

Pharmaceutical Standards and Nomenclature

It is a national responsibility to determine what official specifications for therapeutic and other agents should be adopted and enforced, but it has long been recognized that such standards have disadvantages if they are established without reference to those of other countries. As early as 1865 the First International Pharmaceutical Congress met to discuss the possibility of formulating more generally accepted standards. Progress was slow but, as a result of international conferences held in Brussels in 1902 and 1925, an international agreement for the compilation of an international pharmacopoeia was signed at Brussels in 1929 by twenty-six countries. According to the terms of this agreement, the League of Nations was to be responsible for organizing the technical side of the work and the Belgian Government was to assist with the secretarial arrangements. The actual work of compilation was begun in 1937 by a Technical Commission of Pharmacopoeial Experts, appointed by the Health Organisation of the League of Nations. Much was accomplished during the next few years, though there was a lull during the Second World War, and in 1945 the Commission issued an interim report, which contained the following statement:

There is a desire for a uniform system of nomenclature, and it is specially urged that the same name should, in all countries, designate a drug of the same strength and composition. Differences in national standards for widely used materials constitute a source of danger to travellers . . . [and] are also a hindrance to the spread of medical and pharmaceutical knowledge. A state of affairs under which the same supply of a drug or chemical may be accepted in one country and rejected in another may lead to the retention of lower standards in manufacture, whilst the maintenance of a common high standard would tend to economy of production and would facilitate commerce between the nations.

As is described in Chapter 6, the Interim Commission of the World Health Organization appointed an Expert Committee on the Unification of

Pharmacopœias. After the First World Health Assembly, in 1948, work began in earnest on the final compilation of the International Pharmacopœia. This work involved, among other things, establishing chemical, physico-chemical and biological specifications for important pharmaceutical products commonly met with in international trade and widely used in many countries, and standardizing nomenclature, posology, and methods of assay. Under its new name—Expert Committee on the International Pharmacopœia—the Committee completed the first volume of the *Pharmacopœa Internationalis* in 1951. This volume, which appeared simultaneously in English and French, and was shortly followed by a Spanish edition, contained specifications of physical and chemical properties, identification tests, permissible limits for impurities, and methods of assay for 199 pharmaceutical preparations, with forty-three appendices defining certain tests and methods referred to in the specifications and listing for the various preparations the usual and maximum doses for adults.

The second volume, published in 1955, in English and French, and also followed later by a Spanish edition, contained specifications for a further 210 pharmaceutical preparations and twenty-six additional appendices. A number of important pharmaceutical substances—insulin preparations, antibiotics, and new synthetic drugs—were included in this volume, as well as tables of posology for both adults and children.

Both volumes of the International Pharmacopœia have appeared in German and Japanese translations, prepared by private firms under the supervision of members of the Expert Advisory Panel.

To ensure as wide an international participation as possible, the draft monographs and appendices for Volume II of the International Pharmacopœia were submitted, through the governments of the various Member States, to a large number of pharmaceutical firms and experts for comments. This innovation greatly complicated the process of preparation, but was considered justifiable as a means of facilitating the general acceptance of the International Pharmacopœia as a reference work.

The work of unification is still going on; specifications for ninety-three new pharmaceutical preparations and twelve appendices have been circulated for comment to Member States prior to publication as a supplement to the *Pharmacopœa Internationalis*.

The specifications contained in the *Pharmacopœa Internationalis* are no more than recommendations to serve as a basis for the establishment of national specifications. This has already been done in several countries, and there is encouraging progress towards a reasonable measure of uniformity. In several countries pharmacopœia commissions and other authorities are making

increasing use of the International Pharmacopoeia when drawing up specifications for the examination of pharmaceutical preparations, imported or manufactured locally. Many of the specifications that have been published in national pharmacopoeias and in other official or semi-official works have been largely based on the specifications recommended by WHO.

International Non-Proprietary Names for Drugs

The need for avoiding confusion in medical and pharmaceutical terminology is obvious. Chemists have been largely successful in standardizing chemical terminology, but a very large number of new medicinal substances are introduced into the *materia medica* every year and the matter is now so complicated that no individual pharmacologist, manufacturer, physician or purchaser can readily find his way through the maze. For example, methadone hydrochloride of the *Pharmacopoea Internationalis* (6-dimethylamino-4, 4-diphenyl-3-heptanone) is known in different countries under the names of amidone, miadone, diadone, diamion, mephenon or symoron. The existence of several non-proprietary names for each of a large number of substances, and for the scores of new ones that are added every year, complicates unreasonably the task of the physician and the pharmacist.

A number of countries made attempts to clear up this confusion, but it was evident that the problem called for international co-operation and WHO was accordingly asked to assume responsibility. In 1955, the Executive Board established a procedure for selecting and recommending non-proprietary names for drugs, and since then 482 names have been proposed, after wide consultation with producers in many countries. The basis of this procedure is that, while it is important to obtain agreement on non-proprietary names for drugs as soon as possible after the introduction of a new drug, nothing should be done to interfere with legitimate commercial interests or to infringe registered trade-marks. The system is therefore complicated. When a request is received for the establishment of an international non-proprietary name, WHO first consults members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations, designated for this purpose, and the names selected are submitted to all Member States and printed in the *Chronicle of the World Health Organization* as "proposed international non-proprietary names". Objections and comments received within a certain period after this publication are examined and, finally, when all differences have been settled, the names are included in a list of "recommended international non-

proprietary names", which is again published in the *Chronicle* in the hope that Member States and individual manufacturers will widely accept them. In all, 219 names have so far been selected. They have been widely accepted throughout the world, and are increasingly used in the medical and pharmaceutical literature of many countries.

Centre for Authentic Chemical Substances

The number of substances for which international biological standards have been provided in the past, but whose potency can now be determined by physico-chemical methods, is constantly increasing. The chemical structure of substances such as oestrone, progesterone, tubocurarine and vitamin-A acetate is now well understood and it is no longer necessary to assess their potency against a biological standard. However, it is often desirable to check the purity and potency of these products against some standard, and to meet this need a Centre for Authentic Chemical Substances was established in 1955, under the auspices of WHO, at the Apotekens Kontrollaboratorium in Stockholm. The task of the Centre is to collect, assay, store and distribute a number of pure chemicals required for reference purposes by national and other laboratories or by manufacturing firms. Eight substances are now available; they can be obtained free of charge by non-profit-making laboratories and institutes, and on payment of a nominal charge by commercial firms. The Centre will remain for some time on an experimental basis: few additions will be made to the substances already available, and they will be limited to substances used in the laboratory control of medicaments and for pure research.

Examination of Pharmaceutical Preparations

At the present time, many new therapeutic and prophylactic substances are being produced and put on the market every year. The process is accelerating, the lapse of time between discovery and general use being sometimes no more than a few months. Health administrations are well aware of the importance of the problem and during the past few years WHO has received an increasing number of requests for technical information. In response to these requests a study group was convened in 1956 to study principles which could be of help to national health departments and other authorities dealing with the approval of new pharmaceutical remedies. The study group noted

that a number of other organizations had shown an interest in this problem during recent years, particularly the Pan American Sanitary Organization, the Pan American Medical Federation, the International Pharmaceutical Federation, the Pharmaceutical Products Sub-committee of the Western European Union, and the Pharmaceutical Union of the Arab League. The study group indicated ways and means of establishing a system for the centralization, examination and distribution of information concerning the properties of new pharmaceutical preparations. It was considered that this could best be done through the preparation of information sheets for distribution to governments, laboratories for the control of drugs, and specialists. Speed would be one of the chief requirements for the new service, and it was emphasized that WHO could not carry out its task efficiently without the full collaboration of the pharmaceutical industry, national pharmacopoeial commissions and health administrations, and other bodies, as in the case of the work on non-proprietary names. The information sheets would also serve as useful basic material for future revisions of the International Pharmacopoeia.

Industrial Production of Antibiotics and DDT

A few programmes of WHO, which were designed to meet emergency situations, have been discontinued. An example of such a temporary project is the assistance that was given by WHO in the development of plants for the production of penicillin and DDT.

At the end of the Second World War a number of countries embarked on large-scale campaigns for which considerable quantities of antibiotics or insecticides were needed. In spite of international efforts to provide these countries with the antibiotics and insecticides required at a reasonable cost, it soon became apparent that currency and other difficulties were going to delay the introduction of the campaigns in countries that had not the equipment or technical personnel to manufacture the products themselves. International assistance was therefore called for, and WHO agreed to provide it by helping governments to set up their own plants.

An Expert Committee on Antibiotics met in April 1950 to draw up scientific and technical plans for this emergency aid programme, under which WHO was to take part in the establishment of national centres for the production of antibiotics in several countries, by giving technical advice and financial assistance. Between 1950 and 1953, under the joint auspices of UNICEF and WHO, penicillin plants were established, modernized or expanded in India,

Yugoslavia and Chile, and plants for the production of DDT were set up in Egypt, India and Pakistan. Educational assistance was also provided.

The establishment of penicillin or DDT plants comes naturally within the scope of other international projects, such as those undertaken by UNICEF, or by the United Nations under its Technical Assistance Programme. Following discussions with the United Nations, the Fifth World Health Assembly approved in principle the taking over by the United Nations Technical Assistance Administration of activities connected with the manufacture of antibiotics and insecticides, it being understood that WHO must maintain its function of providing scientific advice.
