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PHARMACEUTICAL LEGISLATION

by

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There is general agreement now in all countries, developed as well as developing, on what should be included in pharmaceutical legislation. In a number of countries, pharmaceutical legislation has been submitted to complete re-examination, in keeping with present trends in pharmaceutical manufacturing, distribution, import and export. This is particularly the case in countries where pharmaceutical manufacturing is a significant part of the economy of the country and where pharmaceutical exports and imports are important. Among these could be mentioned the United States and the United Kingdom, as well as Switzerland, Germany and France.

In addition the World Health Organization has been asked by a number of resolutions of the Executive Board and the World Health Assembly to undertake research and bring about suggestions and principles concerning pharmaceutical problems, particularly in order to protect countries where pharmaceutical control had not yet been fully developed, against the introduction of medicines which may be of insufficient quality, or whose therapeutic efficiency, toxicity and side effects have been insufficiently investigated and defined.

The work of these countries, as well as the suggestions made by WHO experts and included in various reports of WHO Headquarters and Regional

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Organizations, have been following corresponding principles and these can be used as basis for pharmaceutical legislation. Attention is drawn in this connection to the following published reports: "Use of Specifications for Pharmaceutical Preparations, Geneva, 1956", Wld Hlth Org. techn. Rep. Ser., 1957, 138; "The Quality Control of Pharmaceutical Preparations, Warsaw, 1961", Wld Hlth Org. techn. Rep. Ser., 1962, 249; "WHO Expert Committee on Specifications for Pharmaceutical Preparations, Twenty-first Report, Geneva, 1964", Wld Hlth Org. techn. Rep. Ser., 1965, 307; "WHO Expert Committee on Pharmaceutical Preparations, Twenty-second Report, Geneva, 1968", Wld Hlth Org. techn. Rep. Ser., 418; "The Quality Control of Pharmaceutical Preparations, Helsinki, 1968", Report on a Conference, EURO 2032.

Reference is made in these various reports a) to the elaboration of suitable specifications of quality, purity, potency and sterility; b) to manufacturing controls; c) to the inspection of pharmaceutical plants; d) to the work and organization of the official laboratory for pharmaceutical quality control; e) to the qualifications of the staff (pharmaceutical establishments and control laboratories, official laboratories, inspectors).

From these documents a large amount of material is being made available to the Member States of WHO for the inclusion in up-to-date legislation and regulations.

While problems concerning the introduction of drugs on the market of the different countries tend in principle to become similar all over the world, what is very important from the point of view of international health is that pharmaceutical legislation and regulations introduced in the different countries will ensure a sufficient quality of the drugs in international commerce. For that purpose, the pharmaceutical legislation of a country should, by necessity of trade and health protection, have to be in line with the corresponding legislation in other parts of the world, primarily with regard to quality and particularly with reference to manufacturing controls and the inspection of plants.

The pharmaceutical legislation of a country only relates to the pharmaceutical products which have been authorized for sale within the country in question. With rare exceptions or as a result of bilateral agreements, pharmaceutical products which are not on sale in a given country may not come necessarily under official control of this country. This results from a country's policy of not placing obstacles to the export of pharmaceuticals which are being produced in that country.

It is therefore essential for an importing country to assure itself that the provisions of the legislation and regulations of the exporting country are found adequate in order to ensure a satisfactory control over the drug. It should also make sure that these provisions apply to all pharmaceuticals which may be exported to it, whether they are or not on the market in the exporting country, or are there in a different pharmaceutical form. It is of interest to quote the following paragraph of the above-mentioned Report on a Conference EURO 2032, p.2: "Some participants mentioned that in their countries studies were being made of the possibility of covering, under the same legislation and regulations, the quality control of drugs for home consumption and of drugs for export, even when the pharmaceutical substances, their dosages and pharmaceutical forms as introduced on the market in the exporting country differed from those for the home market. The meeting was informed that in one country of the European Region, new legislation had been enacted which could ensure that an equal degree of control would be exercised over the quality of drugs for export as well as for home consumption. However, that aspect of the legislation would not be implemented in that country until a number of similar moves had been taken internationally. Some countries were at present introducing legislation which would allow them to ensure proper standards of manufacturing procedure in the exporting country when requests were received for permission to import drugs manufactured in other countries. Reference was made to the present provisions of the Food, Drug and Cosmetic Act of the United States and to the measures taken in a number of countries of Europe and other regions. In certain European countries, confidential information might be given on the status

of an exporting firm to other interested countries with a specific group. However, that may prove to be difficult to arrange with countries outside the restricted group in question."

Harmonization between national pharmaceutical legislation and regulations of a number of countries is now in process. One of the most advanced movements in this direction in Europe is in the five so-called Nordic countries; they already have a large number of common specifications based on the work of the Nordic Pharmacopoeia Commission. In America mention should be made of efforts towards common legislation in the countries of the common market of Central America. The six countries of the European Economic Community are in the process of harmonizing their pharmaceutical legislations and regulations. They also cooperate, under the auspices of the Council of Europe, with the United Kingdom and Switzerland in the European Pharmacopoeia Commission which has now published a first volume of a so-called European Pharmacopoeia. The "Medicines Act" recently promulgated in the United Kingdom would make a harmonization of pharmaceutical legislation possible with the countries of the European Free Trade Association as well as with countries of the EEC.

In order to give protection to countries importing pharmaceuticals, the validity of certificates issued by the pharmaceutical manufacturers, agents or government authorities in the exporting country had been discussed in 1964 at an Expert Committee of WHO (Twenty-first Report of WHO Expert Committee on Specifications for Pharmaceutical Preparations", Annex 1, Wld Hlth Org. techn. Rep. Ser., 1965, 307). Such certificates would at first sight have appeared to give the importer a valid assurance of quality. It was, however, mentioned that a certificate issued by the exporter or the exporting country may be of practical help to a country that has not yet made arrangements for an adequate quality control laboratory of its own, but only if the importer is satisfied that: (a) pharmaceutical preparations for export have been submitted to the same quality control regulations as those governing domestic use; (b) an efficiently organized quality control exists within the pharmaceutical manufacturing industry, including control of every batch of raw material and of every batch of the pharmaceutical preparations produced in bulk or ready for use; (c) an efficient inspection is carried out by the national authority of all pharmaceutical

manufacturing establishments, as well as of the staff and facilities for quality control; (d) all pharmaceutical preparations for local use or for export have been registered by competent staff, together with adequate physicochemical and biological quality control specifications; (e) the packing of the pharmaceutical preparation is adequate for transportation and storage, especially in tropical countries, and the storage in the importing country is adequate to preserve the drug from loss of potency and from decomposition, which may lead to the production of undesirable or toxic side effects; (f) the certificate of quality concerns the specific batch of pharmaceutical preparation imported. A country importing pharmaceutical preparations should first ascertain that the above requisites exist in the exporting country by studying both the regulations of that country and the standard of quality control in the industrial and official laboratories. There may be significant differences between regulations on pharmaceutical quality control and their application in the laboratory.

The situation is now becoming more satisfactory as regards the quality of drugs exported and a better protection is afforded to the health of importing countries. This is due in no small measure to the considerable work which has been undertaken since 1964 under WHO auspices as reported in the above-mentioned publications. At the last World Health Assembly special consideration was also given to a certification scheme on the quality of pharmaceuticals moving in international commerce (WHA22.50). This scheme could also be used as a basis in regulations on quality control, to apply to manufacturers in the exporting country and to the certification of individual batches.

Another important item in the harmonization of pharmaceutical legislation conerns the definition of a "new pharmaceutical product". In some countries the concept of "new product" has already been defined by law, and any legislation to control "new pharmaceuticals" introduced on the market will have to include such a definition. A new, previously unknown chemical substance, and a known substance never before used as a pharmaceutical product are generally considered to be "new" pharmaceutical products when first used to diagnose, prevent or treat illness. A

pharmaceutical product would also be "new" if recommended to be given by a new route of administration. However, in the following cases complete agreement for regarding a pharmaceutical preparation as "new" may not be so easy to obtain. A new combination of known pharmaceutical preparations should be considered a "new" product if there is evidence from pharmacological or clinical studies, or from previous knowledge and experience with the separate ingredients, that undesirable secondary effects are to be expected, or if there has been no previous experience of giving them together by the same route of administration. A pharmaceutical product may be considered as "new" if it is recommended in a new indication or in a different posology; or if the method of manufacture is changed and may result in impurities not previously present. A difficult question refers to "when is a 'new' pharmaceutical no longer to be considered as 'new'?" The answer to that question may be different for every product, and may require preferably recourse to a body of experts to advise the authority administering the law.

The expressions used in pharmaceutical legislation and regulations to define and design drugs, their various forms, etc., should be chosen so as to correspond closely to expressions for the same object in legislation and regulations of other countries. These expressions may differ in the same language creating possibly a certain confusion whenever comparing legislation and regulations. For instance let us mention the definition of pharmaceutical preparation (drug) in the above-mentioned WHO technical Reports No.138 and No.249: "A drug (or pharmaceutical preparation) is any substance or mixture of substances manufactured, sold, offered for sale or represented for use in: (a) the diagnosis, treatment, mitigation or prevention of disease, abnormal physical state or the symptoms thereof in man or animal; (b) restoring, correcting or modifying organic functions in man or animal". Canada applies a similar definition to "drug" and in French "drogue", whereas a corresponding definitaon applies in the recently promulgated MedicinesAct of the United Kingdom to "medicinal product". One could also mention that in France "drogue" has a more limited and specific meaning. It is

indeed important to give consideration to the selection of expressions which will as much as possible prevent misunderstandings in dealing with other countries.

Let us also mention the advantages of using the international non-proprietary names proposed for pharmaceutical substances by the World Health Organization. They are communicated to all Member States and published at intervals in the "WHO Chronicle", with a request to introduce them whenever possible on the national level. Through these names a useful protection is afforded against the confusion arising from different non-proprietary names for the same substance. They should therefore preferably be used whenever possible in the labelling of drugs for export. In the absence of such a name, or if it cannot be used because of infringement on patent rights or for other reasons, another name official on the national level or used in the national pharmacopoeia or formulary should be used, or if there is no such name then the chemical designation.

Finally reference should be made here to the remarkable "International Digest of Health Legislation", published quarterly by the World Health Organization in English and French, containing pharmaceutical laws and regulations of many countries.