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WHO Expert Committee on Specifications for Pharmaceutical Preparations

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Geneva, 5–10 December 1983

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WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Twenty-ninth Report

The WHO Expert Committee on Specifications for Pharmaceutical Preparations met in Geneva from 5 to 10 December 1983. The meeting was opened on behalf of the Director-General by Dr Lu Rushan, Assistant Director-General, who stressed the need for a realistic approach to quality control of drugs in developing countries. Although the WHO Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce provides valuable assurance to these countries on the quality of imported products, the responsible authorities also need to be in a position to check for themselves the quality of these products. As yet, however, many developing countries do not have suitable laboratory facilities.

In its policy of according preference in the International Pharmacopoeia to classical methods of analysis wherever these can be accepted without lowering of standards, the Committee has previously shown itself sensitive to the need to bring a measure of quality control within the grasp of all countries. By now providing, in this report, recommendations on the design of a modest national quality control laboratory, the Committee offers health administrations in those countries still lacking any appropriate facility a valuable guide to the scale of investment required.

1. NATIONAL LABORATORIES FOR DRUG SURVEILLANCE AND CONTROL

Every national government allocates a substantial proportion of its total health budget to drugs. This proportion tends to be greatest in developing countries where it may exceed 40%.

Without assurance that these drugs are relevant to priority health needs and meet acceptable standards of efficacy and safety, the efficiency of any health service is evidently compromised. In highly developed countries considerable administrative and technical effort

is directed to ensuring that patients receive effective drugs of good quality. It is crucial to the objective of health for all by the year 2000 that a reliable system of drug control be brought within the grasp of every country.

This need calls for the institution of a national drug registration system embodied within a legislative framework that, *inter alia,* contains provisions to assure the quality of all registered products. These provisions must take cognizance of the various ways in which substandard products may arise. The three principal ways are:

—products that initially conform to prescribed specifications may deteriorate before they are used as a consequence of inappropriate formulation, packaging, or storage conditions; this may result in loss of activity and exceptionally in the formation of toxic degradation products;
—failure to institute and maintain good manufacturing practices may result in errors of formulation or labelling;
—illicitly manufactured drugs, which may be substandard or even spurious, may enter the distribution chain.

To be self-sufficient in meeting these contingencies a country must enforce a system of control that provides for:

—regular inspection of all production units to ensure that good manufacturing practices, as exemplified in the code of *Good practices in the manufacture and quality control of drugs* promulgated by WHO (*1*) are maintained;
—spot checks of the quality of all products in the distribution chain through carefully planned sampling programmes.

An account of the various elements of quality assurance in pharmaceutical supply systems is contained in the Committee's twenty-seventh report (*2*). Full implementation of these measures requires both extensive laboratory facilities and a well staffed inspectorate. It is evident, however, that in many countries resources are not available to provide for investment on this scale.

For these countries, the WHO "Certification scheme on the quality of pharmaceutical products moving in international commerce" (*1*, p. 94), offers some safeguard insofar as imported products are concerned. The scheme provides assurance, underwritten by the drug regulatory authority in the country of origin, that a specific product has been manufactured within

premises that are regularly inspected and that conform to internationally recognized standards of operation.

However, the WHO certification scheme has no relevance to locally manufactured products; it provides no safeguard that an initially acceptable product will not deteriorate owing to improper storage; nor does it apply when a product is imported from a trading company located outside the country of original manufacture. In the last two instances it is particularly important to evaluate quality by appropriate analyses of the finished product.

Consequently, every country, regardless of its stage of development, should consider the need for investment in an independent national drug quality control laboratory. The recommendations contained in Annex 1 are directed to the many developing countries that have not as yet created such a facility and that do not command the resources to maintain a comprehensive system of control.

It should be recognized, in particular, that:

— simple procedures, such as tablet disintegration tests, are frequently of critical importance in eliminating seriously substandard preparations;

—a small laboratory directed by a competent, discerning individual will provide a persuasive deterrent to negligent or fraudulent manufacturing or importing practices;

—the availability of complex automated equipment accelerates but does not necessarily raise the standard of analytical work. Moreover, such equipment performs reliably only when it is expertly maintained and its operation may require the use of highly purified and expensive reagents.

1.1 Proposed model laboratories

Staffing and physical facilities

Recommendations on the staffing and organization of two model laboratories for developing countries where no facilities exist are provided in Annex 1. No concession is made in these recommendations towards any relaxation of standards. Even the smaller of the model laboratories provides for the full analysis of more than 75% of WHO's model list of essential drugs (*3*) in accordance with the methods provided in *The international pharmacopoeia* (*4*).

Emphasis is placed upon economy, both of scale and equipment. None the less, it is recognized that efficient temperature and humidity control is imperative in laboratories located in tropical regions, notwithstanding the high capital expenditure and maintenance costs involved and the heavy energy demands. Several analytical techniques (including infrared spectrophotometry) do not provide reliable results in a hot and humid environment which, moreover, promotes corrosion and accelerates deterioration of expensive instruments.

Having regard to the limited opportunity for institutional technical training in developing countries, newly recruited staff will generally require a period of in-service training in a laboratory adapted to their educational background, individual aptitude, and assigned responsibilities.

Good control laboratory practices

The Committee reiterated the request made in its twenty-eighth report (*5*) that guidelines on good control-laboratory practices be elaborated to embrace various aspects of the management of a national drug control laboratory, including advice on sampling procedures.

Legal status

Regardless of the facilities available, the reliability of any analytical laboratory is vitally dependent upon the calibre and experience of its director. A national quality control laboratory has onerous responsibilities that demand reliable judgements: if the need arises, decisions must withstand examination in a court of law.

Because of the legal connotation of the analytical work undertaken in control laboratories, a special status should be accorded by statute to analytical reports issued by them. Such a privilege, which should however remain open to challenge in defined circumstances, will facilitate the resolution of disputes should reports ever be contested by interested parties.

To avoid possible conflicts of interest, a national laboratory should not engage in routine testing of samples at the request of individual pharmaceutical manufacturers. It is, however, an important function of the laboratory to advise the manufacturers on means of improving their quality control procedures.