appropriate scientific and academic experts, health care professionals, representatives of the patient and consumer advocacy groups, and the regulated industry to develop and publish a plan which is to be reviewed biannually. The plan is required to establish objectives and mechanisms to achieve such objectives. The Secretary is also required to prepare and publish an annual report providing detailed data on performance, achievements made as compared to the objectives set out in the plan, and identifying any regulatory policy that has negative impact on compliance.

*Source: 56.*
### Annex 5. Fees collected for drug registration

Table 1. Fees (in US$) collected for product registration in some developed countries

<table>
<thead>
<tr>
<th>Type of service/fee</th>
<th>Australia</th>
<th>Canada</th>
<th>European Medicines Evaluation Agency</th>
<th>New Zealand</th>
<th>Norway</th>
</tr>
</thead>
<tbody>
<tr>
<td>New chemical entities</td>
<td>500 to 56,000(^a)</td>
<td>92,000</td>
<td>170,000</td>
<td>8,000</td>
<td>5,300</td>
</tr>
<tr>
<td>Generic/non-prescription</td>
<td></td>
<td></td>
<td></td>
<td>40,000</td>
<td>5,300</td>
</tr>
<tr>
<td>Variation</td>
<td></td>
<td></td>
<td></td>
<td>50,000</td>
<td>200(^b)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>800(^b)</td>
</tr>
<tr>
<td>Renewal/5 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12,000</td>
</tr>
<tr>
<td>Annual charge</td>
<td>300(^c)</td>
<td>500(^c)</td>
<td></td>
<td>None</td>
<td>0.5% of gross price</td>
</tr>
<tr>
<td>Control and use of fee by drug regulation authority</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

\(^a\)depends on number of pages  
\(^b\)minor variation  
\(^c\)major variation  
\(^d\)non-prescription drugs  
\(^e\)new chemical entities

Table 2. Fees (in US$) collected for product registration in some developing countries

<table>
<thead>
<tr>
<th>Type of service/fee</th>
<th>Colombia</th>
<th>Kenya</th>
<th>Malaysia</th>
<th>Myanmar</th>
<th>Philippines</th>
<th>Singapore</th>
<th>Thailand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registration</td>
<td>Free</td>
<td>500(^1)</td>
<td>62</td>
<td>300</td>
<td>120(^2)</td>
<td>210(^3)</td>
<td>40</td>
</tr>
<tr>
<td>Variation fee</td>
<td>Free</td>
<td>None</td>
<td>62</td>
<td>100</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Annual retention fee</td>
<td>Free</td>
<td>None</td>
<td>62</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Renewal fee</td>
<td>Free</td>
<td>500</td>
<td>200</td>
<td>50</td>
<td>None</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Control and use of by DRA</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

\(^1\)domestic products  
\(^2\)imported products  
\(^3\)new chemical entities  
\(^4\)generic non-branded  
\(^5\)generic, branded  
\(^6\)registration valid for three years

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