This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization.

WHO Expert Committee on Specifications for Pharmaceutical Preparations

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WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Geneva, 26 November–1 December 1979

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WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Twenty-seventh Report

The WHO Expert Committee on Specifications for Pharmaceutical Preparations met in Geneva from 26 November to 1 December 1979. The meeting was opened on behalf of the Director-General by Dr Ch'en Wen-chieh, Assistant Director-General. He recalled that the Twenty-eighth World Health Assembly, in resolution WHA28.65, adopted the "Certification scheme on the quality of pharmaceutical products moving in international commerce" (*1*) proposed in the twenty-fifth report of the Expert Committee (*2*). He informed the Committee that the number of Member States that have agreed to participate in the scheme has grown continuously and now totals 54.

1. QUALITY ASSURANCE IN PHARMACEUTICAL SUPPLY SYSTEMS

In its twenty-sixth report (*3*), the WHO Expert Committee on Specifications for Pharmaceutical Preparations considered various aspects of quality assurance in pharmaceutical supply systems and suggested that to fulfil some of the objectives enumerated in resolution WHA28.66 of the Twenty-eighth World Health Assembly relating to the regulatory control of drugs, a comprehensive review of approaches to quality assurance should be recommended. A document containing such a review was considered at the present meeting; it incorporated comments by members of the Expert Panel on the International Pharmacopoeia and Pharmaceutical Preparations and by persons from other interested institutions.

A question of definition concerning the terms "drug", "medicine", "raw material", "pharmaceutical product", etc., arose early in the discussion. While there was agreement that it would not be useful in the present report to depart from the usage reflected in documents

such as the twenty-second report of the Expert Committee (*4*) and resolution WHA28.66, the Committee urged that steps should be taken to standardize internationally acceptable terms and definitions.

The Committee noted that the process of acquiring a pharmaceutical raw material, converting it into a finished product and making it available to the consumer involves a number of complex operations which require stringent surveillance to ensure that the user receives a satisfactory product. Moreover, these operations may involve a number of enterprises engaged in raw material production, formulation, distribution, etc., before the finished products reach those who prescribe or dispense them to the general public. A number of checks, tests and inspections must be carried out during these processes, some in the manufacturing sector, others by surveillance authorities. For divers reasons, countries have evolved a variety of procedures that they use in the quality assessment of their pharmaceutical supply systems, and yet other countries are now in the process of developing their own methods. To assist in the evolution of such national systems of drug quality assessment the Committee reviewed the document mentioned above, a revised version of which is published in Annex 1. Countries may select from this outline the features that seem appropriate to their needs.

In discussing the terms "assessment" and "assurance" the Committee came to the conclusion that the term "quality assessment" was appropriate to the activities of governmental agencies whose mandate is to assess by inspection, surveillance and other means how closely manufacturers and distributors comply with drug quality requirements. Manufacturers are regarded as fully responsible for the quality of their products and therefore the term "quality assurance" was considered more appropriate to describe their responsibilities.

Generally speaking, the Committee noted that analytical surveillance systems are directed towards finished pharmaceutical products but recognized that the quality of all raw material ingredients (including that of pharmaceutical aids) plays a crucial role in the quality of the final dosage form. The use of the term "drug quality" in the report is intended to convey consideration of all aspects of quality whatever the stage in the production process from raw material to finished product. However, whenever the context requires a clear identification of raw material or pharmaceutical product these designations are used. Because commercially available raw materials may be incorporated into a wide variety of finished products intended for administration in other than human medicine, the degree of control

over the distribution and use of such materials must be linked to their final purpose.

Countries having a quality assessment scheme, or those intending soon to put one into effect, will note the relevance and usefulness of many previous WHO initiatives concerned with aspects of drug quality and its control. The Committee strongly urged greater acceptance of the WHO certification scheme on the quality of pharmaceutical products moving in international commerce (*1*) so that the quality of imported drugs can be assessed as nearly as possible on the same terms as those manufactured locally.

For a variety of reasons, drug quality specifications deemed necessary by one country may differ somewhat from those of other countries. Nevertheless, the Committee urged that, in cases where there were no persuasive reasons to the contrary, a set of generally well-accepted monographs such as those of the International Pharmacopoeia should be considered satisfactory.

The document known as "Good practices in the manufacture and quality control of drugs" (*1*) adopted by the Twenty-eighth World Health Assembly in resolution WHA28.66 has stood the test of time and is now widely accepted as being generally applicable to all manufacturing situations. The Committee noted that the local production of dosage forms in many developing countries is on the increase and some of the enterprises involved produce only a limited number of simple dosage forms. For such situations it would be useful to evolve from the current basic document a guideline for good manufacturing practices in such specific conditions of manufacture.

The Committee was aware of the different national legal requirements imposed in various countries on such persons as the pharmacist or the prescriber, who are involved in the final steps of the distribution of pharmaceutical products. In some countries these persons have statutory responsibilities concerning the product quality, while in others their responsibilities are governed only by professional standards. Under the first system an obligation exists to report to the drug control authority any instance of a defective product that comes to light, and the authority might wish to introduce an arrangement facilitating such reporting. Under the other system, all those who discover defective products in the course of their professional activities should be strongly encouraged to adopt the same reporting procedure.

2. REVISION OF THE INTERNATIONAL PHARMACOPOEIA

2.1 General

In its twenty-sixth report (*3*), the WHO Expert Committee on Specifications for Pharmaceutical Preparations requested the Secretariat to continue the process of revising the International Pharmacopoeia on the basis of the recommendations published in its twenty-fifth report (*2*). In these reports the Expert Committee drew up the production schedule for the third edition of the International Pharmacopoeia, requiring a sustained effort over a number of years on the part of the collaborating experts and institutions and of the Secretariat. As a considerable delay in publication would result if the whole third edition were to appear simultaneously, it was decided to publish the edition as a set of smaller volumes based on draft texts, each volume to be issued as soon as it was completed.

2.2 Methods of drug analysis

The Committee welcomed the progress made in the publication of general methods of analysis in volume 1 of the third edition (*5*) and thanked the specialists and institutions concerned for their collaboration. It also noted that a number of suggestions had been received by the Secretariat from members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations and interested institutions proposing the expansion of the list of methods of analysis included in the International Pharmacopoeia, especially in respect of methods used to test dosage forms, those used to test herbal drugs, and various biological methods used in the testing of pharmaceutical products. It was agreed to recommend that such methods should be elaborated for inclusion in subsequent volumes of the International Pharmacopoeia, priority being given to the methods needed to support individual monographs.

2.3 Monographs for pharmaceutical raw materials

2.3.1 *Progress in the review of quality specifications*

In keeping with the recommendations in the Committee's twenty-fifth report (*2*), the process of reviewing pharmacopoeial monographs must consist of several steps: the initial review of criteria to be used