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DRUG POLICIES AND MANAGEMENT

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1. Introduction

The WHO Programme on Prophylactic, Diagnostic and Therapeutic Substances has undergone profound changes and development over the years. During the early days of WHO, pharmaceuticals were considered only from the point of view of the chemical and physical characteristics of the substances they contained and in connexion with the methods for quality control as described in the national standards and pharmacopoeas. At that time, WHO initiated an international nomenclature of pharmaceutical substances, now known as the International nonproprietary names (INN) for pharmaceutical substances. This nomenclature is now recognized in many countries and greatly facilitates international communication in the field of pharmaceuticals. Since then considerable progress has been achieved regarding the "technical" dimension of pharmaceuticals, but it was eventually realized that controlling the quality of drugs was not enough, particularly when the number of new chemical entities introduced on the market began to increase rapidly.

In the early 1960s a new dimension was added to the technical dimension of pharmaceuticals. This could appropriately be called the "clinical" dimension. After the substances contained in pharmaceutical preparations had been defined, there was a need to increase knowledge regarding the action of these substances on the human body, as the ultimate purpose of administering drugs is to prevent and cure disease and to improve health. The requirements for drug safety were raised constantly, particularly after the thalidomide tragedy, and scientific methods for testing new medicines for safety and efficacy became increasingly important. It was recognized that no active drugs containing specific therapeutic properties could be absolutely safe as they interfered in one way or another with biological processes and were likely to produce adverse effects in some patients.

During this period, national legislation on drugs and drug control was reviewed in many countries and systems of monitoring adverse reactions were developed. Clinical evaluation of drugs was seen as an analysis of the ratio of benefit to risk in the use of the drugs in medical practice.

As knowledge in pharmacodynamics and pharmacokinetics increased, clinical pharmacology developed rapidly and the clinical pharmacological evaluation of drugs became an important issue in drug policies in many countries, particularly where research was based in the pharmaceutical industry. Regulatory demands for the introduction of new drugs have increased and the question whether they are becoming too complex and stringent, and thus giving rise to excessive delays and the curtailment of drug research and development, has often been raised. This applies particularly to toxicological testing, where methods of measurement have sometimes been extrapolated far beyond our ability to interpret their implications for the health of man. Furthermore, repetition of the same routine tests in several countries for registration purposes represents a waste of resources because of the obvious duplication of work.

In the early 1970s, a "socioeconomic" dimension, which included ethical aspects, became apparent in addition to the technical and clinical dimensions. This was, inter alia, the result of an identified need to rationalize governmental expenditure on health. Drug expenditure represents a considerable proportion of national health budgets, although it is generally regarded as a relatively easy component to manage.

The emphasis on the social and economic implications of pharmaceuticals is clearly linked with the evolution of health policies. The Alma-Ata International Conference on Primary Health Care (1978) recognized that "primary health care requires a continuous supply of essential drugs; that the provision of drugs accounts for a significant proportion of expenditures in the health sector; and that the progressive extension of primary health care to ensure eventual national coverage entails a large increase in the provision of drugs". The Conference recommended that "governments formulate national policies and regulations with respect to the import, local production, sale, and

distribution of drugs and biologicals so as to ensure that the essential drugs are available at the various levels of primary health care at the lowest feasible cost; that specific measures be taken to prevent the over-utilization of medicines; that proved traditional remedies be incorporated; and that effective administrative and supply systems be established". (As is well known, WHO is acting, both at the global level and in the regions concerned, in developing the concept of essential drugs.)

These general observations by the Alma Ata Conference must now be looked at in the light of the specific problems and opportunities existing in the European Region. For instance, in relation to the European situation the essential drug concept may have to be viewed from a somewhat different angle, e.g., by using comparative studies to stimulate discussions on differences among countries in drug registration and use.

2. The European situation

National drug legislation is the basis for the formulation of drug policies, but administrative practices of drug regulatory agencies are the real structure for governmental drug policy. To ensure optimal formulation of official drug policy, the basic aims and roles of the various elements of drug management in relation to the health system of a society must be defined.

As a result of the growing internationalization of drug evaluation and control, the harmonization of legislation and administrative practices is being extensively discussed both within and outside the European Region. Subregional intergovernmental organizations and groupings, such as Benelux, EEC, CMEA, Council of Europe, EFTA and the Nordic Council, all have an increasing number of activities concerning drug evaluation and control and drug policies in general. The motivation for such organizations to establish committees and schemes for collaboration in the drug field is clearly based on the need to achieve optimal use of resources.

The WHO Regional Office for Europe has also secured increasing collaboration with nongovernmental industrial organizations in the drug field. Discussions have taken place with the International Federation of Pharmaceutical Manufacturers' Associations (IFPMA) with regard to collaboration in the current series of European studies of drug regulation, and contacts have been established with the European Federation of Pharmaceutical Industries Associations (EFPIA), which is an association of pharmaceutical industries within the EEC and EFTA countries. Collaboration with the World Federation of Proprietary Medicines Manufacturers (WFPMM) and its European branch, the European Proprietary Medicines Association (AESGP), is also being strengthened, particularly in view of the increasing emphasis on self-care.

Although research into new drugs, together with experimental and clinical research on their safety and efficacy, has been greatly intensified during the last two decades, innovations in the pharmaceutical field have almost reached a status quo as regards the number of new chemical entities introduced. Requirements at the national level relating to drug applications have steadily increased, with a consequent increased workload for governmental drug regulatory agencies. This has obviously affected the costs of government drug control; drug prices have increased, with a corresponding rise in the level of expenditure on drugs under the social security schemes. It may, however, be questioned whether the proportion of drug costs in national health budgets has been increasing at the same rate as expenditure on new technologies.

In many Member States the drug sector has existed without adequate coordination with other parts of the health services, one of the reasons being the commercial character of drug procurement and distribution. However, there is now firm evidence of changing attitudes among decision makers, professionals and the public towards the place of drugs in society. The growing costs of drug treatment, better knowledge of the interaction between drugs and the human body, and constraints to which drug regulatory agencies are subject owing to lack of resources, are some factors which have stimulated those involved to reconsider the situation.

Quite controversial opinions exist regarding the effects of drug regulation on public health. It has, for example, been questioned whether the strict criteria for drug approval in some northern and socialist countries of Europe are more likely to benefit public health than the more liberal regulations of some southern European countries. Discussions on this issue have usually taken place without the presentation of hard facts; urgent action is therefore needed to evaluate the effect of approval policies in different countries of the European Region.

It is also thought that the standardization of guidelines for the clinical evaluation of drugs would enhance the harmonization of drug evaluation requirements. The Commission of the European Communities conducts ongoing activities which result in notes for the guidance of applicants wishing to register new drugs. On the other hand, the Regional Office for Europe has entered this area because of recommendations by drug research planning groups concerning the production of

guidelines for the investigator. Guidelines have been produced for the clinical evaluation of antihypertensive drugs in man, and working groups have been established to draft guidelines on nonsteroid anti-inflammatory drugs and on minor tranquilizers and sedatives.

As stated above, the Member States of the European Region are nowadays faced with a serious problem of high expenditure on drugs, this being partly the result of inappropriate utilization. The need to provide appropriate guidance for prescribers with a view to improving rationality in drug prescriptions has been recognized. Research activities on the measurement of degrees of drug utilization have gained higher priority at the national level and substantial improvements have been noted with regard to methodological aspects for measurement of drug use and the harmonization of drug classification. Also, the role of the Regional Office has been expanded with regard to coordination of utilization studies in the context of national drug policies.

3. Activities of the Regional Office for Europe

3.1 Structure of the PDT programme

Although the Regional Office had already undertaken several activities in this field, a significant step was taken when the new unit of Prophylactic, Diagnostic and Therapeutic Substances (PDT) became operational on 1 April 1979. Since that date the activities of the unit have been developing quite rapidly.

Following the WHO programme classification, the PDT programme in the Regional Office is divided into two components: on the one hand, pharmaceuticals and biologicals; on the other, drug policies and management. This division of the programme is however, rather artificial, since most of the subprogrammes in the field of national drug policies, drug utilization, drug evaluation, drug monitoring and clinical pharmacology all include components of a technical and clinical as well as a socioeconomic nature. At present the main thrusts in the programme are in the field of clinical pharmacological evaluation in drug control, drug utilization research, and development of national drug policies. The first two of these programme areas lend themselves very well to wide intercountry consultation, while the formulation of drug policies at the national level is obviously a question of priorities within individual Member States. However, there are numerous possibilities for intercountry collaboration in this field also, but perhaps rather on a subregional level, between countries with similar traditions and administrative systems.

In the past few years, various topics relating to drug utilization, evaluation and control have been reported on extensively in Regional Office publications (see Annex).

3.2 Clinical Pharmacology

During the 1970s the main activities of the Regional Office in the field of pharmaceuticals related to the series of symposia on clinical pharmacological evaluation in drug control which have been organized in the Federal Republic of Germany since 1972. Although these symposia have been largely devoted to the clinical aspects of drug control and the organization of clinical pharmacological services in the Region, they have also focused on other technical and social aspects such as drug utilization and postmarketing surveillance. Starting with the symposium held in 1980, there has been a change in the organization of these meetings so as to relate them directly to certain other programmes of WHO. Accordingly, the 1980 symposium was devoted entirely to drugs in relation to the elderly population; this activity was organized to complement to an Ad Hoc Technical Group on the Use of Medicaments by the Elderly (within the Global Programme for Care of the Aged). The combination of these two activities enabled problems of medication in old age to be discussed from both the clinical and the control standpoints, and with due recognition of the need to establish guidelines for drugs which should be used with the utmost care or in reduced dosage in this age group.

A symposium planned for 1981 will be devoted to the problems of drugs in infants and children; this will be a joint activity of the Regional Office's Maternal and Child Health and PDT programmes.

3.3 Drug utilization research

Drug utilization research gained rapid attention during the 1970s. Both the public health aspects and the socioeconomic implications have motivated decision makers at national and international levels to give such research activities increased priority. Following a WHO Symposium on the Consumption of Drugs (Oslo, 1969), a small expert group on drug utilization was sponsored by WHO headquarters. The group pointed out at an early stage that methodological problems in measuring and comparing drug utilization were potential obstacles in the development of drug utilization research. Also, the sources and availability of data differed considerably.

This expert group, now called the Drug Utilization Research Group (DURG), expanded quite rapidly, and in 1979 the Regional Office assumed the secretarial responsibility for the Group. When the Group met in Prague in 1979 it included scientists from 14 European Member States, and it is envisaged that a number of scientists from other countries within and outside the Region will join the Group at its next meeting in Yugoslavia (April, 1981).

After consultation and close collaboration with the Nordic Council on Medicines, the Group agreed on a classification system and on methodologies for measuring drug utilization. These methodologies are based on defined daily doses (DDDs) as units of measurement. Such doses reflect, in principle, the average daily maintenance dose for a given compound as recommended in the literature and are therefore technical units of measurement.

These methodologies have been tested by members of the Group, and studies have been published on international comparisons of sales of antidiabetic and psychotropic drugs in several European countries. In 1979 the Regional Office published Studies in drug utilization (European Series, No. 8), in which data collection systems in 10 European countries and the results of international comparisons are described.

3.4 National drug policies

The aim of developing national drug policies has been defined as the improvement of the efficiency of the pharmaceutical supply system through definition of the objectives and coordination of its different components, and through cooperation among the different sectors involved, mainly health, social services, trade and industrial production. In this context, the term "pharmaceutical supply system" covers elements like procurement, manufacture, distribution, control (including marketing licences), marketing surveillance (including drug utilization), reimbursement systems, research and development.

A series of studies of drug policies and management was started in 1980. These studies are focused mainly on the practices of drug regulatory agencies in different Member States in an attempt to reveal data on the effects of drug regulation on public health. They concentrate on the fate of drug applications in the various agencies, differences in approval policies, legal aspects concerning confidentiality in the handling of drug applications, etc.

In 1979 the Regional Office issued a publication entitled National drug policies (Public Health in Europe, No. 12), with the aim of presenting the concept of drug policies and stimulating the development of such policies at the national level. This publication contains contributions on the roles of regulatory agencies, health professions, universities, social security schemes, regional economic constellations, industry and the consumer in the pharmaceutical supply system.

At country level, the Regional Office has responded promptly to Member States' requests for advice on the organization of the different elements of drug policies so as to place them in the context of comprehensive drug policies and overall health policies. It is quite clear that an individual country-oriented approach in the formulation of drug policies will be the most appropriate in view of different traditions and needs.

4. Future trends

4.1 Drugs and strategies for health for all by the year 2000

In the regional strategies for attaining health for all by the year 2000, references to the drug component pertain mainly to the supportive nature of drugs in relation to health services. Emphasis is placed on the development of technical cooperation and support in the assessment of new drugs and on monitoring and surveillance after marketing in order to avoid over-sophistication and unnecessary duplication of efforts. In this context the regional potential for drug assessment has a global significance also.

Furthermore, the regional strategy clearly relates to the development of an awareness among people of the problems, risks and benefits of drug treatment and of opportunities to make informed choices regarding self-treatment with drugs. This requires a considerable strengthening of health education programmes and information aimed at improving conditions for self-care and ensuring compliance with instructions for prescribed drugs.

The education of physicians, pharmacists and other health personnel engaged in drug management will also have to be more community-oriented with regard to the use of drugs for prevention, primary care and long-term care and to the provision of information for the public.

4.2 Drug policies and management

The formulation of national drug policies covering all facets of the pharmaceutical supply system within the context of country health programming is a matter of growing concern to many Member States. The organization of the pharmaceutical supply system in all Member States requires a multisectoral approach since it covers nationwide activities in the drug field, including selection, procurement, distribution, manufacture, control, marketing surveillance, research and development. In many Member States the pharmaceutical supply system has been organized separately from or in parallel with the health sector. There is now a clear trend to incorporate drug components when planning for health care delivery in general because, although drugs alone cannot provide adequate treatment, they do play an important role in health care.

There are, indeed, very different traditions and approaches in the Member States with regard to the organization of the pharmaceutical supply system. Selection procedures differ; the approval policies for new drugs are quite stringent in some countries and more liberal in others; some countries have predominantly private systems of procurement, manufacture and distribution, while others have parallel private and public pharmaceutical supply systems, and a number of countries have even nationalized some or all steps in the supply system.

In Europe, drug policies are, generally speaking, closely linked with social security and health insurance schemes, and in many countries there is growing concern that the availability of drugs at a nominal price or even free of charge, combined with commercial pressures, may lead to over-consumption or wastage. In this context, antibiotics and chemotherapeutics are often cited as examples because of the fact that they account for a relatively high proportion of prescriptions and costs. As expenditure on drugs within the social security system increases, means are being sought to save resources through cost-sharing schemes, restricted lists of reimbursable drugs and price controls.

All these aspects of national drug policies require careful study. Such studies should not be isolated but, when possible, should be linked with studies related to model health care programmes. It is also necessary to continue studies on the impact of drug legislation and regulations regarding approval policies, availability of drugs, mechanisms for drug inspection and marketing surveillance techniques in Member States.

4.3 Drug information and drug utilization research

In the general problem definition of the medium-term programme for the Sixth General Programme of Work it is stated that excessive prescribing and the irrational use of drugs due to lack of information has created a growing public demand for drugs, and physicians have tended to prescribe drugs where they are not really indicated. The irrational use of drugs is partly due to a lack of cost-consciousness and there is no way of overcoming this problem unless information and education programmes for the public and the health professions are considerably strengthened.

In most Member States the drug manufacturers have established an effective information network for physicians, pharmacists and other health professionals, and advertisements of over-the-counter products are in general permitted. Although these information activities by the manufacturers are usually regulated in these countries, there is a growing awareness that all concerned should have access to independent, objective information. Such activities are already to be found in many countries in parallel with the activities of industry, whereas in other countries there is a clear need to strengthen such services.

There has also been a trend towards increased and improved patient information, but it has to be realized that the flow of information of varying quality, and sometimes expressing quite controversial opinions, has contributed to confusion among patients as well as imparting knowledge. Although the patients should, in principle, receive information on drugs from the physician or the pharmacist, it has to be acknowledged that self-medication is more widely used than prescribed medication. It is therefore very important to prepare both the physician and the pharmacist better for their educational role vis-à-vis the public and the other health professions.

Methodologies in drug utilization research in the Region have been developed and are now widely accepted. They include the establishment of an anatomical and therapeutic classification system for identifying individual therapeutic substances and widely used combinations, and a system of defined daily doses as units of measurement to facilitate international comparisons of drug consumption. The establishment of these methodologies is an important step towards studying in more detail the social consequences of drug utilization and identifying ways of improving the communication of data to prescribers and users in order to rationalize prescriptions and improve compliance.

The Regional Office could continue to coordinate research projects in drug utilization and update the classification of drugs and systems for measuring drug use in collaboration with intergovernmental and nongovernmental organizations and national bodies. Studies could also be organized, in relation to the health promotion programme, on the role of physicians, pharmacists and other health personnel in public information relating to the rational use of drugs.

4.4 Self-medication (self-care)

Although self-medication is more widely used than prescribed medication, limited attention has been given to this aspect and to the numerous products which are available without prescription. There are very different attitudes in Member States about this, as there are about other therapeutic traditions. However, in both developed and developing countries over-the-counter drugs and popular remedies are widely used. Policies with regard to over-the-counter drugs and popular remedies vary from country to country, and it is important in this connexion to balance the requirements for efficacy with the human aspects of health care and the cultural aspects and traditions of self-care. However, requirements for quality and safety should not be abandoned.

The Regional Office could promote surveys on patterns of self-medication in selected population groups and geographical areas in the Region and promote more effective guidance on the part of the manufacturer and the distributor regarding the use of over-the-counter drugs.

4.5 Essential drugs

The concept of essential drugs has been a fairly controversial issue at the European level. This concept should necessarily be regarded in the light of national drug policies and, as stated above, the Alma-Ata Conference recognized the need for a continuous supply of essential drugs in primary health care. However, it must also be recognized that there are differing views and differing needs in the Region as far as selection of a "hard core" of essential drugs for primary health care is concerned. Many Member States have, in fact, adapted the concept at hospital or even regional level by producing drug formularies for single hospitals or groups of hospitals.

The varying attitudes towards the concept of essential drugs require that the Regional Office should respond to individual country needs. The very considerable difference in policies among Member States of the Region also makes this a particularly interesting area for research and it is felt that studies to compare different national practices with regard to drug committees in primary health care and hospitals and to drug registration would be an important contributory factor in stimulating policy discussions in this field.

The WHO Action Programme on Essential Drugs is clearly oriented towards developing countries and in this context the European Region is mainly regarded as a provider region. In the drug field, as in many other fields of technology, the European Region is, of course, in a special situation, since it possesses considerable scientific and technical potential. This potential is, in fact, being utilized for the benefit of developing countries within and outside the Region by the provision of training and financial and managerial resources, as well as through aid programmes.

European Member States can also clearly assist in the Action Programme by providing facilities for quality assurance of essential drugs, and the Regional Office might play an active role in drug assessment (see 4.6). The Regional Office could also provide continuing advice for the Global Action Programme and stimulate European Member States to provide relevant training facilities for fellows from developing countries who are engaged in pharmaceutical supply and drug control.

4.6 Role of WHO in international drug registration

The economic constraints referred to in this paper stimulate rethinking and call for new collaborative approaches in drug regulatory agencies to avoid overlapping and thereby reduce resource wastage. WHO could well develop an international scheme for the evaluation of drugs in order to facilitate the more rapid transfer of knowledge about new drugs introduced on the market in different countries. The development of an international scheme in this regard should also be seen in the context of WHO's goal of achieving health for all by the year 2000, because it is quite obvious that developing countries have very limited possibilities for establishing adequate regulatory mechanisms for drug evaluation. They will therefore be very dependent on decisions made by other countries with more advanced drug regulatory agencies. However, such agencies in developed countries have serious difficulties, as mentioned above, because of growing workloads and reduced budgets for drug regulation.

A certification scheme for the scientific approval of drugs by WHO might be considered. Such a scheme should not create any obligations for Member States or for any other party, and therefore it should be possible to avoid a number of the problems which usually arise when attempts are made

to harmonize national drug legislation or to establish supranational systems. It would seem natural that the European Region, with its well-developed national drug regulatory agencies and drug industry, should take the lead in such a development. However, this would have to be done in very close cooperation with WHO headquarters, and the practical possibilities of such a development would have to be very carefully studied.

Annex

PUBLICATIONS AND DOCUMENTS OF THE WHO REGIONAL OFFICE FOR EUROPE
IN THE DRUGS FIELD, 1979-1981

Studies in drug utilization, European Series, No. 8, 1979 (English)

National drug policies, Public Health in Europe, No. 12, 1979 (English)

Guidelines for the clinical evaluation of antihypertensive drugs in man, ICP/PHB 003/6 Rev 3 (English)

Clinical pharmacological evaluation in drug control: Report on the Seventh Symposium, EURO Reports and Studies No. 13, 1979 (English/French)

Report on the annual meeting of the WHO Drug Utilization Research Group, Prague, 22-25 August 1979 (D4/76/3) (English)

Summary report on the Eighth European Symposium on Clinical Pharmacological Evaluation in Drug Control, Cologne, 20-22 November 1979, ICP/PHB 006 (English, French, German, Russian)

Report of the Planning Group on Evaluation of Drugs and other Therapeutic and Diagnostic Substances, Copenhagen, 3-5 June 1980 (ICP/RPD 006(3)) (English)

Report of a meeting of the Programme Committee of the WHO Drug Utilization Research Group, Copenhagen, 12 August 1980, ICP/DPM 002 (English)

Summary Report on the Ninth European Symposium on Clinical Pharmacological Evaluation in Drug Control, Schlangenbad, 18-21 November 1980, ICP/PHB 008 (English)

Directory of official drug regulatory agencies in the European Region, EURO Reports and Studies (in press) (E/F/G/R)