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Geneva, 28 November–3 December 1988

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WHO EXPERT COMMITTEE ON SPECIFICATIONS FOR PHARMACEUTICAL PREPARATIONS

Thirty-first Report

The WHO Expert Committee on Specifications for Pharmaceutical Preparations met in Geneva from 28 November to 3 December 1988. The meeting was opened on behalf of the Director-General by Dr V. Fattorusso, Adviser to Dr Hu Ching-Li, Assistant Director-General, who recalled that the supply of good-quality essential drugs—identified at the International Conference on Primary Health Care, Alma-Ata, 1978, as one of the basic prerequisites for the delivery of health care—had long been of fundamental concern to the World Health Organization. Pivotal to its efforts in this connection had been the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. However, rigorous procedures for attesting the quality and provenance of imported products needed to be complemented, wherever possible, by the analytical facilities afforded by a national drug quality-control laboratory and, above all, by a reliable system of licensing pharmaceutical products as a prerequisite for their distribution and sale. For this reason, emphasis had been accorded within WHO's revised drug strategy to the need to prepare guiding principles for small national drug regulatory authorities. The Committee was consequently requested to consider, in addition to various important technical issues relating to quality assurance, some draft guidelines addressing this need that had been prepared as a consultative document and to submit any recommendations it might care to propose to the Director-General.

1. DRUG STABILITY

Inadequate storage and distribution of pharmaceutical products can lead to their physical deterioration and chemical decomposition, resulting in reduced activity and, occasionally, in the formation of toxic degradation products. Degradation is particularly likely to occur under tropical conditions of high ambient temperature and

humidity; and it is not widely recognized that, because of the potential for chemical interaction between the active ingredients and excipients, drug dosage forms can be more vulnerable to degradation than pure drug substances.

The stability of a specific product is thus dependent, in a large measure, on its formulation, and its expiry date should be determined on the basis of stability studies carried out by the manufacturer. Studies undertaken with a view to determining the stability of a product under temperate conditions, however, do not necessarily provide a reliable indication of its shelf-life in tropical climates. In such cases, additional proof of stability should be requested from the manufacturer, who should assume responsibility for formulating a product that is stable under the climatic conditions prevailing in the countries of destination. Relevant information should be specifically requested by the national regulatory authority in the importing country within the context of the WHO Certification Scheme (see section 6 of this report). It is obviously impossible to obtain satisfactory assurances when a product is purchased through an intermediary if its provenance is unknown to the purchaser. For domestically produced products, the regulatory authority should evaluate stability data furnished by the manufacturer. The procurement agencies and the pharmacists responsible for drug distribution should ensure that they are supplied with adequate information concerning the proper storage and handling of each product.

Annex 1, on the stability of drug dosage forms, is a comprehensive statement on both the technical aspects of the subject and the responsibilities that devolve upon the manufacturer and all agencies and individuals responsible for the product throughout the distribution chain up to the time of its administration or delivery to the patient.

Within the distribution chain, the labelled expiry date on a pharmaceutical product has a dual significance: after this date, no formal assurance is provided regarding the condition of the product; and the manufacturer may no longer have legal liability for it. The Committee agreed that the use of time-expired stock should be entertained only in the most exceptional circumstances, when to withhold the stock would have serious consequences for patients. In every instance, the proposal to release such a product must be channelled through a pharmacist or other professional experienced in quality assurance and, when appropriate, referred to the